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FROM THE EDITOR’S DESK

Namaskar Friends,

I want to share with you my vision on Journal of Association of Physicians of India (JAPI) as a New Editor in Chief. As me and my editorial team kick-off the new innings, all our endeavours will be in the pursuit of excellence.

JAPI with improved impact factor, superior visibility on various platform, eminently peer reviewed original research articles pertinent to the Indian subcontinent, larger citation, faster turnaround time through a coherent, secure, and streamlined system, better discoverability, simple direct access, peek in to the latest happening in the medical research world with novel section of postgraduate corner, social media presence, collaborations with international journals, accomplishing bimonthly publication will be my priorities.

While the country is slowly recovering back to normalcy after devastating covid pandemic; it is important to notice that in last decade we faced multiple heat waves, unseasonal rain falls, cyclones, locusts adversely affecting the agriculture and also taking a human toll. Global warming, deforestation, changing ecosystem are threatening the very existence of species. The Sixth Assessment Report of the United Nations Inter-Governmental Panel on Climate Change (IPCC) was released on April 2nd 2022. It highlighted the efforts to minimize the global warming. India pledged for decarbonization and minimizing greenhouse effect. To preserve the ecosystem along with government agencies, we will need sustainable, workable, individual commitments as well.

What should be a rational and logical response to these multiple environmental demurs? With the help of modern technologies and scaled down paper consumption to dwindle deforestation, minimizing our credence on the fossil fuel, employing green energy fuel with renewable adoptable technologies, we can certainly take a step towards mitigating these climatic change challenges. We need to join hands together to save Mother Earth. Medical professionals being the elites; should take upon themselves the responsibility of community awareness to preserve healthy ecosystem. I think, one great support and action would be to move energy generation, transport and industry aggressively green. And as we know transformation should start at home, I also wish to Go Green. We – Team JAPI will attempt to reduce paper consumption by GOING GREEN. And I need your support and an active cooperation! So, through my first message, I sincerely appeal members of our baronial association to join hands with me.

I bow down to memories of my mentor, path-buster Late Prof. Dr. Siddharth N Shah for his unparalleled guidance to me during my API tenure. And I am lucky to have hand-holding by the likes of Prof. Dr. Y. P. Munjal, Prof. Dr. Shashank R Joshi, Prof. Dr. Milind Nadkar, Prof. Dr. B. B. Thakur, Prof. Dr. Alaka Deshpande, Prof. Dr. Shyam Sunder, Prof. Dr. G. S. Wander, Dr. Girish Mathur, Dr. K. K. Pareek, Dr. Pritam Gupta, Dr. Rajesh Upadhyaya, Prof. Dr. Agam C Vora and many more. I express my sincere gratitude to them and request them to bless me and my team with continuous support and guidance.

Long Live JAPI!!!
Long live API!!!

Mangesh Tiwaskar
Editor-in-Chief: JAPI
Cardiac Biomarkers: Role in Risk Assessment, Diagnosis, and Prognostication of Coronary Artery Disease

Gurpreet S Wander*  

The Framingham heart study and the seven countries study were the first ones to identify the risk factors for coronary artery disease (CAD).1–3 Framingham risk score is widely used since then for calculating 10 year risk of CAD.4 This and other risk prediction scores are applicable to both CAD and stroke since they have similar risk factors. The INTERHEART study highlighted the significance of nine risk factors for atherosclerotic cardiovascular disease.5 The risk factors included: smoking, lipids, self-reported hypertension or diabetes, obesity, diet rich in fruits and vegetables, physical activity, alcohol consumption, and psychosocial factors. These risk factors could explain 90% risk of CAD in this study. However, some other studies show that one third of CAD events occur in individuals with none of the traditional risk factors. Hence, the quest for additional risk markers. These are also called the “newer or emerging risk factors”. They are believed to be more important in South Asians.6 These include hyperhomocysteinemia, increased Lp(a) levels, central obesity, hyperinsulinemia, and others.5

In the last 2 decades, there has been a lot of work on genome-wide association studies which have helped us to develop biomarkers with similar risk scores with multiple single nucleotide polymorphisms (SNPs) that correlate with risk of CAD. These genetic scores offer an additional method to identify individuals who are at increased risk of CAD. It is believed that, by combining genetic risk with the conventional and newer risk factors, we will be able to predict and diagnose CAD earlier and more effectively.7–9

The third area which is being evaluated for helping us to predict CAD is evaluation of biomarkers which are released in blood during the process of atherosclerosis. The term biomarker (biological marker) was introduced in 1989 as a Medical Subject Heading (MeSH) term. In 2001, a National Institute of Health (NIH) working group standardized the definition of a biomarker as, “a characteristic that is objectively measured and evaluated as an indicator of—normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.”

A good biomarker that is clinically useful should have the following properties. It should be easily measured and interpretable, have a reproducibility associated with disease/outcome, be informative beyond usual clinical means of risk assessment, reflective of disease presence, severity, risk of progression, risk of events, and possibly be informative with regard to treatment selection. The biomarkers that will be developed in coming times will be assessed in terms of the above-mentioned abilities.

Atherosclerosis is an inflammatory process. It involves cellular migration, adhesion, transformation, and collection of lipids and foam cells in the subintimal part of vessel wall. The initial fatty streak develops into a fibrous plaque over years and subsequently can rupture when it causes acute coronary syndrome (ACS). The triggers (risk factors) for ACS are different from the atherosclerotic risk factors. These include extreme exertion, emotional stress, early morning catecholamine surge, inflammation, and infections.10–12

Biomarkers are proteins detected in the systemic circulation. There can be biomarkers linked to the inflammatory, oxidative, or metabolic processes of atherosclerosis. They are generated by and so reflect the underlying cellular metabolic processes. Various biomarkers of atherosclerosis that have been evaluated till now include:

• Lipid related biomarkers—low density lipoprotein (LDL) remnants, oxidized LDL, Lp(a) levels, apolipoprotein-B, etc.13
• Cellular migration and degradation molecule related biomarkers—intracellular adhesion molecule 1 (ICAM-1) and vascular adhesion molecule 1 (VCAM-1).
• Biomarkers of inflammation—high-sensitivity C-reactive protein (hs-CRP), cytokines like interleukins IL-1, IL-6, IL-8, monocyte chemoattractant protein (MCP-1), serum amyloid A (SAA), placental growth factor (PIGF), and soluble CD40 ligand.
• Biomarkers of oxidative stress—myeloperoxidase (MPO).
• Biomarkers of myocardial stretch—natriuretic peptides, soluble suppression of tumorigenicity 2 (sST2), and growth differentiation factor-15 (GDF-15).
• Biomarkers of myocardial injury—high-sensitivity cardiac troponin I and high-sensitivity cardiac troponin T (hs-cTnT).
• Biomarkers of metabolism—adiponectin, leptin, and insulin.

CAD has different presentations, from asymptomatic stage to acute events and subsequent heart failure. The biomarkers that are relevant in different presentations of CAD are shown in Table 1.

These biomarkers when present and detected in the blood can help in estimation of risk of CAD and related acute events. None of these biomarkers have individually been shown to significantly contribute to the diagnosis and prognosis of CAD. For this reason, multiple biomarker assessments are collated for estimation of risk and prognosis of CAD.

In the article published in this journal the authors Jaishankar et al. have evaluated three such biomarkers, remnant lipoprotein

Table 1: Biomarkers in different stages of CAD

<table>
<thead>
<tr>
<th>Stage of CAD</th>
<th>Biomarkers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable plaque</td>
<td>LDL, oxidized LDL, CRP, IL-6, IL-10, IL-18, fibrinogen, tumor necrosis factor</td>
</tr>
<tr>
<td>Unstable plaque</td>
<td>Matrix metalloproteinases 9, ICAM, VCAM, MPO</td>
</tr>
<tr>
<td>Plaque rupture</td>
<td>Soluble CD40 ligand (sCD40L), PIGF, pregnancy-associated plasma protein-A (PAPP-A), VCAM</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>Plasminogen activator inhibitor (PAI-1), sCD40L, Von Willebrand factor (VWF), D-dimer</td>
</tr>
<tr>
<td>Ischemia</td>
<td>Ischemia modified albumin (IMA), free fatty acid (FFA), choline, brain natriuretic peptide (BNP)</td>
</tr>
<tr>
<td>Necrosis</td>
<td>cTNT, myoglobin</td>
</tr>
<tr>
<td>Left ventricular (LV) remodeling</td>
<td>BNP, NT-ProBNP, matrix metalloproteinases (MMP)</td>
</tr>
</tbody>
</table>

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cholesterol, oxidized LDL as lipid-related biomarkers, and hs-CRP as a marker of low-grade inflammation in young south Asian population with CAD. They observed a significant increase in these three biomarkers in patients with CAD as compared to healthy controls. This is a small study, which does provide evidence in the same direction as multiple other large studies and registries are showing. These are being conducted for finding out the various biomarkers which can be useful to us in future for early detection of CAD, besides the conventional risk factors and the recently evolving genetic risk scores.

Remnant lipoprotein cholesterol was shown to be associated with CAD in the Jackson Heart and in the Framingham Offspring Cohort Studies. The Copenhagen General Population Study showed that one third of total cholesterol in plasma is present in remnant lipoproteins. Remnant lipoprotein cholesterol corresponds to cholesterol in triglyceride-rich lipoproteins including IDL, VLDL, and chylomicron remnants. Remnant lipoproteins can enter the arterial intima at a slower speed than the LDL particles. Thus, they can participate in the atherosclerosis process.14–17

Oxidized LDL is produced by oxidation of LDL and apolipoprotein-B by the free radicals. The oxidized LDL enters the macrophage and forms the foam cells. It initiates the atherosclerotic process. High-sensitivity C-reactive protein is a marker of inflammation. It has an important role in the process of atherosclerosis. It promotes uptake of LDL-C by macrophages. A value of >2 mg/L indicates increased risk of CAD and >10 mg/L of ACS.

In 2008, Paul Ridker showed that hs-CRP is a strong and important predictor of CAD.18–20

The current guidelines do not recommend the routine use of presently known biomarkers in clinical practice for stable CAD. However, emerging evidence is placing these recommendations under closer scrutiny. Even the recent European guidelines for CAD prevention, state that the presently known biomarkers have as yet a limited value for CAD risk prediction. Possibly a multimodel strategy combining many biomarkers can improve risk prediction in CAD. It is a field with significant potential and is being widely explored for risk assessment of CAD in its various stages.

REFERENCES

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<th>Key Parameters</th>
<th>Fexofenadine + Montelukast</th>
<th>Levocetirizine + Montelukast</th>
<th>Bilastine + Montelukast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioequivalence Published Data</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Synergistic effect</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Published efficacy data in Indian patients</td>
<td>92.5%</td>
<td>85.6%</td>
<td>No data</td>
</tr>
<tr>
<td>Published safety data in Indian patients</td>
<td>9.6%</td>
<td>23.2%</td>
<td>No data</td>
</tr>
</tbody>
</table>

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**Reference**

4. Concomitant bilastine and montelukast as additive therapy for seasonal allergic rhinoconjunctivitis and mild-to-moderate asthma. The SKY study. 2019

Assessment of Remnant Lipoprotein Cholesterol and Oxidized Low-density Lipoprotein Associated with Low-grade Inflammation in Coronary Heart Disease Subjects of Young South Indian Population

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Abstract

Background: Coronary heart disease (CHD) is a major disease entity responsible for significant mortality and morbidity in the Indian population. The prevalence of CHD is increasing day by day in India. The hardening of arteries is linked to oxidative variations in low-density lipoproteins (LDLs). Modification of LDL to oxidized LDL (ox-LDL) is a crucial step in the oxidation hypothesis of atherogenesis. Oxidized LDL and remnant lipoprotein cholesterol (RLP-C) stimulate the immune and inflammatory reactions and promote atherosclerosis. Because of its lesser size along with high cholesterol content, and increased residence period in blood the remnant lipoproteins are highly atherogenic. Remnant lipoproteins transport more cholesterol to macrophages compared to LDL particles. Remnant lipoproteins enter into the arterial wall easily and are taken up directly by macrophages. This leads to the formation of foam cells, thus initiating the lipid-laden plaque. High sensitive C-reactive protein acts as a nonspecific inflammatory marker. Oxidized LDL along with RLP-C and high-sensitivity C-reactive protein (hs-CRP) play crucial role in progression of CHD.

Aim of the study: The aim of the study is to assess ox-LDL and RLP-C associated with hs-CRP as potential biomarkers in the development of CHD.

Materials and methods: This cross-sectional study was conducted in Sri Ramaswamy Memorial Medical College Hospital and Research Centre on subjects appearing for master health check-up and medicine. This cross-sectional study was conducted on 273 subjects who were age and sex match in the age group of ≤45 years. 91 Non-Diabetic subjects with CHD, 91 Diabetic subjects with CHD, and 91 normal healthy subjects were selected as control. After overnight fasting, blood fluid samples were collected for analysis for lipid profile, ox-LDL, and hs-CRP. Oxidized LDL and hs-CRP were measured by enzyme-linked immunosorbent assay (ELISA) method and lipid profile was measured using Auto Analyser AU480. Statistical analysis was done using Student’s t-test and Pearson's correlation analysis for the comparison between two groups.

Results: The mean level of ox-LDL, RLP-C, and hs-CRP was significantly elevated in CHD group. A significantly positive correlation was observed between plasma ox-LDL, RLP-C, and hs-CRP.

Conclusion: These results suggest that the link between high ox-LDL, RLP-C, and hs-CRP levels might be interrelated to atherogenesis in subjects with CHD. In addition to conventional parameters, ox-LDL, RLP-C, and hs-CRP can prove to be a valuable tool in risk assessment of CHD.

Introduction

Coronary heart disease is a major cause of death and disability in developed countries. Although CHD mortality rates worldwide have declined over the past 4 decades, CHD remains responsible for about one-third or more of all deaths in individuals over age 35 years.¹

The prevalence of CHD in developed as well as developing countries has presumed to be an important cause of death in India by 2020. Coronary heart disease causes more than 7 million deaths among adult population (21.9% of total deaths, projected to increase to 26.3% by 2030 worldwide every year, and maximum of these deaths arise in developing countries).²

The hydrolyzed products of chylomicron (CM) and very-low-density lipoproteins (VLDLs) are collectively called RLP-C. Remnant lipoproteins are the atherogenic lipoprotein influence mostly intermediate-density lipoproteins and VLDL in fasting state and CMs in the nonfasting state.³ Remnant lipoprotein cholesterol is considered as the one of the ultimate destructive lipoproteins very highly associated in circulation of CHD subjects. Assessment of RLP-C is an advantageous mechanism to evaluate the status of CHD.

Recent studies have more evidence that higher level of cholesterol as remnant-like particles. Remnant lipoprotein cholesterol generates deterioration of endothelial function over the fasting state. Remnant lipoprotein not only raises in abnormality lipoprotein metabolism, it is also combined with the progression of atherosclerosis and CHD.

Elevated RLP-C concentrations in fasting state correlated with existing CHD in dyslipidemia. Kugiyama et al. stated that raised remnant lipoproteins in fasting concludes upcoming coronary crisis in subjects with CHD independent of various other risk issues.⁴

Remnant cholesterol accumulating and infiltrating the endothelial barrier, spurring inflammatory reaction, and atherogenic process in the arterial wall like low-density lipoprotein cholesterol (LDL-C). Remnant particles are larger than LDL and carry ≤40 times as much cholesterol per particle and more atherogenic than LDL.⁵

Remnant lipoprotein is almost massively correlated to most LDL particles, it is especially bad because unlike LDL particles, which have to go through oxidation before they can be taken into the arterial intima by macrophage cells, RLP can be freely scavenged by macrophage cells even when they are not oxidized. Once scavenged by a macrophage, RLP is converted into foam cells which are the building blocks of arterial plaque. In fact, increased RLP has been found in survivors of myocardial infarction and individuals with significant CHD. Additionally, RLP contributes to endothelial dysfunction by damaging the vascular relaxation process as well as strengthening platelet aggregation.⁶

Increased oxidative stress and formation of superoxide anion in vascular cells stimulate...
RLP-C and ox-LDL Associated with Low-grade Inflammation

the alteration of LDL-C to atherogenic ox-LDL. Elevated level of RLP-C and LDL oxidation in the vessel wall results in uptake by scavenger receptor on monocyte-derived macrophages, leads to accumulation of foam cells and fatty streak formation.

Remnant lipoprotein cholesterol and LDL oxidation may be part of local and systemic inflammatory reaction causally correlated to the risk of CHD and low-grade inflammation. C-reactive protein plays an important role in pathogenesis of atherosclerosis. C-reactive protein is a pentraxin family of protein, an acute phase reactant with molecular weight of 23 kDa. It is a highly sensitive marker for inflammation. The level of CRP rises drastically during inflammatory process. The elevated concentration of hs-CRP directly implies subclinical inflammation in individual. We assessed each correlation between RLP-C and ox-LDL associated with hs-CRP in CHD subjects.

Materials and Methods

Study Design and Population

This cross-sectional study was conducted from June 2019 to December 2019 at Sri Ramaswamy Memorial Medical College Hospital and Research Centre, Chennai, Tamil Nadu, India on subjects attending the Cardiology and Medicine department. Totally 273 subjects were included who were age and sex match in the age group of ≤45 years. 91 Non-Diabetic subjects with CHD, 91 Diabetic subjects with CHD, and 91 normal healthy subjects were selected as control. The control subjects were also taken from Master health check-up Programme and the Medicine department in Sri Ramaswamy Memorial Medical College Hospital and Research Centre, Chennai, Tamil Nadu, India. This study obeys with the Declaration of Helsinki and was approved by the institutional ethical committee at Sri Ramaswamy Memorial Medical College Hospital and Research Centre (ECN: 1513/ICE/2018). Written informed consent was collected from all participants at the time of enrollment.

Inclusion Criteria

The CHD subjects including both males and females selected on the basis of coronary angiography.

Group I (healthy controls): the control group consists of persons with no clinical and electrocardiogram (ECC) evidence of CHD and negative history of the past event of CHD or stroke, diabetes mellitus, hypertension, smoking, dyslipidemia, and family history of CHD.

Group II (Non-Diabetic subjects with CHD): CHD subjects who are not identified diabetes or not fulfilling American Diabetes Association (ADA) norms and were selected on the basis of coronary angiography, chest pain lasting for >30 minutes, elevated ST elevation >0.1 mV on at least two adjacent electrocardiographic leads and increase of creatine kinase to peak levels of at least two-fold the upper limit of normal values. Group III (diabetic subjects with CHD): previously known CHD subjects with diabetic duration of ≤5 years.

Exclusion Criteria

The subjects who were on treatment for renal failure, cancer, autoimmune diseases, surgery, fever, alcoholics, smokers, pregnancy, and subjects with corticosteroids, estrogen, and antiretroviral drugs psychotropic medications. Thyroid, arthritis, rheumatoid arthritis, and acute/chronic infection subjects were excluded.

Anthropometric Measurement

Medical and demographic data were collected at the period of enrolment, and documents were deidentified before investigation. Basic info on age, gender, and a history of diabetes, hypertension, and the use of medications were collected using a questionnaire during the clinical appointment. Questionnaires were evaluated by an expert questioner for lost data and entirety, before shifting the data to a database. Arterial blood pressure was measured using standard methods in triplicate, and the averaged values were used for the analysis. Information of laboratory reports was noted for all the subjects. The physical examination consisted of a 12-lead resting electrocardiogram. The fasting samples from cases and controls were taken in the morning taking all aseptic precautions from antecubital vein. The blood was centrifuged for 15 minutes at 2500 rpm; and serum was separated and used for the estimation of glucose and routine lipid profile includes plasma total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C), TC/HDL-C ratio, LDL-C/HDL-C ratio, and HbA1c were measured. Body mass index (BMI) was calculated as weight (in kilograms)/height (in meters). Lipid profiles were estimated using direct antibody inhibition. Total cholesterol was estimated by enzymatic end-point cholesterol esterase–peroxidase method. Triglycerides (TGs) were estimated by enzymatic end-point glycerol phosphate oxidase–peroxidase method (Beckmann Coulter AU480 Analyzer).

The RLP-C was calculated using the formula: RLP-C = TC – (HDL-C + LDL-C).

Measurement of ox-LDL-C

A quantity of 3 mL of blood was allowed to clot for 30 minutes and then centrifuged at 2500 RPM for 10 minutes for the measurement of ox-LDL. Oxidized LDL was estimated using ELISA kit (Bioassay Technology Laboratory Co., Ltd, China) (Catalogue No: C5B-E 07931H) based on direct sandwich method in which two monoclonal antibodies are directed in contrast to separate antigenic factors on the oxidized apolipoprotein B molecule. Absorbance are measured at 450 nm.

Measurement of hs-CRP

A quantity of 3 mL of blood was allowed to clot for 30 minutes and then centrifuged at 2500 RPM for 10 minutes for the measurement of ox-LDL. High-sensitivity C-reactive protein was estimated using ELISA kit (Bio source Laboratory) (Catalogue No: MBS 2506093) based on the direct sandwich technique. Samples are added to the micro ELISA plate wells and combined with the specific antibody. Then a biotinylated detection antibody specific for human hs-CRP and Avidin-Horseradish Peroxidase conjugate are added successively to each microplate well and incubated. The enzyme-substrate reaction is terminated by the addition of stop solution and the color turns yellow. The optical density (OD) value is proportional to the concentration of human hs-CRP. Concentration of human hs-CRP is calculated by comparing the OD of the samples to the standard curve. The OD is measured by spectrophotometer at a wavelength of 450 ± 2 nm.

Statistical Analysis

Data were analyzed using Statistical Package for Social Service (SPSS 16.0). The data collected from the study were shown as mean and standard deviation (SD). Differences were considered as significant if p-value was <0.05. Statistical significance for study group and control was analyzed by Student’s t-test. Pearson’s correlation coefficient was calculated to find out the correlation between different parameters. Correlation between the two parameters was determined by simple linear regression analysis.

Results

A total of 273 subjects were enrolled in this study. A total of 45 (49.4%) were male and 46 (50.5%) were female in non-diabetic subjects with CHD. And 57 (62.6%) were male and 34 (37.3%) were female in diabetic subjects with CHD. And 40 (43.9%) were male and 51 (56%) were female subjects were selected as control. In the subjects group, 26 non-diabetic subjects with CHD having a family history of CHD and 39 diabetic subjects with CHD having a family history of CHD.

The BMI, waist circumference, waist-hip ratio, and systolic blood pressure were
significantly ($p < 0.05$) higher in both diabetic and non-diabetic subjects with CHD subjects as compared to controls as depicted in Table 1.

The study shows fasting blood glucose (FBG), TC, TG, LDL-C, VLDL-C, LDL/HDL ratio, TC (TC)/HDL ratio, and HbA1c are significantly elevated in these subjects compared to control depicted in Table 2. The mean levels of HDL-C levels did not differ significantly among the two groups in diabetic and nondiabetic subjects with CHD.

In diabetic and non-diabetic subjects with CHD, the mean level of RLP-C, ox-LDL, and hs-CRP values show a statistically significant increase when compared to controls.

Pearson’s correlations analysis between CHD biomarkers (RLP-C and ox-LDL) along with conventional biomarker hs-CRP in nondiabetic subjects with CHD

Remnant lipoprotein cholesterol positively correlated with BMI, waist circumference, waist-hip ratio, TC, TG, LDL-C, VLDL-C, TC/HDL Ratio, LDL/HDL Ratio, and HbA1c. And ox-LDL negatively correlated with FBG and HDL-C.

Oxidized LDL positively correlated with BMI, waist circumference, waist-hip ratio, TC, TG, LDL-C, VLDL-C, TC/HDL Ratio, LDL/HDL Ratio, ox-LDL/HDL ratio, ox-LDL/LDL ratio, RLP-C, and hs-CRP. Remnant lipoprotein cholesterol and ox-LDL are positively correlated with the duration of diabetes in CHD subjects with diabetes.

High-sensitivity C-reactive protein positively correlated with BMI, waist circumference and waist-hip ratio, TG, HDL-C, LDL-C, VLDL-C, TC/HDL Ratio, LDL/HDL Ratio, ox-LDL/HDL ratio, ox-LDL/LDL ratio, RLP-C, and hs-CRP. And RLP-C negatively correlated with waist-hip ratio, TC, TG, LDL-C, and HbA1c.

Oxidized LDL positively correlated with BMI, waist circumference, waist-hip ratio, TC, TG, LDL-C, VLDL-C, TC/HDL Ratio, LDL/HDL Ratio, ox-LDL/HDL ratio, ox-LDL/LDL ratio, RLP-C, hs-CRP, and HbA1c. And ox-LDL negatively correlated with waist circumference and HDL-C.

Table 1: Demographics and baseline characteristics CHD subjects and healthy controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy Controls (n = 91)</th>
<th>Non-Diabetic subjects with CHD (n = 91)</th>
<th>Diabetic subjects with CHD (n = 91)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years, mean ± SEM)</td>
<td>31.8 ± 3.75</td>
<td>34.93 ± 5.39</td>
<td>38.6 ± 6.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>40 (43.9%)</td>
<td>45 (49.4%)</td>
<td>57 (62.6%)</td>
<td></td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>51 (56%)</td>
<td>46 (50.5%)</td>
<td>34 (37.3%)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.91 ± 0.37</td>
<td>23.47 ± 0.35</td>
<td>24.03 ± 0.19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>90.9 ± 10.1</td>
<td>93.8 ± 9.6</td>
<td>98.8 ± 4.3</td>
<td></td>
</tr>
<tr>
<td>Waist to hip ratio</td>
<td>0.94 ± 0.02</td>
<td>1.01 ± 0.01</td>
<td>1.05 ± 0.03</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>112.73 ±18.32</td>
<td>119.38 ± 16.57</td>
<td>122.26 ± 13.95</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>74.58 ± 13.26</td>
<td>77.69 ± 7.95</td>
<td>82.16 ± 16.47</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Family history of CHD</td>
<td>Yes</td>
<td>0</td>
<td>26 (28.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>91 (100%)</td>
<td>65 (71.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Comparison of lipid profile in CHD subjects and healthy controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy Controls (n = 91)</th>
<th>Non-Diabetic subjects with CHD (n = 91)</th>
<th>Diabetic subjects with CHD (n = 91)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mg/dL)</td>
<td>95.7 ± 7.68</td>
<td>97.29 ± 6.98</td>
<td>169.98 ± 66.28</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>170.76 ± 16.13</td>
<td>227.01 ± 34.27</td>
<td>242.73 ± 40.33</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>82.74 ± 28.41</td>
<td>140.19 ± 60.71</td>
<td>178.86 ± 90.08</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>46.96 ± 9.4</td>
<td>37.64 ± 4.12</td>
<td>37.83 ± 4.25</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>106.54 ± 12.45</td>
<td>161.31 ± 24.48</td>
<td>164.64 ± 27.32</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>VLDL (mg/dL)</td>
<td>17.26 ± 8.77</td>
<td>28.06 ± 12.14</td>
<td>34.08 ± 14.29</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TC/HDL ratio</td>
<td>3.71 ± 0.70</td>
<td>6.17 ± 1.14</td>
<td>6.50 ± 1.36</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>LDL/HDL ratio</td>
<td>2.35 ± 0.53</td>
<td>4.22 ± 0.75</td>
<td>4.41 ± 0.90</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>RLP-C (mg/dL)</td>
<td>15.69 ± 12.15</td>
<td>35.65 ± 16.11</td>
<td>40.25 ± 24.62</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>ox-LDL (U/L)</td>
<td>16.6 ± 3.54</td>
<td>40.89 ± 8.69</td>
<td>42.82 ± 10.03</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td>1.92 ± 0.47</td>
<td>3.80 ± 1.35</td>
<td>3.93 ± 0.54</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.9 ± 0.17</td>
<td>5.21 ± 0.28</td>
<td>8.49 ± 2.32</td>
<td>&lt;0.0001***</td>
</tr>
</tbody>
</table>

Values are expressed in mean ± SD; *** p-value is considered very highly significant
Table 3: The Pearson’s correlations analysis between ox-LDL and RLP-C with other biochemical parameters in Non-Diabetic subjects with CHD

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ox-LDL r-value</th>
<th>p-value</th>
<th>RLP-C r-value</th>
<th>p-value</th>
<th>hs-CRP r-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>0.156 A</td>
<td>&lt;0.0001***</td>
<td>-0.007 B</td>
<td>&lt;0.0001***</td>
<td>0.173 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.100 A</td>
<td>&lt;0.0001***</td>
<td>0.251 A</td>
<td>&lt;0.0001***</td>
<td>0.123 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>BMI</td>
<td>0.111 A</td>
<td>&lt;0.0001***</td>
<td>0.023 A</td>
<td>&lt;0.0001***</td>
<td>0.141 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.035 A</td>
<td>&lt;0.0001***</td>
<td>0.044 A</td>
<td>&lt;0.0001***</td>
<td>0.065 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.296 A</td>
<td>&lt;0.0001***</td>
<td>0.240 A</td>
<td>&lt;0.0001***</td>
<td>0.286 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>FBG</td>
<td>-0.106 B</td>
<td>&lt;0.0001***</td>
<td>-0.131 B</td>
<td>&lt;0.0001***</td>
<td>-0.152 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TC</td>
<td>-0.050 B</td>
<td>&lt;0.0001***</td>
<td>0.011 A</td>
<td>&lt;0.0001***</td>
<td>-0.071 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TG</td>
<td>0.145 A</td>
<td>&lt;0.0001***</td>
<td>0.065 A</td>
<td>&lt;0.0001***</td>
<td>0.188 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>HDL-C</td>
<td>-0.148 B</td>
<td>&lt;0.0001***</td>
<td>-0.227 B</td>
<td>NS</td>
<td>0.048 A</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>LDL-C</td>
<td>0.996 A</td>
<td>&lt;0.0001***</td>
<td>0.431 A</td>
<td>&lt;0.0001***</td>
<td>0.829 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>VLDL-C</td>
<td>0.144 A</td>
<td>&lt;0.0001***</td>
<td>0.064 A</td>
<td>&lt;0.0001***</td>
<td>0.188 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TC/HDL Ratio</td>
<td>0.680 A</td>
<td>&lt;0.0001***</td>
<td>0.737 A</td>
<td>&lt;0.0001***</td>
<td>0.541 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>LDL/HDL Ratio</td>
<td>0.10 A</td>
<td>&lt;0.0001***</td>
<td>0.220 A</td>
<td>&lt;0.0001***</td>
<td>-0.023 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>HbA1c</td>
<td>-0.030 B</td>
<td>&lt;0.0001***</td>
<td>0.041 A</td>
<td>&lt;0.0001***</td>
<td>-0.039 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>ox-LDL</td>
<td>–</td>
<td>–</td>
<td>0.437 A</td>
<td>&lt;0.0001**</td>
<td>0.853 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>RLP-C</td>
<td>0.437 A</td>
<td>&lt;0.0001**</td>
<td>–</td>
<td>–</td>
<td>0.316 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>hs-CRP</td>
<td>0.853 A</td>
<td>&lt;0.0001***</td>
<td>0.316 A</td>
<td>&lt;0.0001***</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

** p-value is considered highly significant; *** p-value is considered very highly significant; A: Positive correlation; B: Negative correlation; NS: Not significant

Discussion

Remnant lipoprotein not only increases in abnormality of lipoprotein metabolism, it also related with the progression of atherosclerosis and CHD. Low-density lipoprotein particles penetrate the arterial wall simply and they are highly at risk to oxidation. In our study RLP-C, ox-LDL, and CRP were directly associated with waist circumference and waist-hip ratio, TC, TG, HDL-C, and VLDL-C (Table 4).

High-sensitivity C-reactive protein positively correlated with BMI, FBG, LDL-C, TC/HDL Ratio, LDL/HDL Ratio, ox-LDL/HDLD ratio, ox-LDL/LDL ratio, and HbA1c. High-sensitivity C-reactive protein negatively correlated with waist circumference and waist-hip ratio, TC, TG, HDL-C, and VLDL-C (Table 4).

Levels of ox-LDL and RLP-C in the present study were positively correlated with inflammatory biomarker high sensitivity C-reactive protein. In our study, we found the level of hs-CRP were significantly elevated in CHD subjects when compared to control group. Ridker et al. reported that healthy individuals with elevated hs-CRP values are four times possible to have CHD.24 Ndrepepa et al. stated that raised hs-CRP level is associated with the risk of upcoming adverse cardiovascular events (heart attack, stroke, and death) in healthy persons and in subjects with stable CHD.25 The current study demonstrated that increased levels of remnant lipoproteins in fasting serum predicts the development of clinical coronary actions in subjects with CHD independently of other risk factors like ox-LDL and hs-CRP. In our study, we observed a positive correlation between RLP-C and hs-CRP. Recent genetic studies done by Varbo et al. with very large samples also indicate that elevated remnant cholesterol and ox-LDL is associated with low-grade inflammation, whereas elevated LDL-C causes ischemic heart disease without inflammation.26 Zhang et al. found that ox-LDL and hs-CRP were positively correlated and can directly lead to the occurrence of inflammatory reaction.27 Study by Hong et al. stated that remnant cholesterol was positively associate with most important inflammatory biomarkers such as hs-CRP.28 To our knowledge, there have been no previous studies on determining whether the baseline levels of RLP-C and ox-LDL qualified for a useful
Table 4: The Pearson's correlation analysis between ox-LDL and RLP-C with other biochemical parameters in Diabetic subjects with CHD

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ox-LDL r-value</th>
<th>ox-LDL p-value</th>
<th>RLP-C r-value</th>
<th>RLP-C p-value</th>
<th>hs-CRP r-value</th>
<th>hs-CRP p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of diabetes</td>
<td>0.064 A</td>
<td>&lt;0.0001***</td>
<td>0.009 A</td>
<td>&lt;0.0001***</td>
<td>0.512 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>-0.170 B</td>
<td>&lt;0.0001***</td>
<td>0.031 A</td>
<td>&lt;0.0001***</td>
<td>0.017 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>-0.083 B</td>
<td>&lt;0.0001***</td>
<td>0.033 A</td>
<td>&lt;0.0001***</td>
<td>0.068 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>BMI</td>
<td>0.037 A</td>
<td>&lt;0.0001***</td>
<td>0.104 A</td>
<td>&lt;0.0001***</td>
<td>0.142 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>-0.051 B</td>
<td>&lt;0.0001***</td>
<td>0.035 A</td>
<td>&lt;0.0001***</td>
<td>0.084 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.073 A</td>
<td>&lt;0.0001***</td>
<td>0.032 B</td>
<td>&lt;0.0001***</td>
<td>0.148 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>FBG</td>
<td>0.208 A</td>
<td>&lt;0.0001***</td>
<td>0.047 A</td>
<td>&lt;0.0001***</td>
<td>0.069 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TC</td>
<td>0.013 A</td>
<td>&lt;0.0001***</td>
<td>0.050 A</td>
<td>&lt;0.0001***</td>
<td>0.048 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TG</td>
<td>-0.021 A</td>
<td>&lt;0.0001***</td>
<td>0.238 B</td>
<td>&lt;0.0001***</td>
<td>-0.147 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>HDL-C</td>
<td>-0.078 B</td>
<td>&lt;0.0001***</td>
<td>0.312 B</td>
<td>NS</td>
<td>-0.079 B</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>LDL-C</td>
<td>0.110 A</td>
<td>&lt;0.0001***</td>
<td>0.226 A</td>
<td>&lt;0.0001***</td>
<td>0.256 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>TC/HDLD Ratio</td>
<td>0.630 A</td>
<td>&lt;0.0001***</td>
<td>0.746 A</td>
<td>&lt;0.0001***</td>
<td>0.330 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>LDL/HDLD Ratio</td>
<td>0.265 A</td>
<td>&lt;0.0001***</td>
<td>0.165 A</td>
<td>&lt;0.0001***</td>
<td>0.229 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.246 A</td>
<td>&lt;0.0001***</td>
<td>-0.019 B</td>
<td>&lt;0.0001***</td>
<td>0.055 A</td>
<td>&lt;0.0001***</td>
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<tr>
<td>ox-LDL</td>
<td>–</td>
<td>–</td>
<td>0.201 A</td>
<td>&lt;0.0001***</td>
<td>0.269 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>RLP-C</td>
<td>0.269 A</td>
<td>&lt;0.0001***</td>
<td>–</td>
<td>–</td>
<td>0.246 A</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>hs-CRP</td>
<td>0.853 A</td>
<td>&lt;0.0001***</td>
<td>0.246 A</td>
<td>&lt;0.00001***</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

**p-value is considered highly significant; ***p-value is considered very highly significant; A: Positive correlation; B: Negative correlation; NS: Not significant

**Coronary heart disease has been a subjects of research for decades. Its alarming rise in recent years in the Indian population has brought the debate to identify factors which can add conventional risk factors for proper timely diagnose of this multifactorial disease. Current study conclude that the assessment of RLP-C, ox-LDL, and hs-CRP may contribute to early finding of CHD and to reduce morbidity and mortality risk. And discovery of its association with RLP-C, ox-LDL, dyslipidemia, hypertension, and DM have now become emerging areas of concern.**

**References**

10. Sproston NR, Ashworth JI. Role of C-reactive protein at sites of inflammation and infection. Front Immunol 2018;9:754.
Various Factors that are Causing Difference in Prevalence of Coronary Risk Factors among Siblings

Anter Preet¹, Sandeep Chhabra², Shibba T Chhabra³, Narender P Jain⁴, Gurpreet S Wander⁵, Suman Sethi⁶*

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Abstract

Background and aim: Coronary artery disease (CAD) is one of the predominant types of cardiovascular disease (CVD). The aim of present study was to study various factors that are causing difference in prevalence of coronary risk factors among siblings.

Materials and methods: This cross-sectional study was conducted in Dayanand Medical College and Hospital, among the healthy individuals (not known CAD) attending regular health care outpatient department (OPD) and their siblings over a period of 1½ years. All individuals coming for regular health checkup (not known CAD) of age more than 30 years or above and their siblings (with or without known CAD).

