Original Article

Accuracy of Dermoscopy as a Point-of-Care Tool for Distal Subungual Onychomycosis at a Tertiary Hospital

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Abstract

Context: Accurate diagnosis of onychomycosis is important since misdiagnosis can lead to inappropriate therapy, delayed diagnosis of other nail conditions, and antifungal resistance. Dermoscopy is an emerging diagnostic tool, particularly valuable in the resource-poor settings.

Aims: The study aimed to evaluate the accuracy of dermoscopy as a point-of-care tool in diagnosing distal subungual onychomycosis (DSO) at a tertiary hospital.

Settings and Design: An observational, prospective, and cross-sectional study was conducted among 22 clinically diagnosed DSO patients using convenience sampling at a tertiary hospital from November 2019 to September 2021.

Subjects and Methods: Participants underwent gross nail examination, dermoscopy, potassium hydroxide (KOH), and periodic acid-Schiff (PAS) examinations.

Statistical Analysis Used: Sensitivity, specificity, predictive value, and likelihood ratios (LRs) of the dermoscopic patterns were obtained using KOH and PAS results as the reference standard.

Results: Fifty-one nails were submitted but 2 were lost during the processing, leaving 49 nails for analysis. The most common pattern was jagged edge with spikes (65.3%). Individual patterns yielded only low-to-moderate sensitivity (32.4%–73.5%). However, combining all patterns increased sensitivity to 91.2% (95% confidence interval: 76.3–98.1). Ruin appearance showed the highest specificity (100%) and positive predictive value (100%). LRs were not significant enough to draw the conclusions.

Conclusions: Dermoscopy may serve as an on-site, adjunct tool in the diagnosis of DSO, especially when the combination of patterns is considered. Ruin appearance maybe particularly useful in ruling in DSO. However, confirmation using mycological and histopathological tests remains essential.

Keywords: Dermoscopy, onychomycosis, periodic acid schiff, postassium hydroxide

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Introduction

Onychomycosis or fungal infection of the nails affects approximately 5% of the population worldwide, with an incidence of 0.5%–5% in Asian populations.[1,2] It accounts for almost 50% of nail disorders.[3] In the

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Philippines, it is the most common nail disorder treated by Filipino dermatologists.[4] However, the statistics regarding onychomycosis as the most common nail disorder have been recently challenged.[5,6] Nail changes caused by foot and toe malformation may look like onychomycosis, particularly the distal lateral subungual type.[5] Other nail disorders that can mimic onychomycosis are traumatic onycholysis, lichen planus, psoriasis, and trachyonychia.[1] Accurate diagnosis of onychomycosis is paramount because incorrect diagnosis can lead to delay in the diagnosis of other nail conditions, unnecessary long-term expensive treatment, severe side effects from systemic medications, and more recently, the promotion the emerging antifungal resistance.[7] Unfortunately, almost 40% of dermatologists do not perform confirmatory tests for suspected onychomycosis cases.[8]

The current established techniques for the diagnosis of onychomycosis include direct microscopy with potassium hydroxide (KOH), histopathological examination, and fungal culture.[9] Based on the recent meta-analysis of the utility of KOH, culture, and periodic acid-Schiff (PAS) for the diagnosis of onychomycosis, nail clipping with PAS outperformed KOH and fungal culture in terms of validity, performance, and efficiency and therefore can be considered the "gold standard" diagnostic technique.[10]

However, PAS examination is an expensive diagnostic procedure, especially for developing nations. In the United States, PAS and culture examination of nails can cost around 148 dollars.[11] At the time of the study (2021), only a limited number of institutions in the Philippines offer these services, with costs ranging from Php1385 to Php5000 per sample, inclusive of the dermatopathologist's reading fee. This could be one of the factors why some dermatologists do not routinely request for additional tests.

Dermoscopy is commonly used on the skin as tool in distinguishing between benign and malignant neoplasms. Recently, it has been also utilized on the nails to help diagnose onychomycosis.[9] The authors have found that the significant dermoscopic patterns [Table 1], particularly in the most common subtype, the distal subungual onychomycosis (DSO), are the presence of ruin appearance, jagged edge with spikes, longitudinal striae, leukonychia, and distal irregular termination.[12-15] This study aims to evaluate the diagnostic accuracy of these patterns in diagnosing DSO.

