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Basal Cell Carcinoma Type Based on Histopathological Examination: Aggressive vs. Non-Aggressive

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Abstract: Histopathological subtypes of basal cell carcinoma (BCC) help determine prognosis and guide management. This study aimed to describe and compare the clinical and histopathological characteristics of aggressive and nonaggressive BCC. An observational descriptive study was conducted on 26 patients with biopsy-proven BCC. Hematoxylin and eosin (H&E) – stained sections were reviewed by an experienced pathologist. The nonaggressive group included nodular and superficial BCC, while the aggressive group included infiltrative and morpheaform BCC. Clinical and demographic data were recorded, and representative images were selected. Of the 26 cases, 13 were classified as aggressive and 13 as nonaggressive BCC. Female predominance was observed in both groups (61.54% vs. 69.24%). The mean age was 62.08 years in the aggressive group and 69.23 years in the nonaggressive group. Lesions were most frequently located in the nasal and zygomatic regions. The nodular subtype predominated among nonaggressive BCC (76.92%), while infiltrative (53.85%) and morpheaform (46.15%) subtypes were most common in the aggressive group. Histologically, nonaggressive subtypes exhibited well-circumscribed basaloid nests with palisading, whereas aggressive subtypes showed irregular cords within desmoplastic stroma and ill-defined margins. Histopathological examination remains the gold standard for differentiating aggressive from nonaggressive BCC, providing essential guidance for surgical planning and recurrence prevention.

Keywords: Aggressive; Basal Cell carcinoma; Histopathological subtypes; Nonaggressive.

Introduction

Basal cell carcinoma (BCC) is the most frequently diagnosed skin malignancy worldwide and arises from epidermal basal keratinocytes or follicular stem cells, with ultraviolet exposure as the dominant environmental driver (Anggraini & Damayanti, 2024; Irawan et al., 2022; Winaya et al., 2024). Although metastatic spread is rare, BCC causes substantial local morbidity through tissue invasion and cosmetic impairment, particularly when lesions occur on the head and neck (Dai et al., 2018; De Giorgi et al., 2020; Khalil et al., 2024; Kim et al., 2022). Clinically, BCC presents with a wide range of appearances, from translucent pearly nodules to superficial scaly plaques or ulcerated lesions (Knecht-Gurwin et al., 2024; Tanese, 2019; Vornicescu et al., 2018). This phenotypic variability reflects an underlying histologic diversity that plays a decisive role in determining prognosis and guiding appropriate management (Murgia et al., 2023; Naik & Desai, 2022; Reiter et al., 2021; Trieu et al., 2022). Because clinical morphology alone often fails to predict tumor behavior, contemporary guidelines increasingly emphasize subtype-directed treatment planning (Dika et al., 2020; Wunderlich et al., 2024). Nonaggressive variants can generally be treated with standard excision or topical modalities, whereas aggressive subtypes require wider surgical margins or margin-controlled procedures such

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as Mohs micrographic surgery (MMS) to minimize recurrence (Johnson Noah R., 2020; Murray et al., 2018; Naik & Desai, 2022; Papadopoulos et al., 2020). As recurrence risk, surgical margin requirements, and the need for adjuvant therapy correlate more strongly with histopathological pattern than with gross appearance, precise microscopic classification becomes central to accurate clinical decision-making (Heibel et al., 2020; Venturi et al., 2025; WHO, 2018).

Modern histopathologic classifications distinguish BCC into biologically distinct categories (Amici et al., 2021; Pampena et al., 2021). Low-risk or nonaggressive subtypes include nodular and superficial BCC, which typically demonstrate well-circumscribed tumor nests, peripheral palisading, and limited dermal invasion—features associated with predictable growth and simpler excision (Naik & Desai, 2022). In contrast, high-risk or aggressive variants such as infiltrative, morpheaform/sclerosing, micronodular, and basosquamous BCC exhibit thin cords or strands of tumor cells, irregular infiltrative nests, and stromal desmoplasia, often extending far beyond the clinically visible margins (Nicer et al., 2025; Niculet et al., 2024). Basosquamous carcinoma, which contains both basaloid and squamous elements, carries an even higher risk of recurrence and occasional metastasis (Fotiadou et al., 2021; Oldbury et al., 2018). Because mixed-pattern tumors are frequent, pathology reports must document predominant and high-risk components to guide appropriate surgical strategies (WHO, 2018).

