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Clinico-Histopathological Features of Cutaneous Squamous Cell Carcinoma, Keratoacanthoma, and Bowen's Disease

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Abstract

Background: Cutaneous squamous cell carcinoma (SCC) is the second most common form of skin cancer after basal cell carcinoma. Ultraviolet (UV) radiation is the primary risk factor in the development of cutaneous squamous cell carcinoma and its precursor lesions. Bowen disease (BD) is squamous cell carcinoma *in situ*, and keratoacanthoma (KA) is considered a low-grade SCC. The diagnosis of these conditions requires clinical and histological assessment. **Objective:** Clinical and histopathological evaluation of squamous cell carcinoma, keratoacanthoma and Bowen's disease. **Patients and Methods:** This study is a retrospective study carried out at the Dermatology Center, Medical City/Teaching Hospital, including patients diagnosed with SCC, KA, and BD during a period extending from January 2016 until October 2023. A total of 55 patients were included. Clinical information was recorded, and the histopathological slides were reviewed. Other precursor lesions, such as actinic keratosis, were not included in the analysis, as the objective was to examine only lesions with confirmed invasive or in-situ squamous differentiation. This deliberate exclusion was intended to maintain diagnostic consistency and allow for more detailed histopathological comparisons within the selected lesion types. **Results:** Forty-one out of 55 patients were males and 14 were females. Regarding SCC, males constituted 77.8% and females 22.2%. The most common age group was the 7th decade, with a mean age of 60.5 years. The mean duration was 10 months, and the most common site of the lesions was the head (83.3%). Histologically, the most common finding detected was squamous eddies (83%), while nesting was detected in 69.4% and pearl horns in 52.8%. Dermal infiltrate was composed mainly of lymphocytes; plasma cells and eosinophils were also detected. The acantholytic type constituted 19.4% of cases, and one case was spindle cell SCC. Regarding the degree of differen-

tiation, moderately differentiated SCCs were the most common (79.8%). For KA, males constituted 72.8% and females 27.3%. The most common age group was the 6th decade. The mean duration was 4.2 months, and the most common site of the lesions was the head (72.7%). Histologically, a crater, glassy eosinophilic appearance and eosinophilic infiltration were found in all cases. For BD, males constituted 62.5% and females 37.5%. The most common age group was the 7th decade. The mean duration was 9.5 months, and the most common site of the lesions was the head (62.5%). Histologically, the eye liner sign was found in 50% and acantholysis in 37% of cases. **Conclusion:** This paper retrospectively analyzes the clinical and histopathological features of cutaneous squamous cell carcinoma (SCC), keratoacanthoma (KA), and Bowen's disease (BD) in 55 Iraqi patients from 2016 to 2023. The study finds that moderately differentiated SCC was the most common diagnosis, predominantly affecting the head in older males. The paper details the specific histological characteristics observed for each condition and compares these findings to existing literature. Most cases of SCC were moderately differentiated. The head was the most common location for SCC, KA and BD.

Keywords

Squamous Cell Carcinoma, Keratoacanthoma, Bowen Disease, Clinicopathological Feature, Skin Cancer, Cutaneous Lesions, Premalignant Skin Condition

1. Introduction

Squamous cell carcinoma (SCC) is the second most common cutaneous malignancy after basal cell carcinoma, with an increasing incidence worldwide [1]-[3]. Although many factors can increase the risk for SCC, cumulative sun exposure, especially in childhood and youth, is of greatest importance. Moreover, in recent years, immunosuppression, including that associated with organ transplantation, has emerged as an increasingly important contributor to tumorigenesis, and the arousal of SCC in areas of chronic inflammation must also be kept in mind [4].

SCC accounts for most nonmelanoma skin cancer-related metastatic disease; therefore, recognition and treatment of early SCC are important for the prevention of neoplastic progression. Although non-invasive tools have been recently introduced for the diagnosis of SCC, histopathology and surgical excision remain the gold standard for the diagnosis and treatment [5].

