ORIGINAL ARTICLE

The Unexplored Link between Nailfold Capillaroscopy and Acanthosis Nigricans: A Cross-sectional Clinicodermoscopic Study

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Abstract

Introduction: Acanthosis nigricans (AN), a commonly encountered condition in clinical practice, is linked with numerous systemic disorders. Currently, there is a dearth of literature on the correlation of clinical and dermoscopic features of AN with nailfold capillaroscopy (NFC) changes. This study intended to evaluate patients with AN who have underlying microvascular complications as a consequence of metabolic diseases.

Objectives: Primarily to study the association of clinical and dermoscopic findings of AN with NFC and to elucidate the spectrum of NFC changes in patients of AN.

Materials and methods: This was a cross-sectional, hospital-based study with a sample size of 97. Clinical Burke's grading and dermoscopy were performed in clinically diagnosed AN patients. NFC was performed on all 10 fingernails. The fourth and fifth fingernails of each hand were considered for studying the association.

Results: NFC changes seen were tortuous, dilated, cross-linked, ramified capillaries, and dropouts. There was a positive association of clinical Burke's grading (p-value = 0.002) and duration (p-value = 0.003) of AN with dermoscopic features such as depth of sulci cutis, number of hyperpigmented dots, and shape of papillary projections. Tortuous, cross-linked capillaries showed a significant association with the clinical scale of AN (p-value < 0.05). Ramified and cross-linked capillaries showed a significant association with the duration of AN (p-value < 0.05).

Conclusion: Dermoscopy in AN showed gradation in changes corresponding to the clinical Burke's grading and duration. Ramified and cross-linked capillaries showed a significant association with the duration of AN, while tortuous, cross-linked capillaries showed a significant association with the clinical scale of AN. The present study aids in the early detection of microvascular changes in AN, such as tortuous, ramified, and cross-linked capillaries, and proves helpful in referring the patient for screening of diabetic retinopathy and nephropathy at the earliest.

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Introduction

Acanthosis nigricans (AN) is associated with several systemic diseases, hence, its detection is necessary.[1] Endocrine and metabolic disorders such as diabetes mellitus (DM) and polycystic ovarian syndrome are underlying systemic diseases seen in association with AN. It is a dermatological marker of insulin resistance (IR) as well as hyperinsulinemia. Therefore, its utility lies in detecting cases that may progress to have impaired glucose tolerance and frank diabetes, both of which can be associated with microvascular changes.[1] Nailfold capillaroscopy (NFC) is a noninvasive diagnostic technique to evaluate proximal nailfold microvascular complications in DM, metabolic syndrome, and rheumatological disorders.[2] Not much literature is available regarding the correlation of clinical and dermoscopic features of AN with NFC changes. Currently, there is a dearth of literature on NFC in AN and/or IR; hence, we have compared our findings with studies showcasing NFC changes in type 2 DM. The rationale behind this is that AN is a marker of IR, which is a prediabetic state. A study done by Baranowska-Jurkun et al.[3] suggests that individuals with impaired glucose metabolism, whose blood sugar levels exceed optimal values but do not meet the diagnostic criteria for DM, still experience microvascular complications associated with diabetes. The primary objective was to study the association of clinical and dermoscopic findings of AN with NFC changes, and the secondary objective was to study the spectrum of NFC findings in AN.

Materials and Methods

This was a 1-year (July 2022–2023) cross-sectional study carried out in a tertiary care center at the dermatology department with a sample size of 97. The formula used for sample size calculation was:

$$n = \frac{p(100-p)Z^2}{E^2}$$

Where, n was the sample size required, p was the percentage occurrence of a state or condition (proportion or prevalence), E was the percentage maximum error required, and Z was the value corresponding to the level of confidence required.

