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Nevus of Hori in African patients: an entity that is most likely underdiagnosed in clinical practice

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ABSTRACT

Background: Nevus of Hori (HN) has been primarily reported in patients of Eastern Asian descent, with a paucity of data regarding HN occurring in African patients. In this study, we report on South African patients with HN initially thought to have melasma.

Objective: To characterize the histopathological and clinical phenotypes of HN in African patients.

Methods: Retrospective data were collected from patients who met the inclusion criteria. These data entailed the clinical distribution, demographic data, Fitzpatrick skin phototype, and histopathologic features of African patients diagnosed with HN from a single private aesthetic center in Bloemfontein, South Africa.

Results: Thirty patients with an average age of 49 ± 7.37 were included in this analysis. The majority of patients were female (*n* = 29; 96.67%), and most patients were of Fitzpatrick skin phototype V (*n* = 22; 73.3%). The most common clinical distribution pattern was bitemporal (76.7%), followed by the zygomatic pattern (20%), mixed type (16.7%), and finally the central forehead pattern (3.3%). Histopathologically, the dendritic cell type of melanocytes was observed in the majority of patients (*n* = 25; 83.3%), while spindle-shaped cells were observed in few patients (*n* = 7; 23.33%), and none of the patients had bipolar-type melanocytes.

Limitations: This study has limitations inherent to small sample size and its inability to accurately generalize the findings.

Conclusion: HN can clinically mimic melasma in African patients. The most common clinical presentation was bitemporal. To our knowledge, this study is the largest regarding the clinicopathological profile of HN in African patients and it is likely to be the first to report these compelling findings.

Keywords: acquired bilateral nevus of Ota-like macules, acquired circumscribed dermal facial melanocytosis, melasma, nevus fusco caeruleus zygomaticus

Introduction

Nevus of Hori (HN) is an acquired dermal melanocytosis that is characterized by multiple bilateral macules, often speckled blue-gray and brown areas of pigmentation affecting cheeks, temples, the sides of the forehead, the superior aspect of the eyelids, root of the nose, and ala nasi.[1–3]

In 1984, Hori et al.[3] first described the nevus of Ota-like facial dermal melanocytosis occurring later in life, as observed in their study of 22 Japanese patients. Emanating from that study, the term acquired bilateral nevus of Ota-like macules or HN was coined. In 2005, Ee et al.[2] also reported a larger series of 161 subjects with HN, all of whom were of Asian descent. Furthermore, one population-based study has documented that the overall prevalence of HN was 2.5% in Chinese people and further that women (90%) were more affected than males (10%), with a median age of 46 years.[4]

It is generally accepted from the literature that HN is primarily reported in patients of Eastern Asian descent. Apart from a few sporadic case reports, data on African patients is lacking.[5,6] In South Africa, studies conducted by Dlova et al. have reported that pigmentary disorders were among the top 5 presenting complaints of dermatology patients seen in their setting. Of these pigmentary disorders, melasma, postinflammatory pigmentation, and lichen planus pigmentosus were among the conditions that were singled out with no particular mention of HN.[7–9]

What is known about this subject in regard to women and their families?

- Nevus of Hori is primarily described in Eastern Asian descent and to our knowledge, no data exists in a South African population.

What is new from this article as messages for women and their families?

- The study reports a largest cohort primarily affecting women and described for the first time in African patients.

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Table 1
Demographic summaries

	Description	Frequency	Percent
Age group	35–40	4	13.33
	40–45	4	13.33
	45–50	8	26.67
	50–55	7	23.33
	55–60	7	23.33
	Total	30	100.00
Gender	Female	29	96.67
	Male	1	3.33
	Total	30	100.00
Skin phototype	IV	8	26.67
	V	22	73.33
	VI	0	0.00
	Total	30	100.00

The characteristics of the macular pigmentation seen in HN are similar to those of other known dermal melanocytosis, such as Mongolian spot, nevus of Ito, and nevus of Ota. It is therefore imperative to differentiate HN from the typical nevus of Ota, which may be bilateral, as both conditions may affect the face.[2,3,10] HN is typically acquired later in life, in contrast to the nevus of Ota, which is well known to occur as early as prenatally and as late as puberty. Patients with the latter also tend to have ocular mucosal involvement, in addition to cutaneous lesions. We report the occurrence of HN in African patients, wherein there is a higher possibility that clinicians may miss the diagnosis, as the condition can mimic melasma.