A number of studies that dealt with the clinical and histological features of SCC in different countries were published. However, the period of study and the number of patients vary; in addition, genetic and environmental factors may lead to differences in the incidence and the clinic-pathological features of SCC [6]-[8].

BD is an SCC *in situ*. It usually presents on sun-exposed skin of elderly individuals as an erythematous and scaly plaque [9]. KA, on the other hand, is considered by some authors to be a variant of SCC, while others consider it a benign

tumor [10].

The study was conducted to evaluate the clinical and histopathological features of squamous cell carcinoma, keratoacanthoma, and Bowen's disease.

Histologically, these three entities can be differentiated based on key patterns: Bowen's disease (BD), as an *in situ* squamous cell carcinoma, exhibits full-thickness atypia of keratinocytes throughout the epidermis with disordered maturation, numerous mitoses, pleomorphic nuclei, and no invasion past the basement membrane. In contrast, invasive squamous cell carcinoma (SCC) shows atypical and pleomorphic keratinocytes breaching into the dermis, often forming nests or cords, with varying degrees of keratin pearl formation depending on differentiation grade. Keratoacanthoma (KA), although debated as a variant of SCC, typically has a symmetrical crateriform architecture with a central keratin-filled plug, well-differentiated uniform keratinocytes, pushing rather than infiltrative borders, and often a phase of spontaneous regression [11]. So the key feature that distinguishes SCC from BD and KA is invasion beyond the basement membrane. While the key feature in BD is full-thickness atypia and KA is a keratin filled crater.

2. Patients and Methods

The study was based on records from January 2016 to 2021 and new cases in 2022 and October 2023. This retrospective study included a total of 55 patients diagnosed with cutaneous squamous cell carcinoma (SCC), keratoacanthoma (KA), or Bowen's disease (BD). Other precursor lesions such as actinic keratosis were not included in the study because we thought this needs a more extensive study. The study used archived histopathological records from 2016 to 2021 and new histologically confirmed cases from 2022 to 2023. All cases were retrieved from the dermatopathology registry of the Center of Dermatology and Venereology at Baghdad Teaching Hospital/Medical City, Baghdad, Iraq. Biopsies were processed at the National Center Teaching Labs/Medical City, and inclusion criteria were based on confirmed histological diagnosis of SCC, KA, or BD. Ethical approval was granted by the Scientific Council of Dermatology and Venereology, the Iraqi Board for Medical Specializations. Informed consent was obtained from all patients for their images.

In this retrospective study, we collected and reviewed clinical records and histopathological slides of 55 patients diagnosed with squamous cell carcinoma (SCC), keratoacanthoma (KA), and Bowen's disease (BD). Descriptive statistics were used to analyze demographic data, including age, sex, lesion duration, and lesion location. Histopathological evaluation was performed for diagnostic confirmation. A comparative statistical analysis was conducted to evaluate the distribution and clinical characteristics of the different lesion types. Statistical significance was assessed where applicable.

All patients with a confirmed diagnosis of cutaneous SCC, KA, and BD by biopsy were included. Patients whose slides could not be retrieved from the lab were excluded.

The following information was noted: history including age, sex, occupation, and duration of lesions. Results of the clinical examination were recorded, including site and size of each lesion. Clinical images were transferred to a personal computer, arranged, and labeled in organized files. Biopsies were fixed in 10% formalin. They were automatically stained with hematoxylin and eosin (H&E) using the Leica histopathology system.

The following histological features were evaluated among others: in SCC, nests of squamous epithelial cells arising from the epidermis and extending into the dermis; large malignant cells with abundant eosinophilic cytoplasm and a large, often vesicular, nucleus; variable keratinisation (keratin pearls); squamous eddies; acantholysis; dyskeratosis; crater in KA, disordered maturation with atypical keratinocytes through all the epidermal layers in BD; and inflammatory cells in the dermis and the epidermis.