Several microscopic features further predict aggressive behavior and recurrence risk, including infiltrative growth, perineural invasion, micronodular architecture, and deep or subcutaneous extension (Niculet et al., 2024; Pyne et al., 2020). Evidence consistently demonstrates that infiltrative and micronodular subtypes are associated with higher rates of positive surgical margins and local recurrence when treated with standard excision, compared with nodular or superficial lesions. Although perineural invasion is relatively uncommon, its presence signifies poorer prognosis and necessitates wider excision, closer follow-up, or adjuvant radiotherapy in selected patients (Niculet et al., 2024; Pyne et al., 2020). Together, these findings underscore that histologic subtyping is not merely descriptive; it is fundamental to prognosis, surgical planning, and early identification of lesions that require more intensive management.

Despite improvements in dermoscopic evaluation that may occasionally suggest tumor subtype, definitive differentiation between aggressive and nonaggressive BCC still relies on conventional histopathology (Shi-Qi et al., 2022; Wojtowicz & Żychowska, 2025). Routine hematoxylin-eosin sections remain sufficient to visualize hallmark features, such as desmoplasia, strandlike infiltration, or perineural involvement that distinguish high-risk lesions. Additional immunohistochemical or molecular tests are generally reserved for challenging or metatypical cases (Niculet et al., 2024). Given the major therapeutic implications of subtype diagnosis, presenting matched clinical images and representative histologic micrographs in a systematic manner can strengthen diagnostic accuracy, improve clinician–pathologist concordance, and serve as valuable teaching material, particularly in settings where advanced techniques like MMS are limited (Naik & Desai, 2022; WHO, 2018).

Although global literature strongly emphasizes the significance of histologic subtyping, data characterizing the clinical–histopathologic correlation of BCC in many regions, including Indonesia remain limited. Variation in UV exposure patterns, occupational risks, skin phototypes, and access to dermatologic services suggests that local patient profiles may differ substantially from those described in Western populations. Without region-specific evidence, clinicians may underestimate lesion aggressiveness or misjudge the required surgical margins, leading to incomplete excisions and higher recurrence rates. In resource-constrained environments where MMS is unavailable, accurate histopathologic assessment becomes even more critical to prevent reoperations, avoid aesthetic and functional morbidity, and optimize patient outcomes.

The novelty of this study lies in its systematic, side-by-side comparison of the clinical features and histopathologic patterns of aggressive versus nonaggressive BCC using WHO 2018 criteria, complemented by representative clinical photographs and micrographs. Unlike many available reports that focus solely on epidemiology or isolated clinical findings, this study integrates visual, clinical, and microscopic perspectives to highlight morphological cues that can reliably indicate tumor behavior. This approach provides practical, locally relevant data that can assist clinicians and pathologists in early recognition of high-risk subtypes, strengthen surgical decision-making, and contribute to improved treatment strategies in Indonesian healthcare settings.

This study aims to describe and compare the clinical characteristics and histopathological patterns of aggressive and nonaggressive basal cell carcinoma (BCC) based on the WHO 2018 classification. Specifically, it seeks to identify differences in clinical morphology, lesion location, demographic profiles, and key microscopic features that distinguish the two groups. By presenting the correlation between clinical presentation and histopathological findings, this study

is expected to provide a stronger scientific basis for accurate diagnosis, surgical planning, and appropriate management strategies, particularly in healthcare settings with limited access to advanced surgical techniques such as Mohs micrographic surgery.

Method

This study employed an observational descriptive design to characterize BCC based on histopathological examination (Ciążyńska et al., 2020). All cases included in the series were biopsy-proven BCCs diagnosed in the Department of Pathology, Dr. Moewardi General Hospital Surakarta, Indonesia, between April-October 2025. Clinical data, including patient age, sex, and anatomical location of the lesion, were obtained from medical records when available. Representative clinical photographs were also collected for illustrative purposes (Li et al., 2020).

Histopathological evaluation was performed on formalin-fixed, paraffin-embedded tissue sections stained with routine hematoxylin and eosin (H&E). All slides were reviewed independently by a single experienced pathologist to confirm the diagnosis and to classify tumors into aggressive or nonaggressive subtypes. The classification followed the WHO 2018 criteria and established dermatopathology guidelines. Tumors were categorized as nonaggressive when showing nodular or superficial growth patterns, characterized by well-circumscribed basaloid nests or superficial budding from the epidermis with limited dermal infiltration. Aggressive subtypes included infiltrative and morpheaform patterns, identified by thin irregular cords, narrow strands of basaloid cells, or sclerotic stromal reaction with ill-defined margins (Camela et al., 2023).