Material and methods

The study employed a retrospective descriptive design to access and analyze data from 30 adult patients at a single center in Bloemfontein, South Africa. All included patients were above 18 years of age and had records of histopathological confirmation of the diagnosis by means of 2 to 3 mm punch biopsies. The biopsies were taken from the lesional skin of the bitemporal areas or cheeks of the affected patients and reviewed by 2 independent dermatopathologists. Clinical photographs and Fitzpatrick skin phototype (SPT) information were also obtained. Chi-square, which is best applied for small sample sizes, was used to analyze the data. Correlation analysis was applied to categorical data to assess the level of association between the demographic data, clinical patterns, and histological features. The level of significance was set as the level <.05. Descriptive statistics, such as frequency and percentages, were used to analyze the data, which were processed using IBM SPSS Statistics V22.0, New York City, New York.

This study was conducted in accordance with the prescriptions stipulated by the Declaration of Helsinki. Ethical clearance was obtained from the South African Medical Association Research Ethics Committee (SAMAREC 280808016/003/2022). All data were completely anonymized, and formal consent was obtained from patients whose clinical photographs were used in this study. All data were fully anonymized before conducting statistical analysis in consultation with a biostatistician.

Results

Thirty patients diagnosed with HN were included in the analysis. Most of the patients were in 45 to 50 years age group (n = 8; 26.67%). These were followed by patients above 50 years of age (n = 7; 23.33%). The average age was 49 ± 7.37 years with the youngest patient being 35 years old and the oldest being 60 years old. Majority of patients were female compared with male counterparts (n = 29; 96.67%). The most common Fitzpatrick SPT was V (n = 22; 73.3%). Table 1 summarizes the results.

Figure 1 summarizes the clinical distribution patterns present in our cohort of patients. Zygomatic pattern was observed in 20% of the patients compared with the majority (76.7%) counterparts that had a bitemporal pattern. Mixed type constituted 16.67% with the remaining 3.33% representing the central forehead distribution pattern.

On histology, the dendritic cell type of melanocytes was observed in the majority of patients (n = 25; 83.3%), whereas spindle-shaped cells were documented in few patients (n = 7; 23.33%), and none of the patients had bipolar-type melanocytes. Regarding other features, none of the patients had lymphocytic or interface reaction patterns. All histopathological examinations revealed a normal epidermal melanin content. The results are shown in Figure 2.