Table 1: Description of significant dermoscopic patterns in distal subungual onychomycosis from previous studies[12-15]

Dermoscopic pattern	Description
Ruin appearance	Indented areas are seen on the ventral nail (subungual keratosis), and there is distal pulverization characterized by thickening of the nail plate
Jagged edge with spikes	The proximal edge of onycholysis shows jagged margins with spikes. These jagged edges correspond to the fungal invasion in the nail plate
Longitudinal striae/ Aurora Borealis	Presence of multiple striae of same or different colors (yellow, white, brown, etc.) within the onycholytic nail plate. These correspond to the reflections of fungal colonies, invasion, and subungual debris
Leukonychia	Yellowish color change on the nail plate from light yellow to orange
Distal irregular termination	The end of the thickened nail plate ending with an irregular and crumbly appearance

Subjects and Methods

An observational, prospective, cross-sectional study of 22 clinically diagnosed DSO patients, obtained through convenience sampling, was carried out at a tertiary hospital in the Philippines, from November 2019 to September 2021. To strengthen the methodology, the 2015 standards for reporting of diagnostic accuracy studies was adapted.[16] Inclusion criteria include patients ≥18 years old with any clinical signs of DSO of at least one fingernail or toenail. On the other hand, patients <18 years of age, those who received topical or systemic antifungals in the past 1 or 3 months, respectively, and have a presumed or confirmed diagnosis of an inflammatory nail disorder were excluded.

The study was conducted according to the principles of the Declaration of Helsinki and approved by the Institutional Review Board. The study process was carefully explained to all participants and an informed consent was obtained as well. All laboratory examinations were at the expense of the investigator. There were no reported adverse events during the conduct of both index and reference standard tests. All the data gathered are kept confidential and kept in a password-protected computer. A unique patient ID number was used for all specimen labels and electronic data.

Gross cutaneous examination of all fingernails and toenails was done onto each participant. These were documented using a 12-megapixel camera phone (Apple Inc., California, USA). To minimize collection bias when a potential participant has more than 1 nail involved, the following sampling technique was used: if more than 1 nail was involved in the same hand or foot, only 1 nail was included. Hence, the maximum number of nails included from a participant with multiple nails involved, was 4 (1 nail per extremity).

Digital dermoscopic images were obtained using a dermatoscope with ×10 magnification (3Gen Inc., California, USA) manually attached to a 12-megapixel

camera phone (Apple Inc., California, USA). Both polarized and nonpolarized light were used during dry and wet examinations. Nails were photographed on the dorsal aspect and free edge of the nails. The patterns from the images were read initially by the primary investigator and confirmed by a dermoscopy specialist who was blinded on the results of both KOH and PAS examination of the study samples. The same dermoscopy specialist confirmed all images; hence, there was no inter-observer variability.

For PAS examination, using a sterile nail clipper, the nails were cut from the distal portion or free edge, which according to the literature, should be at least 4 mm in length to improve the diagnostic performance.[17] The longest nail was chosen to minimize pain and to facilitate adequate specimen collection. The nail clippings were then placed in a specimen bottle with 10% buffered formalin and were sent to the laboratory to be sequentially be processed and stained with PAS. The slides were read by a dermatopathologist, who was blinded on the results of both dermoscopy and KOH examinations. The presence of intensely stained reddish dots or threadlike structures in between the cells of the nail plate was considered to be a positive result.[10] A sample with positive PAS result was still considered a true positive even if it was negative with KOH test.