Additional histological features such as stromal retraction, ulceration, and perineural invasion were recorded when present. Findings were described qualitatively and presented with representative clinical and microscopic images to highlight the morphologic differences between aggressive and nonaggressive subtypes. Ethical approval was obtained from the institutional review board of Health Research Ethics Committee of Dr. Moewardi General Hospitals (No: 2.195/IX/HREC/2024). All data were anonymized, and the study complied with the principles outlined in the Declaration of Helsinki.

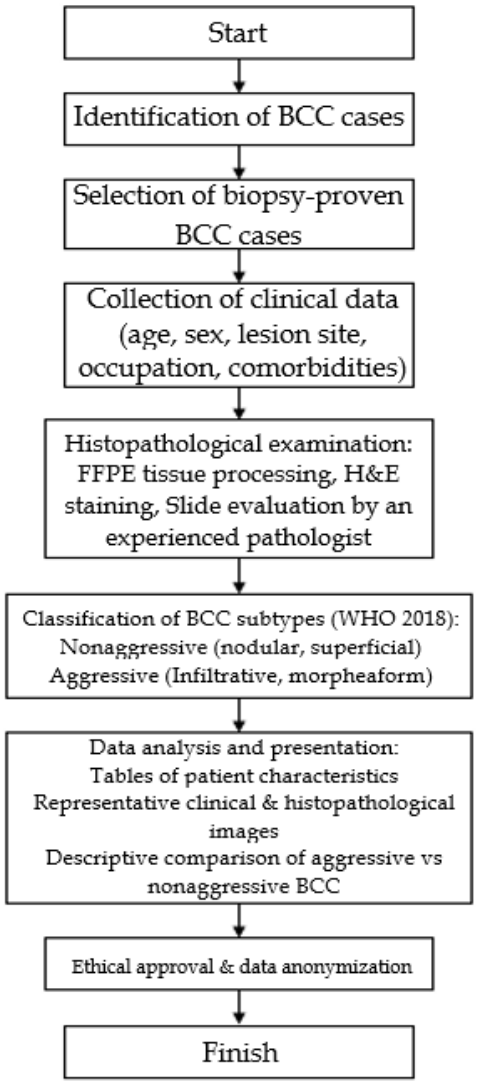

Figure 1. Research Flowchart

Result and Discussion

Subject's Characteristics

A total of 26 subjects with BCC were included in this study, divided equally into 13 cases classified as aggressive and 13 as nonaggressive types. In both groups, female patients were more frequently affected, accounting for 61.54% of cases in the aggressive group and 69.24% in the nonaggressive group. The mean age of patients with aggressive BCC was 62.08 years, whereas those with nonaggressive BCC had a higher mean age of 69.23 years. The most common age categories in the aggressive group were 40–64 years and ≥65 years, while in the nonaggressive group, the majority were ≥65 years.

Occupational background varied between groups. In the aggressive BCC group, the most frequent occupation was trader (38.46%), followed by housewife (23.08%), laborer (23.08%), and farmer (15.38%). In contrast, among patients with nonaggressive BCC

group, the most common occupation was farmer (30.77%), followed by private employee (23.08%), housewife (15.38%), laborer (15.38%), trader (7.69%), and civil servant (7.69%). Educational status was similar across both groups, with elementary school being the most common highest level attained (59.24% in each group).

With respect to comorbidities, hypertension was the most frequently observed condition, present in 30.77% of patients with aggressive BCC and 23.08% of those with nonaggressive BCC. The distribution of lesion sites showed that in the aggressive group, the nasal area (30.77%) and zygomatic region (23.08%) were the most affected. Conversely, in the nonaggressive group, lesions were predominantly located on the zygomatic region (46.15%) and nasal area (30.77%).

Regarding histopathological subtypes, the aggressive BCC group consisted primarily of infiltrative type (53.85%), followed by morpheaform type (46.15%). In the nonaggressive group, nodular BCC was the dominant subtype (76.92%), while superficial BCC accounted for 15.38% of cases. These findings highlight distinct demographic, clinical, and histopathological profiles between aggressive and nonaggressive BCC.