Results: This was a cross-sectional study, conducted among 100 pairs of healthy siblings (not known cases of CAD) who came for health checkup at health center of Dayanand Medical College and Hospital, a tertiary care hospital in North India. Prevalence of obesity was more in siblings living in urban area than their counter siblings living in rural area, but it was statistically insignificant. Six had impaired fasting blood sugar (FBS) and two were diabetic. Among their siblings living in urban area, 21 were nondiabetic, 10 had impaired FBS, and seven were diabetic. This correlation was statistically significant with p-value of 0.02.

Among the CAD negative, out of 23 subjects, two subjects (9.0%) had heavy stress level, while remaining four subjects (17.0%) and 17 subjects (74.0%) had light and moderate stress levels, respectively. Among the CAD negative, out of 23 subjects, 10 subjects (43.0%) had high stress level, while remaining zero subject (0%) and 13 subjects (57.0%) had light and moderate stress levels, respectively. Significant results were obtained while comparing the CAD findings of subjects divided on the basis of stress level.

Conclusion: In our study, among siblings (CAD positive and CAD negative), significant results were obtained for residence, socioeconomic class, physical activity, stress levels, smoking, waist-to-hip ratio (WHR), and diabetes, that is, all these factors have correlation in increasing CAD among siblings.

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Introduction

Cardiovascular disease is the leading cause of death and disability worldwide. It is expected that by 2020, CVD would prevail as the leading cause of death and disability over infectious diseases globally.¹ Coronary artery disease is one of the predominant types of CVD. The two leading manifestations of CAD are angina and acute myocardial infarction.²

The risk factors for CAD can be described as the one that can be controlled (modifiable): high blood pressure (BP); high blood cholesterol levels; smoking; diabetes; overweight or obesity; lack of physical activity; unhealthy diet; and stress.³ Those that cannot be controlled (conventional or nonmodifiable): age (simply getting older increases the risk); sex (males are at greater risk than females); and genetics (family history).

The development of CAD depends on a complex interaction between environmental and genetic factors. Risk factors that are modifiable (hypertension, diabetes, dyslipidemia, obesity, and smoking) can predict 80–90% of risk of coronary heart disease in most population around the world.⁴ Many traditional risk factors for CAD are related to lifestyle, therefore, preventative treatment can be tailored to modify specific factors. It is very important to know these risks to reduce disability and premature deaths from coronary heart disease (CHD), cerebrovascular disease, and peripheral vascular disease in people at high risk, who have not yet experienced a cardiovascular event. People with established CVD are at very high risk of recurrent events.³

Studies have shown the importance of the microenvironment, in particular the family, where genetic influences and lifestyle are equally important. Offspring of parents with systemic arterial hypertension or with dyslipidemia have a greater incidence of diseases whose phenotypes are influenced by the familiar lifestyle. The result of this interaction is responsible for atherosclerotic disease, which normally affects males after the 6th decade and females almost 1 decade later. In younger patients with CAD, a greater participation of the genetic component has been discussed. Despite the existing controversies, a familiar analysis may directly or indirectly facilitate the detection and quantification of which component, genetic, or environmental, has the greatest impact on early atherosclerotic disease, and consequently, on its future control.⁵

Over the past years, there are many studies that have been done on coronary artery risk factors, its epidemiology, and prevalence of risk factors among rural and urban subjects of demographic areas but so far no such study has been conducted among siblings (not known case of CAD). There are many studies conducted among siblings of people with premature coronary heart disease. This particular study “To study the prevalence of coronary risk factors among siblings” is a cross-sectional study conducted among siblings to access the prevalence of coronary risk factors to look for impact of sociodemographic factors, urbanization, and lifestyle on coronary risk factors against similar genetic susceptibility of two siblings.

Materials and Methods

Source of Data

This cross-sectional study was conducted in Dayanand Medical College and Hospital, among the healthy individuals (not known CAD) attending regular healthcare outpatient department (OPD) and their siblings over a period of 1½ years. Patients and their siblings of either sex, aged more than 30 years were included in the study.

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Methods of Collection of Data

Inclusion Criteria
- Individuals coming for regular health checkup (not known CAD) of age more than 30 years or above and their siblings (with or without known CAD).
- Either sex.

Exclusion Criteria
- Patients with any malignancy.
- Patients with chronic renal failure.

Duration of Study
This study was carried out among healthy siblings coming for health checkup at Dayanand Medical College and Hospital, Ludhiana over a period of 1½ years.

Procedure
1. Informed consent was taken from all patient and siblings.
2. Detailed history including history of hypertension, diabetes mellitus, dyslipidemia, smoking, and alcohol intake was taken.

Quantification of smoking was done using the smoking index (SI). Smoking index was defined as the number of bidis/cigarettes smoked per day multiplied by the number of years smoked. Based upon SI, patients were categorized into the following groups:

I. never smokers.
II. light smokers (SI = 1–100).
III. moderate smokers (SI = 101–300).
IV. heavy smokers (SI ≥300).

Quantification of alcohol consumption was done by a questionnaire. Total alcohol intake was computed in gm/day and the amount of alcohol content in different type of beverages calculated as 360 mL (12 oz) of beer contains 13.2 gm of ethanol; 11.3 gm of ethanol for 360 mL (12 oz) of light beer; 10.8 gm of ethanol for 120 mL (4 oz) of wine; and 15.1 gm of ethanol for 45 mL (1.5 oz) of liquor (gin, bourbon, whiskey, vodka, and liqueurs).
3. Socioeconomic status was defined on basis of Kuppuswamy’s Scale (2016).

Socioeconomic classes

<table>
<thead>
<tr>
<th>Score</th>
<th>Socioeconomic class</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. 26–29</td>
<td>Upper</td>
</tr>
<tr>
<td>II. 16–25</td>
<td>Upper middle</td>
</tr>
<tr>
<td>III. 11–15</td>
<td>Lower middle</td>
</tr>
<tr>
<td>IV. 5–10</td>
<td>Upper lower</td>
</tr>
<tr>
<td>V. &lt;5</td>
<td>Lower</td>
</tr>
</tbody>
</table>

4. Level of physical activity was measured as per groups suggested by Dewan et al.6
   I. Heavy activity group—farmers working in field and laborers, both men and women.
   II. Medium activity group—shopkeepers, skilled workers, and women doing household work.
   III. Light activity group—retired men and women living a sedentary life.
5. Personal stress was measured on basis of Perceived Stress Scale score.7
   - 0–13: Low stress
   - 14–26: Moderate stress
   - 27–40: High perceived stress
6. Food frequency questionnaire was used to assess the nutritional status of both patients and their siblings.
7. Clinical examination along with anthropometric evaluation was carried out including height, weight, waist–hip ratio, that is, waist circumference/hip circumference (waist circumference measured between lower limit of rib cage and the iliac crest in centimeters with subject standing using flexible nondistensible tape and hip circumference measured around the widest portion of the buttocks, with the tape parallel to the floor), and BMI was calculated by formula—body weight (in kilogram)/height² (in meter). Any abnormality in these parameters defined as per the World Health organization (WHO) guideline.8
   BMI—18.5–24.9: normal
   >25–29.9: overweight
   >30: obese
   WHR: >0.85 for females
   >0.90 for males
8. Blood pressure (BP) measurement was done after 10 minutes rest in supine position, with no tight clothes, mean of two measurements was registered and hypertension defined by Indian guidelines.

Classification of blood pressure for adults aged 18 and older

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic (mm Hg)</th>
<th>Diastolic (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;130</td>
<td>&lt;85</td>
</tr>
<tr>
<td>High-normal</td>
<td>130–139</td>
<td>85–89</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage II</td>
<td>160–179</td>
<td>100–109</td>
</tr>
<tr>
<td>Stage III</td>
<td>&gt;180</td>
<td>&gt;110</td>
</tr>
<tr>
<td>Isolated systolic hyperten</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>140–159</td>
<td>&lt;90</td>
</tr>
<tr>
<td>Grade II</td>
<td>&gt;160</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>

9. Laboratory investigations.
Fasting blood sugar (FBS) was measured by glucose oxidase peroxidase method and diabetes defined by WHO criteria.9
FBS—<100: nondiabetic
100–125: impaired
>126: diabetic

Lipid Profile
Serum cholesterol was measured by cholesterol oxidase peroxidase method.
Serum triglycerides (TGs) was measured by glycerol phosphate oxidase peroxidase method.
Serum high-density lipoprotein (HDL) was measured by cholesterol oxidase per oxidase method after precipitation.
Serum low-density lipoprotein (LDL) was measured by Friedwald’s equation and derangement in lipid profile defined by adult treatment panel (ATP) III guideline.

ATP III classification of LDL, total and HDL cholesterol (mg/dL)

<table>
<thead>
<tr>
<th>LDL cholesterol</th>
<th>Total cholesterol</th>
<th>HDL cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>&lt;200</td>
<td>&lt;40</td>
</tr>
<tr>
<td>Optimal</td>
<td>Desirable</td>
<td>Low</td>
</tr>
<tr>
<td>Near optimal/above optimal</td>
<td>Borderline high</td>
<td>High</td>
</tr>
<tr>
<td>130–159</td>
<td>&gt;240</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Borderline high</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>&gt;190</td>
<td>Very high</td>
<td></td>
</tr>
</tbody>
</table>

For Triglycerides
<150: normal
150–199: borderline high
200–499: high
>500: very high

10. Twelve lead electrocardiogram (ECG), TMT/2D Echo was done.

Results
This was a cross-sectional study, conducted among 100 pairs of healthy siblings (not known cases of CAD) who came for health checkup at health center of Dayanand Medical College and Hospital, a tertiary care hospital in North India. Study population included 93 (46.5%) females and 107 (53.5%) male siblings.
The baseline characteristics of population was shown in Table 1. Maximum number of subjects belonged to upper middle socioeconomic class 115 (57.5%), followed by...
Level of physical activity was measured as per groups suggested by Dewan et al. It was found out of 200, 51 had light physical activity, 92 subjects had moderate physical activity, and 57 had heavy physical activity.

Further, those 38 pairs were sorted out and statistical analysis was done and prevalence of CAD risk factors was seen among those 38 pairs of siblings who had difference in their residence (Table 2).

Hypertension defined by Indian guidelines for hypertension and patients with past history of hypertension on medication. It was found that out of 200 patients, 57 were normal, 92 subjects had moderate physical activity, while remaining four subjects had light physical activity (4.0%).

Table 1: Prevalence of various CAD risk factors among all the siblings

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–40</td>
<td>61</td>
<td>30.5</td>
</tr>
<tr>
<td>41–50</td>
<td>68</td>
<td>34.0</td>
</tr>
<tr>
<td>51–60</td>
<td>50</td>
<td>25.0</td>
</tr>
<tr>
<td>&gt;60</td>
<td>21</td>
<td>10.5</td>
</tr>
<tr>
<td>Lower middle</td>
<td>34</td>
<td>17.0</td>
</tr>
<tr>
<td>Upper lower</td>
<td>12</td>
<td>6.0</td>
</tr>
<tr>
<td>Upper middle</td>
<td>115</td>
<td>57.5</td>
</tr>
<tr>
<td>Upper</td>
<td>39</td>
<td>19.5</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td>Lower middle</td>
<td>34</td>
<td>17.0</td>
</tr>
</tbody>
</table>

**Smoking**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light</td>
<td>8</td>
<td>4.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>11</td>
<td>5.5</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>179</td>
<td>89.5</td>
</tr>
</tbody>
</table>

**Stress**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>63</td>
<td>31.5</td>
</tr>
<tr>
<td>Light</td>
<td>9</td>
<td>4.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>128</td>
<td>64.0</td>
</tr>
</tbody>
</table>

**Physical activity**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy</td>
<td>57</td>
<td>28.5</td>
</tr>
<tr>
<td>Light</td>
<td>51</td>
<td>25.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>92</td>
<td>46.0</td>
</tr>
</tbody>
</table>

**HTN**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>12</td>
<td>6.0</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>94</td>
<td>47.0</td>
</tr>
<tr>
<td>Stage I</td>
<td>73</td>
<td>36.5</td>
</tr>
<tr>
<td>Stage II</td>
<td>21</td>
<td>10.5</td>
</tr>
</tbody>
</table>

**Diabetics**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiabetic</td>
<td>141</td>
<td>70.5</td>
</tr>
<tr>
<td>Impaired FBS</td>
<td>39</td>
<td>19.5</td>
</tr>
<tr>
<td>Diabetic</td>
<td>20</td>
<td>10.0</td>
</tr>
</tbody>
</table>

**Obesity**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. of cases</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>27</td>
<td>13.5</td>
</tr>
<tr>
<td>Overweight</td>
<td>96</td>
<td>48.0</td>
</tr>
<tr>
<td>Obese</td>
<td>77</td>
<td>38.5</td>
</tr>
</tbody>
</table>

**CAD, Coronary artery disease; HTN, hypertension**

Impact of type of physical activity (there were 19 such pairs), correlation of waist-to-hip ratio (WHR), TG and HDL levels with physical activity was statistically significant and for all others the risk factors came out nonsignificant. That means siblings doing lighter type of physical activity had significantly abnormal WHR and elevated levels of TGs.

Among the CAD negative, out of 23 subjects, two subjects (9.0%) had heavy stress level, while remaining four subjects (17.0%) and 17 subjects (74.0%) had light and moderate stress levels, respectively. Among the CAD negative, out of 23 subjects, 10 subjects (43.0%) had high stress level, while remaining zero subject (0%) and 13 subjects (57.0%) had light and moderate stress levels, respectively. Significant results were obtained while comparing the CAD findings of subjects divided on the basis of stress level (Table 3).

Impact of difference in education status of siblings was studied among those pairs of siblings who had difference in level of physical activity (there were 19 such pairs), correlation of waist-to-hip ratio (WHR), TG and HDL levels with physical activity was statistically significant and for all others the risk factors came out nonsignificant (Table 4).

Impact of difference in socioeconomic class of siblings was studied among those pairs of siblings who had difference in socioeconomic class (there were 33 such pairs), correlation of all the risk factors came out nonsignificant (Table 5).

Impact of difference in level of physical activity of siblings was studied among those pairs of siblings who had difference in level of physical activity (there were 19 such pairs), correlation of WHR, TG and HDL levels with physical activity was statistically significant and for all others the risk factors came out nonsignificant (Table 5).
Coronary Risk Factors

Among the CAD negative, out of 23 subjects, two subjects (9.0%) had heavy stress level, while remaining four subjects (17.0%) and 17 subjects (74.0%) had light and moderate stress levels, respectively. Among the CAD negative, out of 23 subjects, 10 subjects (43.0%) had high stress level, while remaining zero subject (0%) and 13 subjects (57.0%) had light and moderate stress levels, respectively. Significant results were obtained while comparing the CAD findings of subjects divided on the basis of stress level (Table 7).

**Discussion**

In the present study, we studied prevalence of coronary risk factors among 100 pairs of siblings (total 200 subjects). Siblings have equal tendency to acquire any disease from their parents, so impact of environment on coronary risk factors can be better studied among siblings. For this study, we have taken 100 pairs of healthy siblings (those who were not known cases of CAD). Overall prevalence of risk factors of CAD was studied among 200 subjects; maximum number of siblings coming for health checkup belonged to age group of 41–50 years. There were 14 pairs of siblings where both belonged to rural area, came out nonsignificant. That means siblings doing lighter type of physical activity had significantly abnormal WHR and elevated levels of TGs (Table 6).

**Correlation of Sociodemographic Profile among only CAD Positive and Negative Sibling Pairs**

Among the CAD negative, out of 23 subjects, nine subjects (39.1%) had rural residence while remaining 14 subjects (60.9%) had urban residence. Among the CAD positive, out of 23 subjects, two subjects (8.7%) had rural residence while remaining 21 subjects (91.3%) had urban residence. Significant results were obtained while comparing the CAD positive and negative findings subjects divided on the basis of residence.

Among the CAD negative, out of 23 subjects, six subjects (26.1%) had middle class while remaining 17 subjects (73.9%) had upper class. Among the CAD positive, out of 23 subjects, one subject (4.3%) had middle class while remaining 22 subjects (95.7%) had upper class. Significant results were obtained while comparing the CAD findings of subjects divided on the basis of socioeconomic class.

Among the CAD negative, out of 23 subjects, three subjects (13%) belonged to Hindu religion while remaining 20 subjects (87%) belonged to Sikh religion. Among the CAD negative, out of 23 subjects, four subjects (17.4%) belonged to Hindu religion while remaining 19 subjects (82.6%) belonged to Sikh religion. Nonsignificant results were obtained while comparing the CAD findings of subjects divided on the basis of religion.

Among the CAD negative, out of 23 subjects, two subjects (9.0%) had heavy stress level, while remaining four subjects (17.0%) and 17 subjects (74.0%) had light and moderate stress levels, respectively. Among the CAD negative, out of 23 subjects, 10 subjects (43.0%) had high stress level, while remaining zero subject (0%) and 13 subjects (57.0%) had light and moderate stress levels, respectively. Significant results were obtained while comparing the CAD findings of subjects divided on the basis of stress level (Table 7).
Table 3: Comparison of different parameters of sociodemographic profile among those pairs of siblings in whom one subject came out to be CAD positive on evaluation in health checkup

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Classification</th>
<th>TMT</th>
<th>Total</th>
<th>Chi-square value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Socioeconomic class</td>
<td>Lower middle</td>
<td>6</td>
<td>26.1%</td>
<td>1</td>
<td>4.3%</td>
</tr>
<tr>
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<td>Upper</td>
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<td>22</td>
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</tr>
<tr>
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<td>8</td>
<td>34.8%</td>
</tr>
<tr>
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<td>21</td>
<td>91.3%</td>
<td>15</td>
<td>65.2%</td>
</tr>
<tr>
<td>Religion</td>
<td>Hindu</td>
<td>3</td>
<td>13.0%</td>
<td>4</td>
<td>17.4%</td>
</tr>
<tr>
<td></td>
<td>Sikh</td>
<td>20</td>
<td>87.0%</td>
<td>19</td>
<td>82.6%</td>
</tr>
<tr>
<td>Type of family</td>
<td>Joint</td>
<td>12</td>
<td>52.2%</td>
<td>10</td>
<td>43.5%</td>
</tr>
<tr>
<td></td>
<td>Nuclear</td>
<td>11</td>
<td>47.8%</td>
<td>13</td>
<td>56.5%</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Heavy</td>
<td>12</td>
<td>52.2%</td>
<td>6</td>
<td>26.1%</td>
</tr>
<tr>
<td></td>
<td>Light</td>
<td>1</td>
<td>4.3%</td>
<td>9</td>
<td>39.1%</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>10</td>
<td>43.5%</td>
<td>8</td>
<td>34.8%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>No</td>
<td>19</td>
<td>82.6%</td>
<td>18</td>
<td>78.3%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>4</td>
<td>17.4%</td>
<td>5</td>
<td>21.7%</td>
</tr>
<tr>
<td>Level of stress</td>
<td>High</td>
<td>2</td>
<td>8.7%</td>
<td>10</td>
<td>43.5%</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>4</td>
<td>17.4%</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>17</td>
<td>73.9%</td>
<td>13</td>
<td>56.5%</td>
</tr>
<tr>
<td>Obesity</td>
<td>Normal</td>
<td>7</td>
<td>30.4%</td>
<td>3</td>
<td>13.0%</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>7</td>
<td>30.4%</td>
<td>12</td>
<td>52.2%</td>
</tr>
<tr>
<td></td>
<td>Preobese</td>
<td>9</td>
<td>39.1%</td>
<td>8</td>
<td>34.8%</td>
</tr>
<tr>
<td>WHR group</td>
<td>Nonsignificant</td>
<td>6</td>
<td>26.1%</td>
<td>1</td>
<td>4.3%</td>
</tr>
<tr>
<td></td>
<td>Significant</td>
<td>17</td>
<td>73.9%</td>
<td>22</td>
<td>95.7%</td>
</tr>
<tr>
<td>HTN</td>
<td>Normal</td>
<td>2</td>
<td>8.7%</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>Prehypertension</td>
<td>11</td>
<td>47.8%</td>
<td>11</td>
<td>47.8%</td>
</tr>
<tr>
<td></td>
<td>Stage I</td>
<td>9</td>
<td>39.1%</td>
<td>9</td>
<td>39.1%</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>1</td>
<td>4.3%</td>
<td>3</td>
<td>13.0%</td>
</tr>
<tr>
<td>Diabetics</td>
<td>Nondiabetic</td>
<td>19</td>
<td>82.6%</td>
<td>10</td>
<td>43.5%</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>2</td>
<td>8.7%</td>
<td>3</td>
<td>13.0%</td>
</tr>
<tr>
<td></td>
<td>Prediabetic</td>
<td>2</td>
<td>8.7%</td>
<td>10</td>
<td>43.5%</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Borderline high</td>
<td>5</td>
<td>21.7%</td>
<td>7</td>
<td>30.4%</td>
</tr>
<tr>
<td></td>
<td>Desirable</td>
<td>13</td>
<td>56.5%</td>
<td>13</td>
<td>56.5%</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>5</td>
<td>21.7%</td>
<td>3</td>
<td>13.0%</td>
</tr>
<tr>
<td>TG</td>
<td>Borderline high</td>
<td>6</td>
<td>26.1%</td>
<td>5</td>
<td>21.7%</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>4</td>
<td>17.4%</td>
<td>5</td>
<td>21.7%</td>
</tr>
<tr>
<td></td>
<td>normal</td>
<td>13</td>
<td>56.5%</td>
<td>13</td>
<td>56.5%</td>
</tr>
<tr>
<td>HDL</td>
<td>High</td>
<td>3</td>
<td>13.0%</td>
<td>1</td>
<td>4.3%</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>11</td>
<td>47.8%</td>
<td>13</td>
<td>56.5%</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>9</td>
<td>39.1%</td>
<td>9</td>
<td>39.1%</td>
</tr>
<tr>
<td>LDL</td>
<td>Borderline high</td>
<td>6</td>
<td>26.1%</td>
<td>7</td>
<td>30.4%</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>4</td>
<td>17.4%</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>Near optimal</td>
<td>5</td>
<td>21.7%</td>
<td>12</td>
<td>52.2%</td>
</tr>
<tr>
<td></td>
<td>Optimal</td>
<td>6</td>
<td>26.1%</td>
<td>4</td>
<td>17.4%</td>
</tr>
<tr>
<td></td>
<td>Very high</td>
<td>2</td>
<td>8.7%</td>
<td>0</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

CAD, Coronary artery disease; HDL, high-density lipoprotein; HTN, hypertension; LDL, low-density lipoprotein; TG, triglyceride; TMT, treadmill test; WHR, waist-to-hip ratio
Coronary Risk Factors

was high in urban 55% than rural 46%, in urban area. Prevalence of hypertension was studied among only those pairs of sibling who were segregated on basis of difference in their residence, hypertension was prevalent among urban (53%) siblings as compared to their siblings living in rural (42%) area. There were considerable number of siblings in high normal range 23% and 23% in rural and urban siblings, respectively. The results were statistically nonsignificant.

Our results were in concordance with the results obtained by Anchala et al. who found that the overall prevalence of hypertension in India to be 29.8% with significant urban–rural difference. Previous studies in India in the last decade have reported varying prevalence of hypertension ranging from 17 to 47% in the adult population.

Overall prevalence of Hypertension (HTN) among the study participants on the study conducted by Tripathy et al. was found out to be 40.1%.

Previously identified risk factors for hypertension in Indians include increasing age, higher BMI, increased alcohol consumption, sedentary lifestyle, and stress. Our study shows the rising trend of hypertension among rural population as well.

In the present study, prevalence of diabetes among overall population was 10%. A percentage of 1% was unaware of their diabetic status and 14% had impaired FBS status. It was higher among urban subjects (12%) than rural subjects (6%), also higher among males than females. Also prevalence of impaired FBS was higher among urban than rural population. However, the results were statistically insignificant. When studied among siblings separated on residence basis (n = 38 pairs), similar results were obtained; diabetes was more commonly seen among urban siblings (18.4%) than their siblings living in rural area (5.3%).

In the present study, there were considerable number of siblings both in rural and urban areas who had impaired FBS, 13 and 28%, respectively. That means more awareness is needed in both the regions so that occurrence of overt diabetic status is prevented. It was found that difference of socioeconomic status (13 pairs), education status (33 pairs), and physical activity levels (19 pairs) of two siblings had no significant impact on occurrence of diabetes. It was also seen that diabetes was more prevalent among male siblings than their female siblings, but statistically insignificant. Studies have shown large regional and socioeconomic differences in the prevalence of type 2 diabetes in India. Self-reported prevalence is lower in rural area than in urban area ranging from 3.1 in rural area to 7.3% in urban area. The disease appears to be more prevalent in the south of the country as compared to the northern and eastern parts. The WHR is a measure of abdominal obesity and a surrogate measure for visceral

### Table 4: Study CAD risk factors among those pairs of siblings with difference in education status (n = 33 pairs)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Education (33 discordant pairs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diploma or less</td>
<td>Graduation or more</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Normal</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>High normal</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Stage I</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Stage III</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Nondiabetic</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Impaired FBS</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>5</td>
</tr>
<tr>
<td>Obesity</td>
<td>Normal</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Overweight</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>7</td>
</tr>
<tr>
<td>WHR</td>
<td>Normal</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>8</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>Total cholesterol</td>
<td>172.9 ± 34.2</td>
</tr>
<tr>
<td></td>
<td>TG</td>
<td>169.8 ± 58.9</td>
</tr>
<tr>
<td></td>
<td>LDL</td>
<td>112.7 ± 25.1</td>
</tr>
<tr>
<td></td>
<td>HDL</td>
<td>39.7 ± 8.6</td>
</tr>
</tbody>
</table>

CAD, Coronary artery disease; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WHR, waist-to-hip ratio

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Socioeconomic class (n = 13 pairs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diploma or less</td>
<td>Graduation or more</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Normal</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>High normal</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Stage I</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Stage III</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Nondiabetic</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Impaired FBS</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>3</td>
</tr>
<tr>
<td>Obesity</td>
<td>Normal</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Overweight</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>3</td>
</tr>
<tr>
<td>WHR</td>
<td>Normal</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>4</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>Total cholesterol</td>
<td>176.4 ± 32.4</td>
</tr>
<tr>
<td></td>
<td>Triglycerides</td>
<td>173.5 ± 62.6</td>
</tr>
<tr>
<td></td>
<td>LDL</td>
<td>115.8 ± 27.6</td>
</tr>
<tr>
<td></td>
<td>HDL</td>
<td>37.5 ± 7.8</td>
</tr>
</tbody>
</table>

CAD, Coronary artery disease; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WHR, waist-to-hip ratio

48 pairs of siblings where both belonged to urban area, and 38 such pairs where one sibling lived in rural area and other lived in urban area. Prevalence of hypertension was high in urban 55% than rural 46%, which was statistically significant. When prevalence of hypertension was studied among only those pairs of sibling who were segregated on basis of difference in their residence, hypertension was prevalent among urban (53%) siblings as compared to their siblings living in rural (42%) area. There were considerable number of siblings in high normal range 23% and 23% in rural and urban siblings, respectively. The results were statistically nonsignificant.
of urban siblings had abdominal obesity (WHR) and 82% siblings living in rural area had abdominal obesity, when compared statistically not significant. Asian Indians have a greater predisposition to abdominal obesity and accumulation of visceral fat and this has been termed as “Asian Indian phenotype.” In a study conducted in urban north India (New Delhi), the overall prevalence of generalized obesity was 50.1%, while that of abdominal obesity was 68.9%. The Chennai Urban Rural Epidemiology Study conducted in Chennai city in Tamil Nadu reported age-standardized prevalence of generalized obesity to be 45.9%, while that of abdominal obesity was 46.6%. Isolated generalized obesity was found in 9.1% while isolated abdominal obesity was reported in 9.7%. In another study conducted by Pradeepa et al., authors showed a higher prevalence of isolated abdominal obesity than isolated generalized obesity.18–21

While studying dyslipidemias mean total cholesterol levels among cohort (200 population) were 180.80 ± 38.589 (desirable range), mean TG levels were 149.37 ± 69.79 (borderline high), HDL levels were 43.73 ± 14.57, mean LDL levels were 116 ± 30.81 (varied from optimal to borderline high). Lipid levels when compared among total rural and urban cohort significant results were obtained for both total cholesterol group and LDL group. When lipid profile was compared among siblings divided on residence basis (38 pairs), nonsignificant results were obtained for total cholesterol, TG, and HDL Levels. While correlation of LDL levels with siblings divided on residence basis was statistically significant (p-value = 0.008). High levels of LDL were found in 16% of urban siblings and 6% rural siblings. Upon studying impact of education, socioeconomic class of siblings on lipid profile no significant results were obtained, but significant results were obtained while studying impact of physical activity on lipid profile, those siblings doing lighter physical activity had higher total cholesterol, TGs, and LDL levels. While studying only CAD positive and negative sibling

### Table 6: Study CAD risk factors among those pairs of siblings with difference in physical activity class (n = 19 pairs)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Physical activity (19 discordant pairs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Normal 4</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>High normal 6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Stage I 5</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Stage II 4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Stage III 0</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Nondiabetic 13</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Impaired FBS 2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Diabetic 4</td>
<td>1</td>
</tr>
<tr>
<td>Obesity</td>
<td>Normal 9</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Overweight 7</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Obese 3</td>
<td>0</td>
</tr>
<tr>
<td>WHR</td>
<td>Normal 11</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Abnormal 8</td>
<td>2</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>Total cholesterol 180.2 ± 44.3</td>
<td>176.4 ± 34.9</td>
</tr>
<tr>
<td></td>
<td>Triglycerides 171.6 ± 90.6</td>
<td>152.3 ± 38.42</td>
</tr>
<tr>
<td></td>
<td>LDL 118 ± 24.3</td>
<td>115.7 ± 35.6</td>
</tr>
<tr>
<td></td>
<td>HDL 39.5 ± 9.65</td>
<td>42.6 ± 15.3</td>
</tr>
</tbody>
</table>

CAD, Coronary artery disease; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WHR, waist-to-hip ratio

### Table 7: Correlation of sociodemographic profile among only CAD positive and negative sibling pairs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Classification</th>
<th>CAD Negative</th>
<th>CAD Positive</th>
<th>Total</th>
<th>Chi-square value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>15 65.0%</td>
<td>9 39.0%</td>
<td>24</td>
<td>3.164</td>
<td>0.076</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>8 35.0%</td>
<td>14 61.0%</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td>Rural</td>
<td>9 39.0%</td>
<td>2 9.0%</td>
<td>11</td>
<td>5.850</td>
<td>0.015</td>
</tr>
<tr>
<td></td>
<td>Urban</td>
<td>14 61.0%</td>
<td>21 91.0%</td>
<td>35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Socioeconomic class</td>
<td>Middle</td>
<td>6 26.0%</td>
<td>1 4.0%</td>
<td>7</td>
<td>4.2</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>17 74.0%</td>
<td>22 96.0%</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Religion</td>
<td>Hindu</td>
<td>3 13.0%</td>
<td>4 17.0%</td>
<td>7</td>
<td>0.168</td>
<td>0.681</td>
</tr>
<tr>
<td></td>
<td>Sikh</td>
<td>20 87.0%</td>
<td>19 83.0%</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of family</td>
<td>Joint</td>
<td>12 52.0%</td>
<td>10 43.0%</td>
<td>22</td>
<td>0.348</td>
<td>0.555</td>
</tr>
<tr>
<td></td>
<td>Nuclear</td>
<td>11 48.0%</td>
<td>13 57.0%</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td>Light</td>
<td>1 4.0%</td>
<td>9 39.0%</td>
<td>10</td>
<td>8.62</td>
<td>0.013</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>10 44.0%</td>
<td>8 35.0%</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>12 52.0%</td>
<td>6 26.0%</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>No</td>
<td>19 83.0%</td>
<td>18 78.0%</td>
<td>37</td>
<td>0.138</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>4 17.0%</td>
<td>5 22.0%</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of stress</td>
<td>Low</td>
<td>4 17.0%</td>
<td>0 0.0%</td>
<td>4</td>
<td>9.876</td>
<td>0.007</td>
</tr>
</tbody>
</table>

CAD, Coronary artery disease
Coronary Risk Factors

pairs, correlation of lipid profile showed no significant results among siblings in causing CAD. Dyslipidemia has been closely linked to the pathophysiology of CVD and is a key independent modifiable risk factor for CVD.

Urbanization usually involves varying degrees of modernization and westernization which have an impact on dietary habits. The urban environment entails important changes in lifestyles, economic activities, exposure to marketing, and reference group influences. All these impinge on traditional diets and lead to shifts in food consumption patterns. With an ever-increasing incidence of both type 2 diabetes mellitus and CVD in most urban populations, there has been a stressful need for studies that could evaluate risk of CVD—the largest cause of death in developing countries. Moreover, morbidity and mortality due to CVD at premature age are reported to be high in diabetes. Despite high prevalence, there is paucity of studies showing differences in CVD risk factors between urban and rural diabetic population. Moreover, data on AD among diabetic patients in urban and rural area of developing countries, like India, are uncertain. In addition, there are no definitive reports on the variation of emerging cardiovascular indices, such as TG/HDL and atherogenic index among urban and rural diabetic patients versus respective nondiabetic controls from north India. Differential data have been reported in the past literature in relation to the prevalence of smoking habit among Indian population. The prevalence of smoking cigarettes among school-going adolescents in India using the global youth tobacco survey (GYTS) data of 2000 and 2001 have been reported to vary from one state/union to another between 0.5% in Goa and 22.8% in Mizoram, with the north-eastern states/unions having higher rates than the south-western states/unions. Current cigarette smoking was defined as having ever smoked even one puff in the past 30 days preceding the study. Jindal et al. have reported that the prevalence of having ever smoked in northern India was lowest in Punjab (2.9% for boys and 1.5% for girls) and highest in Chandigarh (8.5% for boys and 9.8% for girls). Knowledge of the prevalence of smoking among adolescent is important in estimating the burden of the problem and facilitates evaluation of public health interventions as change in prevalence over time can be assessed.

Alcohol use is an important public health problem, especially in developing countries like India. There was a marked variation between World Health Organization subregions on average volume of alcohol consumption and patterns of drinking. Average volume of drinking was highest in established market economies in western Europe and the former socialist economies in the eastern part of Europe and North America and it was lowest in the eastern Mediterranean region and parts of southeast Asia, including India. A recent study highlighted that in India, health loss from alcohol will grow even larger, unless effective interventions and policies are implemented to reduce these habits. In our study, among siblings (CAD positive and CAD negative), significant results were obtained for residence, socioeconomic class, physical activity, stress levels, smoking, WHR, and diabetes, that is, all these factors have correlation in increasing CAD among siblings.

References

Interrelation of the Risk Factors of NAFLD at various Stages of Progression of the glycemic Status on long-term Follow-up

Gautam Ray1,*, Chandan Kumar2

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Abstract

Background: Though the risk factors for nonalcoholic fatty liver disease (NAFLD) are the same in diabetic and nondiabetic patients, their exact interrelation and weightage in the pathogenesis are unclear.

Methods: A total of 130 nondiabetic and 170 diabetic patients with NAFLD (diagnosed on abdominal ultrasound and severity assessed by NAFLD fibrosis score (NFS)) were recruited from 2009 to 2018 and their baseline risk factors (body mass index (BMI), waist circumference (WC), blood pressure, presence of the metabolic syndrome (MS) and insulin resistance (IR) by Homeostasis Model of Assessment for Insulin Resistance (HOMA-IR), fasting blood glucose (FBG) and lipid levels, and hemoglobin A1c (HbA1c) levels) were noted and their interrelationship studied. The nondiabetic patients were prospectively followed up for alteration of glycemic status.

Results: There was presence of high BMI (>23) in 66%, central obesity in 86% (of whom 59% had normal body weight), low high-density lipoprotein cholesterol (HDL) in 51%, high triglyceride (TG) in 68%, high low-density lipoprotein cholesterol (LDL) in 46.7%, IR in 86%, hypertension in 54%, and the MS in 57%. Hemoglobin A1c was high in 42.3% of nondiabetics. The prevalence of the MS was significantly higher in patients having IR and vice versa but only the MS and its components as also increasing age determined advanced fibrosis. After mean follow-up 7.3 years, progression from prediabetes (PD) to diabetes mellitus (DM) occurred in 10%, from normal glucose tolerance (NGT) to PD in 6.25%, and progression of NFS occurred in 16.9%. Advanced age, low HDL and high TG were associated with IR and were involved in glycemic progression as also obesity in progression from NGT to PD and central obesity from PD to DM.

Conclusion: Though IR and MS go hand in hand in the pathogenesis of NAFLD in both diabetic and nondiabetic patients as well as in the glycemic progression of nondiabetic patients with NAFLD, the MS or its components have more weightage in determining the severity.

Introduction

While NAFLD occurs commonly among patients of DM, it also occurs in nondiabetic persons and the risk factors in both are the presence of the MS, obesity, dyslipidemias, and IR. The exact interrelation of these factors and their individual weightage in the pathogenesis of NAFLD in both these groups of patients is still unclear. A recent study has shown that in nondiabetics (consisting of people with NGT and PD) dyslipidemias and obesity are the prime contributors to genesis of NAFLD though IR is also present in a large proportion of patients and may come into play later in the prediabetic stage.1 To elucidate further, we analyzed the interrelation of the above parameters in a group of NAFLD patients consisting of both nondiabetics and diabetics (to study the interrelation and weightage of these parameters in the entire glycemic spectrum of NAFLD patients) cross-sectionally at baseline. The nondiabetic patients were also followed up longitudinally for the development of PD and DM (called glycemic progression) and also for any alteration of severity of their NAFLD as determined by the NFS.

Nonalcoholic fatty liver disease fibrosis score is a quantifiable noninvasive parameter for assessing the severity of NAFLD (including risk of fibrosis).2 By applying a low cut-off (<−1.455), advanced fibrosis can be excluded with high accuracy (negative predictive value 93%) while a high cut-off threshold (>0.676) offers accurate detection of advanced fibrosis (positive predictive value 90%) (i.e., <−1.455 = absence of significant NAFLD, −1.455 to 0.676 = mild to moderate or indeterminate NAFLD, and >0.676 = severe NAFLD). We chose this parameter to assess the severity of NAFLD due to nonavailability of fibroscan at the time of inception of the study and as none of our subjects consented for liver biopsy.