For KOH examination, the exposed subungual debris was then gently scraped with a Blade #15 and placed directly on a glass slide. According to the literature, it is best to obtain scrapings at the advancing infected edge nearest the cuticle, where fungi are most concentrated.[10] After collecting sufficient amount of scrapings, 1 drop of 20% KOH solution was placed on the slide. A transparent tape was placed gently on top of the sample to secure the sample and drain the excess KOH. The slide was left at the room temperature for 30 min or until softening of the specimen occurred. Slides were microscopically evaluated by a senior dermatology resident, who was blinded of both dermoscopy and PAS results. The presence of branching thread-like structures (hyphae) or beaded spherical structures (spores) was considered to be a positive test.[18]

A minimum of sample size of 45 nails with clinically diagnosed DSO was required for this study. This calculation was based on ruin appearance as the most prevalent dermoscopic pattern in the literature. The prevalence was 72.68% among clinically diagnosed DSO patients. The computation also took into account the 85.97% sensitivity of ruin appearance on the basis of any 1 of the following: a positive culture growth or positive PAS and hematoxylin and eosin stain.[13] This estimation also considered 7.07% confidence interval (CI) width, 80% power, and 10% drop-out rate.[19]

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for the categorical variables; mean and standard deviation (SD) were used for normally distributed continuous variables. Sensitivity, specificity, negative predictive value (NPV), positive predictive values (PPV), and likelihood ratios (LRs) were used to determine the diagnostic accuracy of dermoscopic patterns compared with the reference standard tests, KOH, and PAS examination. CIs around these measures of accuracy were calculated at 95% level to quantify the statistical precision of the measurements. Shapiro–Wilk was used to test the normality of the continuous variables. Missing and indeterminate data were not included. STATA 13.1 (StataCorp LLC, Texas, USA) was used for the data analysis.

Results

Fifty-one nail samples were submitted, but two samples were washed out during PAS processing, thus 49 samples remained for the analysis. The average age of patients in the study was 48.6 years (SD = 17.7) old, with 11 female (55%) and 9 male (45%) patients. The most commonly affected nails are the toenails (9; 45%). Eight patients (40%) did not have any co-morbidities, but the second most common co-morbidities are tinea infections (25.5%).

As shown in Table 2, the average age of patients in the study was 48.6 years (SD = 17.7) old, with 11 female (55.0%) and 9 male (45.0%) patients. The most commonly affected nails are the toenails 9 (45.0%). Eight patients (40.0%) did not

Table 2: Demographic and clinical profile of the patients (*n*=20)

Variable	Frequency (%)
Age	
18–40	8 (40.0)
41–60	7 (35.0)
61 years and above	5 (25.0)
Sex	
Male	9 (45.0)
Female	11 (55.0)
Type of nail involvement	
Fingernail	8 (40.0)
Toenail	9 (45.0)
Both	3 (15.0)
Co-morbidities	
None	8 (40.0)
Tinea corporis/pedis/manum	5 (25.0)
Hypertension	3 (15.0)
Bromhidrosis	1 (5.0)
Immunocompromised state	1 (5.0)
Lichen simplex chronicus	1 (5.0)
Seborrheic dermatitis	1 (5.0)

have any co-morbidities, but the second most common co-morbidities are tinea infections (25.5%).

Among the 49 clinically diagnosed DSO nail samples, the most common dermoscopic pattern identified is the jagged edges with spikes (65.3%) and the least common is ruin appearance (22.5%). The prevalence of laboratory-confirmed onychomycosis among all clinically-diagnosed nail samples was observed to be at 69% (95% CI: 55%–81%) based on the KOH and PAS exam results. Conversely, the prevalence of those without laboratory-confirmed onychomycosis is 30.6% (95% CI: 18.2%–45.4%).

Table 3 shows individual patterns yielded low-to-moderate sensitivity and moderate-to-high specificity. PPVs were moderate to high, while NPVs were low. Positive LRs (PLRs) and negative LRs (NLRs) are >1 and <1, respectively. Combining all 5 dermoscopic patterns increased the sensitivity to 91.2% (95% CI: 76.3–98.1).