Table 1. Subject's Characteristics

Characteristics	Aggressive Group (n=13) %	Nonaggressive Group (n=13) %
Sex		
Male	5 (38.46)	4 (30.76)
Female	8 (61.54)	9 (69.24)
Age	62.08 ± 12.98	69.23 ± 9.22
20-39	1 (7.69)	0 (0)
40-64	6 (46.15)	3 (23.08)
≥ 65	6 (46.15)	10 (76.92)
Occupation		
Housewives	3 (23.08)	2 (15.38)
Private employee	0 (0)	3 (23.08)
Laborer	3 (23.08)	2 (15.38)
Farmer	2 (15.38)	4 (30.77)
Trader	5 (38.46)	1 (7.69)
Civil servant	0 (0)	1 (7.69)
Education		
None	1 (7.69)	0 (0)
Elementary school	9 (59.24)	9 (59.24)
Middle school	1 (7.69)	2 (15.38)
High school	1 (7.69)	2 (15.38)
University	1 (7.69)	0 (0)
Comorbidities		
Hypertension	4 (30.77)	3 (23.08)
Gastritis	1 (7.69)	0 (0)
Diabetes melitus	0 (0)	1 (7.69)
ALL	0 (0)	1 (7.69)
Ischemic stroke	1 (7.69)	0 (0)
None	7 (53.85)	8 (61.54)
Lesion site		
Supraorbital	1 (7.69)	0 (0)
Infraorbital	2 (15.38)	1 (7.69)
Nasal	4 (30.77)	4 (30.77)
Mandibule	1 (7.69))	0 (0)
Zygomaticum	3 (23.08)	6 (46.15)
Frontal	1 (7.69)	2 (15.38)
Cantus	2 (15.38)	1 (7.69)
BCC subtype		
Infiltrative	7 (53.85)	0 (0.0)
Morpheaform	6 (46.15)	0 (0.0)
Nodular	0 (0.0)	10 (76.92)
Superficial	0 (0.0)	3 (23.08)

Clinical Presentation

In the aggressive BCC group, representative clinical images demonstrated both infiltrative and morpheaform subtypes. The infiltrative subtype (Figures 2 A&B) presented as irregular, ill-defined lesions with ulceration and induration, often extending deeper than their visible margins. The morpheaform subtype (Figures 2 C&D) showed sclerotic, plaque-like growth with firm consistency and poorly demarcated borders. The clinical features of both infiltrative and morpheaform subtypes highlight their propensity for local tissue destruction and the difficulty in achieving complete surgical clearance without histopathological margin control.

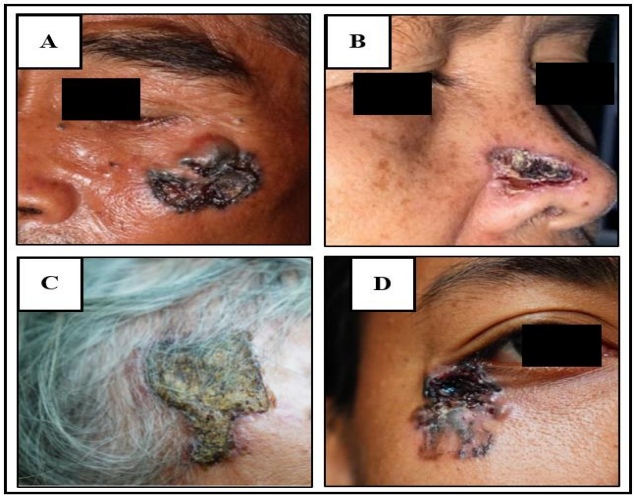

Figure 2. Clinical presentation of aggressive basal cell carcinoma. (A, B) Infiltrative BCC with irregular borders and ulceration. (C, D) Morpheaform BCC with sclerotic plaque-like lesions and indistinct margins.

The nonaggressive basal cell carcinoma group comprised the nodular and superficial subtypes, which typically presented as well-defined lesions with slow growth and limited local invasion. The nodular subtype (Figures 3 A&B) appeared as firm, dome-shaped nodules with a pearly or translucent surface. Some lesions exhibited telangiectatic vessels and rolled borders, characteristic of classic nodular BCC. The superficial subtype (Figures 3 C&D) manifested as erythematous to brownish, scaly plaques with slightly elevated margins and a smooth or ulcerated surface. These lesions were smaller in diameter and more circumscribed than the aggressive variants. Most lesions were located on sun-exposed areas such as the nasal and malar regions. Overall, both subtypes showed clinically distinct, well-demarcated borders, reflecting their noninvasive growth pattern and favorable prognosis compared to aggressive forms.