The prevalence of AN was assumed as 50%. With the percentage of maximum error taken as 10% and at a 95% confidence level, the sample size was given by:

$$n = \frac{50\times(100-50)\times 1.96^2}{(10)^2}$$

$$n = 96.04 \approx 96$$

Convenience sampling was done. Patients with clinically diagnosed AN from the age of 5–70 years who gave written/parental consent were included in the study. Patients with scleroderma, lupus, dermatomyositis, psoriasis, and alopecia areata were excluded. Detailed history, height, and weight were noted. Dermoscopy was done on affected sites using a digital dermoscope (Dinolite AF4115ZT) in polarized and nonpolarized modes, and images were recorded. NFC was performed on all 10 fingers. Findings in ≥3 nailfolds were considered significant.[4] The fourth and fifth nailfolds of both hands were used to study the association due to better visibility.[2] The dermoscopy (Table 1 and Figs 1A to F) and NFC findings (Table 2) were graded with the help of a scale formulated and validated by two expert dermatologists specialized in dermoscopy and NFC. All the data were entered into an Excel sheet

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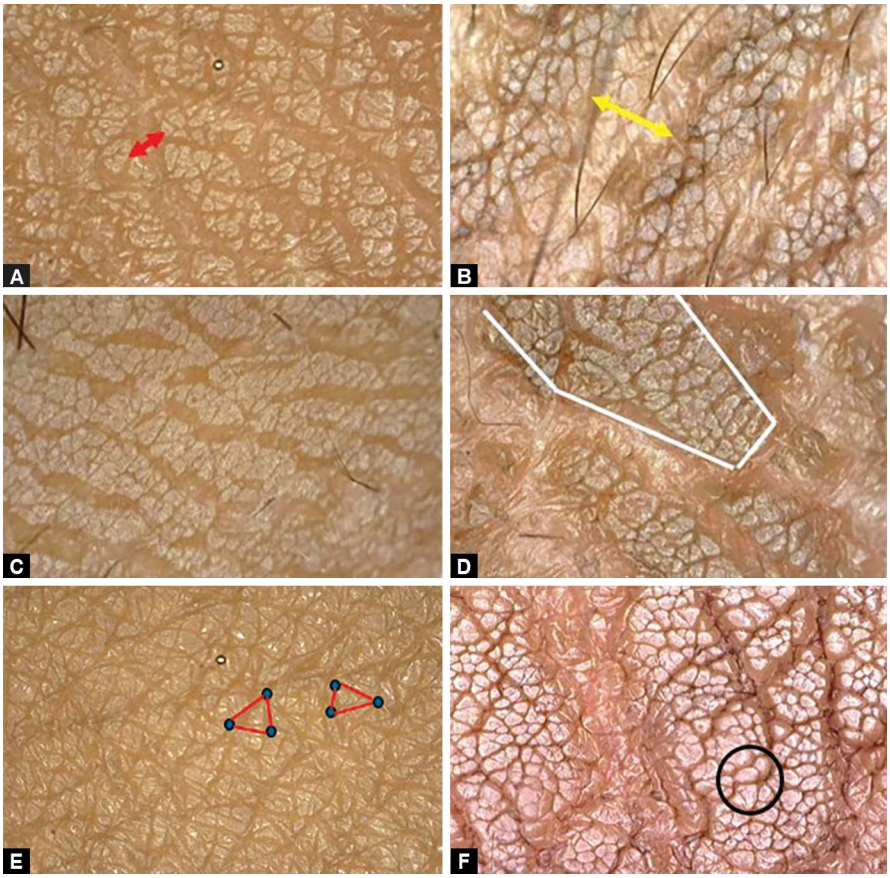
Table 1: Dermoscopic scoring system for AN (self-designed)

	Dermoscopy changes	*0*	*1*	*2*
1.	Sulci cutis	Absent	Prominent	Not prominent
2.	Cristae cutis	Absent	Rhomboid formation present	Rhomboid formation absent
3.	Papillary projections	Absent	Nontriangular	Triangular
4.	Hyperpigmented dots/globules	Absent	<50	>50
5.	Color of hyperpigmented dots/globules	Absent	Dark brown	Light brown
6.	Hyperpigmented blotches	Absent	Present	
7.	Crypts	Absent	Present	
8.	White streaks/globules	Absent	Present	