Methods

The study was undertaken from 2009 to 2018 and consisted of 130 nondiabetics (80NGT and 50 PD) and 170 diabetics recruited from outdoor and indoor hospital services who were diagnosed with NAFLD on abdominal ultrasonogram (USG) in the fasting state while being investigated for various reasons like abdominal symptoms, abnormal liver function tests, fever workup, and preplacement examination. A detailed history taking and clinical examination (especially to exclude endocrine disorders, drugs that may cause NAFLD, and high TGs as also chronic liver disease for which USG was used in addition) were done at initial screening followed by investigation to exclude secondary causes of chronic liver disease like HBsAg, anti-HCV, autoimmune liver disease antibodies, serum ceruloplasmin, and iron studies. In addition to these other exclusion groups were people with ever alcohol intake in any amount and people with any other chronic disease.

Body mass index was calculated as body weight in kg/height in meter2 and patients were graded as underweight (<18.5 kg/m2), normal BMI (18.5–22.9 kg/m2), overweight (23.0–24.9 kg/m2) and obese (≥25 kg/m2) (according to the revised consensus guidelines for obesity for India).3 Blood pressure was measured in sitting position after 30 minutes of rest using a sphygmomanometer. Waist circumference was measured with a non-stretchable tape at the level just above the iliac crest at the end of expiration. The MS was defined by the International Diabetes Federation Global Consensus Definition,4 that is, central obesity (≥90 cm for men, >80 cm for women) plus any two of the following four parameters: (1) raised TG: ≥150 mg/dL or history of specific treatment for this lipid abnormality, (2) reduced HDL: <50 mg/dL in females or history of specific treatment for this lipid abnormality, (3) raised blood pressure: systolic ≥130 mm Hg or diastolic ≥85 mm Hg or on treatment for previously diagnosed hypertension,

References

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and (4) raised FBG ≥100 mg/dL or previously diagnosed DM.

After an overnight fast, blood was collected for the following investigations: (1) FBG and 2-hour postload (75 gm) plasma glucose (oral glucose tolerance test) by glucose oxidase-peroxidase method. (2) Serum total cholesterol (TC), TG, HDL, bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, gamma-glutamyl transpeptidase, total protein, albumin, and globulin (by Autoanalyzer using standard kits). Low-density lipoprotein cholesterol was calculated using the Friedewald equation. (3) Hemoglobin A1c was measured by high-performance liquid chromatography. (4) Serum fasting insulin level was estimated by chemiluminescence immunoassay and IR was calculated using the HOMA-IR formula:

\[ \text{HOMA-IR} = \frac{\text{fasting insulin (mIU/mL)} \times \text{fasting glucose (mmol/L)}}{22.5} \]

Some however prefer to take medicines with recording of body weight, WC, blood pressure, hemoglobin, total cholesterol, TG, HDL, bilirubin, and undergo free investigations at regular intervals or at any convenient time. At least one follow-up visit was needed for inclusion in study. A two-tailed p-value of <0.05 was considered significant. Multivariate analysis of factors predicting glycemic progression was done by logistic regression considering PD and DM as outcome variable. Odds ratio (OR) and confidence intervals (CI) were calculated. All statistical analysis was done with SPSS version 13 (Chicago Inc.).

**Results**

The results are shown in Tables 1 to 3. After mean follow-up 7.3 (±1.4, 6–10) years, new-onset DM occurred in 5/50 (10%), all from the PD group whereas progression from NGT to PD occurred in 5/50 (6.25%), two had IGT, and three had IFG and all were above 45 years of age. There was reversal to normoglycemia from PD in three (6%). None was able to attain ideal body weight and normal WC, only 15 (11.4%) could achieve a maximum of 10% weight loss but WC increased by 2–3 cm in 119 (90%). Mean systolic blood pressure (SBP) was 126.8 (±15.3, 108–146) mm Hg and diastolic blood pressure (DBP) was 85.6 (±10.1, 72–98) mm Hg. There was presence of low HDL in 153 (51%), high TG in 204 (68%), high LDL in 140 (46.7%), IR in 258 (86%), and the number of MS components present were as follows (0 in 15, 1 in 18, 2 in 96, 3 in 33, 4 in 81, and 5 in 57). Hemoglobin A1c was high in 55 (42.3%) nondiabetics. Blood pressure and lipid levels normalized with treatment in all those having high values. As per NFS, overall there was no fibrosis in 45 (15%), indeterminate (F1-F2) fibrosis in 210 (70%), and advanced (F3-F4) fibrosis in 45 (15%) and 43% variability was noted. As per NFS just failed to reach significance. Incidence of IR was 22 (6.9%), to advanced from indeterminate value in four (3.1%) and regression of score in five (3.8%), all in the indeterminate group, but not to normal values. In stepwise logistic regression, age (OR 1.36 (CI 1.05–3.63)), TG (OR 1.58 (CI 1.05–2.17)), and obesity (OR 3.15 (CI 1.22–10.54)) positively predicted progression to PD from NGT group whereas FBS and NFS were also significant by themselves but did not contribute to the model. Age (OR 1.12 (CI 1.08–1.20)), TG (OR 1.04 (CI 1.002–1.074)) and central obesity (OR 5.87 (CI 3.47–12.3)) positively predicted progression to DM from PD though presence of IR and low HDL were also significant by themselves but did not contribute to the model and HbA1c and NFS just failed to reach significance.

**Discussion**

It is thus apparent from this study that though IR and MS go hand in hand in the pathogenesis of NAFLD in both diabetic and nondiabetic groups as well as in the glycemic progression of nondiabetic patients with NAFLD, the MS or its components have more weightage in determining the severity of NAFLD. Tables 1 and 2 show that prevalence of the MS is significantly higher in patients having IR and vice versa but only the MS and its components of central obesity and low HDL as also increasing age determines advanced fibrosis. The probable explanation is that the occurrence of IR may follow the components of the MS, especially obesity.

Similarly advanced age, low HDL, and high TG are associated with IR and are involved in glycemic progression (Table 3). It is interesting to note that whereas obesity is significant in progression from NGT to PD it is central obesity that determines progression from PD to DM.

Multiple studies attest to the results of our study. The progression from NGT to PD was 8.6% after median 3.1 years follow-up and that of DM from PD was 5.1–16% after mean follow-up of 2.7–4.3 years after with MS and NAFLD/nondiabetic obesity being risk factors. Our study had longer follow-up with similar incident DM.

In our study, the NFS by itself is positively associated in glycemic progression from NGT to PD. Similar result is described in another study where NAFLD was higher in PD compared to controls and WC was the best predictor. The progression of NFS to F3–F4 value was noted in only four (3.1%) patients (which parallels the low rate of glycemic progression) and regression in five (3.8%) patients but none in F3–F4 group. The reversion from PD to normoglycemia was 22.2% in a previous study but we had lower reversion, possibly due to underachievement of lifestyle control measures. We did not use metformin as none of our PD patients had BMI >35 and because of the risk of hypoglycemia but our finding of low rate of reversion of PD to normoglycemia and of regression of NFS raises the question about using newer drugs like pioglitazone or saroglitazar (with lesser risk for hypoglycemia) for PD patients with NAFLD at lower BMI.

The strength of our study is a long follow-up in a prospective manner and hence the validity of the outcome. The limitations were use of NFS as severity measure of liver disease instead of regression of score in five (3.8%), all in the indeterminate group, but not to normal values. In stepwise logistic regression, age (OR 1.36 (CI 1.05–3.63)), TG (OR 1.58 (CI 1.05–2.17)), and obesity (OR 3.15 (CI 1.22–10.54)) positively predicted progression to PD from NGT group whereas FBS and NFS were also significant by themselves but did not contribute to the model. Age (OR 1.12 (CI 1.08–1.20)), TG (OR 1.04 (CI 1.002–1.074)) and central obesity (OR 5.87 (CI 3.47–12.3)) positively predicted progression to DM from PD though presence of IR and low HDL were also significant by themselves but did not contribute to the model and HbA1c and NFS just failed to reach significance.

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Table 1: Baseline difference in demography and metabolic factors among different risk groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IR present (n = 258)</th>
<th>IR absent (n = 42)</th>
<th>p-value</th>
<th>Patients with MS (n = 171)</th>
<th>Patients without MS (n = 129)</th>
<th>p-value</th>
<th>None and indeterminate fibrosis (n = 255)</th>
<th>Advanced fibrosis (n = 45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>52.4 ± 8.9</td>
<td>44.3 ± 10.7</td>
<td>0.01</td>
<td>52.8 ± 9.5</td>
<td>49.3 ± 9.31</td>
<td>0.06</td>
<td>49.9 ± 9.2</td>
<td>59.1 ± 6.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>138:120</td>
<td>27:15</td>
<td>0.45</td>
<td>81.90</td>
<td>84.45</td>
<td>0.07</td>
<td>147:108</td>
<td>18:27</td>
<td>0.2</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>98.4 ± 9.6</td>
<td>94.3 ± 12.4</td>
<td>0.25</td>
<td>98.34 ± 8.3</td>
<td>84.4 ± 6.3</td>
<td>0.02</td>
<td>96.9 ± 9.8</td>
<td>102.9 ± 10.1</td>
<td>0.04</td>
</tr>
<tr>
<td>WC (increased/normal)</td>
<td>226.32</td>
<td>32:10</td>
<td>0.08</td>
<td>168.3</td>
<td>90.39</td>
<td>0.003</td>
<td>213.42</td>
<td>45:0</td>
<td>0.01</td>
</tr>
<tr>
<td>Obesity (present:absent)</td>
<td>168.90</td>
<td>30:12</td>
<td>0.5</td>
<td>111.60</td>
<td>84.45</td>
<td>0.9</td>
<td>168.87</td>
<td>30:15</td>
<td>0.9</td>
</tr>
<tr>
<td>BMI</td>
<td>28.1 ± 4.6</td>
<td>27.0 ± 6.01</td>
<td>0.56</td>
<td>28.3 ± 4.5</td>
<td>27.3 ± 5.3</td>
<td>0.32</td>
<td>27.8 ± 4.6</td>
<td>28.4 ± 5.9</td>
<td>0.72</td>
</tr>
</tbody>
</table>
| TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, Low-density lipoprotein cholesterol; HbA1c, Hemoglobin A1c; HOMA-IR, homeostasis Model of Assessment for Insulin Resistance; NFS, NAFLD fibrosis score; BMI, body mass index; FBG, fasting blood glucose; SBP, systolic blood pressure; IR, insulin resistance; DBP, diastolic blood pressure; MS, metabolic syndrome; DM, diabetes mellitus.

Table 2: Baseline levels of metabolic risk factors and their interrelationship

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± standard deviation (range) or %</th>
<th>Univariate OR (CI), p-value</th>
<th>Multivariate OR (CI), p-value</th>
<th>Advances fibrosis OR (CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years</td>
<td>51.34 ± 9.49 (25–74)</td>
<td>1.56 (1.08–1.84), 0.003</td>
<td>1.32 (1.01–1.57), 0.003</td>
<td>1.45 (1.06–1.7), 0.001</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>165:135</td>
<td>1.5 (0.48–5.1), 0.32</td>
<td>1.2 (0.63–2.1), 0.32</td>
<td>1.7 (0.58–5.2), 0.24</td>
</tr>
<tr>
<td>WC (in cm)</td>
<td>88.8 ± 13.1 (72–106)</td>
<td>0.96 (0.9–1.02), 0.16</td>
<td>1.01 (0.17–5.05), 0.2</td>
<td>0.95 (0.9–1.0), 0.052</td>
</tr>
<tr>
<td>BMI</td>
<td>24.2 ± 4.1 (18.4–29.1)</td>
<td>0.92 (0.84–1.09), 0.47</td>
<td>1.05 (0.22–5.75), 0.2</td>
<td>0.98 (0.88–1.08), 0.68</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 23%)</td>
<td>198 (66%), overweight 46%, obese 20%</td>
<td>1.37 (0.79–2.34), 0.17</td>
<td>1.14 (0.84–1.37), 0.16</td>
<td>0.94 (0.87–1.09), 0.68</td>
</tr>
<tr>
<td>Central obesity</td>
<td>258 [86%, 60/102 (59%) with normal body weight]</td>
<td>1.21 (0.86–1.89), 0.16</td>
<td>1.03 (0.82–1.14), 0.17</td>
<td>1.23 (1.11–1.37), 0.04</td>
</tr>
<tr>
<td>Hypertension present</td>
<td>162 (54%)</td>
<td>0.93 (0.9–1.02), 0.12</td>
<td>0.86 (0.73–1.01), 0.12</td>
<td>0.98 (0.95–1.06), 0.15</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.5 ± 2.3 (0.9–6.1)</td>
<td>1.03 (1.01–1.12), 0.04</td>
<td>1.06 (1.01–1.17), 0.03</td>
<td>1.17 (0.79–1.44), 0.44</td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>133.4 ± 46.6 (88–234)</td>
<td>2.34 (1.23–4.42), 0.03</td>
<td>1.96 (1.32–3.270), 0.000</td>
<td>1.18 (1.01–1.36), 0.04</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.96 ± 0.51 (5.1–8.4)</td>
<td>1.45 (1.04–1.83), 0.04</td>
<td>1.12 (1.11–1.32), 0.03</td>
<td>0.82 (0.64–1.2), 0.1</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>212.37 ± 25.42 (156–285)</td>
<td>0.87 (0.86–1.2), 0.02</td>
<td>0.86 (0.79–1.03), 0.12</td>
<td>0.9 (0.85–0.92), 0.3</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>164.1 ± 38.6 (116–246)</td>
<td>1.11 (1.02–1.2), 0.03</td>
<td>1.28 (1.06–1.45), 0.01</td>
<td>1.05 (0.89–1.62), 0.63</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>43.5 ± 9.6 (31–58)</td>
<td>0.81 (0.73–0.98), 0.007</td>
<td>0.91 (0.84–0.97), 0.004</td>
<td>0.87 (0.78–0.98), 0.001</td>
</tr>
<tr>
<td>MS present</td>
<td>171 (57%)</td>
<td>1.48 (1.32–1.67), 0.001</td>
<td>4.34 (1.32–2.64), 0.000</td>
<td>13.67 (1.72–36.62), 0.000</td>
</tr>
<tr>
<td>NFS</td>
<td>−0.45 ± 1.22 (−1.7 to +0.76)</td>
<td>0.83 (0.56–1.22), 0.1</td>
<td>0.78 (0.46–1.24), 0.1</td>
<td>2.16 (1.01–3.78), 0.008</td>
</tr>
</tbody>
</table>

TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, Low-density lipoprotein cholesterol; HbA1c, Hemoglobin A1c; HOMA-IR, homeostasis Model of Assessment for Insulin Resistance; NFS, NAFLD fibrosis score; BMI, body mass index; FBG, fasting blood glucose; SBP, systolic blood pressure; IR, insulin resistance; DBP, diastolic blood pressure; MS, metabolic syndrome; DM, diabetes mellitus.
Table 3: Significance of individual factors in predicting glycemic progression in various groups

<table>
<thead>
<tr>
<th>Factors</th>
<th>NGT to PD</th>
<th>PD to DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.000</td>
<td>0.001</td>
</tr>
<tr>
<td>Sex</td>
<td>0.4</td>
<td>0.7</td>
</tr>
<tr>
<td>BMI</td>
<td>0.43</td>
<td>0.8</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.52</td>
<td>0.8</td>
</tr>
<tr>
<td>TC</td>
<td>0.08</td>
<td>0.3</td>
</tr>
<tr>
<td>TG</td>
<td>0.000</td>
<td>0.04</td>
</tr>
<tr>
<td>Low density lipoprotein</td>
<td>0.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Low HDL</td>
<td>0.4</td>
<td>0.04</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.54</td>
<td>0.05</td>
</tr>
<tr>
<td>FBG</td>
<td>0.04</td>
<td>0.5</td>
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<td>NFS</td>
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<tr>
<td>Hypertension</td>
<td>0.8</td>
<td>0.07</td>
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<tr>
<td>WC</td>
<td>0.21</td>
<td>0.8</td>
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<td>MS</td>
<td>0.13</td>
<td>0.43</td>
</tr>
<tr>
<td>IR presence</td>
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<td>0.04</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.01</td>
<td>0.7</td>
</tr>
<tr>
<td>Central obesity</td>
<td>0.25</td>
<td>0.005</td>
</tr>
</tbody>
</table>

TG, triglyceride; HbA1c, Hemoglobin A1c; HOMA-IR, homeostasis Model of Assessment for Insulin Resistance; NFS, NAFLD fibrosis score; WC, waist circumference; FBG, fasting blood glucose; NGT, normal glucose tolerance; PD, prediabetes; DM, diabetes mellitus.

of fibroscan due to nonavailability at the time of inception of the study or liver biopsy due to nonavailability of consent.

In conclusion, the MS and IR supplement each other both in the pathogenesis of NAFLD as well as in the glycemic progression of NAFLD population but MS is more important in determining the disease severity. Lifestyle measures need strong advocation even before development of PD in those with risk factors. Newer drugs may be needed at lower BMI for PD patients in India.

REFERENCES

Acute Kidney Injury in Dengue Fever: A One-year Hospital-based Prospective Cross-sectional Study

Nikhil Batra¹, Navneet Kaur², Akash Pethekar³
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ABSTRACT

Background and objectives: Dengue fever is amongst the most cardinal arthropod-borne infection among humans. Around the world, an estimated 2.5 billion individuals are at peril of infection, of which approximately 975 million reside in urban areas of tropical and subtropical nations like Southeast Asia, the Pacific, and surprisingly Americas. Acute kidney injury (AKI) is so far not a well-studied dengue complication. The renal abnormalities, though not common, are AKI, proteinuria, glomerulonephritis, and hemolytic uraemic syndrome, which are considered complications of the disease. This study was designed to evaluate the prevalence of AKI in DF and find out the predictors of the development of AKI in patients with DI.

Methodology: This one-year hospital-based cross-sectional study was performed in the Department of General Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala from March 2020 to April 2021. A total of 120 eligible patients with DI were enrolled. These patients were evaluated for AKI based on acute kidney injury network (AKIN) criteria.

Results: The majority of the patients were males 57.5% and the male to female ratio was 1.35:1. Most of the patients were aged between 31 and 50 years (40.8%) and the mean age was 42.23 ± 16.28 years. The majority of the patients (72.5%) had the age of 31 years and above. Most of the patients had dengue fever with warning signs and 14.2% of the patients had severe dengue. The prevalence of AKI was 27.5% in patients with dengue fever. Other than AKI, Acute respiratory distress syndrome (ARDS) (11.7%), Multiple Organ Dysfunction Syndrome (MODS) (3.3%), and sepsis (0.8%) were the complications noted. The majority of the patients (83.3%) improved and were discharged and mortality was noted in 16.7% of the patients. Also, significant differences were noted in patients with and without AKI.

INTRODUCTION

Arboviruses asseverate a pressing public wellbeing predication. These are customarily accompanied by outbreaks that have huge moneymaking and social repercussions in tropical and subtropical areas around the world.¹

Dengue fever is among the most cardinal arthropod-borne infection among humans. Around the world, an estimated 2.5 billion individuals are at peril of infection.² The backcountry is also being progressively contrived in areas of Africa and the Eastern Mediterranean. It is thus appraised that approximately the 50 million positive infections can be thought to occur each year, of which 500,000 inmates are of dengue hemorrhagic fever, for the most part amid child, the case fatality rate of which outstanding 5% in some regions.²⁻⁵

In arrears to jump up the business activities and global trotting around the world, the pathogen has been carried away from the endemic parts to innumerable parts of the whole world.⁶,⁷ DF outbreaks have outstretched more or less in 120 nations and numerous of these countries, with high prevalence.⁸ When overviewing the historical data DF has come out from Africa almost 500–600 years ago, and the first outstretch first stuck out in dissimilar parts around the world such as Asia and South America 1780s concurrently.⁹

During the current decapod, DF has set off the second most widespread mosquito suffering infection after malaria. The total cases of DF have gotten to around 50 million in total. The spread of the virus in nonendemic regions with a high vector (Aedes aegypti and Ae. albopictus) population.¹⁰⁻¹²

The first outstretch of DF in India was observed in 1812.¹³ Despite this the prevention causes steps laid by the specific governments since that time, one by one outstretched have taken place, though it was not proclaimed an epidemic in 2015, the number of cases documented was on the higher side. In India, the occurrence of dengue has expanded year after year. Every monsoon season welcomes an outbreak of DF. New Delhi, from 1967 to 2003 has seen seven major outbreaks.¹⁴,¹⁵ A substantiate the case of dengue fever is a case that is confirmed by dealing with the given laboratory standards, that is, dengue virus isolation from serum or affirmation of tetra fold or greater change in reciprocal of IgG or IgM antibody numerations to other dengue dander in serum samples paired with cerebrospinal fluid (CSF) using techniques like enzyme-linked immunosorbent assay (ELISA).¹⁶,¹⁷

Acute kidney injury (AKI) is so far not a well-studied dengue complication. The renal abnormalities, though not common, are AKI, proteinuria, glomerulonephritis, and hemolytic uraemic syndrome, which are considered complications of the disease.²¹ Furthermore, when given an insight there are only a few cases reports¹⁹⁻²⁶ and also in the literature, very few studies are done on AKI in dengue viral infection (DVI).²⁷⁻³⁰ There are many timely epidemics of dengue infection and a limited database on the inclusion of the renal system in dengue infection. This study was planned to estimate the prevalence of AKI in dengue fever.

METHODOLOGY

This study was done in the Department of General Medicine, Maharishi Markandeshwar Institute of medical science and research, Mullana, Ambala from March 2020 to April 2021.

Study Design
The study design was a hospital-based cross-sectional study.

Study Period and Duration
The present was conducted for a period of 1 year from March 2020 to April 2021.

Source of Data
Patients attending in and/or outpatients Department, Department of General Medicine with clinical suspicion of dengue fever confirmed on NS1/IgM were studied.

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Sample Size
A total of 120 patients with clinical suspicion of dengue fever and confirmed on NS1/IgM fulfilling the selection criteria were selected for the study.

Sampling Procedure
It is assumed that the dengue fever prevalence rate in our hospital is 6.7% based on previous data.

Assumptions:
- Confidence level = 95%
- Precision (d) = ± 5%

For estimation of sample size, the following formula has been used:
\[ n = \left( \frac{Z^2 \alpha \times P \times (1 - P)}{d^2} \right) \]

where
- \( Z_\alpha \) = value of standard normal variate corresponding to a level of significance
- \( P \) = likely value of the parameter
- \( Q = 1 - P \)
- \( d = \) margin of errors which is a measure of precision.

With these assumptions, the sample size works out as 96. So we will take 100 patients. To increase the power of the study sample size increased to 120.

Sampling Method
Patients fulfilling the inclusion criteria were enrolled based on convenient sampling.

Selection Criteria
Inclusion Criteria
- Patients with clinical suspicion of dengue fever confirmed on NS1/IgM.

Exclusion Criteria
- Known cases of diabetic nephropathy, and hypertensive nephropathy.
- Known case of chronic kidney disease.
- Infectious diseases like malaria and enteric fever.
- Known case of cirrhosis and liver dysfunction.
- History of treatment with NSAIDs.

Ethical Clearance
Before the commencement, the study was approved by the Institutional Ethics Committee of Maharishi Markandeshwar Institute of Medical Science and Research, Mullana, Ambala. Written informed consent was obtained on selection criteria. Those who were eligible were briefed about the nature of the study and written informed consent was obtained before the enrolment.

Data Collection and Investigations
Patients were interviewed and demographic data like gender and age were noted. Patients were also interviewed for a detailed clinical presentation, history of associated medical conditions like chronic kidney disease, diabetic nephropathy, and hypertensive nephropathy. A thorough general physical examination was conducted to assess vital parameters, anthropometry, and clinical signs followed by a systemic examination. All these findings were noted on a predesigned and pretested performa.

Investigations
The selected patients underwent the following investigations:
- Complete blood count with platelet count and total count
- Peripheral smear
- Prothrombin time (PT)
- International normalized ratio
- Activated partial thromboplastin time
- Urine analysis - routine and microscopy
- Urine output (per day measurement)
- Serum creatinine and blood urea
- Serum glutamic oxaloacetic transaminase (SGOT)
- Serum glutamic pyruvic transaminase (SGPT)
- Serum electrolytes
- Serum sodium
- Serum potassium
- Serum bicarbonate
- Random blood sugar
- Ultrasound (USG) abdomen (gall bladder wall thickness, pleural effusion, and ascites)
- Liver function test
- Special tests, if required
- Urine myoglobin
- Kidney biopsy

Statistical Analysis
The data obtained were tabulated on a Microsoft Excel spreadsheet. The categorical data were expressed as ratios and percentages. The prevalence of AKI in dengue fever was expressed in terms of percentage. Chi-square test and/or Fisher’s exact test were used to find the association between the predictors of the development of AKI. Continuous data were expressed as mean ± standard deviation (SD) and an independent sample “t” test was used to compare the data. At a 95% confidence interval (CI), a probability value (‘p’ value) of less than or equal to 0.050 was considered to be statistically significant.

Results
This one-year hospital-based cross-sectional study was carried out in the Department of General Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala from March 2020 to April 2021. During the study period a total of 135 adults presented with dengue NS1/IgM tests. Of them, 120 were eligible and 15 were excluded. During the analysis, the majority of the patients were males 57.5% and 42.5% were females with most of the patients being aged between 31 and 50 years (40.8%) followed by <30 years (30%). The mean age was 42.23 ± 16.28 years and the median age was 42 years with a range of 18–78 years. When considering the present complaints fever was manifested by 100% of patients, followed by myalgia,
Acute Kidney Injury in Dengue Fever

The general condition of the patients was assessed based on pallor, icterus, petechial hemorrhage, and rashes and frequency also follow the same trend with numbers standing at 19, 15, 9, 8, respectively. The hematocrit and proteinuria were also observed with 34 patients showing the TLC count <1000/cumm. Hepatic function is assessed based on liver enzymes with ascites present in 36.7%. The majority of patients (74.9%) show normal X-ray findings with ground glass appearance in 1.7% of the patients. The warning signs, dengue with warning signs and patients. Upon diagnosis of dengue without hemorrhage, and rashes and frequency of symptoms is explained in Table 1.

In our study, all the patients presented with fever (100%). The second common clinical presentation was myalgia (62.5%) followed by nausea (47.5%), headache (45.8%), and vomiting (43.3%). The other uncommon clinical manifestations were abdominal pain (42.5%), joint pains (25%), retro orbital pain (19.2%), cough/cold (10%), malena (9.2%), altered mental status (8.3%), and bleeding gums (8.3%). However, very few patients (six patients) presented with rash (6.7%), loose stool (6.7%), oliguria (4.2%), epistaxis (2.5%), and hemoptysis (1.7%). Compared to other studies findings were similar but oliguria was seen in our study. The most common clinical

Discussion

The incidence of dengue is equal in males and females. However, in the present study males (69, 57.5%) were more than females (51, 42.5%) with a male to female ratio of 1.35:1. These findings were comparable with a study conducted by Sharma et al. who reported a male to female ratio of 3:1. Another study conducted by Agarwal et al. also showed a male preponderance with a male-to-female ratio of 1.9:1. In the present study, the age ranged between 18 and 78 years. The common age group was 31–50 years (40.8%) followed by <30 years (30%). Dengue affects people of any age group with a male to female ratio of 1.35:1. These findings were comparable with a study conducted by Sharma et al. who reported a male to female ratio of 3:1. Another study conducted by Chakravarthy A et al. reported the presence of dengue in all the age groups of the study population. The mean age noted in the present study was similar to the study from AIIMS by S. Sharma et al. who reported the median age as 26.3 years and also similar to the Mexico study by Navaretté which is, 26.9 years. These series indicate that the most commonly affected age group is between 20 and 40 years.

Clinical Spectrum

In our study, all the patients presented with fever (100%). The second common clinical presentation was myalgia (62.5%) followed by nausea (47.5%), headache (45.8%), and vomiting (43.3%). The other uncommon clinical manifestations were abdominal pain (42.5%), joint pains (25%), retro orbital pain (19.2%), cough/cold (10%), malena (9.2%), altered mental status (8.3%), and bleeding gums (8.3%). However, very few patients (six patients) presented with rash (6.7%), loose stool (6.7%), oliguria (4.2%), epistaxis (2.5%), and hemoptysis (1.7%). Compared to other studies findings were similar but oliguria was seen in our study. The most common clinical

Table 1: Present complaints of the patients

<table>
<thead>
<tr>
<th>Present complaints</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>120</td>
<td>100.0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>52</td>
<td>43.3</td>
</tr>
<tr>
<td>Headache</td>
<td>55</td>
<td>45.8</td>
</tr>
<tr>
<td>Cough/cold</td>
<td>12</td>
<td>10.0</td>
</tr>
<tr>
<td>RASH</td>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>SOB</td>
<td>28</td>
<td>23.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>57</td>
<td>47.5</td>
</tr>
<tr>
<td>Myalgia</td>
<td>75</td>
<td>62.5</td>
</tr>
<tr>
<td>Joint pains</td>
<td>30</td>
<td>25.0</td>
</tr>
<tr>
<td>Retro orbital pain</td>
<td>23</td>
<td>19.2</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>51</td>
<td>42.5</td>
</tr>
<tr>
<td>Loose stools</td>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>Oliguria</td>
<td>5</td>
<td>4.2</td>
</tr>
<tr>
<td>Urine output</td>
<td>28</td>
<td>23.3</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>2</td>
<td>1.7</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Malena</td>
<td>11</td>
<td>9.2</td>
</tr>
<tr>
<td>Hematemaesis</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>10</td>
<td>8.3</td>
</tr>
<tr>
<td>Bleeding gums</td>
<td>10</td>
<td>8.3</td>
</tr>
<tr>
<td>Visit to endemic area</td>
<td>29</td>
<td>24.2</td>
</tr>
</tbody>
</table>

Table 2: Chi-square values and p-values of parameters

<table>
<thead>
<tr>
<th>Sr. no</th>
<th>Parameter</th>
<th>Chi-square value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Sex</td>
<td>4.319</td>
<td>0.038</td>
</tr>
<tr>
<td>2.</td>
<td>Age</td>
<td>10.029</td>
<td>0.007</td>
</tr>
<tr>
<td>3.</td>
<td>Dengue severity</td>
<td>19.564</td>
<td>0.001</td>
</tr>
<tr>
<td>4.</td>
<td>Creatinine</td>
<td>54.213</td>
<td>0.001</td>
</tr>
<tr>
<td>5.</td>
<td>Urea</td>
<td>44.421</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
sign was pallor (15.8%) followed by icterus (12.5%) and petechial hemorrhage over the body (7.5%).

Several studies have reported varied clinical features of dengue fever. Kumar A et al.37 in his retrospective study conducted in a coastal district of Karnataka to study the clinical manifestations, trend, and outcome of all confirmed dengue cases admitted in a tertiary care hospital assessed the laboratory-confirmed cases from 2002 to 2008 from Medical Records Department (MRD). Of the 466 patients, the most common presentation was fever 462 (99.1%), followed by myalgia 301 (64.6%), vomiting 222 (47.6%), headache 222 (47.6%), and abdominal pain 175 (37.6%). The most common hemorrhagic manifestation was petechiae (67.2%). 22 (33.3%) had ARDS and 20 (30.3%) had pleural effusion. Kalappanavar NK et al. reported 570 patients admitted to tertiary care hospital of S. S. Institute of medical sciences hospital of S. S. Institute of medical sciences and research center, Davangere, Karnataka from June 2009 and May 2010. Among the various clinical features, fever was the most common clinical presentation occurring in all patients on presentation. Other common clinical features were retro-orbital pain (7.5%).

A study from Mangalore by Padabidri VS et al. (1995) fever was found in 100%, abdominal pain in 38%, skin rashes in 36.5%, and bleeding tendency in 70%. In the Chennai study by Narayanam M, fever was found in 98%, headache in 28%, abdominal pain in 20%, a bleeding tendency in 21%.38 In the Mangalore study by Padabidri VS et al. (1995) fever was found in 100%, myalgia in 76%, and headache in 48% of patients. The findings of our study were similar to the other Indian studies.39

Imaging
In the present study pleural effusion, ARDS and ground glass appearance were the findings seen on chest X-rays in 14.2%, 8.3%, and 1.7% of the patients, respectively. On the other hand, Kumar A et al., 55 in their retrospective study reported that, ARDS (4.72%) and pleural effusion (4.29%).

Ultrasound Abdomen
In this study, ascites (36.7%) and thickened gall bladder (39.2%) were the common findings noted on ultrasound abdomen followed by hepatomegaly (25.8%) and splenomegaly (19.2%). On the other hand, Narayanam M. et al.,78 showed hepatomegaly in 60% and a study in Delhi by Tripathi BK et al. in 23% of the cases.40 Similarly, AIIMS study by Sharma et al. showed splenomegaly in 8.2% of the patients, while a study in Delhi by Tripathi BK et al. during the 1996 outbreak showed splenomegaly in 5.71% of cases35 and the Chennai study by Narayanam M. et al. in 11% of the cases. Gallbladder wall thickening in dengue fever may be due to a decrease in the intravascular osmotic pressure and an increase in vascular permeability.

Laboratory Parameters

Urine Analysis
In the present study, urine analysis revealed 21.7% of the patient had 1+ proteinuria while haematuria was evident in 20.8% of the patients. No other previous studies have mentioned urine studies in patients with dengue fever.

Other Laboratory Parameters
At admission platelet count of <20,000 was noted in 14.1% of the patients and 33% of the patients had a platelet count between 20,001 and 49,999/cumm which means nearly half of the patients (47.1%) had low platelet count. The platelet count ranged between 4000 and 319,000/cumm at admission and the mean was lower than the normal reference range (84.1 ± 97.1 × 103/cumm) which gradually increase over a period (111.85 ± 91.08 × 103/cumm) suggestive of improvement. The total cell count was raised in (34 patients, 28.3%) and the mean total count was profoundly high (8759.76 ± 720.54/cumm) suggestive of infection. Also, the majority of the patients had higher SGOT (94 patients, 78.3%) and SGPT (101 patients, 84.2%) levels. Also, the mean SGOT (519.275 ± 2345.11 IU/L) and SGPT (221.27 ± 603.92 IU/L) were very high. A study from Delhi by Sharma et al. showed that SGOT and SGPT were deranged in 8.4% and 76.7% of patients.31

The Severity of Dengue Fever
In this study majority of the patients (87 patients, 72.5%) were diagnosed to have dengue fever without warning signs while (16 patients, 13.3%) of the patients had dengue fever with warning signs and few patients had severe dengue (17 patients, 14.2%).

Complications
In the present study other than AKI most of the patients had ARDS (11.7%). The other uncommon complications noted were MODS (3.3%), sepsis (0.8%), and CAD (0.8%).

Acute Kidney Injury
In this study serum, creatinine levels were estimated at the time of admission and serial measurement were obtained on a day-to-day basis in select cases. The creatinine levels at admission ranged between 0.1 to as high as 9.69 mg/dL but the mean serum creatinine levels were 1.27 ± 1.29 mg/dL and median levels were 0.87 mg/dL suggestive of normal kidney function. However, based on AKIN criteria,41 33 out of 120 patients developed AKI. Hence the prevalence of AKI in dengue fever was 27.5%. Looking at the raised serum creatinine level at admission, it may be hypothesized that, every one out of three patients with dengue fever is likely to present with raised serum creatinine as a consequence of dengue and accordingly are at high risk of developing AKI. This acute nephropathy could be related to prerenal ARF consequent to third space loss of fluid. The spectrum of renal disorders is least studied in dengue infection varies from mild glomerulonephritis and urinary sedimentations to severe AKI. It is a complication of DVI which has not been studied much. Though the prevalence of AKI observed in the present study (27.5%) was this, it was high compared to the studies by Lee et al.32 This wide variation observed in the prevalence rate of AKI can be explained by the varied sample size, different study designs, and different criteria used to address the definition of AKI.

Conclusion
Based on the findings of this study it may be concluded that there is a high prevalence of AKI (27.5%) in patients presenting with dengue fever in the study area hence it cannot be neglected. The significant predictors of AKI in patients with DF are male gender, advanced age, hypotension, high serum creatinine, and blood urea levels at the time of admission and lower platelet count at admission., evidence of polyserositis, and other complications. Laboratory parameters including raised total count, and abnormal liver function tests at admission are also associated with the risk of developing AKI in patients with DF. Persons with dengue fever with warning signs and severe dengue had more evidence of AKI compared to dengue fever. The person who developed AKI had more mortality.

References
Acute Kidney Injury in Dengue Fever

In the management of Heart Failure and T2DM with multiple CV risk factors

Emil Dap
Dapagliflozin 5mg/10mg Tablets
Empower Heart

In Hypertension associated with CHF - Post MI

METPURE-TEL
(+) Metoprolol PR 25 mg & Telmisartan 20/40 mg Tablets
Controls Hypertension, Ensures Cardiac PROTECTION

In Hypertension with Diabetes,

Temsan-AM
Telmisartan 40 mg & (+) Amlodipine 2.5/5 mg Tablets
Swift BP Reduction, Assured Control

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A Clinical Comparison along with Prediction of the Outcome and Prognosis of Anterior and Posterior Circulation Stroke Patients Admitted in Tertiary Care Hospital

Debayan Rarhi1, Prabir Kr Kundu2*, Arup Kr Datta3, Satyaki Basu4, Aniruddha Ray5

Received: 03 February 2021; Revised: 14 August 2021; Accepted: 10 March 2022

ABSTRACT

Introduction: Stroke is the third common cause of death in India after ischemic heart disease and chronic obstructive pulmonary disease. Clinical features and outcomes vary in different types of strokes.