Statistical analysis of the data was carried out using the available statistical package and presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum–maximum values). The study is a descriptive epidemiological study.

3. Results

Patients' demographic and clinical data:

The total number of patients was 55; 36 patients (65.5%) had SCC, 11 patients (20%) had KA, and 8 patients (14.5%) had BD.

The sex distribution of patients is shown in Table 1, while the age is shown in Table 2.

Table 1. The sex distribution of patients with SCC, KA, and BD.

SEX	MALE	FEMALE	TOTAL
SCC	28(77.8%)	8(22.2%)	36(65.5%)
KA	8(72.7%)	3(27.3%)	11(20%)
BD	5(62.5%)	3(37.5%)	8(14.5%)
TOTAL	41(74.5%)	14(25.5%)	55

Table 2. The age distribution of patients with SCC, KA, and BD.

AGE (YEARS)	SCC	KA	BD	TOTAL
21 - 30	1 (2.3%)	0	0	1 (1.8%)
31 - 40	1 (2.3%)	0	0	1 (1.8%)
41 - 50	1 (2.3%)	2 (18.2%)	1 (12.5%)	4 (7.3%)
51 - 60	7 (19.4%)	5 (45.5%)	2 (25%)	14 (25.5%)
61 - 70	14 (38.9%)	3 (27.3%)	3 (37.5%)	20 (36.7%)
71 - 80	10 (27.8%)	1 (9.09%)	1 (12.5%)	12 (21.05%)
81 - 90	2 (5.6%)	0	1 (12.5%)	3 (5.5%)
TOTAL	36	11	8	55

Regarding the duration of lesions, the mean duration of SCC was 10 months, KA was 4.18 months, and BD was 9.5 months.

The head was the most common location for all the lesions (Table 3), while the scalp was the most common area of the head involved (Table 4).

Table 3. The location of lesions with SCC, KA, and BD.

LOCATION	SCC	KA	BD	TOTAL
HEAD	30 (83.3%)	8 (72.7%)	5 (62.5%)	43 (78.2%)
UPPER EXTREMITIES	3 (8.3%)	2 (18.2%)	1 (12.5%)	6 (10.9%)
LOWER EXTREMITIES	1 (2.8%)	0	0	1 (1.8%)
CHEST	0	0	1 (12.5%)	1 (1.8%)
BACK	1 (2.8%)		1 (12.5%)	2 (3.6%)
GENETILIA	1 (2.8%)	1 (9.09%)	0	2 (3.6%)
TOTAL	36	11	8	55

Table 4. The distribution of the lesions of SCC, KA, and BD on the head.

HEAD AND NECK	SCC	KA	BD	TOTAL
SCALP	8 (22.2%)	1 (9.09%)	1 (12.5%)	10 (18.2%)
FORHEAD	7 (19.4%)	0	2 (25%)	9 (16.4%)
NOSE	4 (11.1%)	4 (36.36%)	0	8 (14.5%)
CHEEK	5 (13.8%)	1 (9.09%)	2 (25%)	8 (14.5%)
LIP	4 (11.1%)	2 (18.18%)	0	6 (10.9%)
EAR	2 (5.5%)	0	0	2 (3.6%)
TOTAL	30	8	5	43

Table 5. The largest diameter of lesions of SCC, KA, and BD in centimeters.

DIAMETER (CM)	SCC	KA	BD	TOTAL
0.5 - 1	18	7	4	29
1.1 - 1.5	8	1	3	12
1.6 - 2	6	1	1	8
2.1 - 2.5	4	2	0	6
TOTAL	36	11	8	55

Histological features of SCC, KA, and BD.

Regarding histological features of SCC, squamous eddies were the most common feature (83.3%), followed by squamous nesting as shown in Table 5. Plasma cells were present in (66.7%), while lymphocytes were present in all lesions (Table 6).