Figs 1A to F: Dermoscopy of AN (nonpolarized mode, 80× magnification): (A) Sulci cutis—not prominent (red arrow); (B) Sulci cutis—prominent (yellow arrow); (C) Cristae cutis—rhomboid formation absent; (D) Cristae cutis—rhomboid formation (white rhomboid); (E) Papillary projection—triangular (three blue dots representing corners of the triangle and red lines representing sides); (F) Papillary projection—nontriangular (black circle)

and analyzed using SPSS v21 operating on Windows 10. Categorical data were represented as frequencies and percentages. Continuous data were represented as mean and standard deviation. The Chi-squared test was used to test the association between Burke's clinical scale (neck severity, axilla, and neck texture) and dermoscopy findings of neck and bilateral axilla (sulci cutis, cristae cutis, hyperpigmented dots/globules, number of hyperpigmented dots/globules, hyperpigmented blotches, crypts, and white streaks/globules) and NFC findings (dropouts, tortuous, cross-linked, giant, hemorrhage, ramified, and ectasia). Analysis of variance (ANOVA) test was used to test the association between duration of AN and dermoscopy findings of neck and bilateral axilla (sulci cutis, cristae cutis, hyperpigmented dots/globules, number of hyperpigmented dots/globules, hyperpigmented blotches, crypts, and white streaks/globules) and NFC findings (dropouts, tortuous, cross-linked, giant, hemorrhage, ramified, and ectasia). The *t*-test was used as a test of significance for continuous data between two groups. A *p*-value < 0.05 was considered statistically significant.

Results

In the present study, we observed that the majority of the participants belonged to the age-group of 16–25 years. Females were 71.1% and males were 28.8%. The most common Fitzpatrick skin type noted was type IV, *n* = 64 (66%). Seven (7.21%) patients were known diabetics, and 4 (4.13%) patients were known hypertensives. A total of 36 out of 97 patients consented to get their homeostatic model assessment of insulin resistance (HOMA-IR) done. Of these, 21 had IR (HOMA-IR > 2).

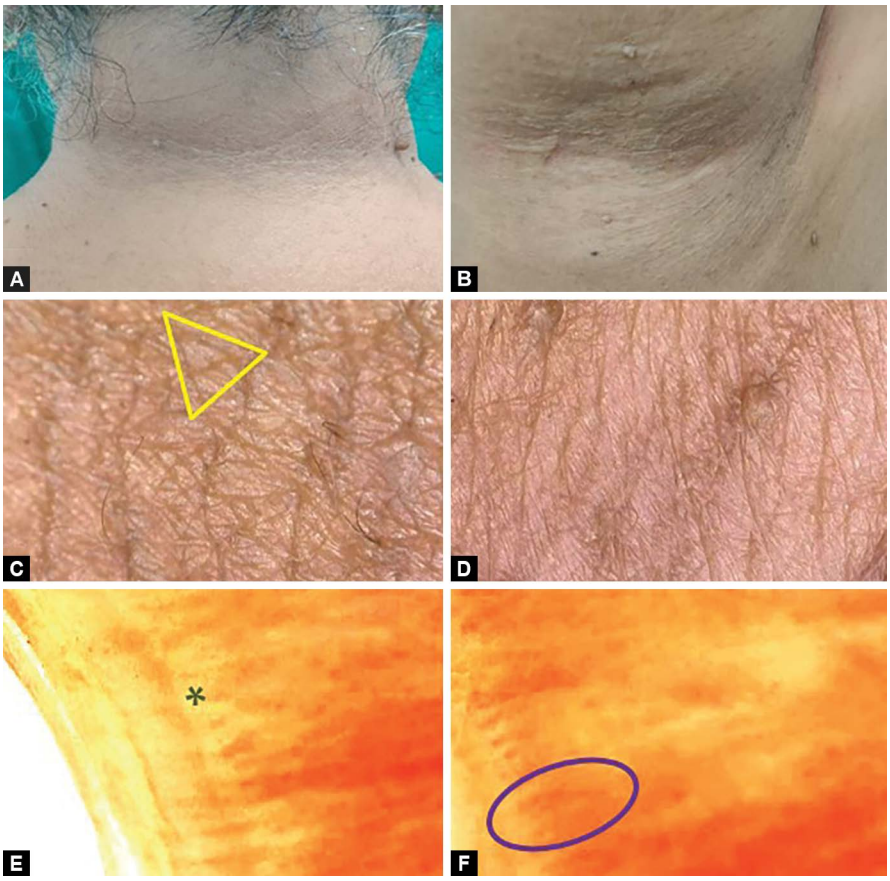
The most common Burke's grade for neck severity was grade III, *n* = 47 (48.5%), for axilla, it was grade III, *n* = 43 (44.3%), and for neck texture, it was grade III, *n* = 58 (59.8%). Sulci cutis was the commonest finding on dermoscopy (97/97, 100%) in the neck, followed by cristae cutis (63/97, 64.9%) and papillary projections (94/97, 96.90%). For axillae, sulci cutis was noted in 78/80 (97.5%) participants. Hyperpigmented dots and globules were seen more in axillae, 59/80 (73.75%), compared to the neck, 55/97 (56.70%).