Objectives: To compare the National Institutes of Health Stroke Scale (NIHSS) score of anterior and posterior circulation stroke patients (confirmed by neuroimaging) on the day of admission, admitted in Department of General Medicine, R. G. Kar Medical College and Hospital (RGKMCH), Kolkata and to predict the prognosis and outcome of the two types of strokes based on the modified Rankin Scale (mRS) on day 5 of admission.

Methodology: After approval from Institutional Ethics Committee and taking written informed consent from participants an observational cross-sectional study was conducted in the Department of General Medicine of a tertiary care hospital over 1.5 years. Clinical features, outcome, and prognosis between anterior and posterior circulation stroke group are compared and results are analyzed.

Results: In anterior circulation, the mean of age (mean ± SD) of patients was 59.2875 ± 6.7790 years; 25 (31.3%) patients were female and 55 (68.8%) patients were male; three (3.8%) patients were Christian, 39 (48.8%) patients were Hindu, and 38 (47.5%) patients were Muslim; the mean of BMI (mean ± SD) of patients was 24.7038 ± 2.3695 kg/m²; 71 (88.8%) patients were from rural area and nine (11.3%) patients were from urban area; 73 (91.3%) patients had hypertension, 51 (63.8%) patients had diabetes mellitus, 24 (30.0%) patients had hypothyroidism, and 56 (70.0%) patients had ischemic heart disease; the mean of NIHSS score on day 0 (mean ± SD) of patients was 13.9875 ± 4.0362, the mean of mRS score on day 5 (mean ± SD) of patients was 2.1125 ± 0.9936. In posterior circulation, the mean of age (mean ± SD) of patients was 59.2167 ± 6.7826 years; 20 (33.2%) patients were female and 40 (66.7%) patients were male; two (3.3) patients were Christian, 29 (48.3%) patients were Hindu and 29 (48.3%) patients were Muslim; the mean of BMI (mean ± SD) of patients was 24.7017 ± 2.3265 kg/m²; 51 (85.0%) patients were from rural area and nine (15.0%) patients were from urban area; 54 (90.0%) patients had hypertension, 37 (61.7%) patients had diabetes mellitus, 18 (30.0%) patients had hypothyroidism, and 42 (70.0%) patients had ischemic heart disease; the mean of NIHSS score on day 0 (mean ± SD) of patients was 23.8833 ± 4.5737, the mean of mRS score on day 5 (mean ± SD) of patients was 4.6333 ± .8227.

Conclusion: Symptoms of PCI stroke patients are more severe than that of ACI stroke patients. The outcome and prognosis of PCI stroke patients are worse compared to the ACI stroke patients.

INTRODUCTION

The World Health Organization defines stroke as rapidly developed clinical signs of focal disturbance of cerebral function, lasting for more than 24 hours or leading to death, with no apparent cause other than vascular origin. Cerebrovascular diseases include some of the most common and devastating disorders: ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysms and arteriovenous malformations. According to World Health Organization factsheet it is the second largest cause of death worldwide killing about 6.7 million people in 2012. Between 1990 and 2010 the number of strokes decreased by approximately 10% in the developed world and increased by 10% in the developing world. It is the leading cause of adult disability and the second leading cause of mortality worldwide. Anterior circulation strokes are defined as strokes involving areas of the brain supplied by anterior cerebral artery and middle cerebral artery. Posterior circulation strokes are defined as strokes involving areas of the brain supplied by the vertebrobasilar artery and posterior cerebral artery. This study compares the severity of these two categories of patients with respect to the NIHSS score and predicts prognosis and outcome with the help of mRS. Very few studies exist till date comparing these two types of strokes with respect to these two mentioned scales. The idea of this study is to clinically compare these two types of stroke patients admitted in RGKMCH based on the NIHSS score on day 0 of admission and subsequent mRS on day 5 of admission and prediction of prognosis based on the result of these scales.

OBJECTIVES

- Comparing the NIHSS score of anterior and posterior circulation stroke patients (confirmed by neuroimaging) on the day of admission, admitted in Department of General Medicine, RGKMCH.
- Predicting the prognosis and outcome of the two types of strokes based on the mRS on day 5 of admission.

METHODOLOGY

An observational cross-sectional study was conducted for 18 months (January 2017–June 2018) in patients above 18 years age admitted with ischemic stroke in General Medicine ward, RGKMCH, Kolkata. A sample size of 140 was taken, samples collected by systematic random sampling. Patients with multiple infarcts, intracranial hemorrhage, and presentation within time-window for thrombolysis, were excluded from the study. A patient admitted with stroke (clinical stroke) was evaluated thoroughly and scoring is done on the basis of NIHSS score. Then neuroimaging is done to confirm the nature of stroke. Then a comparison is done based on the NIHSS score and the severity of the two types of strokes is compared. The patients are given the standard therapy for ischemic strokes. On day 5 of admission evaluation of the patient is done...
A Clinical Comparison of Anterior and Posterior Circulation Stroke Patients

based on mRS and an outcome and prognosis are predicted based on that. If any patient is found to expire before 5 days of hospital stay the mRS of that patient automatically is taken 6 (the worst outcome). If any patient goes to another hospital/healthcare center before day 5 by signing the risk bond, he is automatically excluded from the study. Outcome definitions and parameters were based on the NIHSS score of all ischemic stroke patients admitted in RGKMCH, Department of General Medicine and thus a severity comparison between the anterior and posterior circulation strokes and the prediction of their prognosis based on mRS. The results were analyzed via appropriate statistical software (SPSS 24.0 and GraphPad Prism version 5).

RESULTS AND ANALYSIS

- In anterior circulation, 73 (91.3%) patients had hypertension. In posterior circulation, 54 (90.0%) patients had hypertension. Association of hypertension vs type of stroke was not statistically significant \( (p = 0.8008) \).
- In anterior circulation, 51 (63.8%) patients had diabetes mellitus. In posterior circulation, 37 (61.7%) patients had diabetes mellitus. Association of diabetes mellitus vs type of stroke was not statistically significant \( (p = 0.8006) \).
- In anterior circulation, the mean of NIHSS score on day 0 (mean ± SD) of patients was 13.9875 ± 4.0362. In posterior circulation, the mean of NIHSS score on day 0 (mean ± SD) of patients was 23.8833 ± 4.5737. Difference of mean NIHSS score on day 0 vs type of stroke was statistically significant \( (p < 0.0001) \).
- In anterior circulation, the mean of mRS score on day 5 (mean ± SD) of patients was 2.1125 ± 0.9936. In posterior circulation, the mean of mRS score on day 5 (mean ± SD) of patients was 4.6333 ± 0.8227. Difference of mean mRS score on day 5 vs type of stroke was statistically significant \( (p < 0.0001) \).

DISCUSSION

Considering the NIHSS score on the admission day and the mRS on day 5, there were statistically significant differences when two strokes were compared. The NIHSS score on day 0 was significantly higher in the PCI group compared to the ACI group (Table 1). Subsequently, the mRS on day 5 was higher for the PCI group when compared with the ACI group (Table 2). Thus it was observed from this study that the PCI stroke patients having statistically significant higher scores on both the scales are most likely to have a poorer prognosis than the ACI stroke patients.

The TOAST (Trial of ORG 10172 in Acute Stroke Treatment) study conducted a study comparing the ACI and PCI stroke patients.\(^5\) The analysis included 1,039 patients with AC stroke and 180 patients with PC stroke. There were fewer women in the PC than in the AC groups, but otherwise there were no differences in demographics, risk factors, or stroke subtypes between the two groups. Headache (AC 8.7%, PC 15%, \( p = 0.013 \)) and vomiting (AC 3.5%, PC 17.8%, \( p < 0.001 \)) were more common among PC patients but these results however did not have a statistically significant \( p \) value. Mean baseline NIHSS score was lower (less severe) among PC (6.1) than AC patients (9.5; \( p < 0.001 \)). This result was different from the result obtained in our study. In our study, the NIHSS score was significantly higher in PCI group compared to the ACI group (Fig. 1). However, multivariate analysis, controlling for gender, history of previous stroke, and baseline NIHSS score, showed no difference in outcome between PC and AC stroke.

In a study published in BMJ in 2011, 312 consecutive patients with the first ever ACS and 93 patients with the first ever PCS were prospectively analyzed. The median NIHSS score was 8 in ACS and 4 in PCS \( (p = 0.004) \). Brain imaging revealed more often pathological findings in ACS than PCS. The proportion of nonthrombolyzed patients with a favorable clinical outcome (mRS score 0–2) was similar in ACS and PCS (67.0 vs 78.4%; \( p = 0.08 \)).\(^6\) In this study though there was a higher NIHSS score in ACI patients compared to the PCI, the mRS of both group of patients were similar. However, both these results were not statistically significant considering the insignificant \( p \) values. This result was also different from the result obtained in our study. In our study, both NIHSS (Fig. 1) and mRS (Fig. 2) scores were significantly higher in PCI group compared to the ACI group.

Apart from the above studies, very few studies exist that compared these two types of strokes with respect to their outcome and prognosis. All other studies that compared the ACI and PCI strokes were related to their symptomatology, that is, what symptoms were commoner in which group of patients. In a study of patients with brain stem infarction by Kubik and Adams, disturbances of consciousness were considered to be an important feature of PCI.\(^7\) This was followed by studies of patients with specific vertebrobasilar lesions, including the midbrain, cerebellum, and basilar artery occlusive disease separately; the rate of disturbed consciousness was high, frequently 20%.\(^8\)–\(^11\) In the most extensive of these studies, Archer and Horenstein reported 20 patients with basilar artery occlusion and

| Table 1: The mean of NIHSS score on day 0 vs type of stroke |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Number          | Mean            | SD              | Minimum         | Maximum         | Median          | p-value         |
| NIHSS score on day 0 | Anterior         | 80              | 13.9875         | 4.0362          | 22.0000         | 14.0000         | <0.0001         |
|                 | Posterior        | 60              | 23.8833         | 4.5737          | 29.0000         | 25.0000         |

In anterior circulation, the mean of NIHSS score on day 0 (mean ± SD) of patients was 13.9875 ± 4.0362. In posterior circulation, the mean of NIHSS score on day 0 (mean ± SD) of patients was 23.8833 ± 4.5737. Difference of mean NIHSS score on day 0 vs type of stroke was statistically significant \( (p < 0.0001) \)

| Table 2: The mean of modified rankin scale score on day 5 vs type of stroke |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Number          | Mean            | SD              | Minimum         | Maximum         | Median          | p-value         |
| Modified Rankin Scale on day 5 | Anterior         | 80              | 2.1125          | 0.9936          | 4.0000          | 2.0000          | <0.0001         |
|                 | Posterior        | 60              | 4.6333          | 0.8227          | 6.0000          | 5.0000          |

In anterior circulation, the mean of mRS score on day 5 (mean ± SD) of patients was 2.1125 ± 0.9936. In posterior circulation, the mean of mRS score on day 5 (mean ± SD) of patients was 4.6333 ± 0.8227. Difference of mRS score on day 5 vs type of stroke was statistically significant \( (p < 0.0001) \)
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found 19 of them had various impairment of consciousness. In contrast, Sato et al. reported a much lower rate of disturbed consciousness in patients with PCI than with ACI (18 vs 41%; p = 0.001).

Previous studies, the New England Medical Center Posterior Circulation Registry, and a Qatar study presented within-study comparisons of the frequency of the neurological deficits in PCI cohorts; but, these studies did not compare PCI with ACI patients. In a series of articles from the New England Medical Center Posterior Circulation Registry, unilateral limb weakness (38%) was the most frequent sign in the whole PCI cohort, hemiparesis and tetraparesis (62%) were the most common signs for patients with midbrain infarction, and hemiparesis was present in more than half of patients (50.6%), along with basilar artery occlusive disease.

But none of these studies compared the outcome and prognosis as a whole and also had no comparison with respect to the NIHSS and mRS scale. In this study, by comparing the NIHSS score on admission we can predict the severity as well as comparing the mRS score on day 5 we can predict the outcome and prognosis. The result showed us that both scores were higher in the PCI group and so PCI strokes are likely to have a worse outcome compared to ACI stroke patients.

The region in the posterior circulation stroke involves mainly the brainstem and the cerebellum. Edema in these areas can cause compression of brainstem structures including the reticular activating system which is likely to cause more drowsiness and altered sensorium. Also as in the region of brainstem the descending tracts and ascending tracts are compactly arranged in a small area, edema in this area is likely to cause more neurodeficit compared to ACI strokes. This might be the likely explanation of worse outcome and more score in both NIHSS and mRS scales.

**Conclusion**

The study showed us that the NIHSS score on admission was significantly more in the PCI stroke group than that of ACI stroke group. Also the mRS score of PCI stroke group was significantly more than that of the ACI stroke group. The higher NIHSS score predicts that the symptoms of PCI stroke are more severe than that of ACI stroke patients. The mRS score of PCI stroke patients being higher than ACI stroke patients predicts a likely worse outcome and prognosis of PCI stroke patients compared to the ACI stroke patients.

**References**

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Acute Methanol Toxicity: Clinical Correlation with Autopsy Findings, a Descriptive Study

Medhavi Gautam1, Himanshu Dandu2, Suhail Siddiqui3, Virendra Atam4, Sangeeta Kumari5, Shiuli Rathore6*

Received: 03 August 2021; Revised: 29 January 2022; Accepted: 10 March 2022

Abstract
Background: Methyl alcohol poisoning or deaths from drinking illegally brewed cheap alcohol which is often spiked with chemicals to increase its potency are frequent in India. Many outbreaks from different parts of the country have been reported from time to time. A total of 11,830 lives were lost between 2006 and 2015 due to the consumption of spurious liquor in the country. The symptoms can range from mild to severe depending upon factors like the amount of exposure and time of presentation.

Aims and objectives: The present study was designed to describe the clinical presentation, management, and outcome of the patients during a recent methanol outbreak that can form a basis for diagnosis and management. This study also highlights the salient autopsy findings and their correlation with clinical features.

Materials and methods: It is a retrospective, descriptive study discussing clinical features of patients with methanol intoxication, their outcome, and the clinical correlation with autopsy findings of patients who succumbed to death. The study was conducted at King George’s Medical University, Lucknow. The patients were enrolled from a methanol intoxication outbreak in Barabanki district on 28th May 2019 followed by a similar outbreak in Sitapur district two days later.

Results: A total of 33 patients were included in this study based on predefined clinical characteristics. The average amount of alcohol consumed was about 223 mL (range: 100–300 mL). The majority of patients had onset of symptoms between 12 and 24 hours. All patients had gastrointestinal symptoms, 97% of patients had visual disturbances, 91% of patients had central nervous system manifestation while frank coma was observed in 15% of patients. Decreased urine output was reported in 6% of patients. About 90% of patients had metabolic acidosis. Out of 33 patients included in this study, 30 patients were discharged in stable condition while two died and one absconded. Autopsy findings revealed marked cerebral edema and hyperemia, hyperemic heart, and congested lungs in all the patients. One patient showed putaminal necrosis which is characteristic of methanol poisoning. Kidneys in two cases were hyperemic and show parenchymal degeneration which co-relates with both patients being anuric.

Conclusion: Methanol intoxication is a serious problem in developing countries like ours. Timely intervention is an important factor in reducing mortality among these patients. The study highlights the very important fact that methanol intoxication can be managed at the very ground level with minimal resources (as available) if intervened and recognized in time.

Introduction
Methyl alcohol is a known adulterant of informally produced spirits and illicit liquors. India has a booming moonshine industry and methanol-tainted alcohol has taken the lives of over 12,000 people in the last three decades.1–8 Many outbreaks of methyl alcohol poisoning have occurred from time to time in various developing countries including India and such outbreaks have been responsible for considerable morbidity and mortality. Exact rates of morbidity and mortality are not available.

Methanol per se is mildly inebriating and nontoxic, it is however metabolized to highly toxic compounds, formaldehyde, and formic acid in the body,9 a latent period ranging from 12 to 24 hours therefore is often described between the consumption of adulterated liquor and onset of signs and symptoms.

Central nervous system depression, ocular symptoms, and gastrointestinal complaints are commonly reported initial symptoms.10 A metabolic acidosis with a high anion gap is typical of methanol poisoning.

Several studies11,12 have correlated various biochemical and laboratory markers viz. degree of acidosis, serum bicarbonate levels, or blood methanol concentrations with mortality, and have tried to identify factors associated with poor prognosis.

The present study describes our experience in the management of patients with methyl alcohol poisoning and emphasizes the role of early and aggressive treatment with bicarbonate and hemodialysis (HD) in patients with significant toxicity.

Objectives
- To present epidemiological data from a recent methanol poisoning outbreak
- To describe the clinical presentation, management, and outcome of the patients during the outbreak
- To provide a basis for clinical diagnosis and treatment
- To report autopsy findings and correlation with clinical features.

Material and Methods
This was a retrospective descriptive study for the analysis of clinical features and outcomes of patients admitted to King George’s Medical University, Lucknow during a methanol intoxication outbreak in the adjacent districts in 2019. There was one methanol poisoning outbreak in Barabanki district on 27th May 2019 followed by a similar outbreak in Sitapur district two days later on 30th May 2019. Patients were received in the Trauma center of King George’s Medical University and managed in various wards. Our study does not truly represent the burden of the outbreak as only a fraction of the patients were directed to this institution.

A retrospective search was made for all patients admitted to the institute with the diagnosis of methanol poisoning. A total of 169 patients admitted to the medical emergency (METC) from 28th May 2019 to 30th May 2019, were screened and 33 patients were included in the study. Apart from this, two patients were brought dead to the trauma center with a history of alcohol consumption.

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Demographic data like age, gender, and occupation, were collected, and presenting signs and symptoms were recorded.

All patients/relatives giving a history of liquor intake from the area of the outbreak and showing classical signs and symptoms of methanol intoxication were included in this study. We adhered to previously published clinical criteria for diagnosing methanol intoxication (Table 1). Methanol concentration could not be measured due to the limitation of resources.

The patients were categorized in three groups according to previously published criteria (Table 2) and managed as per the protocol (Fig. 1).

Results
On May 28, 29, 30, and 31, 2019, patients with accidental methanol poisoning from nearby districts of Lucknow were brought to the institute out of which 33 are included in the study and examined for various clinical manifestations. All the study participants were male with a mean age of 36.93 years and a standard deviation (SD) of 10.85 years, ranging between 20 and 65 years. All the individuals who reported were either laborers or farmers. Out of the total, 55% were laborers and the rest were farmers.

The exact quantity of spurious liquor consumed could not be ascertained, but on the basis of the history given by the family, relatives, and the patient, the average amount of alcohol consumed was about 223 mL with an SD of 48.6 (range: 100–300 mL).

The onset of symptoms was not immediate. The interval between the ingestion and onset of symptoms had a range of 5–72 hours. The average time of onset of symptoms after consumption of alcohol was about 20 hours with a median of 12 hours and an SD of 17.26 hours. The average time interval between onset of symptoms and arrival at our institute was 14 hours with an SD of 3.94 hours.

Clinical features are shown in Table 3. All the patients presented with gastrointestinal symptoms like nausea and vomiting while abdominal pain was reported by 91% of the patients (n = 30).

About 97% reported having visual disturbances like blurred vision, decreased vision, and photophobia after the event. Respiratory symptoms including chest tightness, palpitations, and dyspnea were recorded in 91% of patients while CNS symptoms like drowsiness, headache, altered sensorium, or frank coma were seen in only 15% of patients (n = 5). Oliguria was reported in around 6% (n = 2) cases.

None of the patients we received had edema, icterus, pallor, hematuria, flank pain, or any cranial nerve palsies.

Blood gas analysis was performed on all the patients. 90% of the patients had metabolic acidosis at the time of presentation. In the observation group, only one patient had increased anion gap (AG) metabolic acidosis. Among the 15 patients with mild poisoning, all had increased AG metabolic acidosis except one. Likewise, increased AG metabolic acidosis was observed in all the patients with severe poisoning. The mean pH was 7.19 with an SD of 0.144 (range = 0.5). The bicarbonate levels were depressed in patients with both mild and severe poisoning. Mean bicarbonate levels were 11.1 mmol/L with an SD of 6.8 (range: 3–29). There were no significant differences between the pCO2, sodium, and potassium levels between the three groups. Despite some differences in hemoglobin and platelet levels, there were no apparent abnormalities in any patients. However higher total leukocyte counts were observed in severely intoxicated patients. Abnormal liver function indicated by abnormal transaminases and increased bilirubin was detected to varying degrees among patients. Patients in the severe poisoning group had remarkably raised levels of urea and creatinine as compared to the mild toxicity and observation group.

The decreased vision was reported by all except one patient. Superficial hemorrhage was found in one patient from the observation group, while among the patients with mild poisoning, tortuous blood vessels were observed in one, bilateral optic neuropathy in one, and grade 1 papilledema was seen in two patients. Likewise, grade 1 papilledema was seen in three and optic neuropathy in two patients in the severe toxicity group. Out of 22 patients that went through fundus examination, 10 had abnormalities.

Out of 33 patients included in this study, 30 patients recovered and were discharged in stable condition. One patient absconded from the treatment. Two patients needed ventilatory support and could not recover, both were from the severe toxicity group.

Two expired on the day of arrival.

The mean duration of stay of individuals was approx. Three days with a standard deviation of 1.042. However, the minimum duration of stay was 1 day and the maximum duration of stay was around 6 days. It can

Table 1: Criteria for diagnosis of methanol intoxication

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Value</th>
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<tbody>
<tr>
<td>A. Severe metabolic acidosis, i.e., Arterial pH</td>
<td>&lt; 7.3</td>
</tr>
<tr>
<td>B. Serum bicarbonate &lt;20 mmol/L (mmol/L)</td>
<td></td>
</tr>
<tr>
<td>C. Osmolal gap &gt;10 mOsm/kg</td>
<td></td>
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Table 2: Criteria for diagnosis of methanol poisoning with at least two of the following criteria

<table>
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<tr>
<th>Criteria</th>
<th>Value</th>
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<tbody>
<tr>
<td>A. Severe metabolic acidosis, i.e., Arterial pH</td>
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</tr>
<tr>
<td>C. Osmolal gap &gt;10 mOsm/kg</td>
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be said that many individuals stayed at least 3 days for the treatment.

An autopsy was performed on two decedents. Autopsy revealed marked cerebral edema and hyperemia. The heart was hyperemic and the lungs congested and edematous in both cases. Fatty changes in the liver were seen in one case.

Looking at the specific findings, case 1 showed putaminal necrosis which is characteristic of methanol poisoning and hemorrhage along with cerebral edema and hyperemia. On the other hand, case 2 exhibits marked cerebral edema and hyperemic brain changes. Both these patients presented with a coma. The kidney in both the cases was hyperemic and show parenchymal changes. Both these patients presented with frank coma died indicating that methanol toxicity coma is related to poor prognosis. Most other studies reported similar findings.16,19,20,23

In line with previous studies, the amount of alcohol ingested and the rapidity of the appearance of signs and symptoms after the ingestion of toxic alcohol did not appear to have any correlation with the prognosis. An arterial gas serves as an important tool not only in diagnosing but also in classifying the victims when caring for a large number of patients simultaneously as happens in mass methanol intoxication.8,17,20 In our study, out of 33 patients, 30 had metabolic acidosis with an elevated anion gap. Nazir et al. stated that diagnosis of methanol intoxication should not depend upon testing of drug levels as the facility for such testing are not always available, moreover if handy, the clinical decision-making cannot be delayed till the time results close in. Lab abnormalities like metabolic acidosis with an elevated anion gap and osmolar gap are a significant clue when treating a patient with suspected methanol intoxication.24

Activated charcoal, gastric lavage, and syrup of ipecac have no role in the management of toxic alcohol exposures.13 The American Academy of Clinical Toxicology recommends ethanol or fomepizole as a treatment of methanol intoxication, however, fomepizole is preferred over ethanol unless fomepizole is unavailable or the patient is allergic to fomepizole.9 Neither ethanol nor fomepizole was used during the management in the current study as both were not available locally. All alcoholics have a low molecular weight which is efficiently removed by HD.20 Intermittent HD is the most efficient method for decreasing serum levels of toxic alcohols, and formate and correcting metabolic acidosis.9 As a facility for serum methanol levels was not available, patients received bicarbonate and HD in line with the clinical features and acidosis in blood gas analysis. The American Academy of clinical toxicology recommends HD in presence of metabolic acidosis with blood pH between 7.25 and 7.30, visual abnormalities,
renal failure, or electrolyte imbalance that is unresponsive to conventional therapy or a serum methanol concentration >50 mg/dL. In our study, we had dialedyzed two patients, both in the severe intoxication group. They were dialedyzed consecutively for two days each with a duration of 3.5–4 hours. Their metabolic acidosis improved and they did not require any further sessions of dialysis.

Regarding the duration, 8 hours of HD is recommended if methanol levels are not required. The duration of HD can otherwise be estimated using a formula based on serum alcohol concentration, blood flow, gender, age, height, weight, and urea clearance of dialyzer:

\[ \text{Time (h)} = \frac{-V \ln (S/A)}{0.06 \, k} \]

Where \( V \) is total body water in liters; \( A \) is the serum alcohol concentration in mmol/L; \( k \) is 80% of dialyzer urea clearance in mL/min.

The metabolism of formate is hypothesized to be enhanced by folic acid and given the lack of any deleterious effects, administration of leucovorin as adjunctive and given the lack of any deleterious effects, hypothesized to be enhanced by folic acid is 80% of dialyzer urea clearance in mL/min.

serum alcohol concentration in mmol/L; \( k \) is recommended if methanol levels are not require any further sessions of dialysis.

The metabolism of formate is hypothesized to be enhanced by folic acid and given the lack of any deleterious effects, administration of leucovorin as adjunctive and given the lack of any deleterious effects, hypothesized to be enhanced by folic acid is 80% of dialyzer urea clearance in mL/min.

Time (h) = \( -V \ln (S/A)/0.06 \, k \)

Where \( V \) is total body water in liters; \( A \) is the serum alcohol concentration in mmol/L; \( k \) is 80% of dialyzer urea clearance in mL/min.

The metabolism of formate is hypothesized to be enhanced by folic acid and given the lack of any deleterious effects, administration of leucovorin as adjunctive therapy seems reasonable. Administration of bicarbonate is recommended in the management of metabolic acidosis and to expedite the removal of formate from kidneys. Both leucovorin and bicarbonate were used in the current study as well.

Pulmonary injury, optic atrophy, and coma are described as a classical triad of methanol intoxication. This is in accordance with findings reported from one of the cases, with coma on presentation and hemorrhagic putaminal necrosis on autopsy.

There were multiple limitations to this study. First of all, the study is limited by its retrospective nature and certain confounders were inevitable. One potential limitation of this study is that it does not truly represent the outbreak, as only a number of patients were directed to our institution. Another limitation involves the issue of the sample size which was not very large, more so when classified into groups providing insufficient data to generate any cause and effect theory. Moreover, all data was not collected from every patient, for instance, an ophthalmic examination for all the patients was not done. Besides, blood levels of methanol, formate, and ethanol were not done. Despite these limitations, however, we could summarize the clinical features of methanol toxicity and an association between coma on admission and poor outcome. To our knowledge, this is one of the very few studies which have tried to correlate the clinical profile of the patients with the autopsy findings. Moreover, given the nature of the problem, a planned prospective study seems difficult.

**Data Management and Analysis**

All the data was entered in Microsoft Excel sheet 2016 and statistical analyses were performed through IBM SPSS version 25.0 (IBM, Chicago, IL, USA). As the sample size was very less (\( n = 33 \)), descriptive statistics were used for the analysis of the data. Data are expressed as median with a range and mean and standard deviation as appropriate.

**Ethical Clearance**

The study was conducted after approval by the Institutional Ethics Committee, KGMC. Details of the sample population were concealed and kept in a strictly confidential manner.

**Implications of this Study**

Our society has seen several outbreaks of methanol intoxication in the last few decades that has to lead to significant morbidity in society both financially as well as physically. People from remote areas either do not have enough knowledge about the harmful effects of methanol or they are not financially sound enough to access better sources of alcohol. In this in turn can result in their loss of life or significant comorbidity for later life (e.g., permanent visual impairment).

With this study, we aim in addition to early identification of symptoms of methanol intoxication, for early intervention. This will help in proper counseling of patients regarding methanol intoxication.

The patients can be followed to observe for any late sequel and its outcome that can be a further study.

Also, this study was carried out in a pilot study and following further outbreaks in and around the district we can make a definite protocol for the management of any such future outbreak both at the CHC level (with minimum facilities) and at the institutional level (where maximum amenities are available).

**Conflict of Interest**

None.

**References**

5. BBC News India doctors fight to save west Bengal alcohol victims. 16 December 2011
7. Spurious liquor kills six, 18 other critical in Burdwan. 2017-03-03
A Comparative Study of the Patterns of Mortality in COVID-19 Patients in Juxtaposition with Non-COVID-19 Mortality in the First and Second Waves of the Pandemic

Ritu Gupta1, Silas S Nelson2, Ila Upadhyay3, Trisha Chatterjee4, Sahitya Rao5
Received: 13 November 2021; Revised: 02 February 2022; Accepted: 10 March 2022

Abstract

Background and objectives: The Coronavirus disease 2019 (COVID-19) pandemic has posed an unprecedented challenge to the public healthcare system worldwide like none before, producing far-reaching global economic, humanitarian, and social crises. It is estimated to have affected more than 1.8 million people worldwide. India has faced two phases of the pandemic, being the country with 2nd most number of deaths with varying mortality patterns across the two waves. In this study, we compare the patterns of mortality between the two phases of pandemics in association with COVID-19 and non-COVID-19 deaths.

Materials and Methods: A retrospective observational study at a tertiary care center in Central India was carried out. Demographic patterns of mortality have been studied in each of the groups, and a comparative analysis was done between COVID-19 and non-COVID-19 mortality patterns in each phase of the study, that is, from 20th March 2020 to 19th September 2020 and from 20th September 2020 to May 2021, as well as between the two phases.

Results: The case fatality rate of COVID-19 positive patients in the second phase of the study was 22.04%, whereas the those of non-COVID-19 patients in the second phase were found to be 15.95%. A maximum number of COVID-19 positive deaths during the first wave of the pandemic occurred in September 2020 and during the second wave in April 2021. In the first phase of the study, 69.6% of patients who died were males, and 30.3% were females, whereas in the second phase among COVID-19 positive subjects, 65% deaths were among males, and 35% deaths were among females. COVID-19 positive mortality in the second phase showed, 26.53% to be hypertensive, while 13.8% were diabetic.

Conclusion: It was found that most of the deaths in both phases of COVID-19 amongst COVID-19 positive patients and non-COVID-19 patients were amongst the elderly population (≥ 60 years) with male predominance. Most deaths in both populations occurred during the first 3 days of admission whereas it was relatively less in the second phase. Noncommunicable diseases like systemic hypertension, and DM had a significant influence on all-cause mortality and morbidity in both COVID-19 positive and non-COVID-19 patients in the first and second waves of COVID-19. Noncommunicable diseases thus played a major role in mortality among both the populations under study.

Introduction

Coronavirus disease 2019 (COVID-19) is defined as an illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China. On March 11, 2020, the WHO declared COVID-19 a global pandemic, its first such designation since declaring H1N1 influenza a pandemic in 2009.

As the pandemic curves through its highs and lows, a significant difference in the pattern of mortality has been observed in deaths caused by COVID-19 and deaths due to systemic illnesses in COVID-19 negative patients. Studying such mortality patterns can help to discern the changing high-risk groups and prediction trends in the pandemic.

A study conducted in the US showed a 22.9% increase in all-cause mortality reported, far exceeding annual increases observed in previous years (≤2.5%). In addition, the study also found that death rates from several non-COVID-19 diseases (e.g., heart disease, Alzheimer’s disease) increased during surges. The study claimed that excess deaths not attributed to COVID-19 could reflect either immediate or delayed mortality from undocumented COVID-19 infection, or non-COVID-19 deaths secondary to the pandemic, such as from delayed care or behavioral health crises.

A UK-based study comparing deaths due to COVID-19 and non-COVID-19 deaths revealed differing magnitudes of association with demographic factors and comorbidities between the two groups. In the study, older age was more strongly associated with COVID-19 death than non-COVID death, as were male sex, deprivation, obesity, and some comorbidities. Smoking, history of cancer, and chronic liver disease had stronger associations with non-COVID than COVID-19 death.

Coming to all in all mortality between the two waves of the pandemic, an Indian study comparing differences in mortality patterns between the first and second wave of COVID-19 showed several obvious differences. In the 2nd wave, the pediatric and younger individuals were getting infected, in addition to older ones. The symptoms of the COVID 2nd wave are also variable in the two waves, especially gastrointestinal.

During the pandemic, studies did not cast much importance on mortalities due to causes other than COVID-19, which in turn, showed changing trends over the months with regard to demographic statistics as well as disease predictions. This arena showed a major gap in the literature as mortalities due to other systemic illnesses showed a significant change from the figures in the nonpandemic era. This study aims to review and analyze comparative patterns of such deaths in both the waves of the COVID-19 global pandemic, in order to better understand the drivers of excess mortality during the COVID-19 pandemic in different periods of time, considering healthcare supply and demand.
demand (including changes in consultations, surgery, and emergency services used by patients) and social, behavioral, and economic changes that may impact mortality through different mechanisms.

**AIM AND OBJECTIVES**

- To study the mortality patterns in COVID-19 positive and non-COVID-19 patients in the two phases of the pandemic pertaining to their demographic characteristics.
- To compare the mortality patterns and their association with comorbidities amongst COVID-19 positive and non-COVID-19 deaths in the two phases of the pandemic.

**MATERIALS AND METHODS**

The study was conducted in the Department of General Medicine in Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh in two phases, in order to differentiate mortality patterns and variations in severity in different demographic groups in the two waves of the COVID-19 pandemic. The first phase of the study was from 20th March 2020 to 19th September 2020, coinciding with the first wave and the first peek of the pandemic. The second phase of the study started on 20th September 2020 and continued till May 2021, coinciding with the second wave of the COVID-19 pandemic.

The study population was divided into two groups in each of these phases, COVID-19 positive patients and COVID-19 negative patients admitted to the non-COVID general wards and ICU. A comparative analysis was done between COVID-19 and non-COVID-19 mortality patterns in each phase of the study as well as between the two waves focussing on the trends in mortality based on gender, age-groups affected, duration of stay in the hospital, and comorbidities.

**Observations**

A total of 3,311 patients were admitted to COVID-19 Wards, and 6,256 patients in non-COVID-19 General Medicine wards during the period 20th September 2020 to May 2021 (Fig. 1 and Table 2). Whereas during the first COVID-19 wave, that is, from March 2020 to 19th September 2020, 1,840 patients were admitted to COVID-19 and 5,084 patients in General Medicine wards.

Comparing the case fatality rates between patients admitted in COVID-19 Wards and non-COVID-19 General Medicine wards, it has been seen that there was a higher percentage of deaths in COVID-19 negative General Medicine wards in both the phases of the study. Also, the case fatality rate in Medical College, Jabalpur for COVID-19 positive deaths was higher in the second phase of the study, that is, from 20th September 2020 to May 2021, which can be attributed to the greater severity of cases being admitted (and referred from the peripheral centers). The case fatality rate of COVID-19 positive patients in the second phase of the study was 22.04%, whereas the case fatality rates of non-COVID-19 patients in the second phase were 15.95% (Table 1).

A maximum number of COVID-19 positive deaths during the first wave of the pandemic occurred in September 2020 and during the second wave in April 2021.

The first phase of the study showed 64.93% (474) Male deaths against 35.06% (256) female deaths and in the second phase of the study 58.01% (579) male deaths were recorded against 41.98% (419) female deaths. Males showed increased mortality rates in both COVID-19 and non-COVID-19 diseases in the second phase of the study.

Maximum deaths among COVID-19 positive patients occurred in the age group of >60 years in both the phases of the study (Fig. 2 and Table 3). Also, it was observed that most deaths occurred during the first 3 days of admission among both positive and negative deaths in both phases of the study. Out of total COVID-19 positive deaths occurring from 20th March 2020 to 19th September 2020, 71.4% deaths occurred in less than 3 days of hospital stay. In coherence with this finding, in the second phase of the study, 54.93% of deaths occurred in less than 3 days of hospital stay.

In the first phase among COVID-19 positive patients, 19.01% of patients who died were diabetic while 14.08% of individuals were hypertensive. 22.4% of the same population suffered from > 1 comorbidity, while 22% of patients who died had no predefined

**Table 1:** Case fatality rates and mortality of COVID-19 positive and negative patients during the two phases of study

<table>
<thead>
<tr>
<th></th>
<th>20th March, 2020–19th September, 2020</th>
<th>Case fatality rate (%)</th>
<th>Percentage of total admissions (%)</th>
<th>20th September, 2020–May, 2021</th>
<th>Case fatality rate (%)</th>
<th>Percentage of total admissions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 positive deaths</td>
<td>168</td>
<td>9.13</td>
<td>2.42</td>
<td>730</td>
<td>22.04</td>
<td>7.63</td>
</tr>
<tr>
<td>Non-COVID-19 deaths</td>
<td>889</td>
<td>17.48</td>
<td>12.83</td>
<td>998</td>
<td>15.95</td>
<td>10.43</td>
</tr>
</tbody>
</table>

**Fig. 1:** Comparative study of admissions and deaths between COVID-19 positive and non-COVID-19 subjects from 20th September to May, 2021.
Mortality in COVID-19 in Juxtaposition with Non-COVID-19 Mortality

Table 2: Admissions and deaths between COVID-19 positive and non-COVID-19 subjects from 20th September to May 2021

<table>
<thead>
<tr>
<th></th>
<th>COVID-19 Positive</th>
<th>Non-COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admissions</td>
<td>3,311</td>
<td>6,256</td>
</tr>
<tr>
<td>Deaths</td>
<td>730</td>
<td>998</td>
</tr>
</tbody>
</table>

comorbidities. Among COVID-19 negative deaths in the same duration of the study, 28.5% of patients were hypertensive, while 23.4% of patients were diabetic (Fig. 3). In the second phase of our study, 26.53% of COVID-19 positive patients had hypertension, while 13.8% of COVID-19 positive individuals were diabetic (Fig. 4). Here, in concordance with the previous phase, 20.46% of patients had >1 comorbidity, whereas 19% of deaths occurred in individuals having no comorbidities. In the COVID-19 negative population, 24.74% were suffering from hypertension, whereas 16.73% population had diabetes mellitus (Table 4).