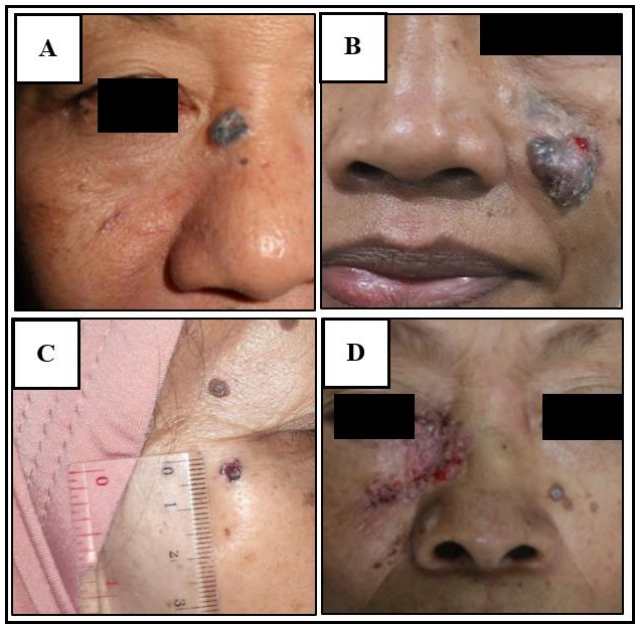

Figure 3. Clinical presentation of nonaggressive basal cell carcinoma. (A, B) Nodular BCC showing well-defined, pearly nodules with central ulceration. (C, D) Superficial BCC presenting as erythematous to brownish, scaly plaques with clear margins.

Histopathological Presentation

Histopathological examination confirmed the distinct growth patterns differentiating nonaggressive from aggressive BCC. The nodular subtype (Figures 4A and 4B) displayed large, well-circumscribed nests of basaloid cells with peripheral palisading and retraction artifact separating tumor islands from the surrounding stroma. These features represent the classic morphology of nonaggressive BCC, typically associated with a favorable prognosis and relatively low recurrence risk. The morpheaform subtype (Figure 4C) demonstrated narrow strands and cords of basaloid cells embedded within a densely fibrotic stroma. The tumor margins were indistinct, with infiltrative growth extending into the dermis. This subtype is considered aggressive because of its tendency to extend beyond clinically visible margins, making complete surgical excision more challenging. The infiltrative subtype (Figure 4D) was characterized by irregular cords and thin strands of basaloid cells invading deeply into the dermis, often surrounded by a desmoplastic stromal reaction. The poorly defined tumor borders observed microscopically highlight the aggressive nature of this growth pattern and its higher risk of recurrence compared with nonaggressive types.

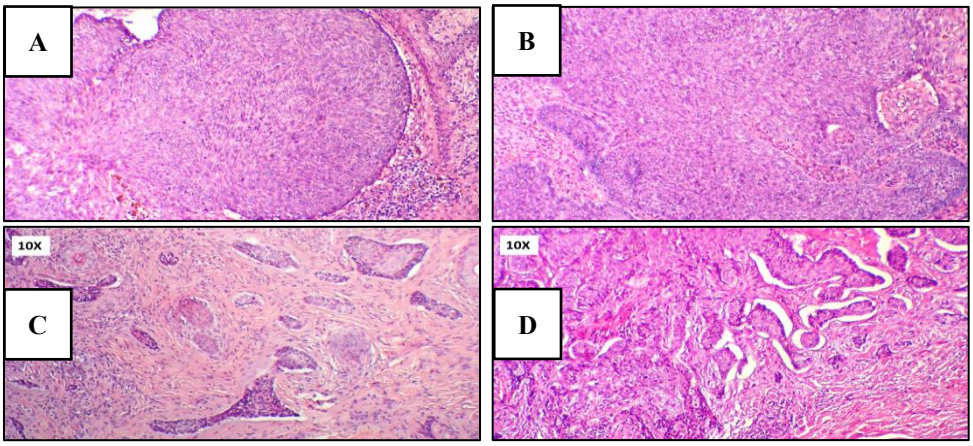

Figure 4. Histopathological features of basal cell carcinoma subtypes (H&E, 10x). (A–B) Nodular BCC showing large tumor nests with peripheral palisading and stromal retraction. (C) Morpheaform BCC composed of narrow strands of basaloid cells within dense fibrous stroma and ill-defined margins. (D) Infiltrative BCC with irregular cords of tumor cells extending into the dermis with desmoplastic stroma (H&E; 10x).