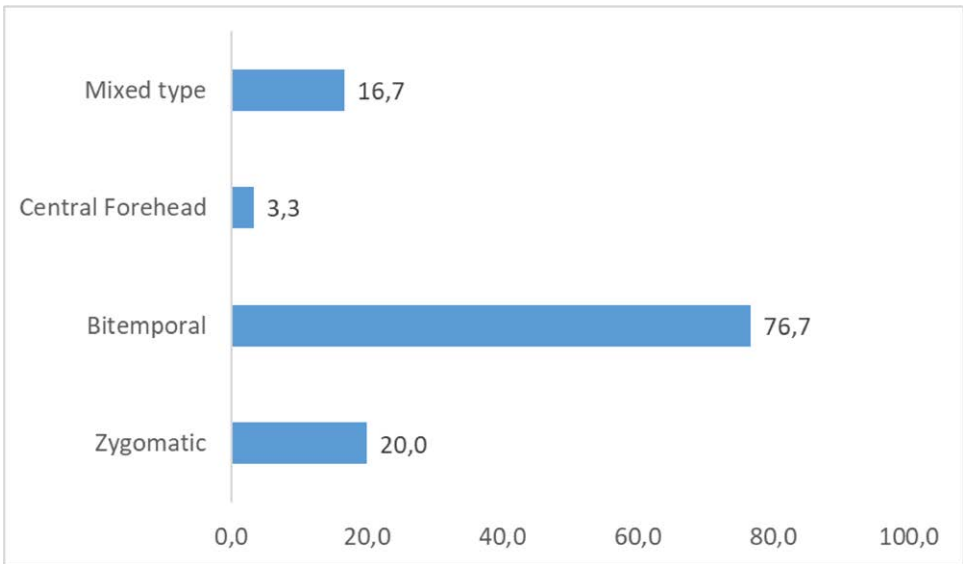

Fig. 1. Clinical distribution pattern of lesions.

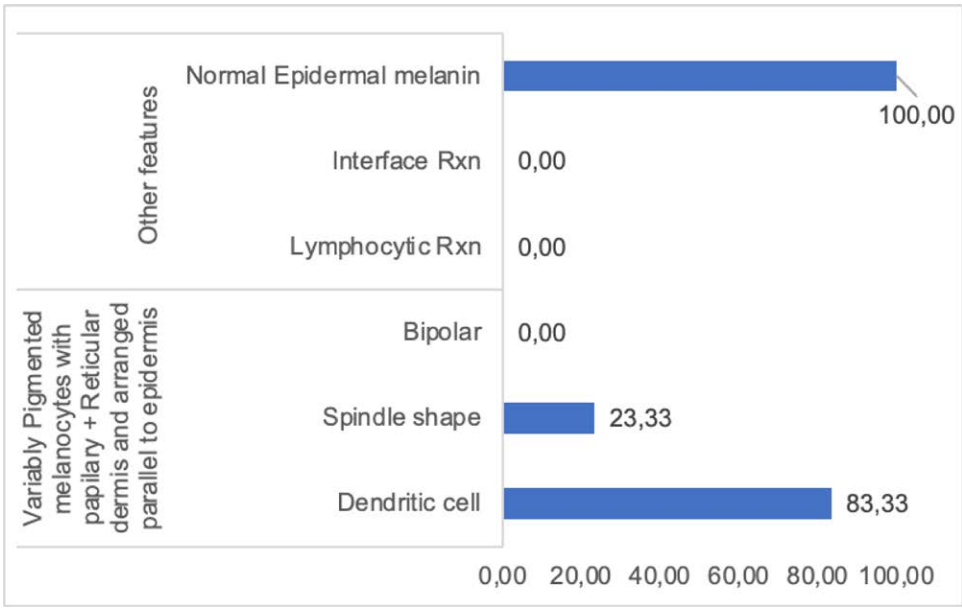

Fig. 2. Histopathological features of HN lesions. HN, nevus of Hori.

Discussion

HN is an acquired dermal melanocytosis that is commonly reported in patients of Eastern Asian descent.[5,6] In general, dermal melanocytic lesions may be subclassified as congenital or acquired. The congenital entities are the nevus of Ota, nevus of Ito, Mongolian spot, and blue nevus. Acquired dermal melanocytosis may also be further subdivided into facial and extra-facial variants. HN is classified as acquired facial dermal melanocytosis.[1,10] Most HN cases are diagnosed clinically based on factors such as history taking, treatment response, and the use of 365-nm Wood's lamp.[11] Melasma may show enhancement under Woods' lamp if it is epidermal, whereas HN