**Discussion**

India has faced two waves of the global pandemic with the second phase being more severe, more transmissible, and with a different pattern of mortality. In this study, we have evaluated the difference in patterns of mortality in the two waves amongst the COVID-19 positive patients and non-COVID-19 patients.

We found that there was a higher percentage of deaths in COVID-19 negative General Medicine wards as compared to COVID-19 positive wards in both phases of the study. The highest number of deaths occurred in April 2021 during the second phase of the study. Most deaths occurred during the first three days of admission among both positive and negative deaths in both phases of the study. In the first phase, 70.83% of COVID-19 positive deaths occurred in the first 3 days of study, whereas 74.9% of deaths in General Medicine wards also occurred in the first 3 days of admission. Also, in the second phase of the study, we found that 54.93% of COVID-19 positive deaths occurred in the first 3 days of admission whereas 65.33% of total deaths occurred in General Medicine wards. The reduction in numbers in the second phase may be due to increased awareness of the disease amongst the general population, availability of better preparedness for the pandemic, availability of better infrastructure, and vigorous treatment in the institution.

We found that most, that is, 65% of the deaths were attributed to the male gender in the COVID-19 positive group in the second phase of the study. These findings were similar in the COVID-19 negative group, where 58% of deaths had occurred in the male population. In consistence with the second phase of the study, the first phase showed that 69.6% of patients who died were males, among COVID-19 positive mortality, while in non-COVID19 mortality in General Medicine wards, 57% were males. This male preponderance in both COVID-19 positive wards and General Medicine wards can be attributed to high-risk behavior among males, like smoking, tobacco chewing, alcohol consumption, lifestyle-related non-communicable diseases (NCDs), and exposure to work and travel, these factors being more in males than females.9-11 Also, immunological differences among male and female genders have also been pointed out to be a cause of such preponderance.

In both the phases, a maximum number of deaths occurred in the age group>60 years, with more attribution of non-COVID-19 illnesses. In this age population, in the first phase, 20.76% of deaths were COVID-19 positive, whereas 79.23% of deaths were due to other systemic illnesses. In the second phase of the study among individuals aged >60 years, 46.97% of deaths occurred in the COVID-19 positive population, while 53.02% of deaths occurred in the COVID-19 negative group. Stark et al.12 reported that there was indeed an age-related risk of COVID-19 severity. Total deaths including both COVID-19 positive and COVID-19 negative showed the least numbers in the age group of 15–30 years, with more predominance in the COVID-19 negative population. Mortality in the first phase of the study in the 15–30 years age group showed 5.35% deaths due to COVID-19 and 94.97% deaths due to non-COVID-19 illnesses. In the second phase, the mortality in the 15–30 years age group in the COVID-19 positive population increased to 11.83%. Non-COVID-19 mortality still had a significant proportion, that is, 88.16% in the second phase. COVID-19 positive mortality among the 45–60 years age group also showed an increase from 22.9% in the first phase to 37.39% in the second phase. We thus see a rise in mortality in both the young and middle-aged in the second phase of the study.

As per the World Health Organization, MOHFW and the CDC, noncommunicable diseases have overtaken communicable diseases as the major cause of death worldwide. Changing social, economic, and cultural factors such as urbanization and the adoption of unhealthy lifestyles have fuelled the NCD crisis that kills 15 million people prematurely (before...
Mortality in COVID-19 in Juxtaposition with Non-COVID-19 Mortality

Mortality in COVID-19 in Juxtaposition with Non-COVID-19 Mortality

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while 13.8% of COVID-19 positive individuals had diabetes mellitus. Here, in concordance with the previous phase, 20.46% of patients had >1 comorbidity. In the COVID-19 negative population, 24.74% were suffering from hypertension, whereas 16.73% population suffered from >1 comorbidity.

Among COVID-19 negative deaths in the same duration of the study, 28.5% of patients had hypertension as comorbidity, while 23.4% of patients had diabetes as a comorbidity. In the second phase of our study, 26.53% of COVID-19 positive patients had hypertension, while 13.8% of COVID-19 positive individuals had diabetes mellitus. Here, in concordance with the previous phase, 20.46% of patients had >1 comorbidity. In the COVID-19 negative population, 24.74% were suffering from hypertension, whereas 16.73% population were diabetic.

WHO has emphasized that people with NCDs are more likely to become severely ill and die due to coronavirus. In the present study, in the first phase, 19.01% of patients who died were diabetic while 14.08% of individuals were hypertensive (considering single comorbidity). About 22.4% of the same population suffered from >1 comorbidity. Among COVID-19 negative deaths in the same duration of the study, 28.5% of patients had hypertension as comorbidity, while 23.4% of patients had diabetes as a comorbidity. In the second phase of our study, 26.53% of COVID-19 positive patients had hypertension, while 13.8% of COVID-19 positive individuals had diabetes mellitus. Here, in concordance with the previous phase, 20.46% of patients had >1 comorbidity. In the COVID-19 negative population, 24.74% were suffering from hypertension, whereas 16.73% population were diabetic.

Table 4: Distribution of comorbidities in COVID-19 positive and COVID-19 negative mortality in the two phases of the study

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HTN</td>
<td>DM2</td>
</tr>
<tr>
<td>COVID-19 positive deaths (%)</td>
<td>14.08</td>
<td>19.01</td>
</tr>
<tr>
<td>COVID-19 negative deaths (%)</td>
<td>28.5</td>
<td>23.4</td>
</tr>
</tbody>
</table>

Fig. 3: Distribution of comorbidities in COVID-19 positive and COVID-19 negative mortality from 20th March 2020 to 19th September, 2020

Fig. 4: Distribution of Comorbidities in COVID-19 positive and COVID-19 negative mortality from 20th September 2020 to May, 2021
NCDs were hence found to be associated with an increase in disease severity and deaths in both general medicine wards and COVID-19 positive deaths but a significant rise was seen in the second wave. These noncommunicable diseases can be controlled by modification of lifestyle, physical exercise, dietary modification as well as proper treatment, which can thus prevent morbidity and mortality due to both COVID-19 and non-COVID illnesses.

However, our study also showed COVID-19 positive mortality among subjects with no comorbidities. In the first phase of the study, 22% of patients who died had no comorbidities. This was congruous with the results in the second phase, in which 19% mortality was among individuals with no comorbidities.

Thus, we conclude that the second wave of COVID-19 differed from the first wave by being slightly more transmissible, affecting the young and the middle-aged in significant numbers in addition to the elderly. There was a significant association of comorbidities with severe COVID disease in both the first and second waves of COVID-19.

REFERENCES
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A Comparative Study of efficacy and safety of different Sodium Glucose Co-transporter 2 (SGLT-2) Inhibitors in the Management of Patients with Type II Diabetes Mellitus

Deepak Bhosle1*, Sanjeev Indurkar2, Umar Quadri3, Bhakti Chandekar4

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ABSTRACT

Background: There are a handful of sodium glucose co-transporter 2 (SGLT2) inhibitors available in the global and Indian markets to manage type II diabetes mellitus (T2DM). However, head-to-head comparison between different SGLT2 inhibitors is scarce. Therefore, the present study was aimed to evaluate the effect of different SGLT2 inhibitors on glycemic control and body weight in Indian patients with T2DM.

Methods: This was a prospective, interventional, nonrandomized study that included patients (N = 480) of either sex, aged ≥30 years, with inadequately controlled T2DM having HbA1c > 8.5%, and were receiving either Canagliflozin, Empagliflozin, Dapagliflozin or Remogliflozin on the background of triple-drug therapy. In this study, patients were evaluated for HbA1c, fasting blood sugar (FBS), post-prandial blood sugar (PPBS), body weight, and systolic and diastolic blood pressure at baseline, 12 and 24 weeks.

Results: A total of 480 patients who received either Canagliflozin (n = 120), Empagliflozin (n = 120), Dapagliflozin (n = 120), or Remogliflozin (n = 120) were included in this study. There was a significant reduction in levels of HbA1c, FBS, PPBS, body weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) at week 12 and 24 in all treatment groups. The difference in mean values of glycemic parameters and body weight was comparable across the treatment groups at week 12 and 24 but was not significant. Out of all 480 patients, 10 patients (2.08%) reported urinary tract infection (UTI), and five (1.04%) reported genital mycotic infection. All the five patients were females and treatment for UTI and mycotic infection was provided as required. Rest of the patients tolerated the therapy well.

Conclusion: Overall observations indicate that all the four SGLT2 inhibitors are effective in reducing HbA1c, FBS, PPBS, body weight SBP, and DBP. Therefore, gliflozins can be the best choice to start early in patients with inadequately controlled T2DM receiving triple-drug therapy which helps in controlling the parameters of glycemia and significantly reducing the body weight. Hence SGLT2 Inhibitors could be considered as an add-on to all antidiabetic agents currently used for the management of diabetes in Indian setting.

INTRODUCTION

Sodium glucose co-transporter 2 (SGLT2) inhibitors are recently approved oral anti-hyperglycemic agents by US Food and Drug Administration (FDA) (2013). Owing to their non-pancreatic action SGLT2 inhibitors have demonstrated efficacy and safety in the management of T2DM through the reduction of hypoglycemia risk. These agents are recommended along with diet and exercise by various international as well as Indian guidelines for diabetes management. In a recent update of the ADA 2020 guideline of diabetes management, SGLT2 inhibitors are recommended especially in patients with diabetes with high cardiovascular risk.1 Likewise, the use of SGLT2 inhibitors in patients with type II diabetes has been recommended by the Research Society for the Study of Diabetes in India.2

Unlike the other oral hypoglycemic agents, SGLT2 inhibitors have a novel mechanism of action that reduces blood glucose levels without triggering insulin secretion.3 In addition, several SGLT2 inhibitors have benefits in terms of reduction in body weight, blood pressure, and cardiovascular risk. Assessment of the safety profile indicates genitourinary infection is more commonly observed among patients with diabetes receiving treatment of SGLT2 inhibitors followed by mycotic infection, polyuria, volume depletion, hypotension, and dizziness.4–6

Currently, there are a handful of SGLT2 inhibitors including Canagliflozin, Empagliflozin, Dapagliflozin, and Remogliflozin available in the global and Indian market to manage type II diabetes either as monotherapy or with concomitant medication.7 Recent real-world studies from Ireland and Southern Europe on the clinical efficacy of SGLT2 inhibitors reported a significant reduction in HbA1c and body weight in patients with type II diabetes.8,9 Similarly, real-world experience from India reported the effectiveness of SGLT2 inhibitor in terms of significant improvement in glycemic control and weight reduction with the insignificant incidence of adverse events.3

AIM OF THE STUDY: To analyze the efficacy and safety of different SGLT2 inhibitors in patients with T2DM.

OBJECTIVE: To study the effect of different SGLT2 inhibitors on glycemic parameters, body weight, and blood pressure in patients with T2DM.

METHODS

This was a prospective, interventional, nonrandomized study conducted in MGM Medical College and Hospital, in collaboration with the Department of Medicine and Deogiri Diabetes Care Centre, Aurangabad, Maharashtra, India, between November 2019 and November 2020.

The study protocol was approved by MGM Ethics Committee for Research on Human Subjects (MGM. ECRHS).

STUDY POPULATION AND DATA COLLECTION

Patients (N = 480) of either sex, aged ≥30 years, with inadequately controlled T2DM having HbA1c > 8.5%, and BMI > 25 kg/m² who were receiving either Canagliflozin (100 mg OD), Empagliflozin (25 mg OD), Dapagliflozin (10 mg OD) or Remogliflozin (100 mg BD) (N = 120 for each group) on the background of triple-drug therapy were included in this study. Newly diagnosed T2DM patients (N = 480) of either sex, aged ≥30 years, with inadequately controlled T2DM having HbA1c > 8.5%, and BMI > 25 kg/m² who were receiving either Canagliflozin (100 mg OD), Empagliflozin (25 mg OD), Dapagliflozin (10 mg OD) or Remogliflozin (100 mg BD) (N = 120 for each group) on the background of triple-drug therapy were included in this study. Newly diagnosed T2DM patients (N = 480) of either sex, aged ≥30 years, with inadequately controlled T2DM having HbA1c > 8.5%, and BMI > 25 kg/m² who were receiving either Canagliflozin (100 mg OD), Empagliflozin (25 mg OD), Dapagliflozin (10 mg OD) or Remogliflozin (100 mg BD) (N = 120 for each group) on the background of triple-drug therapy were included in this study.
patients, type 1 diabetes mellitus, gestational diabetes, patients with eGFR value less than 45 ml/min/1.73 m² calculated by MDRD formula, patients on insulin therapy, patients with recurrent UTI, and patients with a history of diabetic ketoacidosis or other comorbid cardiac, hepatic, and renal diseases were excluded.

Data collection included body weight in Kgs measured with the electronic weighing machine, and laboratory data included parameters determining glycemic control [HbA1c % measured using High Performance Liquid Chromatography method (Bio-Rad D 10), FBS, PPBS in mg% were analyzed with fully automated Vitros 250 Dry Chemistry analyzer], SBP and DBP measured with a sphygmomanometer in mm of Hg. These parameters were recorded at different time points, at baseline, at week 12 and 24. Safety assessment was performed by general and systemic examination and as per adverse drug reaction reported by patients.

### Statistical Analysis
Data were analyzed using Statistical Package for The Social Sciences (SPSS) software, version 24.0. Quantitative data were presented as mean [standard deviation (SD)] while qualitative data were presented as number. We have applied paired t-test for within-group comparison (before and after therapy) ANOVA test for intergroup comparison and a comparison of two groups was done using post hoc test of LSD (Latin Square Design). A p-value < 0.05 was considered statistically significant.

### Results
A total of 480 patients who received either Canagliflozin (n = 120), Empagliflozin (n = 120), Dapagliflozin (n = 120), or Remogliflozin (n = 120) were included in this study. The mean (SD) age of the patients was 52.1 (9.35) years in Canagliflozin (C), 51.8 (10.74) years in Empagliflozin (E), 52.0 (12.33) years in Dapagliflozin (D), and 51.9 (12.19) years in Remogliflozin (R) groups. All four groups were having comparable ages (p-value 0.361) with a slightly higher proportion of men than women in each group.

Though the difference in mean values of glycemic parameters like FBS, PPBS, HbA1c, and other parameters such as body weight, SBP and DBP was comparable across the treatment groups at 12-week and 24-week follow-up from baseline; the intergroup comparison between all four groups did not demonstrate a significant difference (Tables 1 and 2).

Similarly, two groups comparison using a post hoc test of LSD observed nonsignificant differences in the mean values of all the parameters except C vs R and E vs R groups where a significant reduction was observed in mean FBS values at 24 weeks.

A significant reduction was observed within the groups in the HbA1c values at the end of 24 weeks with a total mean reduction of 3.08, 2.87, 2.74, and 2.79% in Canagliflozin, Empagliflozin, Dapagliflozin, and Remogliflozin groups, respectively (Table 3). An overall highly significant reduction was recorded in the mean values of other glycemia parameters like FBS and PPBS within all four groups (Table 3). Similarly, body weight reduction was also observed in all the patients along with a reduction in SBP and DBP with highly significant differences within individual groups from baseline to the end of 24 weeks (Table 3). Out of a total of 480 patients enrolled in all the four groups 10 patients (2.08%) reported UTI and 5 (1.04%) patients reported genital mycotic infection. All the five patients were females.

### Table 1: Comparison of mean values of glycemic parameters in all groups (ANOVA)

<table>
<thead>
<tr>
<th>Glycemia Parameters</th>
<th>No. of visits</th>
<th>Canagliflozin (Mean ± SD) (C)</th>
<th>Empagliflozin (Mean ± SD) (E)</th>
<th>Dapagliflozin (Mean ± SD) (D)</th>
<th>Remogliflozin (Mean ± SD) (R)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting blood sugar (FBS) (mg%)</td>
<td>Baseline (visit 1)</td>
<td>195.94 ± 23.69</td>
<td>193.93 ± 22.52</td>
<td>198.58 ± 27.52</td>
<td>200.42 ± 27.17</td>
<td>0.201</td>
</tr>
<tr>
<td></td>
<td>12 weeks (visit 2)</td>
<td>164.11 ± 25.14</td>
<td>161.62 ± 23.77</td>
<td>167.50 ± 30.32</td>
<td>167.31 ± 29.90</td>
<td>0.291</td>
</tr>
<tr>
<td></td>
<td>24 Weeks (Visit 3)</td>
<td>140.32 ± 24.99</td>
<td>139.77 ± 24.71</td>
<td>143.82 ± 36.51</td>
<td>148.31 ± 29.72</td>
<td>0.095</td>
</tr>
<tr>
<td>Post prandial blood sugar (PPBS) (mg%)</td>
<td>Baseline (visit 1)</td>
<td>291.37 ± 62.54</td>
<td>287.72 ± 65.02</td>
<td>289.23 ± 61.36</td>
<td>287.91 ± 63.37</td>
<td>0.968</td>
</tr>
<tr>
<td></td>
<td>12 weeks (visit 2)</td>
<td>246.41 ± 65.92</td>
<td>245.62 ± 66.18</td>
<td>248.63 ± 65.72</td>
<td>248.37 ± 65.90</td>
<td>0.987</td>
</tr>
<tr>
<td></td>
<td>24 weeks (visit 3)</td>
<td>205.94 ± 70.31</td>
<td>203.71 ± 68.65</td>
<td>205.44 ± 70.32</td>
<td>206.8 ± 70.27</td>
<td>0.988</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>Baseline (visit 1)</td>
<td>11.7 ± 1.79</td>
<td>11.6 ± 1.76</td>
<td>11.5 ± 1.80</td>
<td>11.6 ± 1.81</td>
<td>0.854</td>
</tr>
<tr>
<td></td>
<td>12 weeks (visit 2)</td>
<td>10.23 ± 1.62</td>
<td>10.31 ± 1.68</td>
<td>10.83 ± 1.75</td>
<td>10.3 ± 1.52</td>
<td>0.747</td>
</tr>
<tr>
<td></td>
<td>24 weeks (visit 3)</td>
<td>8.62 ± 1.57</td>
<td>8.73 ± 1.70</td>
<td>8.76 ± 1.67</td>
<td>8.81 ± 1.74</td>
<td>0.837</td>
</tr>
</tbody>
</table>

Two groups comparison using a post hoc test of LSD observed nonsignificant differences in the mean values of all the parameters except C vs R (0.036) and E vs R (0.025) groups where the significant reduction was observed in mean FBS values at 24 weeks.

### Table 2: Comparison of mean values of other parameters in all groups (ANOVA)

<table>
<thead>
<tr>
<th>Other Parameters</th>
<th>No. of visits</th>
<th>Canagliflozin (Mean ± SD) (C)</th>
<th>Empagliflozin (Mean ± SD) (E)</th>
<th>Dapagliflozin (Mean ± SD) (D)</th>
<th>Remogliflozin (Mean ± SD) (R)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bodyweight (Kg)</td>
<td>Baseline (visit 1)</td>
<td>72.81 ± 9.88</td>
<td>73.12 ± 13.06</td>
<td>71.82 ± 12.15</td>
<td>72.74 ± 13.11</td>
<td>0.879</td>
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<tr>
<td></td>
<td>12 weeks (visit 2)</td>
<td>70.43 ± 14.52</td>
<td>71.24 ± 14.54</td>
<td>69.13 ± 13.82</td>
<td>70.24 ± 14.48</td>
<td>0.724</td>
</tr>
<tr>
<td></td>
<td>24 weeks (visit 3)</td>
<td>68.22 ± 13.87</td>
<td>68.43 ± 13.78</td>
<td>67.62 ± 12.34</td>
<td>69.23 ± 13.38</td>
<td>0.828</td>
</tr>
<tr>
<td>Systolic blood pressure (SBP) (mm of Hg)</td>
<td>Baseline (visit 1)</td>
<td>138.81 ± 5.31</td>
<td>139.32 ± 5.78</td>
<td>139.11 ± 5.36</td>
<td>138.94 ± 5.68</td>
<td>0.940</td>
</tr>
<tr>
<td></td>
<td>12 weeks (visit 2)</td>
<td>136.90 ± 7.46</td>
<td>137.44 ± 6.40</td>
<td>136.63 ± 5.66</td>
<td>136.0 ± 6.67</td>
<td>0.345</td>
</tr>
<tr>
<td></td>
<td>24 weeks (visit 3)</td>
<td>134.71 ± 8.35</td>
<td>135.21 ± 6.64</td>
<td>134.94 ± 6.38</td>
<td>134.82 ± 7.32</td>
<td>0.863</td>
</tr>
<tr>
<td>Diastolic blood pressure (DBP) (mm of Hg)</td>
<td>Baseline (visit 1)</td>
<td>89.31 ± 5.90</td>
<td>87.63 ± 6.17</td>
<td>87.53 ± 7.92</td>
<td>87.64 ± 7.75</td>
<td>0.163</td>
</tr>
<tr>
<td></td>
<td>12 weeks (visit 2)</td>
<td>88.14 ± 6.06</td>
<td>86.01 ± 5.92</td>
<td>86.34 ± 8.35</td>
<td>86.23 ± 8.09</td>
<td>0.084</td>
</tr>
<tr>
<td></td>
<td>24 weeks (visit 3)</td>
<td>86.61 ± 6.14</td>
<td>85.22 ± 4.85</td>
<td>85.11 ± 8.56</td>
<td>85.32 ± 8.96</td>
<td>0.343</td>
</tr>
</tbody>
</table>
Sodium Glucose Co-transporter 2 in Type II Diabetes Mellitus Patients

Table 3: Comparison of mean difference in values of all parameters within groups (Paired t-test)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of visits</th>
<th>Canagliflozin (C)</th>
<th>Empagliflozin (E)</th>
<th>Dapagliflozin (D)</th>
<th>Remogliflozin (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS (mg%)</td>
<td>Baseline vs 24 weeks</td>
<td>55.62 ($p&lt;0.001^{**}$)</td>
<td>54.16 ($p&lt;0.001^{**}$)</td>
<td>54.79 ($p&lt;0.001^{**}$)</td>
<td>52.12 ($p&lt;0.001^{**}$)</td>
</tr>
<tr>
<td>PPBS (mg%)</td>
<td>Baseline vs 24 weeks</td>
<td>85.43 ($p&lt;0.001^{**}$)</td>
<td>84.01 ($p&lt;0.001^{**}$)</td>
<td>83.79 ($p&lt;0.001^{**}$)</td>
<td>81.11 ($p&lt;0.001^{**}$)</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>Baseline vs 24 weeks</td>
<td>3.08 ($p&lt;0.001^{**}$)</td>
<td>2.87 ($p&lt;0.001^{**}$)</td>
<td>2.74 ($p&lt;0.001^{**}$)</td>
<td>2.79 ($p&lt;0.001^{**}$)</td>
</tr>
<tr>
<td>Bodyweight (Kg)</td>
<td>Baseline vs 24 weeks</td>
<td>4.59 ($p=0.0035^{*}$)</td>
<td>4.69 ($p=0.0073^{*}$)</td>
<td>4.20 ($p=0.0084^{*}$)</td>
<td>3.51 ($p=0.0412^{*}$)</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>Baseline vs 24 weeks</td>
<td>4.10 ($p&lt;0.001^{**}$)</td>
<td>4.11 ($p&lt;0.001^{**}$)</td>
<td>4.17 ($p&lt;0.001^{**}$)</td>
<td>4.12 ($p&lt;0.001^{**}$)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>Baseline vs 24 weeks</td>
<td>2.70 ($p&lt;0.001^{**}$)</td>
<td>2.41 ($p&lt;0.001^{**}$)</td>
<td>2.42 ($p&lt;0.001^{**}$)</td>
<td>2.32 ($p&lt;0.001^{**}$)</td>
</tr>
</tbody>
</table>

Within group comparison using a paired t test observed significant differences ($p<0.001^{**}$) in the mean values of all the parameters except body weight in all groups where the reduction was non significant at 24 weeks

Table 4: Adverse drug reactions (ADRs) in each group

<table>
<thead>
<tr>
<th>ADR</th>
<th>Canagliflozin</th>
<th>Empagliflozin</th>
<th>Dapagliflozin</th>
<th>Remogliflozin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital mycotic infection</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

and treatment for UTI and mycotic infection was provided as required. The rest of the patients tolerated the therapy well (Table 4).

Discussion

An extensive literature search has revealed that there is a scarcity of data that compared the efficacy of several available gliflozins in a single study at the global as well as national levels. The use of gliflozins varies widely due to varied clinical inertia toward a marketed drug. A real-world study from Southern Europe carried out the clinical effectiveness of dapagliflozin in various countries and reported geographical diversity may have a significant impact on gliflozins on glycemic control.

In view of this lacuna, the present study attempted to evaluate the effect of SGLT2 inhibitors on glycemic control and body weight in Indian patients with diabetes. The overall observations of this study suggest a reduction in glycemic level at all visits in all the treatment groups indicating the effectiveness of gliflozins on glycemic control. At 12 and 24 weeks of follow-up, all the four gliflozins in this study showed a significant reduction in HbA1c, blood glucose levels, and body weight from baseline indicating the efficacy of these drugs in achieving good glycemic control and weight reduction. These findings corroborate with the previous studies where each of these gliflozins has shown improvement in glycemic control and better influence on weight reduction.

Empagliflozin is the first gliflozin approved by USFDA followed by Canagliflozin and Dapagliflozin. However, Remogliflozin is recently approved SGLT2 inhibitor by USFDA for the management of diabetes. In the present study, the mean difference in HbA1c at 6-months was comparable across the treatment groups. Similarly, a real-world observational study of 120 Indian patients with uncontrolled type II diabetes that compared Remogliflozin 100 mg with Canagliflozin 300 mg reported similar effectiveness between these two agents in terms of reducing HbA1c level, PPBS, FBS, and body weight. India is a developing country with a large proportion of the patient population from lower socioeconomic classes, and the cost-effectiveness of drugs is a crucial factor attributable to drug compliance. Remogliflozin and dapagliflozin were more cost-effective and can be used as alternative SGLT2 inhibitor options. SGLT2 inhibitors have also been observed to address cardiovascular and renal outcomes in terms of safety and efficacy through various global cardiovascular outcome trials. Another previous clinical trial (open-labeled, 52-week study) comparing Empagliflozin with dapagliflozin as add-on therapy in patients with uncontrolled type II diabetes showed both SGLT2 agents as effective as previous antidiabetic agents. However, the authors further demonstrated Empagliflozin is more effective in improving glycemic control and other cardiometabolic outcomes along with a reduction in body weight compared to dapagliflozin. On the contrary present study reported all the four gliflozins are comparable in terms of achieving glycemic control and weight loss. A recently published randomized active-controlled trial compared Remogliflozin vs dapagliflozin for 6 months in patients with uncontrolled type II diabetes demonstrated noninferiority of Remogliflozin over dapagliflozin in terms of reducing HbA1c, FBS, PPBS, and body weight. Similarly, in the present study, the mean difference of HbA1c, FBS, PPBS, and weight were comparable between Remogliflozin and dapagliflozin at 12 and 24 weeks follow-up from baseline.

Sodium glucose co-transporter 2 inhibitors are associated with significant weight reduction in patients with diabetes. Likewise, a previous real-world study conducted on 30 Irish patients with diabetes reported a reduction in HbA1c and body weight over 15 months of exposure to SGLT2 inhibitors. This is in accordance with the present study that reported all the four gliflozins to have significant weight loss at 12 and 24 weeks follow-up from baseline.

Several limitations of this study should be considered and observations should be interpreted vigilantly. The most important limitation of our study was the small sample size and duration of the study. More prospective clinical studies with head-to-head comparisons of SGLT2 inhibitors will be helpful in validating these observations.

Conclusion

Overall observations indicate all the four gliflozins (Canagliflozin, Empagliflozin, Dapagliflozin, and Remogliflozin) were similarly effective in achieving target glycemic levels and reduction in body weight. A reduction was also observed in blood pressure with the use of all the four gliflozins. Therefore, gliflozins can be a possible choice for the management of diabetes in Indian settings.

References


Effect of Mycobacterium w on IL-6 and Oxygen Requirement in COVID-19

Shailaja Behera1*, Mukesh K Gupta2, Hardik Dudhatra3, Raj K Ayyappan4

Received: 10 December 2021; Accepted: 10 March 2022

ABSTRACT

The efficacy and safety of heat-killed Mycobacterium w (Mw) in severe COVID-19 were evaluated. Twenty-five hospitalized patients (mean age, 52.9 ± 13.1 years) with severe COVID-19 and having multiple comorbidities were intradermally injected with 0.3 mL of Mw daily for three consecutive days. Changes in leukocyte and platelet counts; C-reactive protein (CRP), interleukin-6 (IL-6), serum creatinine, and liver enzyme levels; and oxygen saturation were compared before and after treatment. An ordinal scale assessed the clinical response.

There were significant improvements in the IL-6 level and oxygen saturation following treatment (p < 0.001). There were marked improvements in the platelet count, CRP level, serum aspartate transaminase level, and ordinal scale score. Eighty percent of patients who were on oxygen support were successfully shifted to room air within 5.6 days of treatment and discharged. No systemic adverse events were noted. Thus, Mw treatment could be a promising therapeutic modality in severe COVID-19.

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INTRODUCTION

COVID-19 has taken a havoc toll and there is an unmet need for an effective therapy. A dysregulated host immune response predominantly caused organ damage in COVID-19.1 Patients with severe COVID-19 have a higher level of inflammatory cytokines,2 and thus, immunomodulator therapy is of a potential value.

A heat-killed Mw, also known as Mycobacterium indicus pranii, acts through the toll-like receptor (TLR) pathway and enhances the host-T cell response.3 It is clinically effective in gram-negative sepsis.4 The clinical efficacy of Mw in COVID-19 has been demonstrated in some preliminary studies;4–6 however, its role in modulating inflammatory cytokine levels and oxygen saturation in severe COVID-19 has not been established. We evaluated the efficacy and safety of Mw therapy in severe COVID-19.

CASE DESCRIPTION

Twenty-five hospitalized patients with severe COVID-19, some with comorbidities, were studied. All patients were intradermally injected with 0.3 mL (0.1 mL each on three different sites) of Mw (heat-killed) injection (Sepsivac™, Cadila Pharmaceuticals Ltd., Ahmedabad, India) daily for three consecutive days along with the standard of care. The total leukocyte and platelet counts; CRP, IL-6, serum creatinine, serum aspartate transaminase, and serum alanine transaminase levels; and oxygen saturation before and after treatment were compared using paired t-test (SPSS version 23, IBM, Armonk, NY). An ordinal scale (Table 1) was used to assess the clinical response.

The mean age of the patients was 52.9 ± 13.1 years; 22 (88%) of them were male. Breathlessness, weakness, cough, and fever were present in 100%, 12%, 32%, and 40% of the patients, respectively. Ten patients (40%) had type 2 diabetes mellitus, eight (32%) had hypertension, two (8%) had tuberculosis, one (4%) had obesity, and one (4%) had coronary artery disease. Twenty-one patients (84%) had at least one organ (lungs, kidney, or liver) dysfunction. Five patients had renal and respiratory compromise, 13 had liver and respiratory compromise, while four had renal, hepatic, and respiratory compromise. Twenty patients (80%) had respiratory compromise (one on nasal cannula, 15 on non-rebreather mask, and four on noninvasive ventilation) requiring oxygen support. Neutrophil-predominant leukocytosis and lymphocytopenia were noted at baseline; CRP and IL-6 levels were elevated (Table 1).

Following Mw treatment, there was a significant reduction in the IL-6 level (320.8 ± 214.4 vs 3.1 ± 2.3 pg/mL, p < 0.001) and a significant improvement in oxygen saturation (87.2 ± 6.3 vs 94.4 ± 3.4%, p < 0.001) on the fourth-day posttreatment as compared to the values before treatment. Improvements in platelet count, CRP level, and serum aspartate transaminase level were also observed; however, these changes were not statistically significant (Table 1). There was no significant change in the neutrophil:lymphocyte ratio. Changes in the ordinal scale score further suggested the beneficial effects of Mw (Fig. 1). In 16 patients, the mean score was reduced from 4 to 3 in 5 days; in two, it was reduced from 5 to 3; in three, it was maintained; and in four, it was increased in 6 days. Furthermore, there was a reduction in the use of vasopressor agents following Mw treatment. No significant systemic adverse events were noted. However, in four patients, the clinical response worsened (Fig. 1).

Twenty patients (80%) who required oxygen support were shifted to room air within 5.6 days (mean) after treatment and discharged. Four patients (16%) died (three from sudden cardiac arrest and one from type 1 respiratory failure, acute kidney injury, and septic shock). The patients died on the fifth, third, sixth, and eighth day of completion of treatment with Mw. All these patients had existing comorbidities like hypertension, diabetes, obesity, and hypothyroidism. They had multiorgan failure and raised inflammatory markers at the time of admission. The mean IL-6 level in these patients was very high at baseline (219, 788.4, 318, and 289 pg/mL) which was significantly reduced after Mw treatment (403.6 ± 259.9 pg/mL vs 90.5 ± 78.7 pg/mL, p < 0.001). The causes of death could not be because of Mw treatment as patients died of cardiac arrest, respiratory failure, and acute kidney injury.

DISCUSSION

We report a series of 25 patients with severe COVID-19 who were successfully treated with adjunctive Mw. This treatment significantly reduced IL-6 levels and improved oxygen saturation. Furthermore, there were improvements in the platelet count, CRP level, and serum aspartate transaminase level.

Patients with severe COVID-19 have peripheral lymphocytopenia.7 There is also a reduction in the peripheral CD8 and CD4 T-cell counts. The role of Mw in these patients is not known. In our study, there was a significant reduction in the IL-6 level (p < 0.001) and a significant improvement in oxygen saturation (p < 0.001) in the IL-6 level and oxygen saturation following treatment (p < 0.001). The causes of death could not be because of Mw treatment as patients died of cardiac arrest, respiratory failure, and acute kidney injury.

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Effect of Mycobacterium w on IL-6 and Oxygen Requirement in COVID-19

We report a series of 25 patients with severe COVID-19 having multiple comorbidities who were treated with Mw. Eighty percent of them who required oxygen support were shifted to room air and discharged. There were significant improvements in the IL-6 level and oxygen saturation following Mw treatment in severe COVID-19.

**Table 1: Changes in the laboratory parameters before and after administration of Mycobacterium w (Mw) (n = 25)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pretreatment values</th>
<th>Posttreatment values at 4 days</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen saturation (%)</td>
<td>87.2 ± 1.3</td>
<td>94.4 ± 0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interleukin-6 level (pg/mL)</td>
<td>320.8 ± 42.9</td>
<td>3.1 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total leukocyte count (cells/μL)</td>
<td>10,403.9 ± 834.4</td>
<td>12,194.4 ± 929.5</td>
<td>0.196</td>
</tr>
<tr>
<td>Neutrophil: lymphocyte ratio</td>
<td>8.27 ± 1.16</td>
<td>10.73 ± 0.99</td>
<td>0.541</td>
</tr>
<tr>
<td>Platelet count (cells/μLx10^9)</td>
<td>2.3 ± 0.3</td>
<td>2.7 ± 0.4</td>
<td>0.063</td>
</tr>
<tr>
<td>C-reactive protein level (mg/L)</td>
<td>121.4 ± 14.9</td>
<td>95.6 ± 9.6</td>
<td>0.443</td>
</tr>
<tr>
<td>Serum creatinine level (mg/dL)</td>
<td>1.1 ± 0.1</td>
<td>1.2 ± 0.3</td>
<td>0.667</td>
</tr>
<tr>
<td>Serum aspartate transaminase level (mg/dL)</td>
<td>60.4 ± 6.9</td>
<td>47.6 ± 4.4</td>
<td>0.051</td>
</tr>
<tr>
<td>Serum alanine transaminase level (mg/dL)</td>
<td>73.7 ± 13.6</td>
<td>74.0 ± 9.9</td>
<td>0.984</td>
</tr>
</tbody>
</table>

The results are represented by the mean ± standard error of the mean. Significance of bold value is improvement in oxygen saturation and reduction of IL-6 suggest faster recovery post Mw administration.

**Fig. 1:** Changes in the ordinal scale score before and after 4 days of administration of Mycobacterium w (n = 25)

CD4 T-cell counts. Furthermore, there is a hyperinflammatory response. The virus invades and enters the type II alveolar epithelial cells and virus-laden pneumocytes release various cytokines and inflammatory markers. The cytokine storm acts as a chemoattractant for neutrophils, CD4 helper T cells, and CD8 cytotoxic T cells, which get sequestered in the lung tissue, causing inflammation and injury. Considering such pathogenesis, an immunomodulator therapy is of potential value.

Heat-killed Mw has an immunomodulating effect. It is a potent TLR-2 agonist. It increases the expression of IL-1 receptor-associated kinase-1 and tumor necrosis factor receptor-associated factor-6 that are required for TLR-4 downstream kinase activation along with activation of TLR-4 downstream signaling, activating translocation of nuclear factor κB. It also upregulates the inhibitor κ kinase-α and -β. Mw induces apoptosis of activated macrophages by suppressing IL-β. Also, it might enhance viral clearance by activating the Th1-mediated innate immune response. Reduced mortality was observed following Mw treatment in severe COVID-19. This is the first report of significant improvements in IL-6 level and oxygen saturation following Mw treatment in COVID-19.

**Conclusion**

We report a series of 25 patients with severe COVID-19 having multiple comorbidities who were treated with Mw. Eighty percent of them who required oxygen support were shifted to room air and discharged. There were significant improvements in the IL-6 level and oxygen saturation. No adverse event was noted. Thus, adjunctive Mw treatment can be an effective and safe therapeutic modality in severe COVID-19.
Highlights
We highlight the efficacy and safety of Mw treatment in the management of hospitalized patients with severe COVID-19. Critical prognostic markers were significantly improved following treatment. Further studies are required to validate these findings.