In 14/97 (14.43%) participants, all 10 nailfolds were not visible. All 83 patients showed dropouts in ≥3 nailfolds. About 61/83 (73.49%) patients showed tortuous capillaries in ≥3 nailfolds. Again, 55/83 (66.26%) patients showed cross-linked capillaries in ≥3 nailfolds. Then, 26/83 (31.3%) showed ramified capillaries, 7/83 (8.4%) giant capillaries, and 6/83 (7.22%) hemorrhages in ≥3 nailfolds.

There was a significant association between Burke's scale and duration of AN on dermoscopy. As the grade of clinical scale and duration increased, sulci cutis became prominent, cristae cutis showed rhomboid formation, and papillary projections became nontriangular from triangular (*p*-value < 0.05) (Figs 2A to F and 3A to F). Tortuous capillaries showed a significant association with Burke's clinical grade of AN (neck severity, *p*-value = 0.001; neck texture, *p*-value = 0.001). Cross-linked capillaries also showed a significant association with Burke's

Table 2: Nailfold capillaroscopic scoring for NFC in AN (self-designed)

	NFC changes	*0*	*1*
1.	Dropouts	Absent	Present
2.	Tortuous capillaries	Absent	Present
3.	Cross-linked capillaries	Absent	Present
4.	Giant capillaries	Absent	Present
5.	Hemorrhage	Absent	Present
6.	Ramified capillaries	Absent	Present
7.	Ectasia	Absent	Present



Figs 2A to F: (A) Involvement of neck, Burke's grading neck severity 3, neck texture 2; (B) Involvement of axilla, Burke's grading axilla 2; (C) Dermoscopy of neck (nonpolarized mode, 80× magnification): sulci cutis—not prominent, cristae cutis—rhomboid formation absent, papillary projections—triangular (yellow triangle); (D) Dermoscopy of axilla (nonpolarized mode, 80× magnification): sulci cutis—not prominent, cristae cutis—rhomboid formation absent, papillary projections—absent; (E) NFC (polarized mode, 80× magnification)—dropouts (green asterisk); (F) NFC (polarized mode, 80× magnification)—cross-linked capillary (purple oval)

clinical grade of AN (neck severity, neck texture, and axilla, p-value = 0.001). As the clinical grade increased, the presence of these findings in nailfolds increased. As duration increased, the presence of cross-linked (p-value = 0.001) and ramified capillaries (p-value = 0.003) in nailfolds increased (Figs 2 and 3).

Discussion

Out of a total of 97 patients, the majority were observed to be between the age-group of 16–25 years, 38/97 (39.17%). These findings are similar to a study by Tank et al.,[5] where the most common age-group with AN was 11–20 years, with 32.9% of patients and 24.9% of patients between 21 and 30 years. Out of the 97 patients, 71/97 (71.13%) were females, and 26/97 (26.80%) were males. Similar findings were found in a study done by Puri,[6] where females were 18/30 (60%) and males were 12/30 (40%). Female preponderance in our study may be due to the possibility that females presented more with AN as a cosmetic concern. The neck was involved in all patients, 97/97 (100%), whereas the involvement of the axilla was seen in 80/97 (82.47%) patients in the present study. In a study done by Varthakavi et al.,[7] the neck involvement was 100%, and axilla involvement was 80.6%, which was similar to our finding. In a study done by Puri,[6] the neck (93.3%) was the commonest site, followed by the axilla in 66.6%. Sulci cutis was the common finding on dermoscopy, 97/97 (100%) in the neck, followed by cristae cutis (63/97, 64.9%), and papillary projections (94/97, 96.90%). Sulci cutis was observed in 78/80 (97.5%) in both axillae. Similar findings were seen in a study done by Pardeshi et al., where sulci cutis on the neck were seen in 100% of patients, followed by cristae cutis seen in 99% of patients. Hyperpigmented dots were seen in 46.6% of patients. We attribute the presence of white globules/streaks to scarring due to scratching or hair removal techniques. As the clinical grade increased, sulci cutis became prominent (p-value = 0.001), and cristae cutis showed rhomboid formation (p-value = 0.001). Papillary projections became nontriangular from triangular as clinical grade increased (p-value = 0.01). The number of hyperpigmented dots/globules increased as neck texture and clinical grade of axilla increased (p-value < 0.05). The presence of crypts and hyperpigmented blotches increased as the clinical grade increased. Similar findings were seen in a study by Shah et al.,[8] where the association of changes in dermoscopy of facial AN with Sharqie's grading of AN was studied. The study highlighted the following findings: in mild clinical grade, follicular plugging and less prominent sulci with irregular brown globules were seen. In the moderate clinical grade of AN, prominent sulci and large brown globules were seen, and the severe grade showed markedly depressed sulci and prominent cristae, which led to the formation of rhomboid-shaped islands.[8]