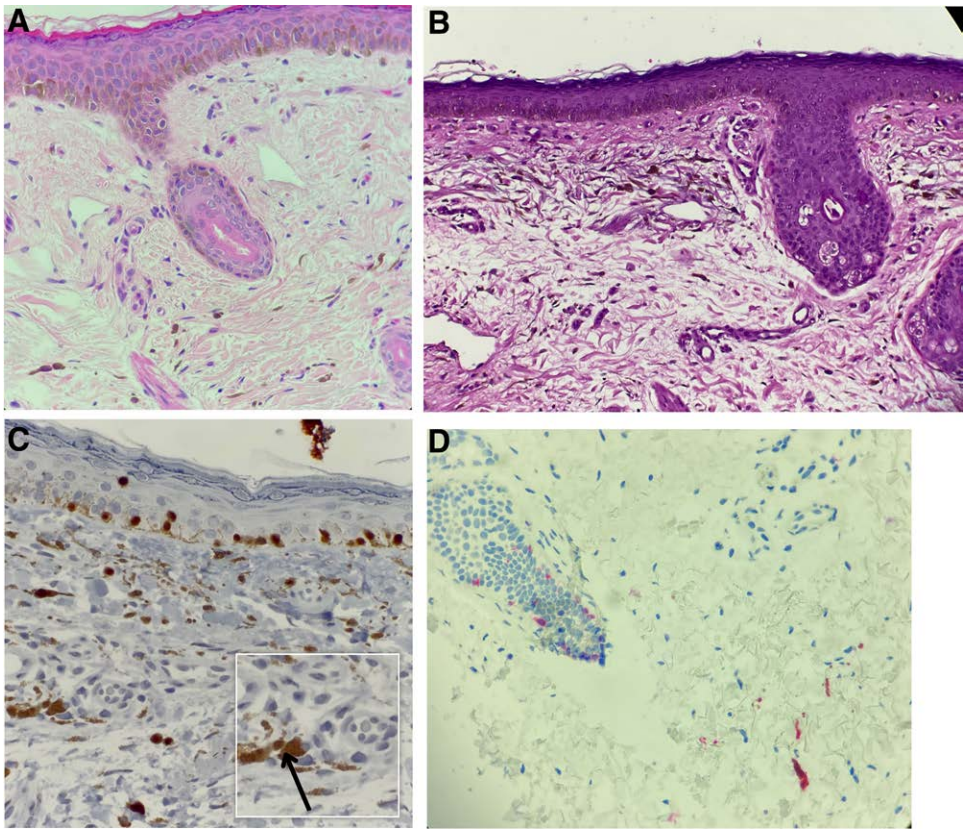

Fig. 3. (A) High power illustration of dermal melanocytes orientated parallel to the epidermis. (B) High-power microscopy illustrating dendritic melanocytes in between collagen fibers. (C) SOX-10 immunohistochemical stain highlighting variably pigmented dermal melanocytosis. (D) Melan-A expression is noted within the dermal loose-lying melanocytes. Normal follicular melanocytes are also demonstrated.