Discussions

This study highlights the clinical and histopathological features that differentiate aggressive from nonaggressive BCC. The nodular and superficial variants, grouped as nonaggressive subtypes, typically displayed well-circumscribed basaloid nests with peripheral palisading and limited stromal invasion, corresponding clinically to dome-shaped or plaque-like lesions with distinct borders. In contrast, aggressive subtypes such as infiltrative and morpheaform BCC revealed irregular cords or strands of basaloid cells with poorly defined margins and desmoplastic stromal reaction. Clinically, these subtypes presented as indurated or scar-like plaques with indistinct edges, which often underestimated their subclinical spread. These findings are consistent with previous reports indicating that nonaggressive subtypes are more amenable to local excision, while aggressive subtypes require margin-controlled techniques such as Mohs micrographic surgery to reduce recurrence risk (Collier & Rhodes, 2020; Fotiadou et al., 2021; Pyne et al., 2020).

The distribution of cases in this cohort underscores certain demographic and clinical patterns. Both aggressive and nonaggressive BCCs were more frequent among older adults, reflecting cumulative ultraviolet radiation exposure as a major etiologic factor. Female predominance was noted in both groups, which contrasts with studies from Western populations that often report a male predominance (Bassukas & Tatsioni, 2019; Kasumagic-Halilovic et al., 2019; Naik & Desai, 2022; Shi-Qi et al., 2022). Occupational exposure, particularly among farmers and traders, was also evident in this series, suggesting a role for chronic sun exposure in outdoor workers. Lesion location was concentrated on the nasal and zygomatic areas, sites recognized as high-risk due to embryonic fusion planes and the cosmetic and functional challenges they pose (Baba et al., 2024; Schmults et al., 2023). These patterns suggest that socioeconomic and environmental factors contribute to disease distribution and emphasize the importance of targeted public health education and early detection in high-risk groups.

From a prognostic standpoint, aggressive histopathological subtypes carry greater risks of incomplete excision, local recurrence, and, in rare cases, perineural spread. In this cohort, morpheaform and infiltrative BCCs demonstrated features associated with higher recurrence, including stromal desmoplasia and poorly circumscribed margins. Such findings align with international series reporting recurrence rates up to 25–30% for aggressive subtypes when treated with standard excision, compared with much lower rates in nodular or superficial types (Paul & Knight, 2023; Schmults et al., 2023). These results reinforce the value of histopathological confirmation not only for diagnosis but also for guiding surgical strategy and follow-up. Given that resources for advanced techniques such as MMS remain limited in many Indonesian centers, raising awareness of histologic aggressiveness may support more judicious treatment planning, wider excision margins, and closer post-treatment surveillance. Ultimately, this descriptive analysis underscores the central role of pathology in bridging clinical presentation with therapeutic outcomes in BCC.

Conclusion

This study demonstrates clear clinical and histopathological distinctions between aggressive and nonaggressive basal cell carcinoma (BCC). Nonaggressive subtypes, particularly nodular and superficial BCC, exhibited well-circumscribed basaloid nests with peripheral palisading and limited dermal invasion, findings that align with their predictable

growth pattern and generally favorable prognosis. In contrast, aggressive subtypes, namely infiltrative and morpheaform BCC, were characterized by irregular strands of basaloid cells, desmoplastic stroma, and poorly defined margins, features associated with subclinical extension and a higher risk of recurrence. These differences confirm that histopathological examination remains the gold standard for accurately distinguishing BCC subtypes and guiding appropriate management. More broadly, the findings of this study reinforce international evidence showing that high-risk histologic patterns correlate with increased recurrence rates, a greater likelihood of positive margins, and the need for wider or margin-controlled excision techniques. The demographic patterns observed—particularly the predominance of head and neck lesions—highlight the importance of early detection in sun-exposed populations. Practically, these results underscore the critical role of precise histologic subtyping in settings where advanced surgical options such as Mohs micrographic surgery are limited. Accurate identification of aggressive features can inform decisions about wider excision margins, closer follow-up, and patient counseling regarding recurrence risks. Strengthening clinicopathologic correlation through routine documentation of subtype-specific morphological cues may improve treatment outcomes and reduce the need for reoperation. Overall, this study provides locally relevant evidence that can support clinicians in optimizing the diagnosis and management of BCC in resource-constrained environments.

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Author contributions
F.F.H. designed the study, collected clinical data, and drafted the manuscript. N.D. performed histopathological evaluation and contributed to data interpretation. P.M. and E.Y.E. assisted in clinical assessment, data validation, and critical manuscript revision. S.W. supervised the overall research process and provided final approval of the manuscript. All authors read and approved the final version of the manuscript.

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Conflict of Interest
The authors declare that they have no conflict of interest related to this study.

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