Discussion

In the present study, the average age of patients presenting clinically with DSO (48.6 years old) is similar with the studies conducted by Kaynak *et al.* and Chetana *et al.*[13,14] The age range (18–40 years old) is slightly lower than studies of Jesús-Silva *et al.* (50–59 years old) and Piraccini *et al.* (56–69 years old) probably because of COVID-19 pandemic restrictions for the elderly during the study period.[15,20] Older age predisposes a person to have onychomycosis because of weakening immune system, higher risk of diabetes, impaired peripheral circulation, slower nail growth, and higher frequency of arthritis, which affects physical flexibility, and hence, digital deformities, especially for the toes.[5] Female predominance was also observed in this study, consistent with previous authors.[14,15,20] However, other studies noted higher rate in males than females.[12,21] This difference might be related to cultural differences between sexes in the studies' population, such as occupation, footwear, and participation in sports. The predominant type of nail is the toenail which is consistent with similar studies.[13,21] This probably reflects the greater incidence of tinea pedis than that of tinea manuum. Finally, the co-existence of an existing fungal infection, particularly tinea pedis was also observed. The findings suggest that fungus on the skin of the foot spreads to toenails and vice versa.[22]

In this study, the most frequently observed pattern in DSO is jagged edge with spikes (65.3%) similar to previous studies.[20,23,24] Jagged edge with spikes corresponds to the behavior of the migrating fungus sharply and irregularly tunneling under the nail plate and extending proximally usually along the area with onycholysis [Figure 1].[13] The second most common is longitudinal striae or aurora borealis pattern (53.1%) which is caused also by the migration of the fungus toward the proximal end, but this time creating longer and wider parallel bands of fading color [Figure 2].[25] Ruin appearance corresponds to the keratotic debris formed by the fungus after invading the nail bed, which causes the stratum corneum to thicken [Figure 3].[25] Leukonychia are white punctate or patchy areas corresponding to the growth of fungi as seen in a culture medium.[25] Distal irregular termination relates to the distal crumbling pattern made by the invading fungus to thickened nail plate.[25] Its low frequency (34.7%) in this study is probably because it is rather more common in total dystrophic onychomycosis than distal subungual type.[15] For these reasons, dermoscopy can indeed guide clinicians on the selection of the best site for mycological and histopathological sampling, because the patterns correspond to the behavior of the invading fungus.

Since dermoscopy yielded low-to-moderate sensitivity, the mnemonic high sensitivity, negative test, rule out, cannot be used to interpret a negative test in a clinical setting.[26] However, in this study, it was found out that the presence of ruin appearance pattern has a high specificity (100.0%).

Table 3: Sensitivity, specificity, predictive values, likelihood ratios, and accuracy of each of the dermoscopic patterns in the present study

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	PLR (95% CI)	NLR (95% CI)	Accuracy (%)
Ruin appearance	32.4 (17.4–50.5)	100.0 (78.2–100.0)	100.0 (71.5–100.0)	39.5 (24.0–56.6)	Undefined	0.68 (0.54–0.85)	53.1
Jagged edges with spikes	73.5 (55.6–87.1)	53.3 (26.6–78.1)	78.1 (50.0–90.7)	47.1 (23.0–72.2)	1.58 (0.89–2.81)	0.50 (0.24–1.03)	67.3
Longitudinal striae/ aurora borealis	64.7 (46.5–80.3)	73.3 (44.9–92.2)	84.6 (65.1–95.7)	47.8 (26.8–69.4)	2.43 (1.01–5.82)	0.48 (0.28–0.83)	67.3
Leukonychia	52.9 (35.1–70.2)	80.0 (51.9–95.7)	85.7 (63.7–97.0)	42.9 (24.5–62.8)	2.65 (0.92–7.64)	0.59 (0.38–0.91)	61.2
Distal irregular termination	41.2 (24.6–59.3)	80.0 (51.9–95.7)	82.4 (56.6–96.2)	37.5 (21.1–56.3)	2.06 (0.69–6.12)	0.74 (0.50–1.07)	53.1
Combined dermoscopic patterns	91.2 (76.3–98.1)	40.0 (16.3–67.7)	77.5 (61.5–89.2)	66.7 (29.9–92.5)	1.52 (0.99–2.33)	0.22 (0.06–0.77)	75.5

CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predicted value, PLR: Positive likelihood ratio, NLR: Negative likelihood ratio

Hence, the mnemonic high specificity, positive test, rule in, can be used, that is, its presence is most useful in ruling in DSO because of its high specificity.[26] This is consistent with the observation of Freedman and Tosti that even though its absence does not necessarily rule out the diagnosis, its presence is highly indicative of a positive diagnosis of DSO.[8] Pewsner *et al*. however pointed out, that care should be taken if highly specific tests are not sufficiently sensitive, similar to this present study.[26] In such cases, according to Trevethan, PPV and NPV should be computed and be the metrics of choice in such context, as this current study had done.[27]