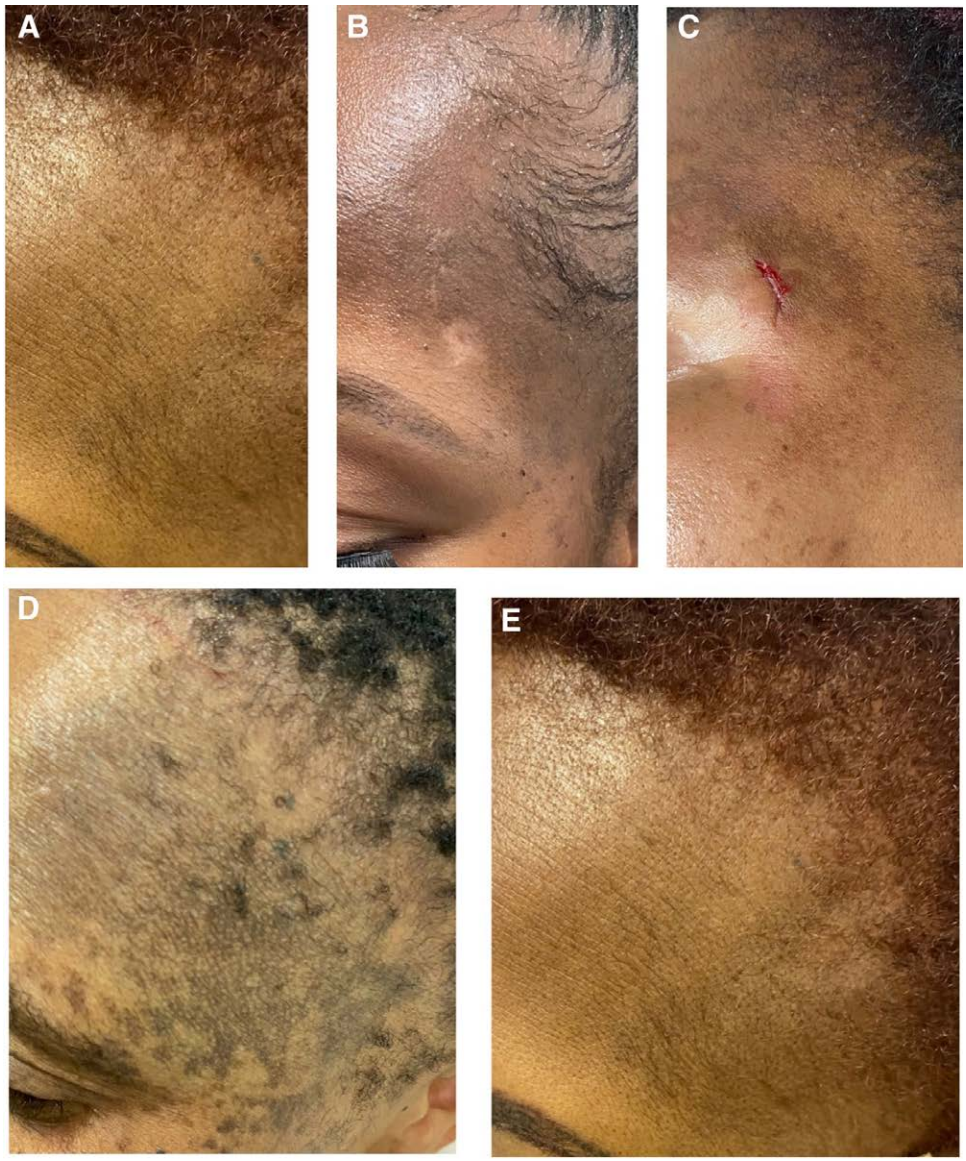

Fig. 4. (A–C) Bitemporal distribution pattern: lateral view. (D, E) Variation in morphology of bitemporal distribution pattern: lateral view.

generally does not, as the pigment is in the deeper dermal layers. It is challenging to differentiate the dermal and the mixed type of melasma lesions from HN under Woods' lamp.[11,12] However, a biopsy of the lesional skin remains the gold standard for the diagnosis of HN.[12,13]

Demographic data

This study is the first to report the occurrence of HN in African patients (n = 30). The average age was 49 ± 7.37 years and the youngest patient was 35 years old, while the oldest patient was 60 years old, which is fairly comparable with the data from a population-based study by Wang et al. in 2011.[4]

In keeping with the reported gender predilection in literature, the majority of patients in the present study were females (n = 29; 96.67%) compared with male counterparts.[4–6]

Interestingly, all patients were initially diagnosed with and treated for melasma. The diagnosis of HN was only established after lesional biopsies were performed in all subjects who were deemed to be recalcitrant cases of melasma, thereby highlighting that HN in African patients may very well mimic melasma and therefore likely to be clinically misdiagnosed and subsequently underreported in the literature. The authors also noted that most patients presented with a preconceived self-diagnosis of melasma. In this situation, the clinician's objective assessment becomes sacrosanct when arriving at a correct diagnosis.