References
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Ref: 1. J Am Coll Cardiol 2021 Mar; 77 (10) 1300-1301
2. Data on File
In hypertensive patients with CAD

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Ref:
1. J Hypertens 38:982-1004
2. European Heart Journal 2016; 37: 1-8
4. Data on file

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Spontaneous Ascitic Fluid Infection: Are we Experiencing an Epidemiological shift in Causative Organisms?

Noopur Mehta1*, Aminoddin Siddiqui2, Pravin Rathi3, Niranjan Banka4, Ameetkumar Mandot5, Vaibhav Somani6, Nitin Aherrao7

Received: 27 June 2021; Accepted: 10 March 2022

Abstract

**Background:** Spontaneous ascitic fluid infection (SAI) is common in cirrhotic patients leading to significant morbidity and mortality. Third-generation cephalosporins are currently recommended as first-line therapy. This is a retrospective observational study that aims to determine bacterial etiology, susceptibility patterns of SAI, and its correlation with model for end-stage liver disease-sodium (MELD-Na) and Child–Turcotte–Pugh (CTP) score.

**Materials and methods:** The present study was conducted on 274 consecutive cases admitted in Bombay Hospital and Medical Research Centre, Mumbai, India. Cases of cirrhosis (irrespective of etiology) with ascites between the ages of 18–85 years were included in this study. Ascitic fluid of every patient was aspirated under all aseptic measures and was sent for biochemical, culture, and cytological analysis.

**Results:** Of the 274 patients studied, 34 (12.4%) patients were diagnosed to have SAI. Culture-negative neutrocytic ascites (CNNA) was present in 27 patients, spontaneous bacterial peritonitis (SBP) was present in six patients, and monomicrobial bacteriases was seen in one patient. Mean age of patients enrolled was 56.05 ± 2.47 years. Eighty-two percent were males and 18% were females. Alcohol (45.45%) was the leading cause of cirrhosis followed by nonalcoholic steatohepatitis (NASH) related cirrhosis (26.47.7%) and hepatitis C virus (HCV) related cirrhosis (11.46%) and cryptogenic cirrhosis (8.82%). Average MELD-Na score was 25 and the CTP class C was most common. Klebsiella pneumoniae was the most commonly isolated organism followed by Escherichia coli. The various factors that predispose to development of SBP include low ascitic fluid protein concentration, a high level of serum bilirubin, deranged serum creatinine, high Child–Pugh score, and high MELD-Na score.

**Conclusion:** Ascitic fluid analysis remains the single most important test for identifying and assessing a course of SBP. Early diagnosis and treatment will reduce the mortality rate in these patients.

**Introduction**

Spontaneous bacterial peritonitis has been defined as a bacterial infection of ascitic fluid without a clear intra-abdominal surgically treatable source of infection.1 Spontaneous bacterial peritonitis almost always occurs in patients with end-stage liver disease (ESLD), and it is associated with significant morbidity and mortality. Multiple factors contribute to increased risk of SBP, among them reduction of intestinal motility leading to bacterial overgrowth as well as alteration of the gut’s barrier function and local immune responses.1 At present, gut dysbiosis, with overgrowth of aerobic species such as E. coli, is regarded as a common first step in SBP development. Following translocation across the gut wall, bacteria can then colonize mesenteric lymph nodes, enter the systemic circulation, and reach the ascitic fluid through the liver.2,4 The diagnosis of SAI is made with an ascitic polymorphonuclear leukocyte count (PMN) ≥250/mm³, with or without an ascitic bacterial isolate. The criteria for a diagnosis of monomicrobial non-neutrocytic bacteriases (MNB) include a positive ascitic fluid culture for a single organism, an ascitic fluid PMN count <250 cells/mm³, and no evident intra-abdominal source of infection that requires surgical treatment.5 Culture-negative neutrocytic ascites was diagnosed in the past when: (i) the ascitic fluid culture grows no bacteria; (ii) the ascitic fluid PMN count is ≥250 cells/mm³; and (iii) there was no other explanation for an elevated PMN count (e.g., hemorrhage into ascites, peritoneal carcinomatosis, tuberculosis (TB), or pancreatitis).6 This variant of ascitic fluid infection is nowadays considered a form of SBP.8 The current guidelines and recommendations for the clinical management of SBP consider the three most common SBP culture isolates, that is, nonmultidrug-resistant (MDR) E. coli, K. pneumoniae, and Streptococcus pneumoniae.3,9 In the last decade, however, the number of cases due to gram-positive bacilli and MDR bacteria has increased.3,9 The extensive use of quinolones as prophylaxis, rising numbers of ESLD patients, and increasing severity of ESLD cases, have all been implicated in this epidemiologic shift.3 For this reason, use of third-generation cephalosporins or amoxicillin/clavulanic acid as empiric therapy for SBP must be carefully considered within the context of local epidemiology and local antibiotics susceptibility profile, in particular in healthcare-related settings.3,9

**Materials and Methods**

The present study is a retrospective observational study, involving 274 consecutive patients with ascites due to cirrhosis of liver admitted to Bombay Hospital and Medical Research Centre, Mumbai, Maharashtra from 1st January 2018 to 31st December 2020.

**Inclusion criteria:**
- Age between 18 and 85 years of age.
- Ascites due to cirrhosis of liver, irrespective of the etiology.

**Exclusion criteria:**
- Age less than 18 years and more than 85 years.
- Ascites not due to cirrhosis of liver.
- Patients having secondary peritonitis due to appendicitis, gastrointestinal perforation, abdominal tuberculosis, septicemia, intestinal obstruction, trauma, and malignancy.

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Ascitic fluid aspiration was done under all aseptic precautions and fluid was sent for culture/sensitivity, routine/microscopic examination. Bedside inoculation of ascitic fluid in blood culture bottle was not done.

The severity of disease was assessed using CTP and MELD-Na scores.

**Results**

Of the 274 patients studied, 34 (12.4%) were diagnosed to have SAI. Culture-negative neutrocytic ascites was present in 27 (79.41%) patients, SBP is present in six (17.64%) patients, and MNB was seen in one (2.94%) patient. As depicted in Table 1 and Figure 1.

Mean age of patients enrolled was 56.05 ± 2.47 years. Twenty-eight (82.35%) were males and 6 (17.64%) were females. Alcoholic liver disease was the leading cause of cirrhosis (n = 15, 45.45%), followed by NASH-related cirrhosis (n = 9, 26.47%), HCV-related cirrhosis (n = 4, 11.46%), cryptogenic cirrhosis (n = 3, 8.82%), autoimmune cirrhosis (n = 2, 5.88%), and HBV-related cirrhosis (n = 1, 2.94%). Refer to Table 2.

*K. pneumoniae* was the most commonly isolated organism followed by *E. coli*. *K. pneumoniae* was isolated in four cases (57.14%) and *E. coli* was isolated in three cases (42.85%). Both *E. coli* and *K. pneumoniae* were resistant to ampicillin and amoxicillin/clavulanic acid in all the seven (20.58%) cases of SBP and MNB. In two (28.58%) patients the isolated *K. pneumoniae* was multidrug-resistant. In one (14.28%) case it was sensitive only to meropenem, doripenem, and ertapenem and in the other case it was sensitive only to tigecycline, doxycycline, erythromycin, vancomycin, teicoplanin, and chloramphenicol. *E. coli*, isolated in three (42.85%) cases was sensitive to third-generation cephalsporins, carbapenems, fluoroquinolones, and piperacillin/tazobactam.

Most of the patients had an elevated MELD-Na and CTP scores. Average MELD-Na score was 25 ± 0.7 and the CTP class C was most common. Nineteen (55.88%) patients had MELD-Na score greater than 25 and 15 (44.11%) patients had MELD-Na score less than 25. Similarly, 19 (55.88%) patients had CTP class B and 15 (44.11%) patients had CTP class C. The various factors that predispose to development of SAI include low ascitic fluid protein concentration, a high level of serum bilirubin, deranged serum creatinine, high Child–Pugh score, and high MELD-Na score. For details refer to Table 3.

**Discussion**

Ascites is a common diagnostic and therapeutic challenge to the internist and gastroenterologist. In patients with cirrhosis, it is associated with significant morbidity and mortality. Approximately one-half of patients develop ascites within 10 years of diagnosis of compensated cirrhosis. Appearance of ascites connotes development of decompensated cirrhosis. Once ascites is present, the expected mortality is ~50% in just 2 years.

Ascitic fluid infection can be classified into four categories based on culture, PMN count, and the presence or absence of a surgical source of infection. An abdominal paracentesis must be performed and ascitic fluid must be analyzed before a confident diagnosis of ascitic fluid infection can be made. A “clinical diagnosis” of infected ascitic fluid without a paracentesis is not enough.

The prototype form of SAI is SBP. This diagnosis is made when there is an elevated ascitic fluid absolute PMN count (≥250 cells/mm³) with or without positive ascitic fluid culture and without an evident intra-abdominal source of infection that requires surgical treatment.

Culture-negative neutrocytic ascites was diagnosed in the past when: (i) the ascitic fluid culture grows no bacteria; (ii) the ascitic fluid PMN count is ≥250 cells/mm³; and (iii) there was no other explanation for an elevated PMN count (e.g., hemorrhage into ascites, peritoneal carcinomatosis, TB, or pancreatitis). This variant of ascitic fluid infection is nowadays considered a form of SBP.

All cirrhotic patients with ascites can develop SBP. The prevalence of SBP in hospitalized patients ranges between 10 and 30%. In this study, the occurrence of SAI was 12.4% of the patients with cirrhotic ascites.

The prevalence of SBP depends on severity of liver dysfunction, being higher in advanced liver disease. Jain et al. reported that the prevalence of SBP was 34.92% out of 63 patients. All patients who had SBP were in Child–Pugh class C. Puri et al. reported 21 (30%) out of 70 had SBP or its variants and 77% of their patients were in class C. In our study, 55.88% of patients were Child–Pugh class C.

In our study, out of 34 cases of SAI, 27 (79.41%) had CNNA which is slightly higher than some other studies as many of these patients had received antibiotics before paracentesis.

In our study, out of 34 cases of SAI, organisms were isolated in seven cases (20.58%). Most of them were gram-negative, mainly *K. pneumoniae* n = 4 (57.14%), *E. coli* n = 3 (42.85%).

In two (28.58%) cases multidrug-resistant *K. pneumoniae* was isolated. The other five (71.42%) cases were sensitive to commonly used antibiotics including third-generation cephalosporins, carbapenems, and fluoroquinolones.
In contrast to commonly available data wherein, *E. coli* is the most commonly isolated organism in patients with SBP, in our study the most common organism was found to be *K. pneumoniae* followed by *E. coli.* Third-generation cephalosporins still remain one of the most effective antibiotics for use in SBP and can be used as first-line therapy for empirical therapy in patients with suspected SAI.1,3

This study depicts a real-world scenario of patients with cirrhosis of liver with ascites and suspected SAI. It also highlights the importance of ascitic fluid analysis and culture sensitivity and this investigation is mandatory in all patients of cirrhosis presenting with ascites. It also highlights the variation of organisms and their antibiotic sensitivity which can be encountered from center to center.

**Future Directions**
Our observations suggest a possible epidemiological shift in causative organisms of SAI which need to be validated in future studies, by involving large number of patients with cirrhosis and SAI. Also, more data on local antibiotic susceptibility will guide us in selecting appropriate initial empiric antibiotics which remains an important stem of current antibiotic stewardship.

**Conclusion**
Ascitic fluid analysis remains the single most important test for identifying and assessing a course of SBP. Ascitic fluid analysis helps in identifying the organism and culture and sensitivity. Early diagnosis and appropriate treatment will reduce the mortality rate in these patients.

**References**
A Study on FibroScan and Endoscopic Finding in Patients of Chronic Liver Disease attending Tripura Medical College and Dr. B.R. Ambedkar Memorial Teaching Hospital

Goutam Debnath1, Avik Chakraborty2*

Received: 10 August 2020; Accepted: 15 March 2022

ABSTRACT

Introduction: Chronic liver disease (CLD) represents different liver disorders of varying severity and etiology in which hepatic inflammation and fibrosis continue at least for 6 months. Portal hypertension is one of the important complications of CLD and its early recognition is of paramount importance. Though liver biopsy remains the gold standard for diagnosing liver fibrosis and upper gastrointestinal (GI) endoscopy plays an important role in diagnosing different findings of portal hypertension, various noninvasive methods like FibroScan are being increasingly used to diagnose liver fibrosis.

Aims and objectives: Study the FibroScan and endoscopic findings in patients of CLDs and the objectives are to find the prevalence of portal hypertension and to find various grades of esophageal varix and portal hypertensive gastropathy (PHG) and its relationship with liver fibrosis by FibroScan.

Materials and methods: A total of 114 patients of CLD and compensated cirrhosis having child-turcotte-pugh (CTP) stages A and B were included in the study fulfilling inclusion and exclusion criteria, after calculating the sample size of 100. All the patients underwent detailed history, physical and gastrointestinal examination. Complete blood count (CBC), liver function test (LFT), kidney function test (KFT), viral markers were done. Aspartate aminotransferase (AST) to platelet ratio index (APRI) score was calculated, liver fibrosis was estimated by FibroScan and evidence of portal hypertension was documented by upper GI endoscopy. Cutoff value of FibroScan, APRI score, and model for end-stage liver disease (MELD) score for portal hypertension was decided by receiver operating characteristic (ROC) curve.

Results: Alcoholic liver disease (ALD) was the most common cause (43%) of CLD closely followed by nonalcoholic fatty liver disease (NAFLD) in 42% cases followed by chronic viral hepatitis, 75% patients had evidence of portal hypertension with PHG being the most common followed by esophageal varix. F4 fibrosis was found in 73% of cases followed by F3, F2, and F1 fibrosis. FibroScan value of 12.2 kPa was predictive of presence of portal hypertension and value of 26.6 mm predicted the presence of large esophageal varices.

INTRODUCTION

Chronic liver disease represents a series of liver disorders of varying causes and severity in which hepatic inflammation and fibrosis continue at least for 6 months. Cirrhosis is the result of a variety of liver diseases characterized by fibrosis and architectural distortion of the liver with the formation of regenerative nodules and can have varied clinical manifestations and complications.1 Though liver biopsy remains the gold standard for diagnosing fibrosis and cirrhosis various noninvasive tests like APRI score, fibrosis-4 calculator (FIB-4), FibroMeter, Hepascore, FibROspect II, transient elastography (FibroScan), acoustic radiation force impulse (ARFI), 2-D shear wave elastography, magnetic resonance elastography, and recently molecular imaging (positron emission tomography (PET) and translocation protein 18kDa (TPSOI)) are used to document liver fibrosis.2 Among them, diagnostic accuracy of FibroScan for advanced fibrosis is good with pooled estimated sensitivity and specificity approaching 90%. The large dynamic range provided by FibroScan facilitates longitudinal follow-up of patients by assessing the change in liver stiffness over time. It has an advantage over liver biopsy because it is a direct measure of fibrosis (i.e., stiffness), whereas liver biopsy stages fibrosis based on the pattern but not the absolute amount scar.3 FibroScan appears to be more accurate than serum biomarkers in predicting cirrhosis, and the most accurate method for early detection of cirrhosis.4

AIMS AND OBJECTIVES

The aim of our study was to evaluate the FibroScan and endoscopic findings in patients of CLDs. The objectives of the study were to find out various grades of fibrosis by FibroScan and its correlation with endoscopic manifestations of portal hypertension and to compare FibroScan values with other noninvasive markers of liver fibrosis. The study would also find out the various causes of CLD attending our hospital.

MATERIALS AND METHODS

As per sample size calculation, minimum of 100 patients needed to be included in the study. A total of 140 patients of CLD and compensated cirrhosis in CTP stages A and B were initially chosen, after fulfilling the inclusion and exclusion criteria finally 114 patients were enrolled in the study. Detailed history, physical, anthropometric measurements, and GI examination were done. All the patients underwent fasting CBC and peripheral blood smear (PBS), blood sugar, LFT, KFT, thyroid function tests, lipid profile, viral markers, and other specific tests to find the etiology of CLD. FibroScan was performed with FibroScan 402 machine which is an easy-to-use device based on a robust technology: Vibration-Controlled Transient Elastography (VCTE™). Upper GI endoscopy was performed with Olympus CV-170 scope.

The study was a cross-sectional study where collected data of 114 study subjects were checked for consistency and completeness and were entered in Microsoft Excel datasheet. Data were organized and presented using the principles of descriptive statistics in the form of frequency and percentage and in tables and diagrams. Diagrams were done by Microsoft Excel software. Categorical data were expressed in proportions. Mean and standard deviation was used for continuous data.

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A Study on FibroScan and Endoscopic Finding

**Table 1: Background characteristics of the study subjects**

<table>
<thead>
<tr>
<th>Background characteristics</th>
<th>Frequency</th>
<th>n = 114</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (in years)</td>
<td></td>
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</tr>
<tr>
<td>&lt;40</td>
<td>7</td>
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<tr>
<td>≥40</td>
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<td>Sex</td>
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</tr>
<tr>
<td>Female</td>
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<tr>
<td>Male</td>
<td>85</td>
<td>74.6</td>
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<td>Religion</td>
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<tr>
<td>Hindu</td>
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<tr>
<td>Others*</td>
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<tr>
<td>Occupation</td>
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<td>Business</td>
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<td>Employee</td>
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</tr>
<tr>
<td>Housewife</td>
<td>22</td>
<td>19.3</td>
<td></td>
</tr>
<tr>
<td>Others#</td>
<td>13</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>114</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

*M included Muslim, Christian, and Buddhist; # included daily workers and students

Mann–Whitney U test (for data not normally distributed) and independent sample t-test (for normally distributed data) were applied to test significance. ROC curve was used for determining cutoff value of FibroScan finding, APRI score, and MELD score to detect portal hypertension and esophageal varices of different grades. p-value less than 0.05 was considered as statistically significant. Analysis of the data was done by IBM SPSS version 20.

The study protocol was approved by the Human Ethics Committee of the Tripura Medical College and Dr. B.R. Ambedkar Memorial Teaching Hospital and written informed consent were obtained in all cases.

**Results**

Among 114 patients, majority (74%) were male (Table 1), ALD was the commonest cause of CLD found in 43% of cases closely followed by NAFLD in 42% cases and chronic viral hepatitis in 10% cases (Fig. 1). Most of the patients had CTP stage B and fibrosis score of F4 (72.8%) followed by F3 (15.8%), F2 (9.6%), and F1 (1.8%) fibrosis (Table 2). This study showed that the cutoff value of FibroScan was 12.2 kPa to detect the portal hypertension. The sensitivity and specificity were 87.5% and 69%, respectively. The cutoff value of APRI score was 1.0 with 70.4% sensitivity and 59% specificity while the cutoff value for MELD score was found as 10.5 (74.2% sensitivity and 58.6% specificity) to detect portal hypertension (Fig. 2). FibroScan was found to be more sensitive and specific than APRI and MELD score to detect portal hypertension. In this study, it was found that cutoff value of FibroScan to detect portal hypertension gastropathy was 11.4 kPa, for esophageal varices 15.8 kPa and both portal hypertension gastropathy with esophageal varices was 15.8 kPa, respectively. The FibroScan value to detect large esophageal varix was 26.6 kPa (Table 3). Mean findings of FibroScan, APRI, and MELD score were higher among the portal hypertensive group compared to the negative ones. The differences were found to be statistically significant (p < 0.05) (Table 4).

**Discussion**

In the present cohort, majority of patients were in the age group of 41–50 years followed by those in the 51–60 years age group. Three quarters of the patients were males (74.6%). Similar age and sex distribution have been observed in other studies from India.5 The commonest cause of admission in the cohort was ethanol (43%) followed by NAFLD (42.1%). High levels of CLD due to alcohol were also seen in a study by Goel et al.5 in tertiary centers.
from South and North India. However, the prevalence of hepatitis B and C infections in the present cohort was much less than in both these studies. In a meta-analysis by Mukherjee et al., alcoholism (34.3% of 4,413) was the commonest cause of cirrhosis while hepatitis B (33.3%) was the predominant cause of CLD in general and noncirrhotic CLD (40.8% out of 8,163). There were significant interregional differences (hepatitis C in North, hepatitis B in East and South, alcohol in North-east, and NAFLD in West) in the predominant cause of CLD.6 In our study population of 114 persons, portal hypertension was found in 74.6% cases out of which 71% had PHG, 52.6% had gastroesophageal varix (GOV), and 50% had both PHG and GOV. Among the patient with esophageal varix, all had gastroesophageal varices grade I, grade II, and grade III varices. Moderate PHG was the commonest presentation in 49% of cases followed by mild PHG in 37% and moderate PHG in 14% cases. Most of the patients had CTP stage II and fibrosis score of F4 (72.8%) followed by F3 (15.8%), F2 (9.6%), and F1 (1.8%) fibrosis (Table 2). This study showed the cutoff value of FibroScan was 12.2 kPa with AUROC of 0.875 and sensitivity and specificity were 87.5% and 69%, respectively to detect the portal hypertension and the value of APRI was 1.1, sensitivity of 70.4%, specificity of 59%, and AUROC 0.67, and for MELD score the AUROC was 0.742 with sensitivity of 74.2% and specificity of 58.6% (Fig. 2). In this study it was found that cutoff value of FibroScan to detect portal hypertension gastropathy was 11.4 kPa, for esophageal varices 15.8 kPa and both portal hypertension gastropathy with esophageal varices was 15.8 kPa which was found to have excellent sensitivity of 91.6%, specificity of 82.8%, and area under receiver operating characteristic (AUROC) of 0.916. (Table 3). In this study the cutoff values of FibroScan to detect esophageal varices grade I, grade II, and grade III were 15.8 kPa, 16.6 kPa, and 26.6 kPa, respectively. In a study by Ghamdi et al. in Saudi Arabia, the mean stiffness score was higher in patients with GOVs or PHG than in patients without esophageal varices or PHG (34.5, SD 18.3 and 25.8, SD 14.9, respectively, p = 0.027) which is like the present study. Several investigators in previous reports have suggested different cutoff FibroScan scores for the detection of GOVs in CLD patients. Castera et al.8 suggested a cutoff value of 21.5 kPa for the prediction of grades II and III varices. In a similar report, Saad et al.9 suggested a cutoff value of 29.7 kPa for the prediction of varices and a cutoff value of 38.2 kPa for the prediction of large varices.

**Table 3:** FibroScan findings of portal hypertension gastropathy, esophageal varices, both portal hypertension gastropathy and esophageal varices and large esophageal varix

<table>
<thead>
<tr>
<th>Methods</th>
<th>Cutoff value (in kPa)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portal hypertension gastropathy</td>
<td>11.4</td>
<td>87.1%</td>
<td>62.1%</td>
</tr>
<tr>
<td>Esophageal varices</td>
<td>15.8</td>
<td>91.8%</td>
<td>82.8%</td>
</tr>
<tr>
<td>Both portal hypertension gastropathy and esophageal varices</td>
<td>15.8</td>
<td>91.6%</td>
<td>82.8%</td>
</tr>
<tr>
<td>Large esophageal varix</td>
<td>26.6</td>
<td>95.6%</td>
<td>86.8%</td>
</tr>
</tbody>
</table>

**Table 4:** Comparison of means of FibroScan findings, APRI score, and MELD score among two independent groups

<table>
<thead>
<tr>
<th></th>
<th>Portal hypertension (yes)</th>
<th>Portal hypertension (no)</th>
<th>Test applied</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FibroScan (kPa)</td>
<td>39.9 ± 22.7</td>
<td>13.6 ± 11.7</td>
<td>Mann–Whitney U test</td>
<td>0.000</td>
</tr>
<tr>
<td>APRI score</td>
<td>2.1 ± 5.5</td>
<td>0.97 ± 0.59</td>
<td>Mann–Whitney U test</td>
<td>0.003</td>
</tr>
<tr>
<td>MELD score</td>
<td>15.4 ± 6.7</td>
<td>10.7 ± 3.4</td>
<td>Independent sample</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**CONCLUSION**

Alcohol remains the most important risk factor of CLD but NAFLD was found to be the second most cause of CLD in our study probably due to changing lifestyle and mass vaccination against hepatitis B in our state. Noninvasive markers like FibroScan and APRI score can be of valuable tool in detecting portal hypertension and predicting high-risk varices.

**REFERENCES**

Atherosclerosis and Associated Cardiovascular Risk Factors in Nonalcoholic Fatty Liver Disease and Metabolic Syndrome

Sarita Bajaj1, Sandeep K Prajapati2*

Received: 16 December 2021; Accepted: 20 April 2022

ABSTRACT

Objectives: Nonalcoholic fatty liver disease (NAFLD) is a well-known contributor for the development of cardiovascular disease (CVD). Nonalcoholic fatty liver disease is considered as the liver component of metabolic syndrome (MetS). This study aimed to assess the influence of NAFLD and MetS on markers of subclinical atherosclerosis, including carotid intima-media thickness (CIMT), ankle-brachial pressure index (ABI), and to investigate the impact of NAFLD and MetS on left ventricular (LV) diastolic and systolic function.

Study design: A case-control study.

Materials and methods: In this case-control study, 120 cases and 90 healthy controls in the age group ranging from ≥18 to ≤65 years were included. Metabolic syndrome was assessed using International Diabetes Federation (IDF) criteria. Height, weight, waist circumference, body mass index (BMI), and blood pressure were measured. Liver ultrasonographic scanning was used for assessing fatty liver. To assess atherosclerosis, CIMT and ABI were used.

Results: The prevalence of NAFLD was 66.7%. As compared with control subjects, patients with NAFLD had a significantly greater (p = 0.02) mean CIMT while in patients with MetS, it was not significant. Left ventricular diastolic and systolic function were significantly impaired (p = 0.03, p = 0.04, respectively) in NAFLD while only LV diastolic function was significantly (p = 0.04) impaired in MetS. There was a strong positive correlation between CIMT and triglyceride (TG) (r = 0.46, p = 0.0001), total cholesterol (TC) (r = 0.47, p = 0.0001), low density lipoprotein cholesterol (LDL-C) (r = 0.46, p = 0.0001), very low density lipoprotein cholesterol (VLDL-C) (r = 0.259, p = 0.001), BMI (r = 0.21, p = 0.03), and age (r = 0.22, p = 0.002).

Conclusions: Carotid intima-media thickness, ABI, and LV diastolic function were affected in patients with NAFLD and MetS.

INTRODUCTION

Nonalcoholic fatty liver disease is characterized by an accumulation of fat in liver and is one of the most common forms of chronic liver disease in developed countries.1 With increasing urbanization and behavioral changes such as decreased physical activity, high-energy fat diet, and increased occurrence of diabetes mellitus type 2 (T2DM), its prevalence has increased in the Asian region.1–3 Nonalcoholic fatty liver disease is a well-known contributor for the development of CVD.4 Metabolic syndrome is defined by a constellation of interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic CVD, T2DM, and all-cause mortality.5,6 Carotid intima-media thickness is a known marker for early atherosclerosis and its progression. The first clinical manifestation of CVD often arises in a stage of well-advanced atherosclerosis. The importance of NAFLD and its relationship with MetS is now increasingly recognized, as the recent studies suggest that NAFLD is linked to increased cardiovascular risk independent of the broad spectrum of risk factors of MetS.7–10 In recent years, case-control studies have shown a relationship between NAFLD and the presence of early manifestations of atherosclerosis indicated by CIMT measurement.11,12

MATERIALS AND METHODS

All individuals aged ≥18 to ≤65 years of either sex with NAFLD diagnosed ultrasonographically13 and MetS diagnosed as per IDF (2005)14 criteria were included in the study as cases. In this study, carotid subclinical atherosclerosis was defined as a mean CIMT ≥0.9 mm or the existence of a carotid plaque.15 Ankle-brachial pressure index was defined as the ratio of noninvasively assessed ankle to brachial (arm) systolic blood pressure. The ratio of the ankle and brachial artery pressure was 1.00–1.40 in normal individuals. Ankle-brachial pressure index values of 0.91–0.99 were considered “borderline,” and those ≤0.90 were abnormal and diagnostic of peripheral artery disease (PAD).16 Two-dimensional echocardiography (2D-ECHO Sonosite Machine) was used to assess LV systolic and diastolic function.17

RESULTS

Characteristics of study subjects: 120 cases were included in the study. They were divided into three groups: 42 NAFLD, 40 MetS, and 38 combined NAFLD with MetS. Majority (57.5%) of patients were in the age group of 30–39 years. Nonalcoholic fatty liver disease was found more in males (35.8%) as compared to females (30.8%) while male to female ratio was equal in MetS group.

The mean age of patients with NAFLD was 37.92 ± 15.66 years and for controls was 35.03 ± 15.50 years (p = 0.14). Patients with NAFLD had a higher elevated systolic blood pressure than normal subjects (p = 0.0001). In patients with NAFLD, serum TG (p = 0.0002), TC (p = 0.0001), high density lipoprotein

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cholesterol (HDL-C) ($p = 0.0001$), LDL-C ($p = 0.0001$), and VLDL-C ($p = 0.0001$) were significantly higher. The mean BMI in patients with NAFLD was $26.01 \pm 3.42$ kg/m$^2$ and in the control group was $25.28 \pm 2.12$ kg/m$^2$; but this difference was not statistically significant ($p = 0.06$). Patients with NAFLD had a greater mean CIMT ($0.93 \pm 0.34$ mm) than control subjects ($0.81 \pm 0.36$ mm; $p = 0.02$). The mean ABI value in patients with NAFLD was $0.95 \pm 0.34$ and in the control group $1.07 \pm 0.24$; $p = 0.0001$ (Table 1).

The mean age of patients with MetS was $35.65 \pm 10.78$ years ($p = 0.97$). Patients with MetS had a significantly higher elevated blood pressure ($p = 0.0001$). The mean BMI in patients with MetS was $26.42 \pm 2.02$ kg/m$^2$ and in the control group was $25.28 \pm 2.12$ kg/m$^2$; $p = 0.0001$. Mean FPG was significantly higher ($p = 0.001$) in patients with MetS ($107.20 \pm 13.46$ mg/dL). In patients with MetS, serum TG ($p = 0.0001$), TC ($p = 0.0001$), and LDL-C ($p = 0.001$) were significantly higher but HDL-C was significantly lower ($p = 0.0001$) than in control subjects. Patients with MetS had a greater mean CIMT ($0.90 \pm 0.44$ mm) than control subjects ($0.81 \pm 0.36$ mm; $p = 0.08$). The mean ABI value in patients with MetS was $0.99 \pm 0.02$ and in the control group was $1.07 \pm 0.24$; $p = 0.02$ (Table 2).

It was found that increased CIMT ($p = 0.0001$) and low ABI ($p = 0.0002$) were significantly associated with NAFLD (Tables 3 and 4). Our findings also indicate that LV systolic ($p = 0.04$) and diastolic function ($p = 0.03$) were significantly impaired in NAFLD patients (Tables 5 and 6).

Similarly, MetS was significantly associated with increased CIMT ($p = 0.0001$) and low ABI ($p = 0.02$) while systolic function was not significantly ($p = 0.75$) impaired in patients with MetS but LV diastolic function was significantly ($p = 0.04$) impaired in patients with MetS.

In Spearman’s correlation analysis, there was a strong positive correlation between CIMT and TG ($r = 0.46, p = 0.0001$), TC ($r = 0.47, p = 0.0001$), LDL-C ($r = 0.46, p = 0.0001$), VLDL-C ($r = 0.26, p = 0.001$), BMI ($r = 0.21, p = 0.003$), and age ($r = 0.22, p = 0.002$), and there was statistically nonsignificant negative correlation between HDL-C and CIMT ($r = -0.13, p = 0.05$).

**Discussion**

There was a slightly greater preponderance of NAFLD in males as compared to females while male to female ratio was equal in MetS. Similarly, in a study conducted by Singh et al., it was shown that fatty liver was seen more commonly in males (26.9%) than in females (13.8%). Nonalcoholic fatty liver disease was documented in 66.7% of participants. In an observational study by Kim et al., prevalence of NAFLD was 72.7%.

Previous studies have demonstrated a strong relationship between CIMT and the risk of myocardial and cerebral infarction. Carotid intima-media thickness can identify patients at high risk for coronary artery disease. Many studies have evaluated the correlation between atherosclerotic risk factors and CIMT. Carotid intima-media thickness increases with age, gender, hypertension, diabetes mellitus, and hyperlipidemia. Patients with NAFLD had a significantly greater mean CIMT ($0.93 \pm 0.34$ mm) than control subjects ($0.81 \pm 0.36$ mm; $p = 0.02$). Similar results were found in a study conducted by Mohammadi et al. They observed that CIMT ($0.80 \pm 0.14$ mm) in patients with NAFLD was significantly higher ($p = 0.001$) than in gender and age-matched control group ($0.58 \pm 0.15$ mm). It was shown that NAFLD and MetS were significantly ($p = 0.0002, p = 0.02$).

### Table 1: Clinical characteristics of NAFLD subjects and controls

<table>
<thead>
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<th>Control (n=90)</th>
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<td>Age (years)</td>
<td>Mean 37.92</td>
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<td></td>
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<td>15.50</td>
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<tr>
<td>SBP (mm Hg)</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>SD 16.30</td>
<td>17.66</td>
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<tr>
<td>WC (cm)</td>
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<td></td>
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<tr>
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<td>SD 30.56</td>
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<td>SD 1.22</td>
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<td>TG (mg/dL)</td>
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<td>SD 29.6</td>
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<td></td>
<td>SD 27.08</td>
<td>15.84</td>
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</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>Mean 104.50</td>
<td>88.08</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>SD 42.36</td>
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<tr>
<td>VLDL-C (mg/dL)</td>
<td>Mean 37.02</td>
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<tr>
<td></td>
<td>SD 13.26</td>
<td>6.4</td>
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<td>CIMT (mm)</td>
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<td>0.02</td>
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<td></td>
<td>SD 0.34</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>ABI</td>
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</tr>
<tr>
<td></td>
<td>SD 0.34</td>
<td>0.24</td>
<td></td>
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</tbody>
</table>

SBP, Systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; PPG, post prandial glucose; A1C, haemoglobin glycosylated; HDL-C, high density lipoprotein cholesterol; FPG, fasting plasma glucose; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.
Atherosclerosis and Associated Cardiovascular Risk Factors

There was a strong positive correlation between CIMT and TG (r = 0.46, p = 0.0001), TC (r = 0.47, p = 0.0001), LDL-C (r = 0.46, p = 0.0001), VLDL-C (r = 0.26, p = 0.0001), BMI (r = 0.21, p = 0.003), and age (r = 0.22, p = 0.002), respectively associated with low ABI. Similar result was also found in a cross-sectional study by Zou et al.25 in which their analyses showed that patients with NAFLD had a significantly higher prevalence of PAD compared with those without NAFLD (12.8 vs 7.8%).

Left ventricular diastolic and systolic function were significantly (p = 0.03, p = 0.04, respectively) impaired in NAFLD patients. While LV systolic function was not significantly (p = 0.75) impaired in MetS but LV diastolic function was significantly (p = 0.04) impaired in MetS. In a study on 180 obese adolescents and 68 healthy controls conducted by Sert et al.26 it was observed that the NAFLD group had normal LV systolic function, impaired diastolic function, and altered global systolic and diastolic myocardial performance.

There was a strong positive correlation between CIMT and TG (r = 0.46, p = 0.0001), TC (r = 0.47, p = 0.0001), LDL-C (r = 0.46, p = 0.0001), VLDL-C (r = 0.26, p = 0.0001), BMI (r = 0.21, p = 0.003), and age (r = 0.22, p = 0.002), and there was statistically nonsignificant

### Table 2: Clinical characteristics of MetS subjects and controls

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<th>MetS</th>
<th>Control</th>
<th>p</th>
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<td>n = 90</td>
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<td>0.97</td>
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<td>SD</td>
<td>10.76</td>
<td>15.5</td>
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<tr>
<td>SBP (mm Hg) Mean</td>
<td>131.70</td>
<td>118.31</td>
<td>0.0001</td>
</tr>
<tr>
<td>SD</td>
<td>15.12</td>
<td>18.9</td>
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<tr>
<td>DBP (mm Hg) Mean</td>
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<td>77.51</td>
<td>0.0001</td>
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<td>SD</td>
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<td>17.66</td>
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<td>WC (cm) Mean</td>
<td>92.53</td>
<td>88.64</td>
<td>0.0001</td>
</tr>
<tr>
<td>SD</td>
<td>6.96</td>
<td>9.10</td>
<td></td>
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<tr>
<td>Weight (kg) Mean</td>
<td>74.10</td>
<td>70.44</td>
<td>0.02</td>
</tr>
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<td>SD</td>
<td>12.20</td>
<td>12.26</td>
<td></td>
</tr>
<tr>
<td>Height (cm) Mean</td>
<td>1.67</td>
<td>1.67</td>
<td>0.98</td>
</tr>
<tr>
<td>SD</td>
<td>0.16</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²) Mean</td>
<td>26.42</td>
<td>25.28</td>
<td>0.0001</td>
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<tr>
<td>SD</td>
<td>2.02</td>
<td>2.12</td>
<td></td>
</tr>
<tr>
<td>FPG (mg/dL) Mean</td>
<td>107.20</td>
<td>100.02</td>
<td>0.0006</td>
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<tr>
<td>SD</td>
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<td>20.44</td>
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<tr>
<td>PPG (mg/dL) Mean</td>
<td>152.73</td>
<td>123.79</td>
<td>0.0001</td>
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<td>26.72</td>
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<tr>
<td>A1C Mean</td>
<td>5.75</td>
<td>5.65</td>
<td>0.73</td>
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<tr>
<td>SD</td>
<td>0.56</td>
<td>0.86</td>
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<td>TG (mg/dL) Mean</td>
<td>159.98</td>
<td>124.76</td>
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<td>SD</td>
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<td>TC (mg/dL) Mean</td>
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<td>158.53</td>
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<td>SD</td>
<td>16.22</td>
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<tr>
<td>HDL-C (mg/dL) Mean</td>
<td>39.18</td>
<td>46.94</td>
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<td>SD</td>
<td>6.86</td>
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<tr>
<td>LDL-C (mg/dL) Mean</td>
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<tr>
<td>SD</td>
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<tr>
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<td>SD</td>
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<td>CIMT (mm) Mean</td>
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<td>0.81</td>
<td>0.08</td>
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<tr>
<td>ABI Mean</td>
<td>0.99</td>
<td>1.07</td>
<td>0.02</td>
</tr>
<tr>
<td>SD</td>
<td>0.32</td>
<td>0.24</td>
<td></td>
</tr>
</tbody>
</table>

SBP: Systolic blood pressure; DBP: diastolic blood pressure; WC: waist circumference; A1C: haemoglobin glycosylated; HDL-C: high density lipoprotein cholesterol; FPG: fasting plasma glucose; LDL-C: low density lipoprotein cholesterol; VLDL-C: very low density lipoprotein cholesterol
negative correlation between HDL-C and CIMT ($r = -0.13, p = 0.05$). These results were similar in a study conducted by Mohammadi et al. They observed that there was a strong positive correlation between CIMT and TG ($r = 0.18, p = 0.0001$), TC ($r = 0.19, p = 0.0001$), BMI ($r = 0.39, p = 0.0001$), and age ($r = 0.44, p = 0.0001$), and there was a strong negative correlation between HDL-C and CIMT ($r = -0.32, p = 0.0001$).