Table 6. The histological features of SCC lesions.

HISTOTLOGICAL FEATURE	NUMBER OF LESIONS	PERCENTAGE
NEST	25	69.4
STRANDS	13	36.1
ACANTHOLYSIS	7	19.4
PEARL HORNS	19	52.8
SQUAMOUS EDDIES	30	83.3
ABNORMAL MITOSIS	17	47.2
DYSKERATOTIC CELLS	10	27.8
2 NUCLEOLI	9	25
MELANIN INCONTINENCE	7	19.4
SPINDLE CELLS	1	2.7
PERIVASCULAR INVASION	4	11.1
PERIFOLLICULAR INVASION	1	2.7
INFLAMMATORY CELLS		
MILD LYMPHOCYTIC INFILTRATION	23	63.9
HEAVY LYMPHOCYTIC INFILTRATION	13	36.1
PLASMA CELLS	24	66.7
EOSINOPHILS	15	41.7
NEUTROPHILS	9	25

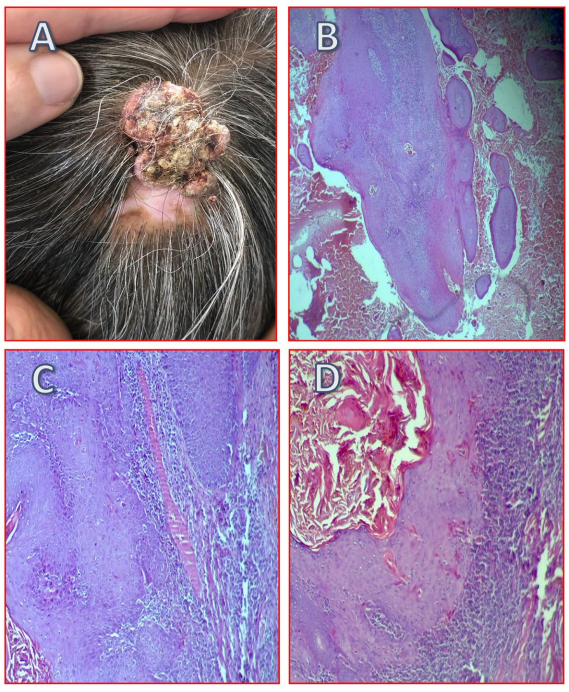

Figure 1. SCC on the scalp. (A) Clinical photograph. (B), (C), (D) Histopathology of the lesion showing moderately differentiated SCC with nests of epithelial cells with prominent nuclear atypia (B). Squamous eddies with lymphocytic, eosinophilic, and plasma cell infiltration (C). And dyskeratotic cells (D).