In general, the sensitivity of each individual dermoscopic patterns ranges from low to moderate, (32.4%–73.5%), compared to that of culture (29.0%–82.0%) [Table 4]. However, when these patterns are combined, the sensitivity increases (91.2%), a finding also demonstrated by Kayarkatte *et al*. (91.7%).[28] This finding can be a groundwork for larger studies in developing a diagnostic criteria for onychomycosis based on multiple dermoscopic patterns.

The major limitation of both sensitivity and specificity is that they are not practically useful in the clinical setting because they are only concerned with the intrinsic accuracy of a diagnostic test relative to the gold standard.[27] It does not answer the clinician's question of: "Given this positive test result of this patient (presence of dermoscopic pattern), what is the chance or probability that the patient does have onychomycosis?" To answer this, predictive values were computed, which are the most useful clinical parameters.[30] In this study, all five dermoscopic patterns showed moderate-to-high PPV, ranging from 78.1% to 100.0% and low-to-moderate NPV, ranging from 39.5% to 47.8%. Similar findings were observed with Nada *et al*. and Kaynak *et al*. with PPV: 75.3%–100.0% and NPV: 37.7%–66.6%.[13,31] However, different finding was observed with Kayarkatte *et al*. with high PPV: 91.7%–98.1% but low NPV: 13.2%–36.85%.[28] This discrepancy could be explained by the influence of prevalence of onychomycosis in each of the studies. Because unlike sensitivity and specificity, predictive values vary with changing disease prevalence.[27]

Table 4: Sensitivity and specificity of the present study, other dermoscopy studies, potassium hydroxide, periodic acid-Schiff, and culture in diagnosing onychomycosis

Diagnostic test	Sensitivity (%)	Specificity (%)
Dermoscopy (present study)	91.2	40.0
Dermoscopy[28,29]	72.7–91.7	72.9–100.0
PAS[10]	61.0–98.0	44.0–100.0
KOH[10]	44.0–100.0	7.0–100.0
Culture[10]	29.0–82.0	83.0–100.0

PAS: Periodic acid-Schiff, KOH: Potassium hydroxide

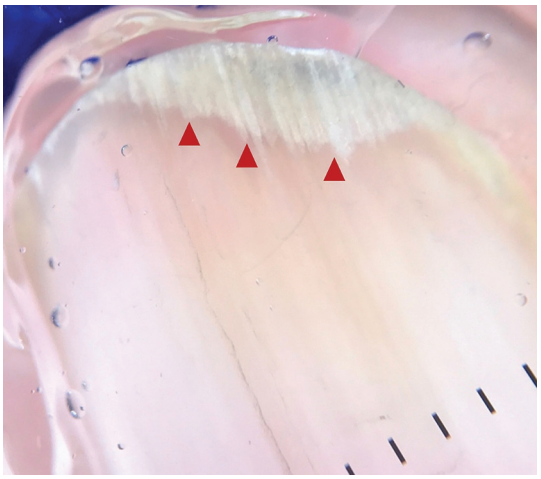

Figure 1: Jagged edges with spike (red triangles) demonstrates the sharp movement of the fungus underneath the onycholytic nail plate from distal to proximal (×10, polarized, wet)

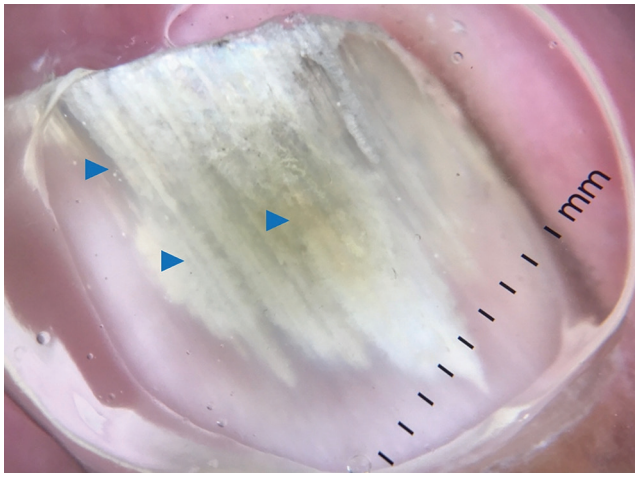

Figure 2: Longitudinal striae or aurora borealis pattern is similar to jagged edges with spike but with longer and wider bands of fading color (blue triangles). This reflects the expansion of the fungal colonies (×10, polarized, wet)