**Limitations of the Study**
Ultrasound was used to assess the presence of NAFLD but liver biopsy, which is an invasive procedure, was not performed. This study showed that NAFLD is independently associated with an increased CIMT, however, major adverse cardiovascular events could not be assessed due to time-bound period of study.

**Conclusions**
Prevalence of NAFLD was found to be higher in male patients. Carotid intima-media thickness had significant positive correlation with lipid

---

**Table 3: Association of NAFLD with CIMT**

<table>
<thead>
<tr>
<th></th>
<th>CIMT</th>
<th>Total</th>
<th>$p$</th>
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<tbody>
<tr>
<td></td>
<td>&lt;0.9 mm</td>
<td>≥0.9 mm</td>
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<tr>
<td>NAFLD (n) (%)</td>
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<td>22</td>
<td>42</td>
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<tr>
<td>Control (n) (%)</td>
<td>76</td>
<td>14</td>
<td>90</td>
</tr>
<tr>
<td>Total (n) (%)</td>
<td>96</td>
<td>36</td>
<td>132</td>
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**Table 4: Association of NAFLD with ABI**

<table>
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<tr>
<td></td>
<td>1.0–1.4</td>
<td>0.91–0.99</td>
<td>≤0.9</td>
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<td>NAFLD (n) (%)</td>
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<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Control (n) (%)</td>
<td>(33.33%)</td>
<td>(23.81%)</td>
<td>(42.86%)</td>
</tr>
<tr>
<td>Total (n) (%)</td>
<td>74</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>(56.1%)</td>
<td>(21.2%)</td>
<td>(22.7%)</td>
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</table>

**Table 5: Association of NAFLD with LVEF**

<table>
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<td>55–65%</td>
<td>45–54%</td>
<td>30–44%</td>
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<td>NAFLD (n) (%)</td>
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<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Control (n) (%)</td>
<td>(42.9%)</td>
<td>(33.3%)</td>
<td>(23.8%)</td>
</tr>
<tr>
<td>Total (n) (%)</td>
<td>75</td>
<td>38</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>(56.8%)</td>
<td>(28.8%)</td>
<td>(14.4%)</td>
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**Table 6: Association of NAFLD with LVDD**

<table>
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<td>Grade I</td>
<td>Grade II</td>
<td></td>
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<td>NAFLD (n) (%)</td>
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<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Control (n) (%)</td>
<td>(28.57%)</td>
<td>(47.62%)</td>
<td>(23.81%)</td>
</tr>
<tr>
<td>Total (n) (%)</td>
<td>59</td>
<td>45</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>(44.7%)</td>
<td>(34.1%)</td>
<td>(21.2%)</td>
</tr>
</tbody>
</table>
parameters, that is, TG, TC, LDL-C, and VLDL-C, but had nonsignificant negative correlation with HDL-C. It was also found that advancing age had significant positive correlation with CIMT. There was significant association of NAFLD with increased CIMT and low ABI. Metabolic syndrome also had significant association with both increased CIMT and low ABI. Left ventricular systolic and diastolic functions were significantly impaired in patients with NAFLD while LV systolic function was not affected in MetS but LV diastolic function was significantly impaired in MetS. The present study showed the significant impact of NAFLD and MetS on subclinical atherosclerosis, and suggests that individuals with NAFLD alone and with MetS should be more closely monitored and might be the target for intervention.

REFERENCES

12. Kim JH, Kim SY, Jung ES, et al. Carotid intima-media thickness is increased not only in non-alcoholic fatty liver disease patients but also in alcoholic fatty liver patients. Digestion 2011;84(2):149–155.
Improving the Quality of Life in the Management of Allergic Rhinitis: New Perspective on Cetirizine

Vikas K Agrawal1, Suheb Patel2, Anup U Petare3*, Krishna C Veligandla4
Received: 18 October 2021; Revised: 01 February 2022; Accepted: 18 February 2022

Abstract
Background: Allergic rhinitis (AR) is associated with disturbed sleep and subsequent functioning, and an impaired quality of life (QoL). The symptoms of AR exhibit prominent circadian variations, with symptoms being more common at the night-time or early morning. Addressing these allergy-related sleep issues, impaired QoL, and circadian variation in symptoms is important from the patient perspective and should be considered in the management of AR.

Objective: To review the efficacy of cetirizine, a second-generation antihistamine and selective H1-receptor antagonist, in relation to improvement in the QoL of the patients, addressing the sleep disturbances and circadian variations in the symptoms of AR in clinical practice, and establishing its role as a contemporary antihistamine for the management of AR compared to newer antihistamines.

Methods: Systematic literature review of the databases such as PubMed/MEDLINE, Google Scholar, and the Cochrane Central Register of Controlled Trials from 1990 to 2020.

Results: The symptoms of AR exhibited a circadian variation, with symptoms being worse during the night and early morning. Patients with AR encountered several sleep-related symptoms, including poor sleep quality, daytime somnolence, fatigue, and impaired productivity and QoL. Impaired QoL in AR was related to the disease severity. Administration of cetirizine at bedtime provides effective control of sleep impairment and symptoms of AR, besides improving the QoL. The efficacy of cetirizine has been demonstrated to be superior or comparable to the newer second-generation antihistamines. Cetirizine exhibits a tolerability profile comparable to the newer antihistamines.

Conclusion: With long years of clinical experience and a good tolerability profile, cetirizine represents a valuable therapeutic option for the management of AR, even 30 years after its introduction. Cetirizine is included in the National List of Essential Medicines of India for the management of allergic disorders in view of its established efficacy and safety profile as well as being a cost-effective option.

Journal of the Association of Physicians of India (2022): 10.5005/japi-11001-0026

Introduction

Allergic rhinitis (AR), a chronic inflammatory condition, is often undetected in the primary medical care.1,2 Globally, AR is reported to affect about 10–25% of the population, representing about 55% of all the allergies. Approximately 20–30% of the Indian population are reported to suffer from AR.3 Clinically, AR is characterized by nasal symptoms such as congestion, nasal itch, rhinorrhea, and sneezing, along with ocular symptoms such as itching/redness and/or lacrimation.4 AR adversely impacts the general well-being and quality of life (QoL) of the patients, affecting sleep, lifestyle, and work performance.4,5 The economic consequences of AR include direct costs related to the treatment and indirect costs associated with absence from work as well as loss of productivity at school and work.5

The first-generation H1-receptor antagonists (antihistamines) were developed as the primary medical treatment for AR. Their sedative and anticholinergic adverse effects led to the evolution of the second-generation antihistamines.6,7 By virtue of their poor penetration into the blood-brain barrier, the second-generation antihistamines have fewer sedative effects and are thus recommended by various guidelines as the first choice for managing AR (Table 1).1,4,6,7

Cetirizine, with its potent and selective blocking activity at the H1 receptors, a rapid onset and long duration of action, documented efficacy against allergic symptoms, cost-effectiveness, and once-daily dosing, is a preferred antihistamine for managing AR. Besides, it is devoid of cardiac safety concerns, has minimal/no sedative activity, and thus is not associated with cognitive or psychomotor impairment.5

This review aims to validate that despite 30-year of clinical usage, cetirizine remains a contemporary antihistamine, with established advantages over the first-generation as well as newer antihistamines, and improves the QoL. The review also provides an insight into the circadian rhythm of AR symptoms and its impact on sleep and QoL, which can be managed by tailoring the administration of cetirizine at bedtime.

Methods
A qualitative systematic review was conducted to identify published articles on comparing the efficacy of cetirizine with the first-generation as well as newer antihistamines, its role in improving QoL, addressing the circadian rhythm of AR symptoms, and improving the sleep-related symptoms of AR. A systematic literature search was conducted on PubMed/MEDLINE, Google Scholar, and

Table 1: Guideline recommendations on second-generation antihistamines6,7

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Recommendations</th>
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<tr>
<td>ARIA</td>
<td>Second-generation antihistamines as first-line therapy for intermittent and persistent AR, regardless of the disease severity</td>
</tr>
<tr>
<td>EAACI/GA2LEN/EDF/WAO</td>
<td>Second-generation antihistamines as first-line treatment, considering not only efficacy but also safety and QoL of patients</td>
</tr>
<tr>
<td>AAO-HNSF clinical practice guideline</td>
<td>Oral second-generation/less sedating antihistamines should be recommended in patients with AR and primary complaints of sneezing and itching</td>
</tr>
</tbody>
</table>

ARIA, Allergic Rhinitis and its Impact on Asthma; EAACI/GA2LEN/EDF/WAO, The European Academy of Allergology and Clinical Immunology/the Global Allergy and Asthma European Network/the European Dermatology Forum/the World Allergy Organization; AAO-HNSF, American Academy of Otolaryngology—Head and Neck Surgery Foundation; AR, Allergic rhinitis; QoL, Quality of life

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Management of Allergic Rhinitis: New Perspectives on Cetirizine

the Cochrane Central Register of Controlled Trials from 1990 to 2020. The following search terms were used: “Cetirizine,” “second-generation antihistamines,” “antihistamines,” “allergic rhinitis,” “sleep impairment,” and “quality of life.” The search terms were kept broad to encompass all the possibilities for applicable studies. Some records were also retrieved via cross-references from the published papers.

Findings

Circadian Variation of Allergic Rhinitis Symptoms and Its Impact on Sleep and Quality of Life

The symptoms of AR worsen at night and in the early morning, leading to poor night-time sleep and impaired QoL during daytime.6,5 This circadian variation in the symptoms of AR has been shown to be controlled using night-time dosing of antihistamines.6,8 Impact of Allergic Rhinitis on Sleep and the Quality of Life

Several studies have noted sleep impairment and daytime somnolence in patients with AR (Table 2), causing an impairment of QoL in patients with AR.10–13 Findings of a systematic review: A systematic review and meta-analysis of observational studies involving 19,444,043 patients with AR examined the associations of AR with sleep duration and impairment. AR was associated with higher risk of nocturnal dysfunctions, including insomnia, nocturnal enuresis, restless sleep, sleep-disordered breathing, obstructive sleep apnea, and snoring as well as with daytime dysfunction, including difficulty waking up, daytime sleepiness, morning headache, and the use of sleep medications.14

Sleep problems in perennial allergic rhinitis: In patients with perennial AR, a high sleep-related burden, leading to disruption of day-to-day activities is related to the symptoms such as stuffy/runny nose or itching of the nose/palate and other head-symptoms. The nature of sleep disturbances reported by patients with perennial allergy are presented in Table 3 and Figure 1. Addressing these allergy-related sleep issues is important from the patient perspective and should be considered in the treatment.15

Impact of sleep disorders in allergic rhinitis: Sleep disorders associated with AR are often under-reported.12 Sleep disorders result in poor sleep quality, daytime somnolence, fatigue, impaired productivity, and an increased risk of associated diseases. A direct correlation has been observed between the degree of sleep disturbance and disease severity.16

Mechanism of Sleep Impairment in Allergic Rhinitis

In patients with AR, the allergen causes a cascade of events leading to mucus secretion, inflammation, vascular permeability, and nasal disease severity.16

Table 2: Effect of allergic rhinitis on night-time sleep and daytime sleepiness

<table>
<thead>
<tr>
<th>Investigator(s)</th>
<th>Study design and patients</th>
<th>Assessments</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stuck et al., 200410</td>
<td>Prospective, controlled, comparative trial involving 25 patients with SAR and 25; healthy controls</td>
<td>Epworth sleepiness scale questionnaire; polysomnography</td>
<td>Increased daytime sleepiness and impairment of QoL, correlated with the severity of the disease</td>
</tr>
<tr>
<td>Colas et al., 201211 (SOMNIAAR study)</td>
<td>A prospective, observational, multicenter survey of 2,275 patients with AR</td>
<td>TSS, specific QOL (RQLQ), sleep quality (Pittsburgh scale), and diurnal somnolence using a scale based on Epworth’s</td>
<td>Sleep quality was worse in moderate-to-severe AR. Nasal obstruction and deterioration in RQLQ were associated with poorer sleep quality</td>
</tr>
<tr>
<td>Leger et al., 201712</td>
<td>A prospective, cross-sectional, observational study in 1750 participants (children and adults) with HDM allergy.</td>
<td>Self-administered questionnaires to assess sleep: ESS, ISI, and a modified version of the HD-42 sleep disorder questionnaire</td>
<td>Sleep disorders (poor sleep quality, snoring, nocturnal awakening, and difficulty in falling to sleep) were a major reason to seek physician consultation</td>
</tr>
<tr>
<td>Meltzer et al., 200913</td>
<td>Pediatric Allergies in America survey involving 500 children with HCP-diagnosed nasal allergies and 504 children without nasal allergies</td>
<td>A survey amongst HCPs and parents of young and older children (aged 10–17 years)</td>
<td>An association between nasal allergy symptoms and sleep disruption in children suffering from AR was reported</td>
</tr>
</tbody>
</table>

AR, Allergic rhinitis; SAR, Seasonal allergic rhinitis; TSS, Total Symptoms Score; QoL, Quality of life; RQLQ, Rhinitis Quality of Life Questionnaire; HDM, House dust mites; ESS, Epworth Sleepiness Scale; ISI, Insomnia Severity Index; HD-42, Hotel Dieu-42; HCP, Healthcare provider; SOMNIAAR, Effect of allergic rhinitis and its treatment on sleep

Table 3: Sleep disturbances in patients with perennial allergy (n = 511)15

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Observations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects using OTC medications as sleep aids</td>
<td>50.3</td>
</tr>
<tr>
<td>Subjects reporting sleep issues</td>
<td>66.1</td>
</tr>
<tr>
<td>Subjects reporting difficulties in falling asleep at least most of the time</td>
<td>66</td>
</tr>
<tr>
<td>Subjects who were rarely or never able to get back to sleep after waking in the night</td>
<td>40.8</td>
</tr>
<tr>
<td>Subjects reporting difficulties waking in the morning most or all of the time</td>
<td>69.2</td>
</tr>
<tr>
<td>Subjects with sleep problems reported disturbances in daily functioning</td>
<td>85.5–95</td>
</tr>
<tr>
<td>Average work absenteeism over the past 7 days</td>
<td>12</td>
</tr>
<tr>
<td>Impairment while working</td>
<td>46.9</td>
</tr>
<tr>
<td>Activity impairment (nonwork-related) due to health</td>
<td>47.1</td>
</tr>
</tbody>
</table>

*Commonly used OTC medications: Oral antihistamines (59.1%), decongestants (52.1%), corticosteroids nasal and oral sprays/drops (47.5%), and eye drops (27.6%). OTC, Over-the-counter
congestion and obstruction, with increased airway resistance during the inspiratory effort. Impaired QoL in patients with AR is attributed to nasal obstruction, which contributes to sleep-disordered breathing and impaired sleep (Fig. 2). The chemical mediators involved in AR have been reported to affect the sleep pattern. Stimulation of H1 receptors by histamine affects the regulation of arousal, cognition, and sleep-wake pattern. Besides, the changes in cytokine levels also correlate with an increased latency to rapid eye movement sleep, decreased time spent in rapid eye movement sleep, and decreased latency to sleep onset in patients with AR. The levels of interleukin (IL)—1b, IL–4, and IL–10 were increased in patients with AR and correlated with disturbed sleep.

Cetirizine in the Management of Allergic Rhinitis

Cetirizine is one of the forerunners among the second-generation antihistamines formulated to selectively inhibit the H1 receptor without causing CNS depression. It has a more favorable pharmacological profile, is well-tolerated, and is at least equally or more efficacious in attenuating/inhibiting the nasal and ocular symptoms and improving the QoL in patients with AR as compared to majority of the other second-generation antihistamines. Moreover, cetirizine is often employed as the main comparator active drug in the majority of clinical trials examining the effect of second-generation antihistamines in patients with AR. Effect of cetirizine on diurnal variations of symptoms of allergic rhinitis: Considering the diurnal variations of seasonal AR symptom, a post hoc analysis of a clinical study with cetirizine administered as a morning or bedtime dose was undertaken. Cetirizine improved the symptom severity, especially overnight and in the early morning, regardless of the dosing schedule. There was a numerically greater reduction in the total symptom severity complex assessed in the morning (a reflection of overnight and early morning symptoms) when cetirizine 10 mg was administered at bedtime compared to the previous morning. Thus, an intentional administration of the antihistaminic at bedtime will help in the amelioration of insomnia as well as allergy symptoms.

Effect of cetirizine on nasal obstruction in allergic rhinitis: It is noteworthy that not all antihistamines are very effective in reducing nasal obstruction, an important symptom associated with sleep impairment. Cetirizine has been shown to improve congestion to some degree.

Safety Aspects of Cetirizine

Cetirizine is well tolerated, with adverse effects being mild-to-moderate in intensity. It is devoid of potential for cardiotoxicity. Sedation: The incidence of somnolence with cetirizine is dose-related and is similar to that seen with other second-generation antihistamines. The slight increase in sedation seen at higher doses can be advantageously exploited by timing the administration of the drug at bedtime objective assessments have confirmed the lack of psychomotor impairments with cetirizine. Use in pregnant and lactating women: There have been no reports on the harmful effects of cetirizine in pregnant or lactating women. In a cohort study involving 196 pregnant women, an exposure to cetirizine in the first trimester of pregnancy was not associated with an increased risk of abortions or fetal malformations. Cetirizine is classified as a category B drug as per the Food and Drug Administration pregnancy category (i.e., not known to cause harm to an animal fetus and no human studies available). Other second-generation antihistamines, such as desloratadine and fexofenadine are in classified as category C (i.e., harmful to an
Management of Allergic Rhinitis: New Perspectives on Cetirizine

Table 4: Impact of cetirizine on sleep quality in patients with allergic rhinitis

<table>
<thead>
<tr>
<th>Investigator(s)</th>
<th>Study design and patients</th>
<th>Interventions</th>
<th>Study outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al., 2019</td>
<td>A prospective, double-blind, placebo-controlled, randomized, clinical study in 212 children with PAR</td>
<td>2 x $10^7$ CFU of Lactobacillus paracasei (LP-33) OR Cetirizine, 2.5 or 5 mg once daily for 4 weeks</td>
<td>Significant improvement in AR symptoms and sleeping difficulties</td>
</tr>
<tr>
<td>Murray et al., 2002</td>
<td>Double-blind, placebo-controlled, parallel-group study in 865 adult patients with SAR</td>
<td>Cetirizine or placebo for 2 weeks</td>
<td>Treatment with cetirizine resulted in greater ($p &lt; 0.001$) improvement in the overall RQLQ and individual domain scores (activities, sleep, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional difficulties) compared to placebo</td>
</tr>
<tr>
<td>Malizia et al., 2018</td>
<td>Single-center, open-label, randomized controlled study involving 128 children with PAR</td>
<td>Beclomethasone dipropionate nasal spray, 100 μg per nostril OR Cetirizine, 10 mg once daily for 21 days</td>
<td>An improvement in sleep quality was noted with cetirizine treatment (mean change from baseline in PSQI total score: −0.19)</td>
</tr>
<tr>
<td>Noonan et al., 2003</td>
<td>A randomized, placebo-controlled, parallel-group study involving 611 patients with SAR</td>
<td>Cetirizine, 10 mg; OR placebo once-daily for 2 weeks</td>
<td>Patients treated with cetirizine achieved clinically meaningful improvements in 7 domains of HRQL: activities, practical problems, symptom distress, sleep problems, and emotional difficulties</td>
</tr>
</tbody>
</table>

PAR, Perennial allergic rhinitis; CFU, Colony forming units; PSQI, Pittsburgh sleep quality index; HRQL, Health-related quality of life; AR, Allergic rhinitis; SAR, Seasonal allergic rhinitis; RQLQ, Rhinoconjunctivitis quality of life questionnaire

animal fetus and with unknown effects in humans. Cetirizine, given at the minimum possible dose and for the shortest possible time, has been recommended as the antihistamine of choice in breastfeeding women by the British Society for Allergy and Clinical Immunology.

Use in children: The early treatment of the atopic child (ETAC) study was one of the longest clinical trials with any antihistamine enrolling children aged 18–24 months. In this study, long-term treatment with cetirizine (>18 months) had no adverse effects on the natural development milestones, and neurological and behavioral events. The proportion of treatment-emergent adverse events was similar between the cetirizine and placebo groups.

Cetirizine: An Essential Drug in India

Cetirizine is included in the National List of Essential Medicines of India, a list designed for India in line with the World Health Organization essential drug list. This is based on the efficacy, safety, favorable risk/benefit ratio, cost-effectiveness, ability to be used in population at large in India and its inclusion in the current recommendations for the disease.

Conclusion

Cetirizine, a potent second-generation H1 antihistamine, has been demonstrated to be clinically efficacious for managing moderate-to-severe AR in pediatric, adolescent, and adult patients, including in patients refractory to other antihistamines. It improves the sleep disturbances seen in AR and improves the QoL. It has a rapid onset of action, and its longer half-life allows for once-daily dosing. Cetirizine is the most widely used antihistamine worldwide and is recommended by almost all the evidence-based guidelines. It is well-tolerated with a low incidence of sedative effects. Administration of the drug at night-time can improve the sleep disturbances associated with AR and address the circadian variations of AR symptoms. Therefore, even after 30 years, cetirizine is still considered to be the first-choice antihistamine for the management of AR.
two randomized trials. Allergy Rhinol (Providence) 2018;9:2152656718783630.
116 not out: A Case of long COVID Syndrome

Nirmal B Taparia*
Received: 08 January 2022; Accepted: 25 January 2022

ABSTRACT
COVID-19 pandemic has caused havoc worldwide with huge health and financial losses to patients and relatives. It has wide clinical spectrum with acute respiratory distress syndrome (ARDS) as its primary manifestation. This also includes secondary infections developing post-COVID. Overall 10–15% of patients develop severe COVID and 5% become critically ill. Usually it takes 2–4 weeks to resolve. But few patients take unusually longer period to recover due to severe and serious complications. Some of them require prolonged ventilatory support and home oxygen and recover gradually with very high morbidity rates.

We report a case of a 35-year-old male patient who was COVID-19 positive and took a long period of 116 days in-hospital stay to recover from illness in spite of having all possible complications.

INTRODUCTION
COVID-19 causes respiratory infection and distress in patients who are moderately to severely affected with the disease. There is acute lung injury followed by ARDS in such patients. Cytokine storm causes severe hypoxemia with tachypnea, tachycardia, fever, body ache, and multi-organ involvement in such patients. They require very high oxygen support with some requiring invasive ventilation to support respiration. Mortality rates among such ventilated patients are extremely high. Those who survive may develop complications like secondary infections with bacteria as well as fungus, pulmonary embolism, pneumaticthorax, and lung fibrosis. Not all patients develop all complications but these add to the days of recovery and increased mortality. Our patient presented with moderate COVID-19 computerized tomography (CT) score of 18 on admission (Fig. 1) which progressed to severe illness and later developed all respiratory complications over the course of illness. The chances of survival with so many complications with such a long duration are very bleak. But this patient sustained all these adversities and survived.

CASE DESCRIPTION
A 35-year-old male patient who came to our hospital for acute febrile illness was detected as having COVID-19 on reverse transcriptase polymerase chain reaction (RT-PCR). This gentleman came on 7th May 2021 to our COVID casualty with a short history of fever, cough, dyspnea, and body ache since 5 days with a positive COVID-19 report. He was admitted and treatment started according to COVID guidelines.1 His oxygen saturation on room air was 82% on admission. Oxygen with non-rebreather mask (NRBM) was given along with steroids 1 mg/kg of solumedrol, inj Remdesiver 100 mg iv od, inj low molecular weight heparin in prophylactic dose of 0.4 cc s/c od, multivitamins, zinc, IV antibiotic ceftriaxone 1 gm iv bd, along with iv fluids and covid awakening repositioning/ proning protocol (CARP) protocol. But he quickly worsened and his oxygen requirement gradually increased to above 10 L on NRBM, so he was shifted to intensive care unit (ICU) and high flow nasal oxygen (HFNO) was applied. Initial high resolution computerized tomography (HRCT) scan showed COVID pneumonia with C-reactive protein of 271.6 and D-dimer of 1213, IL6 of 456 on admission, other routine investigations like complete blood count, renal function test, liver function test, 2D-ECHO, and procalcitonin (PCT) being normal. After 3–4 days of maintaining oxygenation above 94% with an respiratory rate (RR) of 30–35 and increasing oxygen requirement he started to worsen again. Bilevel positive airway pressure (BIPAP) ventilation was applied, but improvement was marginal. His second HRCT with pulmonary angiography revealed bilateral pneumonia with ARDS, a CT score of 23 with pulmonary embolus (PE) in anterior segment of right lung (Fig. 2). Patient was in cytokine storm and inj Toculizumab 400 mg iv was given on day 12 of admission after PCT came normal and inflammatory markers were on the rise. Heparin dose was increased to therapeutic dosage of 0.4 cc sc bd. Post-Toculizumab blood culture, serum PCT, and sr Galactomannan levels were sent and all came negative. He somewhat settled in a few days when on day 17 of admission he developed surgical emphysema around his neck. X-ray chest showed right pneumothorax and pneumomediastinum. Intercostal drain (ICD) was inserted and conservative treatment was continued with a close watch for worsening (Fig. 3). Oxygen requirement was still high but inflammatory markers were settling down. Patient was on 30 L of oxygen on noninvasive ventilation with a SpO2 of around 88–92%.

After 18 days of COVID stay his RT-PCR was repeated which came negative and patient was shifted to post-COVID isolation ICU. Patient was still tachypneic with RR of 35–40 and saturation above 90%. Over the next few days, we attempted to decrease oxygen below 15 L. But patient got fatigued, developed type I & type II respiratory failure with PaO2 < 60 and PaCO2 > 60. Decision to electively intubate and ventilate was taken.

Fig. 1: CT thorax with ARDS

Fig. 2: CT pulmonary angio right artery thrombus

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Much is still unknown about how COVID-19 affects people over time and more research and multiyear studies are needed to understand;③
- long-term effects of COVID-19,
- why symptoms persist or recur,
- how these health problems affect patients,
- clinical course and likelihood of full recovery,
- implication of long-term health effects on return to work.

Though protective measures continue to be important in preventing COVID-19, the best way to prevent post-COVID conditions is to prevent COVID-19 illness. For people who are eligible, getting vaccinated against COVID-19 as soon as you can is the best way to protect yourself from severe COVID-19 disease and it can also help protect those around you. Much is still unknown about how COVID-19 affects people over time and this will untangle with further research.

**Conclusion**

In spite of all the dreaded complications like cytokine storm, pulmonary embolism, B/L pneumothorax with three ICDs, prolonged ventilation with hospital-acquired serious bacterial and fungal infections, multiple weaning failures, and depression, we continued our relentless efforts for patient’s survival. Finally, we could successfully treat him through all these and discharge him in good condition after a marathon 116 days of his hospital stay. Overall a holistic approach and support system is required.

**Ethical Committee**

Consent taken.

**Conflicts of Interest**

None.

**References**

CASE REPORT

Community-acquired round Pneumonia in a 63-year-old Female

Sameer Verma1, Agam Vora2*
Received: 13 December 2021; Revised: 16 February 2022; Accepted: 10 March 2022

Abstract
Round pneumonia is a radiological manifestation of pulmonary lesion. This is found as spherical or oval-shaped radio-opacity on chest X-ray. Round pneumonia has been reported in literature uncommonly.
Round pneumonia was first time reported in the radiology literature in 1954 (Wagner et al., 1998). It was first recognized in children. In 1973, Rose and Ward reviewed 21 cases of round pneumonia in children. Radiological findings resembled pulmonary and mediastinal masses. Since then, time and again, round pneumonia has been reported in children; but, this is also found rarely in adults. There are many causes of round pneumonia in adults, for example, infectious and noninfectious. It may mimic pulmonary neoplasms due to its radiological appearance. Hence, the usual diagnostic challenge of round pneumonia is to differentiate pneumonia from bronchogenic carcinoma.
Here we present an interesting case of round pneumonia in an adult female.

Case Description
A 63-year-old female was admitted with high spiking fever, dry cough, sometimes productive of mucoid and blood-tinged sputa for 3–4 days. She also had shortness of breath since the last 4–5 days.
She reported recent travel to Gujarat, 3 days prior to her illness. She denied any significant medical problem in past. She took both her COVID-19 vaccinations more than 3 months prior to her this illness.
Her chest X-ray was performed on admission, which revealed right lower zone round opacity.
Vital signs revealed a temperature of 38°C, a pulse of 108 beats/min, a blood pressure of 110/70 mm Hg, respiratory rate of 22 breaths/min, SpO2 93–94% at room air (RA) and 97% on O2. Her physical examination revealed bilateral rales, right lower zone rales much more than left side.

Complete blood count (CBC) revealed a white blood cell count of 15.5 × 10^9/mL, hemoglobin of 13.1 g/dL, hematocrit of 39.1%, and platelet count of 201 × 10^9/mL. Erythrocyte sedimentation rate (ESR) was 90 mm/hr and C-reactive protein (CRP) 12.44 mg/dL. Her dengue nonstructural protein (NS1), peripheral smear (PS) for malaria parasite (MP), and malarial antigens were negative.
Liver function tests (LFT) and renal function tests (RFT) were normal, except moderately severe hypokalemia (potassium 3.0 mEq/L). Arterial blood gas (ABG) showed compensated metabolic acidosis and respiratory alkalosis (pH 7.46, pCO2 27, pO2 83, and HCO3 18.9).
Provisional diagnosis was round pneumonia with moderately severe leukocytosis, high ESR and CRP, and moderately severe hypokalemia.

Figure 1 shows her chest X-ray on admission.
Computed tomography (CT) scan of chest with IV contrast was also done on the day of admission (in the evening), which revealed a large irregular area of lung consolidation with air bronchogram in the superior segment of the right lower lobe. The consolidation showed homogenous postcontrast enhancement (Figs 2A and B).

After sending her blood and urine cultures, she was started empirically with piperacillin–tazobactam and clarithromycin combination during her inpatient care, assuming to cover both typical and atypical infectious etiologies of round pneumonia. Her serial chest X-rays were taken to evaluate therapeutic response of antibiotics on round pneumonia.

Her sputum examination showed pus cells >25/hpf, epithelial cells 2–4/hpf, red blood cell (RBC) and yeast cells absent.

How to cite this article: Verma S, Vora A. Community-acquired round Pneumonia in a 63-year-old Female. J Assoc Physicians India 2022;70(6):85–88.
acid-fast bacillus (AFB) was negative and Gram’s stain revealed Gram-positive cocci in pairs and short chains.

Urine for Legionella and Streptococcus pneumoniae antigens were negative. Real-time polymerase chain reaction (PCR) for Legionella, Coxiella burnetii, and SARS-CoV-2 were also negative. Blood and urine cultures were negative.

Repeat chest X-ray taken 3 days later demonstrated good resolution of round pneumonia (Fig. 3).

A specific etiology was identified after sputum culture and sensitivity report, which revealed Pseudomonas aeruginosa. Same treatment regimen was continued since the organism was sensitive to the antibiotics.

Repeat chest X-ray was taken again 4 days later (i.e., 7 days after antibiotics) demonstrated further resolution of round pneumonia (Fig. 4) and patient was asymptomatic clinically. There was no fever, cough became very occasional and no breathlessness, so patient was discharged on cephalosporin and quinolone combination.

### Discussion

Round pneumonia comprises less than 1% of all “coin lesions” seen radiologically. Whenever a coin lesion (Fig. 1) is found, lung carcinoma is the most common provisional diagnosis made by both clinicians and radiologists. CT scan of the chest, followed by further diagnostic procedures like percutaneous or bronchoscopic biopsy are needed to clinch the final diagnosis and to rule out bronchogenic carcinoma.

### Incidence

Round pneumonia occurs most commonly (more than 90%) in children (patients younger than 12 years). The mean age of patients with round pneumonia is 5 years. Because collateral airways develop by the age of 8 years, round pneumonia is uncommon after this age.

### Pathology

The reason for developing round pneumonia much more frequently in children than in adults relates to the development of collateral ventilation (interalveolar communications) and collateral airways. Collateral ventilation is thought to occur through alveolar pores of Kohn, interbronchiolar Martin’s channels, and bronchoalveolar Lambert’s channels (Fig. 5). Pores of Kohn and Lambert’s channels are absent in newborns, and they develop at around 4 years of age. When they develop, they allow air drift between the parenchymal subsegments. In adults, these allow lateral dissemination of infection throughout a lobe, leading to lobar pneumonia. In children, where these pores and channels have not developed, the limited spread of infection results in round pneumonia. This is why pneumonia in young children is often not seen as lobar pneumonia, they just form localized “round” pneumonia.

### Etiology

More than 75% of round pneumonia have no proven etiology. Causes of round pneumonia can be infectious and noninfectious/non-neoplastic.

- **Round pneumonia due to infection:** If history suggests infective etiology, the workup should include:
  - S. pneumoniae,
  - Haemophilus influenzae,
  - Q fever, and
  - Legionella micdadei.

- **Noninfectious/non-neoplastic causes of round pneumonia include:**
  - Atelectasis and

#### Clinical Features

Patients with round pneumonia due to infection often present with fever and cough for 1–2 weeks. The clinical symptoms of round pneumonia can be mild, mimicking a viral syndrome or bronchitis. Some patients with round pneumonia will have no clinical symptoms at initial presentation.

Many times cough and fever with chills for 1 week or more may be treated with antibiotics without undergoing chest radiography. This may be the reason of discrepancy between the estimated prevalence of round pneumonia and the number of cases seen by radiologists. Noninfectious/non-neoplastic
Community-acquired round Pneumonia in a 63-year-old Female

causes of round pneumonia may also be an incidental finding.

**Differential Diagnosis of round Pneumonia in Adults**

- Bacterial infection
- Pulmonary masses
- Bronchogenic carcinoma
- Pulmonary metastases
- Bronchogenic cyst
- Pleural fibroma
- Fungal infection
- Round atelectasis
- Radiation pneumonitis
- Pulmonary pseudotumor

In our case of round pneumonia, no organisms were isolated in urine or blood cultures. All serological tests were also negative. Specific etiology was identified only after sputum culture report, which revealed *P. aeruginosa*.

Final diagnosis was round pneumonia due to community-acquired *P. aeruginosa* infection. Hence, it was community-acquired pneumonia (CAP) due to *P. aeruginosa* presenting as round pneumonia in an elderly female with no risk factors or comorbidities.

*P. aeruginosa* is a common nosocomial pathogen that often causes pneumonia in hospitalized patients, most of whom have underlying medical conditions or risk factors for *Pseudomonas* infection.

*P. aeruginosa* is an established causative pathogen of hospital-acquired pneumonia (HAP) and health care-associated pneumonia (HCAP), but CAP caused by this organism in healthy individuals is rare. However, few case reports described healthy individuals developing CAP caused by *P. aeruginosa*.

Because pathogenicity of most *Pseudomonas* is based on opportunism, it is very rare in previously healthy patients. *P. aeruginosa* usually causes infections in patients who have structural changes in lungs, who are immunocompromised, or who have other specific risk factors.

Since CAP due to *P. aeruginosa* is seen in patients with structural lung diseases, chronic obstructive pulmonary disease (COPD) or cystic fibrosis; 2007 American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines recommended empirical treatment against *P. aeruginosa* in CAP patients with the following specific risk factors:

- Structural lung disease, like bronchi,
- Exacerbations of COPD requiring corticosteroid/antibiotic treatment,
- Antibiotic use before admission,
- Immunocompromised status.

Other risk factors for CAP due to *P. aeruginosa* are malnutrition, chronic heart failure, cerebrovascular disease, advanced age, and smoking.

Influenza may be a risk factor for *P. aeruginosa* infection. There are some reports of *P. aeruginosa* coinfection with influenza A (H1N1). Pathogenesis lies in influenza viral infection causing respiratory epithelial cell dysfunction through disruption of protein synthesis and induction of apoptosis, predisposing to increased bacterial adherence and invasion.

Compared to pneumonia caused by other pathogens, *P. aeruginosa* CAP may progress rapidly. *P. aeruginosa* CAP may have a poor prognosis with mortality of approximately 18–61%. Advanced age (>65 years), chronic liver disease, acute renal failure, requirement of intensive care unit (ICU) admission, and improper initial antibiotic use might be risk factors for poor prognosis. In a few cases, patients develop necrotic pneumonia with cavity formation.

Regarding treatment of *P. aeruginosa* CAP, IDSA/ATS guidelines recommend empirical treatment for those who have risk factors for *P. aeruginosa* infection. Early administration of proper antibiotics may improve the outcomes for such patients. For patients with suspected *P. aeruginosa*-caused severe pneumonia, combination antibiotic therapy should be administered within an hour. For critically ill patients admitted to the ICU, guidelines recommend use of an antipseudomonal β-lactam (piperacillin–tazobactam, cefepime, imipenem, or meropenem) plus an antipseudomonal fluoroquinolone; or the above β-lactam plus an aminoglycoside and azithromycin; or the above β-lactam plus an aminoglycoside and a fluoroquinolone. Once *P. aeruginosa* is confirmed pathogenic agent, antibiotic regimen should be adjusted to be more targeted.