Sulci cutis and cristae cutis showed a significant association with the duration of AN. As the duration increased, sulci cutis became prominent and cristae cutis showed rhomboid formation. Papillary projections became nontriangular from triangular as clinical grade increased (p-value < 0.05). The number of hyperpigmented dots/globules increased as duration increased in the present study (p-value < 0.05). These findings are similar to the study done by Shah et al.[8] where chronic variants showed prominent sulci, dark brown globules, and exophytic papillary structures. The number of crypts increased as the duration increased (p-value < 0.05). These dermoscopy changes that were observed as duration increased may be attributed to the increase of hyperkeratosis, papillomatosis, acanthosis, and increased basal pigmentation

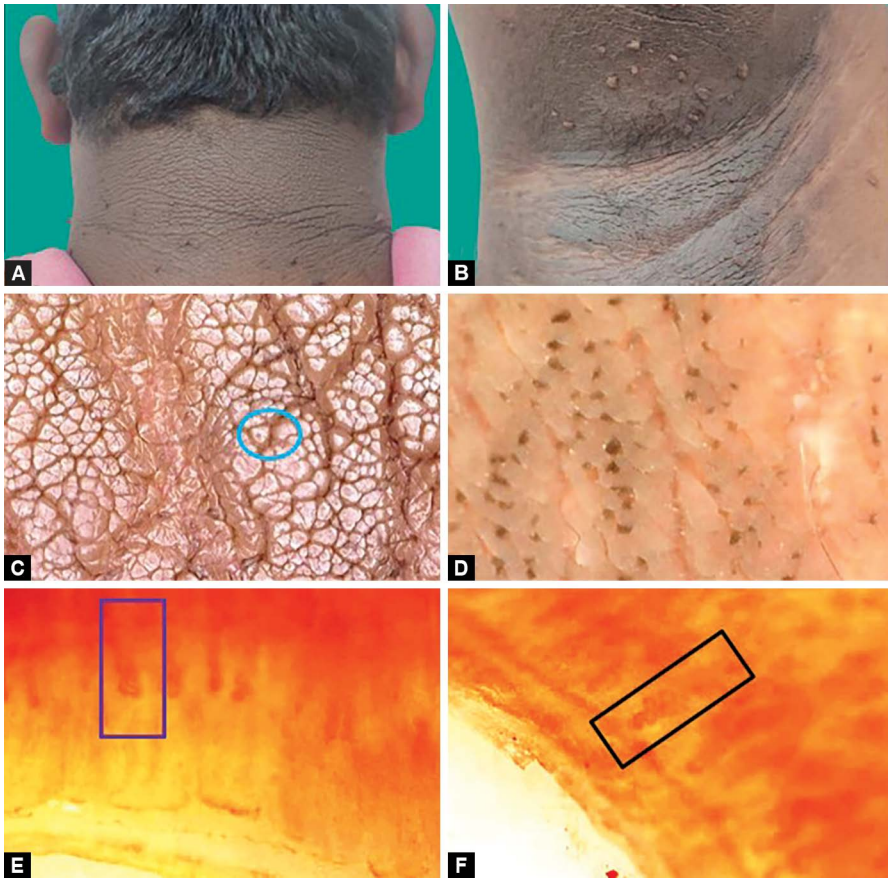
on histopathology as the duration of AN increases. In our study, 7/97 participants were known diabetics. Out of 97 patients, 36 gave consent to get their HOMA-IR done, and 21 had IR (HOMA-IR > 2).