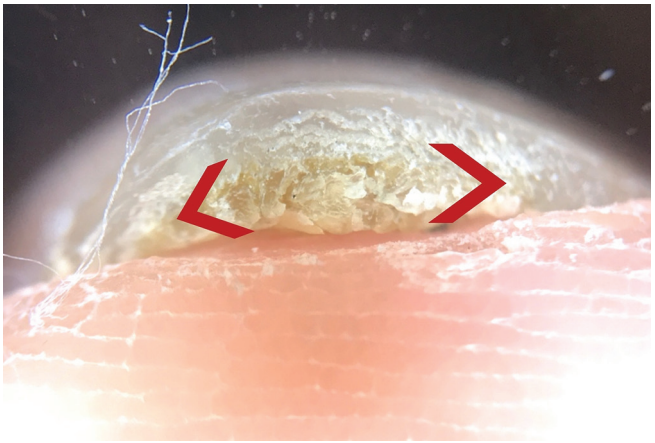

Figure 3: Ruin appearance seen on the distal free edge of the nail plate with thickening and pulverization of the its ventral aspect (red bracket). This corresponds to the accumulation of nail bed debris as a reaction from the invading fungus (×10, polarized, dry)

While all five dermoscopic patterns demonstrate moderate to high PPV, dermoscopy should be viewed as an adjunctive tool rather a replacement for a confirmatory test. Its strength lies in guiding the practicing dermatologist toward optimal sample site selection. For example, instead of sampling the nail randomly, clinicians can target specific areas such as the proximal base of "jagged spikes," zones exhibiting the "ruin appearance," or regions where the "aurora borealis" pattern is most prominent. This can potentially reduce false negatives and can enhance the diagnostic accuracy of a chosen confirmatory test.

Similar to predictive values, LRs are clinically more useful than sensitivity and specificity.[27] Leukonychia is more likely to occur in nails with DSO based on its PLR of 2.65. However, although it is >1, literature says that a value of >10 is generally considered to significantly increase the probability of disease.[32] Longitudinal striae has the lowest NLR of 0.48. This means that a negative test is less likely to occur in nails with onychomycosis. Based on the literature, the significant NLR is <0.1, which was not seen in this case.[32] Since to the author's knowledge, and to date, this is the first study on the diagnostic accuracy of dermoscopy in DSO that reported LRs, no comparison can be made regarding this result.

Conclusion

Dermoscopy may serve as an on-site, adjunct tool in the diagnosis of DSO. It can guide the clinician on the selection of the best site for mycological and histopathological sampling, because the patterns correspond to the behavior of the invading fungus. However, there is a need to combine the patterns to increase the sensitivity. Addition of mycological and histopathological tests is still warranted for confirmation.

The first limitation in this study is the nail sample processing. Locally, not all laboratories are adept in processing nails. In this study, the technicians had difficulty in the adherence of the nail plate to the slide and the take-up of PAS stain in the specimen. Improvement of laboratory protocols and techniques is recommended to lessen technical bias. Second, dermoscopy although useful, cannot identify or distinguish dermatophyte and nondermatophyte fungal organisms, unlike culture studies.

The authors encourage the use of dermoscopy in dermatology clinics and training institutions when diagnosing onychomycosis, especially for cases in which confirmatory tests are not readily available. In addition, the present study recommends exploring other confirmatory tests such as fungal culture, Grocott's methenamine silver stain, or polymerase chain reaction. For other future diagnostic accuracy studies, it is recommended to report not only sensitivity and specificity but also other more clinically relevant measures of accuracy.

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Conflicts of interest

There are no conflicts of interest.

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