The clinical quandary of HN in darker SPTs

The characteristic slate-gray, brown-blue, or blue-gray color is difficult to appreciate in patients with a higher Fitzpatrick SPT. Our study comprised mainly of the patients with SPT V (n = 22; 73.3%), and the remainder had SPT VI (n = 8; 26.7%). To compound this matter further, there are also other differential diagnoses that clinicians need to keep in mind when diagnosing HN. Perspicacious clinicians should be able to rule out melasma, lentigines, maturational hyperpigmentation, ochronosis, lichen planus pigmentosus, Riehl melanosis, ashy dermatosis, macular blue nevus, blue macules of progressive scleroderma, and nevus fuscoceruleus ophthalmomaxillaris (nevus of Ota).[2,3,14] HN is particularly differentiated from the nevus of Ota by its late onset, lack of scleral involvement, and bilateral, speckled, or confluent distribution in nature.[2,3,11] Wood's lamp and

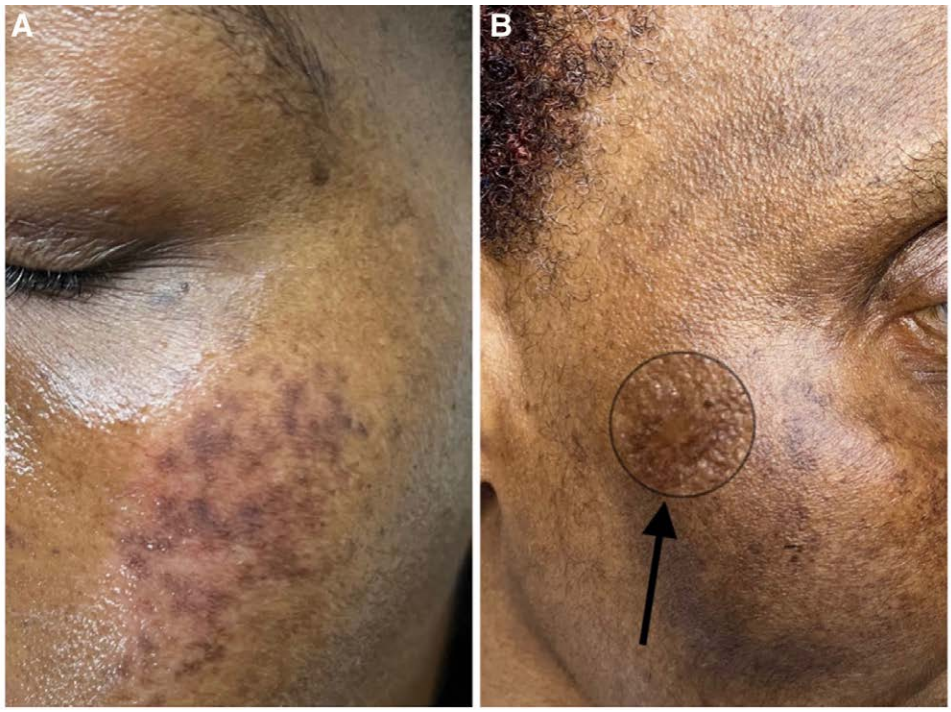

Fig. 5. Malar distribution pattern (note the biopsy site [arrow]).

dermoscopy, although not performed in the present retrospective study, could also provide auxiliary differentiating features to help exclude melasma. Dermoscopic evaluation of HN may feature uneven pigment distribution with follicular involvement and no typical reticular pattern, whereas melasma displays perifollicular sparing with an even pigment distribution and a characteristic reticular pattern.[15]

The pathogenesis, risk factors, and histopathology of HN

To understand the histopathology of HN in our cohort, it is imperative to first consider the current insights into the pathogenesis of HN. Although our study did not focus on the pathogenesis of HN in African patients, the grim reality is that it remains poorly understood, even in patients of Eastern Asian descent. This dearth of data gave rise to the following postulate pathomechanisms suggesting that: (1) there is epidermal melanocytes migration into the dermis, the so-called "dropping off"; (2) the dermal melanocytosis seen is from migrating melanocytes from the adjacent hair bulbs, and lastly that (3) there might be activation of dormant dermal melanocytes caused by some unknown factors.[1–3,14–16] Genetic factors, hormonal fluctuations, and sun exposure have been thought to influence melanogenesis via the induction of tyrosinase activity by melanocyte-stimulating hormone.[1–3,11,14–16] It was beyond the scope of the present retrospective study to elicit family history, sun exposure habits, and the age at which pigmentation was first noticed by the patients. Perhaps these factors, when elicited, could also help further rationalize the clinical phenotypes of HN in our cohort of African patients.