Targeted therapy recommended by guidelines includes an antipseudomonal β-lactam plus an aminoglycoside or a fluoroquinolone, with the alternative being an aminoglycoside plus a fluoroquinolone. In view of rapid progression and poor outcome, patients with such conditions should be monitored closely and with frequent organ function evaluations.

According to our case and related literature review, we conclude that:

- Round pneumonia is uncommon in adult, and our case is community-acquired round pneumonia in an adult female.
- Community-acquired pneumonia due to *P. aeruginosa* is very rare in adult, and present case report is community-acquired round pneumonia due to *P. aeruginosa* in an elderly female without any underlying risk factors or comorbidities.
- A sputum Gram's stain showing mainly polymorphonuclear leukocytes in conjunction with a culture positive for *P. aeruginosa* in this setting suggests a diagnosis of acute *P. aeruginosa* pneumonia. There is no consensus about whether an invasive procedure (e.g., bronchoalveolar lavage or protected-brush sampling of the distal airways) is superior to tracheal aspiration to obtain samples for lung cultures in order to substantiate the occurrence of *P. aeruginosa* pneumonia (Harrison’s Internal Medicine, 20th ed.).
- Close attention should be paid to community-acquired *P. aeruginosa* round pneumonia because of its rapid progression and poor prognosis.

**Summary**

- Round pneumonia is a benign cause of coin lesions seen on chest X-ray, but may be difficult to distinguish from bronchogenic carcinoma.
- It is more common in children and is relatively uncommon in adults. This entity is seen in most radiology practices and may lead to CT and biopsy.
- Round pneumonia appears as single or multiple nodular densities, and occur predominantly in the lower lobes, mainly because gravity causes infected fluids to concentrate in the most dependent bronchi. Upper lobe round or oval X-ray opacities are more likely to suggest a malignant rather than infectious etiology.
- Apart from *S. pneumoniae* and *H. influenzae*, common causes of round pneumonia in adults are Q fever and *L. micdadei*, so in adults with round pneumonia, *C. burnetti* and *Legionella species* titers should be sent.
- Because round pneumonia is easily treated with antibiotics, this diagnosis should be considered in all patients with a coin lesion, keeping in mind that bronchogenic carcinoma is also frequent.
- A trial of antibiotics followed by serial chest X-rays may be considered in all patients with a solitary pulmonary nodule. Serial chest X-rays are helpful in differentiating malignant from benign causes of round pneumonia.
Persistence and progression of round pneumonia on chest X-ray favors a malignant process, whereas decreased size or resolution of round pneumonia on chest X-ray favors an infectious etiology.

Community-acquired round pneumonia caused by *P. aeruginosa* is rare. Despite its poor outcome, if diagnosis is established on time, and appropriate antibiotics administered, it may be treatable.

**References**

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Sir Charles Scott Sherrington (1857–1952) was born in Islington, London. He obtained his medical degree from Cambridge in 1885 and traveled to Berlin to study under Rudolf Virchow and Robert Koch, and gained experience in neurophysiology, pathology, and bacteriology. In 1895, he was appointed Professor of Medicine at Liverpool (1895–1913) and Oxford University (1913–1935).

Sherrington was primarily interested in the working of nervous system. Modern knowledge of neurophysiology dates largely to him as knowledge of neurohistology to Golgi and Cajal. The whole range of concepts and words in neurology are due to Sherrington including, synapse, proprioception, motor units, and many others. In 1894, he demonstrated that one-third to one-half fibers in a nerve leading to muscle were sensory. He explained that they carry proprioception and kinesthetic impulses to the brain, like muscle tension, joint position in order to maintain equilibrium of the body. In 1906, he developed the theory of reflex behavior of antagonistic muscles which explained this coordinating guidance of nervous system. His book “The integrative action of the nervous system” (1906) is a neurology classic.

Sherrington also mapped out with greater accuracy than had been done before, the motor areas of the cerebral cortex showing which region governed the body motion of which parts. His investigations of nearly every aspect of mammalian nervous system directly influenced the development of neurosurgery and the treatment of many neurological disorders.

Sherrington started 3-year mammalian physiology courses which consisted of various procedures on animals in 1914. This taught students to handle living nervous tissues with great care and carry out research. Many well-known future neurologists including Wilder Penfield the great neurosurgeon had enrolled and completed Sherrington’s courses.

Sherrington: Outstanding Neurophysiologist

Jayant Pai-Dhungat

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Correspondence

Caspr2 autoimmune encephalitis with COVID-19 infection

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Sir,

Autoimmune encephalitis refers to a group of conditions that occur when the body’s immune system mistakenly attacks healthy brain cells, leading to inflammation of the brain. Autoimmune encephalitis may be associated with antibodies to proteins on the surface of nerve cells, or within nerve cells. Contactin-associated protein-like 2 (Caspr2) is a membrane protein expressed in the central nervous system (CNS) and peripheral nervous system. Contactin-associated protein-like 2 is essential for the proper localization of voltage-gated potassium channels (VGKC). The coronavirus disease 2019 (COVID-19) pandemic has caused a sudden significant increase in hospitalization for pneumonia in patients with multi-organ disease. Though the major clinical manifestations of COVID-19 infection are pulmonary, COVID-19-associated CNS complications have also been reported. Acute cerebrovascular disease and encephalitis are observed with severe COVID-19 illness (in up to 8% of patients). We describe a rare presentation of Caspr2 autoimmune encephalitis with COVID-19 infection.

A 47-year-old man was brought to the emergency department with a history of postural imbalance, difficulty walking, irrelevant talk, slurred speech, involuntary movements of the lower limb, and sleep disturbance for 1 week. On general physical examination, the patient was afebrile with a heart rate of 86 beats per minute and blood pressure of 120/70 mm Hg. On neurological examination, patient was conscious, oriented to person but not to time and place. He was irritable, with dysarthric speech, and had intact comprehension. On motor system examination, tone and power were normal, while deep tendon reflexes were sluggish with equivocal plantar reflex. Continuous myokymic movement was noticed in the calf and hamstrings muscles of bilateral lower limbs. Sensory examination and cranial nerve examination were normal. The patient had unsteady gait with impaired tandem walking. Other systems examination was normal. Mental status examination revealed increased psychomotor activity with second person auditory hallucination present. A differential diagnosis of autoimmune/infectious/subacute encephalitis was considered. The patient was admitted in ICU for further management.

Reverse transcription polymerase chain reaction (RT-PCR) for COVID-19 was done on day 1 of admission which was negative. Brain magnetic resonance imaging revealed few discrete, nonspecific T2-fluid-attenuated inversion recovery (FLAIR) hyperintensities in left frontal lobe white matter and chronic small vessel ischemic changes. Electroencephalogram (EEG) pattern was unremarkable. Nerve conduction studies showed decreased compound action potential in the bilateral common peroneal nerve with normal sensory-motor conduction. Electromyography (EMG) showed normal insertional activity. However, myokymic discharges of frequency of 20–40 Hz were noted in gastrocnemius and hamstring muscles. Autoimmune workup was carried out. Cerebrospinal fluid (CSF) revealed normal glucose and protein levels, mildly elevated chloride levels with lymphocytic cell count of 2 cells/μL. Serum samples showed high positive titers for Caspr2 and VGKC antibodies. The remaining surface, onconeural and intracellular antibodies (NMDA, LGI1, AMPA1, and GABAβ1) were negative both in serum and CSF.

The patient was treated with intravenous methylprednisolone 1 gm/day, and intravenous immunoglobulin 400 mg/kg/day for 5 days, and there was a significant clinical improvement. On the 5th day of admission, the patient developed fever and loose stools. RT-PCR for COVID-19 was repeated and was found to be positive. A final diagnosis of Caspr2 autoimmune encephalitis with COVID-19 infection was made. The patient was shifted to the isolation ward and was treated with standard COVID-19 protocols. The patient’s clinical condition improved gradually over 1 week and was discharged in stable condition. On further follow-up after 2 weeks; there was no myokymic movement, the patient was able to walk independently with clinically significant cognitive improvement.

Coronavirus disease 2019 infection may be asymptomatic or it may cause a wide spectrum of symptoms, such as mild symptoms of the upper respiratory tract, gastrointestinal, neurological disease, and life-threatening sepsis. Coronavirus disease 2019 may also present with a variety of neuroimmunological conditions like Guillain-Barré syndrome (GBS), myopathy, encephalopathy, meningoencephalitis, encephalomyelitis, and acute myelitis. Autoimmune encephalitis may be associated with antibodies to proteins on the surface of nerve cells, or within nerve cells. Contactin-associated protein-like 2 and leucine-rich glioma inactivated 1 are identified as the main target antigen of neuronal VGKC complex autoantibodies. There have been a few case reports of autoimmune encephalitis following viral infections such as herpes simplex virus 1 infection. A unique case report of parainfectious autoimmune encephalitis has also been reported.

In our case, the onset of COVID-19 symptoms was 12 days after the onset of symptoms of encephalitis. Considering the incubation period of COVID-19 infection being 4–14 days, it is difficult to establish the temporal correlation between the onset of encephalitis symptoms and the COVID-19 infection. Due to lack of temporal association, it was difficult to differentiate between parainfectious autoimmune encephalitis associated with COVID-19 and an incidental coexistence of autoimmune encephalitis with COVID-19 infection, leading to a diagnostic dilemma.

Our case highlights a novel presentation of autoimmune encephalitis along with COVID-19 infection.

Conflict of Interest
Authors have no conflict of interest.

Ethical Consideration
A written informed consent has been obtained from the patient for reporting and publishing the case details.

References
Comparison of Pattern of Mortality in COVID-19 Patients with Patients in General Medicine Wards in Netaji Subhash Chandra Bose Medical College Jabalpur

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Sirs,

Coronavirus disease 2019 (COVID-19) pandemic has created a much increase in morbidity and mortality worldwide. We conducted a retrospective observational study “Comparison of Pattern of Mortality in COVID-19 Patients with Patients in General Medicine Wards in Netaji Subhash Chandra Bose Medical College Jabalpur.”

Coronavirus disease 2019 claimed more than 1.37 million lives as of November 2020.

A retrospective observational study was carried out in which mortality pattern was analyzed and comparison was done between COVID-19 patients in COVID wards and non-COVID patients in General Medicine wards in Netaji Subhash Chandra Bose Medical College Jabalpur.

In the present study, it was found that diabetes was the most prevalent comorbidity in COVID patients, that is, 47%, followed by systemic hypertension, that is, 41%. In non-COVID patients in General Medicine wards, the most prevalent comorbidity was systemic hypertension which is 40.6% followed by diabetes 32.2% (Fig. 1).

Thus, we have concluded that most of the deaths in both COVID and non-COVID patients were in elderly age group and in males as compared to females. Also, there was a strong association of NCDs as comorbidity in both COVID and non-COVID deaths, predominantly, diabetes and hypertension.

Lifestyle measures have been shown to be effective in preventing and delaying the onset of NCDs. People should maintain healthy body weight, physical activity, eat healthy diet, and avoid tobacco use and smoking. This will also prevent the death in COVID infection, as NCDs were mostly associated with adverse outcome of COVID-19.

REFERENCES
2. https://www.who.int/news/item/01-06-2020-
covid-19-significantly-for-noncommunicable-
diseases

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1Senior Professor; 2Senior Resident; 3Senior Specialist, Department of General Medicine; 4Assistant Professor, Department of Geriatric Medicine, SMS Medical College and Attached Hospital, Jaipur, Rajasthan, India

Sirs,

A new variant of SARS-CoV-2, B.1.1.529 (Omicron) was first reported to the World Health Organization (WHO) by South Africa on 24th November 2021. In conclusion, Omicron is found to be a less severe but rapid transmissible variant of concern that might escape from natural immunity or vaccine-derived immunity.1 On 26th November 2021, WHO designated Omicron as a variant of concern.2 On 1st December, the first case of COVID-19 attributed to the Omicron variant was reported in the United States. In India, the first Omicron case of COVID-19 was reported on 2nd December 2021. At present Omicron spread so rapidly that indicates community transmission.

The principal concerns about Omicron include whether it is more infectious or severe than other variants of concern and whether it can circumvent vaccine protection. Although immunological and clinical data are not yet available to provide definitive evidence, we can extrapolate from what is known about the mutations of Omicron to provide preliminary indications on transmissibility, severity, and immune escape. Implementation of concurrent prevention strategies, including vaccination, masking, increasing ventilation, testing, quarantine, and isolation, are recommended to slow transmission of SARS-CoV-2, including variants such as Omicron, and to protect against severe illness and death from COVID-19.

To accelerate detection of COVID-19 cases attributed to the Omicron variant until they are common enough to be reliably measured by routine genomic surveillance, enhanced surveillance was initiated through National SARS-CoV-2 Strain Surveillance on 28th November. The method is based on rapid screening for S-gene target failures (SGTFs) by polymerase chain reaction (PCR)—based diagnostic assays to flag potential cases of Omicron variant infection for confirmation by genomic sequencing.3 Specimens that display SGTFs have a higher likelihood to be Omicron (although SGTFs are not unique to Omicron) based on a mutation (69–70 deletion) that reduces S-gene target amplification in some PCR assays. A retrospective study was conducted on 104 patients of Omicron variant.
of COVID-19 at SMS Medical college, Jaipur and we found that the mean age of Omicron infected patients was 37.96 years (37.96 ± 19.57) with female preponderance (61.54%). A percentage of 90.38% patients were found to be asymptomatic and 69.23% patients were fully vaccinated. A percentage of 80% patients were remained unexposed to previous COVID-19 infection. COVID-19 related inflammatory markers were not raised significantly. All patients are discharged safely at home after an average seroconversion period of 5.65 days without any adverse event. In conclusion, Omicron is found to be less severe but highly transmissible variant of concern which might escape from natural immunity or vaccine derived immunity.

Although previous variant of concerns emerged in a world in which natural immunity from COVID-19 infections was common, this fifth variants of concerns has emerged at a time when vaccine immunity is increasing in the world. The preliminary indications suggest that Omicron spreading rapidly against a backdrop of ongoing Delta variant transmission and high levels of natural immunity to the Delta variant. If this trend continues, Omicron is anticipated to displace Delta as the dominant variant in world. In India, initially the Delta variant accounted for >99.9% of circulating SARS-CoV-2 variants but cases of new Omicron variants have been in increasing trend in last 8–10 weeks. At present, proportion of Omicron variant crossed to Delta variant with reversal of ratio from beginning of third wave in India and now >90% cases have Omicron variants in the community. The potential impact of Omicron on the clinical efficacy of COVID-19 vaccines for mild infections is not clear. Thus far, most COVID-19 vaccines have remained effective in preventing severe COVID-19, hospitalization, and death from all previous variants, because this efficacy might be more dependent on T-cell immune responses than antibodies.

Analysis of APACHE II Score to Decide Step Down of Patients from Intensive Care Unit: A Retrospective Study from a Tertiary Care Hospital

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Table 1: Distribution of APACHE II scores at admission and comparison of actual with predicted mortality

<table>
<thead>
<tr>
<th>APACHE II (predicted mortality)</th>
<th>Number of patients</th>
<th>% of total</th>
<th>Patients died</th>
<th>Actual mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–14 (15%)</td>
<td>19</td>
<td>15%</td>
<td>4</td>
<td>21%</td>
</tr>
<tr>
<td>15–19 (25%)</td>
<td>15</td>
<td>12%</td>
<td>8</td>
<td>53%</td>
</tr>
<tr>
<td>20–24 (40%)</td>
<td>40</td>
<td>33%</td>
<td>19</td>
<td>47%</td>
</tr>
<tr>
<td>25–29 (55%)</td>
<td>19</td>
<td>15%</td>
<td>5</td>
<td>26%</td>
</tr>
<tr>
<td>30–34 (73%)</td>
<td>18</td>
<td>14.8%</td>
<td>12</td>
<td>66%</td>
</tr>
<tr>
<td>&gt;34 (85%)</td>
<td>10</td>
<td>8%</td>
<td>7</td>
<td>70%</td>
</tr>
</tbody>
</table>
is of paramount importance in developing countries. Further studies are needed to derive the exact cutoff values of APACHE II scores to decide the step down of patients.

Authors’ Contributions

MK—literature search, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review.

MD—concept, design, definition of intellectual content, and guarantor.

KN—data analysis and statistical analysis.

BD—data acquisition.

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References


Role of Nursing Education towards Behavior Change and Reduction in Central Lines-associated Bloodstream Infections

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Sir,

Nursing care and nurses form backbone of any healthcare organization. Implementation of policies and practices related to patient care lies on their shoulders. Continuous nursing education and training have been associated with better implementation of clinical nursing practice at patient level. Training and education with respect to infection control practices lead to decrease in healthcare-associated infections (HAIs) to a great extent.

Healthcare-associated infections are either device (Foleys catheter, central line, and ventilator) related or procedure (surgery) related. Healthcare-associated infection-bloodstream infection is due to a central line put in the patient (>48 hours) for rapid drug delivery; also known as central line-associated bloodstream infection (CLABSI). Central line-associated bloodstream infection is defined as a laboratory-confirmed bloodstream infection (LCBSI) where a micro-organism is identified and central line is present on the LCBSI date of event or the day before.1

Central line-associated bloodstream infection remains a leading cause of HAIs in critical units in India, the rate being 79 per 1000 central line days.2 It is the fourth most common HAI as per Center for Disease Control and Prevention (CDC). It is a major contributor to in-hospital morbidity and mortality and is associated with increased expenditure and length of intensive care unit (ICU) stay.3

Though less published data on developing countries are available, the pooled CLABSI rate ranges from 1.6 to 44.6 per 1000 catheter days in adult and pediatric ICUs.3,4

It has been proved in various literatures and published data strongly support the concept of regular training and retraining of all the healthcare workers. With continuous education and training, most cases are preventable with proper aseptic techniques, surveillance, and management strategies.5,6 As per CDC, educating healthcare workers regarding the indications for intravascular catheter use, proper procedures for insertion and maintenance of intravascular catheters, and appropriate infection control measures can help in reducing CLABSI.7

Litteratures suggest that up to 70% of CLABSI could be prevented if adequate measures are undertaken.8 This study was therefore done to find the association of nursing training on CLABSI rates. A total of 40 nurses were enrolled in this study. Permission from Institutional Review Board was taken and informed consent was taken from nurses who were enrolled in the study from December 2016 to January 2017. They were trained on hand hygiene, personal protective measures (PPM) to be taken, and infusion practice which included right site selection, proper dressing of lines, labeling, flushing of lines, and complications.

Study revealed that CLABSI rate/1000 catheter days reduced from 3.8 to 2.63. A total of 64 cases and 47 cases with central lines (>48 hours) were obtained before and after training. The CLABSI cases confirmed were 37 (57.8%) and 15 (31.9%), respectively. Hand hygiene compliance increased from 56 to 66% (p-value 0.145), PPM compliance increased to 40 as compared to 55% (<p-value 0.206), labeling compliance increased to 40 as compared to 15% (<p-value 0.001).

The CLABSI rate per thousand device days obtained in this study was comparable to study done by Mehta et al. Another study by Singh et al. reported a CLABSI rate of 0.48 per 1000 central line days.2,8 The rate of this study is ranging from 2.63/1000 catheter days to 3.8/1000 catheter days. This rate is comparable to study done by Mehta et al. in Indian cities.2

Our study reinforces the concept of training and education among nursing staff to increase compliance to infection control protocols. It was observed that post-training CLABSI rate/1000 device days decreased considerably. The published literature and International Consortium on Infection Control reiterate the need for regular training in the form of lecture series or bedside trainings by infection control department. Support from the management of the hospital to drive trainings forms the core in implementation of best infection control practices.

References


Plant-based Diets: “Fad or fabulous”

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Disclaimer: We are not “nutrition experts.” This narrative is based on the conflicting scientific data and our clinical experience of advising our patients on diet. Our sole aim is to promote a healthy lifestyle and improve the quality of life.

INTRODUCTION

Unhealthy lifestyle has led to a pandemic of noncommunicable diseases, like diabetes, hypertension, obesity, dyslipidemia, coronary heart disease, etc. A healthy lifestyle which consists of a balanced, nutritious diet, regular physical activity and reducing sedentary time, stopping smoking and abuse of alcohol and addicting drugs, and reducing stress by meditation or Yoga, can mitigate the pandemic of noncommunicable diseases.

How India Eats

There is abundant growth of vegetables, grains, and beans in India since 1000 BC; hence, it makes sense to utilize this in our densely populated country. According to the Sample Registration System Baseline Survey released by the Registrar General of India, in 2014, 71% of Indians over the age of 15 are nonvegetarians. However, a similar survey done in 2004 showed that this figure was 75%. How significant is a drop of 4%, is not known, but there is definitely a trend to vegetarianism.

Types of Plant-based Diets

There are a variety of plant-based diets: (1) vegan (total vegetarian; excludes all animal and dairy products), (2) lacto-vegetarian (includes milk products), (3) ovo-vegetarian (includes eggs), (4) lacto-ovo-vegetarian (includes both milk products and eggs), (5) pesco-vegetarian (semiplant diet and includes fish and seafood), and (6) whole-food plant diets.

Nutrient Intake

The vegetarian diet consists of more carbohydrates and dietary fiber, but less proteins and compared to omnivores total fat is similar but the composition of fat differs with higher ratio of polyunsaturated fats to saturated fats (PUFA:SFA ratio) and lower intake of cholesterol. A low-fat, high-carbohydrate diet is also bad, as it acts on the hepatic fructose metabolism, leading to increased uric acid and decreased nitric oxide, causes de novo lipogenesis, increases the hepatic steatosis, increases insulin resistance in muscle and liver, and antagonizes leptin and satiety.

Clinical Evidences

According to one 25-year median follow-up observational study it was found that long-term low-carbohydrate diets with low plant and increased animal products and fats stimulate inflammatory pathways, oxidative stress, and biological aging.1 In the Oxford Vegetarian Study, consisting of a prospective cohort of 6,000 vegetarians subjects compared to 5,000 subjects who ate meat, the former group had low levels of serum cholesterol, low prevalence of obesity, lower mortality rates, and enjoyed better quality of life. The exclusion of meat in diet can reduce coronary heart disease risk by 15–25%. Meta-analysis of intervention trials has also shown that plant-based diets lead to a significant reduction in obesity-related inflammatory biomarkers including CRP, IL6, soluble intercellular adhesion molecule, and TNF-alpha.2 The PORTFOLIO Diet of 2,000 calories, consisting of 45 gm of nuts, 50 gm of plant protein such as soy or pulses (beans/peas), 20 gm of viscous soluble fiber like oats, apples, eggplant, and 2 gm of plant sterols, reduce morbidity and mortality from coronary heart disease by 40%, reduces weight and risk of hypertension by 34%.1 One 16-week randomized clinical trial had shown that a plant-based diet decreased body weight, fat mass, homeostasis model assessment-estimated insulin resistance Homeostasis model assessment-estimated insulin resistance (HOMA-IR) significantly in participants representing vegan group.3 It had been suggested that being rich with good gut microbiota is more important than being rich with rupees for good metabolic health.4 In a randomized controlled trial enrolling 168 participants had shown statistical significant reduction in body weight in the vegan group with a reduction in fat mass and visceral fat. Insulin sensitivity index was increased in the vegan group with an increment of relative abundance of Faecalibacterium prausnitzii and less decrement of relative abundance of Bacteroides fragilis in the vegan group making the treatment effect positive. In this study, it was concluded that a low-fat vegan diet had resulted in significant changes in gut microbiota environment which were related to decrease in weight, fat composition, and insulin resistance.5

CONCLUSIONS

Despite so many evidences, no professional body like the American Heart Association or American College of Cardiology or the European Society of Cardiology has ever endorsed a plant-based diet. Whether plant-based diets are fabulous or just a fad, need to be explored by well-designed studies. Single healthy diet, predominantly plant-based, cuts along various disease categories, not only to lower risk associated with many chronic diseases, but also for improving the quality of life.

REFERENCES


Psoriasiform Skin Eruptions Following COVID-19 Vaccination Unveiled Previously Undiagnosed post-COVID-19 Psoriatic Arthritis

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Sir,

Both new-onset as well as exacerbation of existing psoriasis have been reported so far in subjects vaccinated against COVID-19.1,2 We herein report a case of psoriatic arthritis, which was diagnosed after the appearance of psoriasiform skin eruptions within the first week of receiving the AstraZeneca vaccine.

A 55-year-old Indian man presented with recent onset, dry, raised, red skin patches (lesions) covered with silvery scales (Fig. 1). The plaques were itchy, nontender, and multiple in number, distributed over the scalp (Fig. 1A), forearm (Fig. 1B), lower limbs and toes (Fig. 1C and D), and lower back (Fig. 1E). The nail examination showed pitting, subungual hyperkeratosis, onycholysis, and yellowish-brown discoloration (Fig. 1F). Candle grease, Auspitz, and Koebner signs were positive. The clinical diagnosis was plaque psoriasis. These lesions appeared within the first week following vaccination with the first dose of COVISHIELD (Oxford-AstraZeneca) vaccine. He had suffered COVID-19 six months ago, which was mild in severity, and did not require any hospitalization. However, history revealed he was having intermittent multiple joint pain and swelling predominantly involving the distal interphalangeal joints of both fingers and toes for almost the last six months, just following COVID-19 infection. Of note was that he had recently observed that his fingertips were getting a “tapered” appearance. Relevant investigations established the diagnosis of psoriatic arthritis, where inflammatory arthritis preceded the skin manifestations.

The patient was prescribed tofacitinib, methotrexate, tacalcitol, pimecrolimus (1% w/w) cream, and coal tar (5% v/v) lotion. He showed significant improvement and currently has minimal lesions and no joint pains or deformity.

Several case reports have documented psoriatic flares as well as arthritis following COVID-19.3 Our case is unique in that unlike previously reported post-COVID arthritis, the skin lesions appeared after the first dose of vaccination. However, since the patient arrived only after the appearance of psoriatic lesions, the diagnosis of psoriatic arthritis was made after the vaccination.

Psoriasis is influenced by many factors, including genetics, infection, medications, and lifestyle. Causal links have been suggested between vaccines and psoriasis. Recently, COVID-19 vaccination has been associated with cutaneous manifestations. Psoriasis flare-up was reported in a 34-year-old Taiwanese woman after receiving the first dose of the AstraZeneca vaccine.1 Similar flare-up has been noticed with CoronoVac.2 Vaccines may trigger inflammatory diseases through the activation of cellular and humoral immune system.

Although a direct causal or pathological association between COVID-19 vaccine and psoriasis exacerbation cannot be inferred, the absence of any triggers and a close temporal relationship between the exacerbation of the lesions and the receipt of the vaccine implies an immunological relation. In our patient, COVID-19 infection might have triggered the psoriatic arthritis, while the vaccination, acting as a confounder, exacerbated it, resulting in the appearance of skin manifestations. In general, COVID-19 vaccines are safe in moderate-to-severe psoriasis on treatment; however, isolated reports of psoriatic flares or new-onset reactions should alert the physicians to look out for exacerbation of lesions.

**Author Contributions**

All authors contributed to the study conception. Patient information, diagnosis and management, and data collection were carried out by RG. The first draft of the manuscript was written by RG and edited by DR, AR, and JBL. Visualization was done by DR. All authors read and approved the final manuscript.

**Consent**

Informed consent was obtained from the patient for inclusion into this study.

---

**Figs 1A to F:** Multiple scaly psoriatic plaques present over the scalp (A); forearm (B); lower limbs (C and D); lower back (E); and fingernails (F). Swollen distal interphalangeal joints of both hands with tapered fingertips are visible (F)
Sir,

Early and accurate diagnosis of COVID-19 is important for limiting spread and improving health outcomes. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) assays assess the presence of two or more SARS-CoV-2 genes in a sample.\textsuperscript{1} If single gene target shows weak signal and other targets are not detected, the result is termed as inconclusive.\textsuperscript{2} Different terminologies are used for inconclusive SARS-CoV-2 results such as invalid, indeterminate, presumptive positive, near-source corona positive, etc. Inconclusive results can occur due to a low viral load, improper sample collection, issues with RNA extraction, presence of a PCR-inhibitory substance, differences in analytical sensitivity of individual viral target genes, and nonspecific amplification at late phase of amplification cycle. In such cases, samples need to be retested and still the result remains inconclusive, additional confirmatory testing should be conducted or second sample should be collected.

We performed a retrospective analysis of RT-PCR testing data of 355 inconclusive samples of the 6,209 samples referred to our center for COVID-19 testing from 1st May to 6th July 2020. These 6,209 samples were tested by RT-PCR, Standard mCoV Detection which detects E and ORF1ab genes. In 355 inconclusive samples, repeat testing was performed using LabGun COVID-19 RT-PCR Kit. The test was interpreted as positive, negative, or invalid/inconclusive based on detection of E gene and RdRp gene. About 80 (22.5\%) samples were found to be positive, 183 (51.55\%) were negative, and 92 (25.92\%) remained inconclusive (Fig. 1). We were able to resolve 263 (74.05\%) cases as positive or negative. As per existing literature, up to 5\% of COVID-19 RT-PCR results may be inconclusive.\textsuperscript{3}

In our study, 5.71\% results were found to be inconclusive, requesting for repeat samples after 2–4 days in such situation would have resulted in further spread of the infection. Different specificity could be due to primer targeting different regions, PCR conditions, and reaction components. Majority of the patients with initial inconclusive results were symptomatic 242 (68.16\%) and 113 (31.83\%) were asymptomatic. Out of which, 11.3\% were positive, 57.392\% were negative, and 30.4307\% were still inconclusive on retesting. Out of 242 symptomatic inconclusive cases, 27.7\% were positive, 48.7\% were negative, and 23.6\% were inconclusive on retesting. About 71 patients had underlying medical conditions or comorbidities. Delay in management of symptomatic high-risk individuals with comorbid conditions could lead to various adverse outcomes. Indeterminate/inconclusive results most likely reflect low levels of the virus in the sample or low viral shedding in the nasopharynx/oropharynx early or late in the course of the infection. This strategy has resolved inconclusive results to a definitive diagnosis which together with

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**An Approach to Resolve Uncertainty in COVID-19 Diagnosis due to Inconclusive Results from RT-PCR Test**

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1Scientist-D; 2Scientist-B, Genetic Research Centre; 3Scientist-B, Department of Clinical Research; 4Technical Officer, Department of Clinical Research; 5Technical Officer, Department of Biochemistry; 6PhD Student, Department of Biochemistry; 7Technical Officer, Department of Infectious Biology; 8Technical Officer, Department of Neuroendocrinology; 9Senior Technical Officer, Department of Molecular Immunology and Microbiology; 10Scientist-E, Department of Biochemistry; 11Scientist-D, Department of Molecular Immunology and Microbiology; 12Scientist, ICMR Emeritus Scientist, Division of Structural Biology; 13Scientist-B, Department of Clinical Research, ICMR-National Institute for Research in Reproductive and Child Health, Parel, Mumbai, India

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**References**


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**Fig. 1:** Distribution of results of retesting of initial inconclusive samples. Number of symptomatic and asymptomatic cases in each (positive/negative/inconclusive) is shown as “S” or “AS”, respectively

**Fig. 2:** Protocol/algorithm followed to resolve the issue of “inconclusive results” of RT-PCR test for detection of SARS-CoV-2
clinical history can be used by clinician to provide optimum management. If COVID-19 is still suspected based on exposure history together with other clinical findings in case with negative results on retesting, repeat sample after 2–4 days need to be advised. This should be mentioned in patient reports. In conclusion, the ongoing outbreak of the recently emerged novel coronavirus, inconclusive COVID-19 testing reports result in diagnostic dilemma. As highlighted above retesting of the same sample using different kits having multiple and varied target regions can improve success rate and resolving capacity of the test, either as positive or negative out of simply inconclusive results. This strategy may save time, additional resource, increases accuracy, avoids unnecessary psychological anxiety due to uncertainties in the results-related delays, and helps in taking immediate management stand if the case is found positive. Based on our findings, we suggest a testing protocol to resolve the issue of uncertainty in diagnosis due to inconclusive results (Fig. 2).

**REFERENCES**


**Ethics**

The study was approved by the Institutional Ethics of ICMR-NIRRCH, Mumbai.

**Acknowledgment**

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We are thankful to the Director ICMR-NIRRCH for the support.

Will They? Won’t They? COVID-19 Vaccine Intent among Unvaccinated Young Indian Adults

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Sir,

In June 2021, the Indian Government started COVID-19 vaccination in the age group of 18–44 years. The success of any vaccine program depends upon the uptake by the target population. Individuals in this age group are the major contributors to the present and future economic growth of the country. It is important to understand their COVID-19 vaccine intent and the reasons for refusal of vaccination, if any.

We conducted a cross-sectional study between May and June 2021. A Google form with 15 questions was sent to individuals between 18 and 24 years of age outside the healthcare setting (those who were not doctors, nurses, paramedical workers, etc.) and had not yet received their first dose of the COVID-19 vaccine. We received 1,193 responses using a snowballing technique. We collected demographic data and data pertaining to COVID-19 appropriate behavior, belief in vaccines in general, history of COVID-19 in the respondent and their family, and history of vaccination of family members followed by questions about vaccine acceptance or refusal and reasons for the same.

The mean age of the respondents was 20.9 years ± 1.9 years (age range 18–24 years) and 595 (49.9%) were males. A majority [538 (45.1%)] were graduates, followed by 478 (40.1%) standard 12 students. A huge majority of the respondents were students, with or without a temporary job [985, 82.6%]. Almost everyone [1,162, 97.4%] always wore a mask when outside their homes. A minority, 251 (21%) respondents reported that they had been infected with SARS-CoV2, while 472 (39.6%) reported infection by a family member. It was seen that 954 (80%) of the respondents either worried occasionally or most of the time, while 20% “never” worried about contracting the infection.

It was found that 1,036 (86.8%) respondents were willing to get vaccinated against COVID-19. Figure 1 shows the

**Fig. 1:** Reasons for acceptance and refusal of vaccination
distribution of reasons for acceptance (n = 2113) and refusal (n = 228) to get vaccinated, respectively. The most frequent reason for acceptance of vaccination was to prevent from getting severe COVID-19 [837, 39.6%], followed by “so that I can have a normal social life again” by 536 (25.4%) respondents. The main reasons for refusing to get vaccinated were found to be “I believe COVID-19 will soon go away and hence, a vaccine is not necessary” by 80 (35%) respondents and “I am worried about the side effects of the vaccine” and “I don’t believe the vaccine can protect me” by 74 (32.4%) respondents.

As seen in Table 1, being a graduate and postgraduate [aOR 1.93, 95% confidence interval (CI) 1.20–3.10, p = 0.010 and adjusted odds ratio (aOR) 2.03, 95% CI 1.01–4.07, p = 0.038, respectively], having a family member vaccinated against COVID-19 [aOR 2.24, 95% CI 1.51–3.32, p < 0.001] and believing that vaccines, in general, can prevent diseases [aOR 3.19, 95% CI 1.93–5.29, p < 0.001] were significant predictors of vaccine acceptance. Wearing a mask only “sometimes” or “never” when outdoors was found to be a significant predictor of refusal of vaccination [aOR 2.39, 95% CI 1.03–5.56, p < 0.001]. Also, “never” worrying about getting COVID-19 was a significant predictor of vaccine refusal [aOR 2.48, 95% CI 1.69–3.65, p < 0.001].

Several studies have found that belief in the efficacy and perceived protective benefits of the COVID-19 vaccine have been found to be associated with greater acceptance.1–4 Believing that vaccines, in general, can prevent diseases was a significant predictor of vaccine acceptance in our study. Concerns about the safety and efficacy of the COVID-19 vaccine were the important reasons for vaccine refusal. Low perceived risk of infection was a significant predictor of vaccine refusal, and believing that COVID-19 “will soon go away” and hence, “a vaccine is not necessary” were a few worrying reasons for vaccine refusal.

Vaccine hesitancy is a huge concern in the global fight against the COVID-19 pandemic. We believe that concerted efforts are required to advocate vaccine acceptance to achieve universal vaccine coverage. Targeted behavior—change communication strategies can increase the perceived severity of COVID-19 in this age group and promote COVID-appropriate behavior. The immense social media presence and excellent networking skills of this age group can be put to good use to address the knowledge gaps and enable the swift dissemination of accurate information about COVID-19 vaccination.

**REFERENCES**


<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>Yes n (%)</th>
<th>No n (%)</th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Highest education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 12th</td>
<td>397 (83.1)</td>
<td>81 (16.9)</td>
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<td></td>
</tr>
<tr>
<td>Graduate</td>
<td>481 (89.4)</td>
<td>57 (10.6)</td>
<td>1.93 (1.20–3.10)</td>
<td>0.010</td>
</tr>
<tr>
<td>Postgraduate</td>
<td>158 (89.3)</td>
<td>19 (10.7)</td>
<td>2.03 (1.01–4.07)</td>
<td>0.038</td>
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<tr>
<td>Has any family member been vaccinated against the coronavirus?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>866 (89.6)</td>
<td>100 (10.4)</td>
<td>2.24 (1.51–3.32)</td>
<td>0.001</td>
</tr>
<tr>
<td>Do you believe that vaccines (in general) can prevent diseases?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>971 (88.7)</td>
<td>124 (11.3)</td>
<td>3.19 (1.93–5.29)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Do you wear a mask when you step outside your home?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always</td>
<td>1017 (87.5)</td>
<td>145 (12.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sometimes + Never</td>
<td>19 (61.3)</td>
<td>12 (38.7)</td>
<td>2.39 (1.03–5.56)</td>
<td>0.044</td>
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<tr>
<td>Are you worried about getting infected with the coronavirus?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most of the times</td>
<td>859 (90.0)</td>
<td>95 (10.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>177 (74.1)</td>
<td>62 (25.9)</td>
<td>2.48 (1.69–3.65)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Bold p-values are statistically significant.
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