Table 3 gives a comparison of NFC findings in AN in the present study with two other studies depicting NFC changes in DM. The slightly higher frequency of findings in our study may be attributed to the undetected prevalence of diabetes in the remaining 61 patients, as the diabetic status was not known at the time of conclusion, since they did not undergo blood investigations for IR. In our study, ramified capillaries were seen in 26/83 (31.32%). This finding was similar to a study done by Ahmad et al.,[9] where ramified capillaries were seen in 35.4%. Dropouts were the most common findings in our study. Their high presence in our study may be due to the less visibility of a capillary at the end of the dermoscopic image due to the panoramic view. Vascular damage is initiated by endothelial hypoxia, causing a decrease in capillary density (dropouts) and release of vascular endothelial growth factor (VEGF), endothelin-1. These factors aid in the growth of new capillaries. Compensatory neoangiogenesis begins, characterized by ramifications and capillary dilatation, which if left uncontrolled, can lead to microvascular complications.[10]

As the clinical stage increased, the presence of findings such as tortuous and cross-linked capillaries in the nailfolds increased (p-value < 0.05). Currently, there is absence of literature on the grade of AN and its association with NFC changes.

As the duration of AN increased, the presence of cross-linked capillaries (p-value = 0.001) and ramified capillaries (p-value = 0.003) in the number of nailfolds increased. This can be attributed to untreated or unnoticed IR as the duration of AN increases. Similar findings were seen in a study done by Shah et al.,[11] where the duration of DM was statistically significant in context to NFC findings (p-value = 0.027), demonstrating that NFC findings such as tortuous capillaries, avascular areas, and ramified/bushy capillaries were more common in chronic diabetic cases.

The limitations of this study are: (1) all patients were not evaluated for HOMA-IR and metabolic syndrome, (2) more female representation was seen due to cosmetic concerns. This bias can be reduced by taking a larger sample size in future studies, and (3) this is a cross-sectional study and lacks longitudinal data.



Figs 3A to F: (A) Involvement of neck, Burke's grading neck severity 4, neck texture 3; (B) Involvement of axilla, Burke's grading axilla 4; (C) Dermoscopy of neck (nonpolarized mode, 80× magnification): sulci cutis—prominent, cristae cutis—rhomboid formation present, papillary projections—nontriangular (blue circle), hyperpigmented dots—<50 in number; (D) Dermoscopy of axilla (polarized mode, 80× magnification): sulci cutis—prominent, cristae cutis—rhomboid formation present, papillary projections—nontriangular, hyperpigmented dots—>50 in number; (E) NFC (polarized mode, 80× magnification)—tortuous capillary (purple rectangle); (F) NFC (polarized mode, 80× magnification)—ramified capillary (black rectangle)

Table 3: Comparison of NFC findings in AN in the present study with other studies

NFC changes	*Present study*	*Maldonado et al.*[10]	*Ahmad et al.*[9]
Dropout capillaries	83/83 (100%)	48% (Mentioned as avascular areas)	Not seen
Tortuous capillaries	61/83 (73.49%)	63%	46.1%
Cross-linked capillaries	55/83 (66.26%)	59%	30.9%
Giant capillaries	7/83 (8.43%)	11%	Not seen
Hemorrhage	6/83 (7.2%)	Not mentioned	28.6%
Ramified capillaries	26/83 (31.32%)	Not mentioned	35.4%
Ectasia	6/83 (7.22%)	39%	28.2%

Conclusion

Nailfold capillaroscopy in AN and its clinical and dermoscopic correlation is an uncharted territory. This study provides an insight and scope for the same. The findings of the present study will aid in the early detection of microvascular changes in cases of AN (suggestive of IR) using NFC, a bedside procedure, which can further help in deciding patient referrals for early screening of diabetic retinopathy and diabetic nephropathy. Changes in AN can be monitored

in patients on treatment using dermoscopy. More studies with a larger sample size, with prior evaluation for IR and metabolic syndrome status, are required to strengthen the findings of this study.

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