Histopathologically, the dendritic cell type of melanocytes was observed in the majority of our patients (n = 25; 83.3%), while spindle-shaped cells were seen in a minority (n = 7; 23.33%), and none of the patients had bipolar-type melanocytes (Fig. 2). These melanocytes are found within the dermis and parallel to the epidermis. Figure 3A–C displays SOX-10 and Melan-A (Fig. 3D) positivity, highlighting the melanocytes in the dermis. These findings are consistent with the typical description of pigment-bearing cells that are bipolar or irregular, dendritic or spindle shaped, and scattered throughout the dermis.[3,17,18] Melanocytes in HN are interstitially dispersed between the collagen fibers within the dermis and parallel to the long axis of these collagen fibers. Electron microscopy was not performed in this study. However, in HN, the electron microscopy typically shows melanosomes in earlier stages (II–IV) of melanization. In the nevus of Ota, the melanosomes are, however, in the late stages of melanization. This feature may help distinguish the nevus of Ota from that of HN.[1,2,12,19] Consistent with the respective pathogenic factors, melasma lesions demonstrate histological features such as solar elastosis, mast cell infiltrate, and damage to the basement membrane, with no presence of dermal melanocytosis.[10]

Clinical distribution patterns

The bitemporal clinical distribution pattern was present in 76.7% of the patients (Figs. 4–6). Contrary to the distribution pattern reported in a previous study wherein 99% of the patients had zygomatic involvement, our cohort only had 20% of the patients with zygomatic involvement.[4] Interestingly, the same study then documented 11% of the forehead's clinical distribution pattern compared with only 3.3% in the present study. Apart from the differences in the SPT and perhaps the geogenetic profiles of the patients studied, the reasons for the differences in clinical distribution patterns remain unclear.

To determine the relationship between sex and clinical distribution patterns, the chi-square test was used, and the results showed that sex had a significant association with zygomatic clinical distribution pattern (P = .04193, <.05) (Table 2). Thus, patients with a zygomatic clinical distribution pattern were more likely to be female than male, although the majority may still not be affected by this pattern. In addition, Pearson correlation analysis showed that there was a significant negative correlation between sex and mixed-type clinical pattern of 41% (P = .023, <.05). A further significant positive (51%) correlation was present between the zygomatic distribution pattern and spindle cell-shaped melanocytes (P = .004, <.05) (Table 3). This suggests that African patients with zygomatic clinical

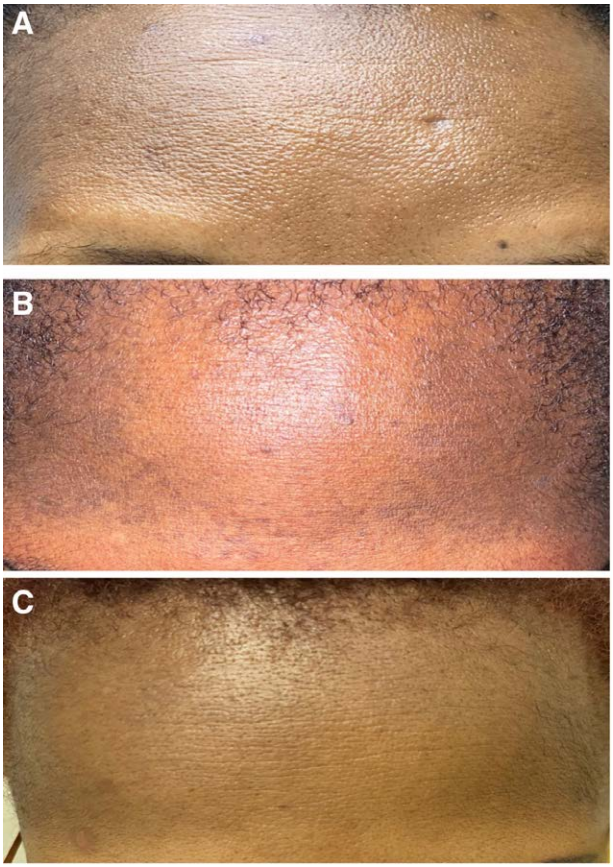

Fig. 6. Bitemporal distribution: anterior view.

distribution patterns have a higher proclivity of spindle cell-type melanocytes on histopathology. The interpretation of these results is cognizant of the inherent limitations of a small sample size as well as the single center and retrospective nature of the study design.

Therapeutic implications for HN in African patients

Topical therapeutic agents, such as skin lighteners, cryotherapy, chemical peels, and dermabrasion, have all been used with variable and often disappointing clinical outcomes. Laser treatments (eg, Q-switched Nd:YAG, 1064 nm picosecond laser, and Er:YAG plus Nd:YAG) have played a significant role and are by far considered the most effective treatments available for HN.[10–13,20–22] Nonetheless, great caution must always be exercised when employing laser devices as the treatment armament for the skin of color patients in general. These devices may result in postinflammatory hyperpigmentation and scarring.[10,12,20]

Conclusion

HN can occur in African patients with a female sex predilection and a bitemporal clinical distribution as the most common presenting pattern described in our cohort. At first glance, the majority of these patients are likely to be misdiagnosed with recalcitrant melasma. To our knowledge, the present study is the first to report the clinical distribution patterns and histological characteristics of HN from a single center in South Africa. In African patients, a punch biopsy (2–3 mm) proved to be the ideal method of diagnosis, as the lesions may not have the exact clinical characteristics originally described by Hori in 1984. The age of onset, family history, and dermoscopic features still need to be elucidated to spur the development of noninvasive diagnostic methods for HN in African patients.

Study limitations

This study has important limitations that must be acknowledged. First, the retrospective nature of the research introduces inherent biases, as we relied on existing data, which may not have been collected with the specific objectives of this study in mind. This limits our ability to control for all potential confounding factors, and as a result, the conclusions drawn should be interpreted with caution. Second, the study was conducted at a single center, which limits the external validity of our findings thereby restricting the generalizability of our results to broader populations. Furthermore, the small sample size presents a significant limitation. With fewer participants, the study may lack the statistical power necessary to detect subtle but clinically important differences, increasing the likelihood of type II errors. Future research with larger, multicenter cohorts will be necessary to further validate our findings and enhance their applicability across different settings.

Conflicts of interest

None.

Funding

None.

Study approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the South African Medical Association Ethics Committee (SAMAREC 280808016/003/2022).

Author contributions

FM and ND contributed to the design and implementation of the research. TRFM and BCM contributed to the analysis of the results and the writing of the manuscript. FM conceived the original and supervised the project.

Table 2

Chi-square results among sex, clinical patterns, and histological features

	Variable	Description	Pearson chi-square	Degrees of freedom	*P* value
Sex	Clinical pattern	Zygomatic	4.138[a]	1	.04193
		Bitemporal	0.315[a]	1	.57472
		Central forehead	0.036[a]	1	.85019
		Mixed type	0.207[a]	1	.64921
	Histologic features	Dendritic cell	0.207[a]	1	.64921
		Spindle shape	0.315[a]	1	.57472

[a] *P* value is measured and found to be statistically significant.

Table 3

Pearson correlation analysis for sex, melanocyte' shape, and clinical distribution pattern

		Bitemporal	Mixed type	Dendritic cell	Spindle shape
Sex	Pearson correlation	.337	−.415[a]	−.083	.102
	P value	.069	.023[a]	.663	.590
	N	30	30	30	30
Zygomatic	Pearson correlation	−.118	−.224	−.224	.512[a]
	P value	.534	.235	.235	.004[a]
	N	30	30	30	30

[a] *P* value is measured and found to be statistically significant.

Patient consent

Written informed consent was obtained from respective patients for the purpose of this publication.

Data availability

All relevant data are within the article and its supporting information files.

Acknowledgments

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