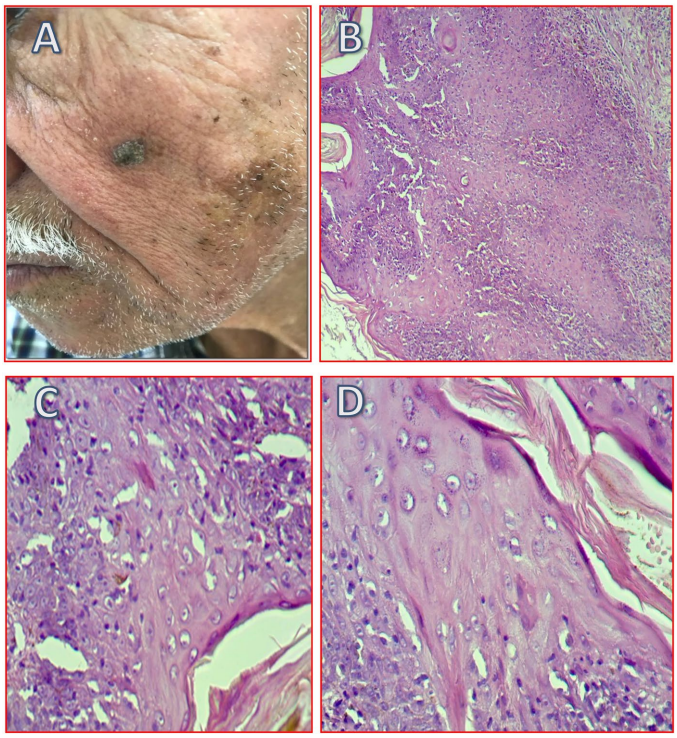

Figure 2. SCC on the cheek. (A) clinical photograph. (B), (C) and (D) histopathological photographs. Moderately differentiated SCC with nests of atypical epithelial cells (B), dense inflammatory infiltration (C) and dyskeratosis and abnormal mitosis (D).

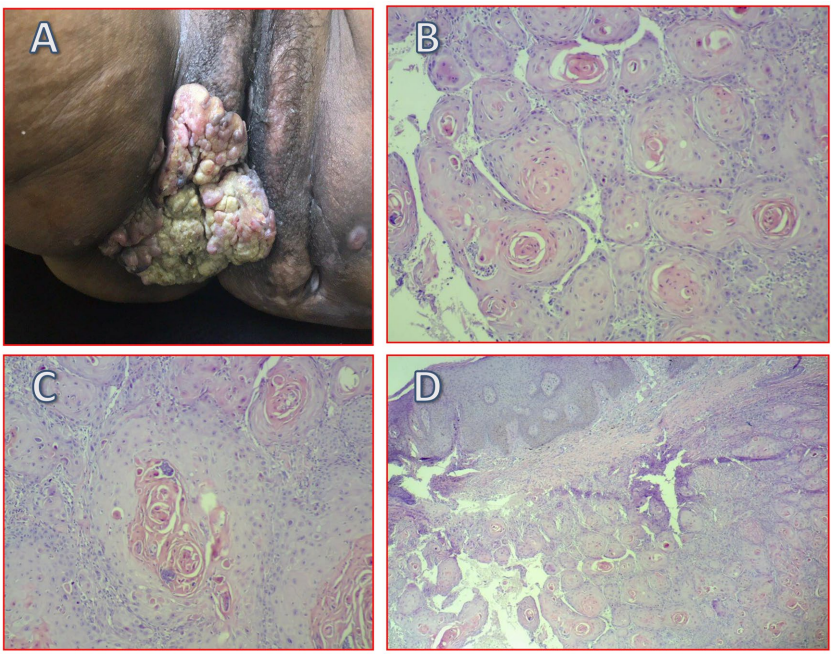

Figure 3. SCC on the genitalia. (A) clinical photograph. (B), (C) and (D) histopathological photographs. (B) shows well-differentiated SCC, (C) shows squamous eddies and horn pearls, and (D) shows inflammatory infiltration.

About differentiation of SCC, 28 lesions (77.8%) were moderately differenti-

ated, as shown in Figures 1-2; 6 lesions (16.7%) were well differentiated (Figure 3), and 2 lesions (5.6%) were poorly differentiated.

Regarding the histological features of KA, a crater, a glassy eosinophilic appearance of cells, and eosinophilic and lymphocytic infiltration in the dermis were found in all lesions (Table 7). These features are shown in Figure 4.

Table 7. The histopathological features of KA lesions.

HISTOTLOGICAL FEATURE	NUMBER OF LESIONS	PERCENTAGE
CRATER	11	100
GLASSY EOSINOPHILIC APPERANCE	11	100
DYKERATOTIC CELLS	4	36.3
MINIMAL ATYPIA	8	72.7
INFLAMMATORY CELLS		
HEAVY LYMPHOCYTIC	3	27.3
MILD LYMPHOCYTIC	8	72.7
EOSINOPHILS	11	100
NEUTROPHILS	5	45.5
PERIFOLLICULAR	3	27.3
DILATED BLOOD VESSELS	3	27.3

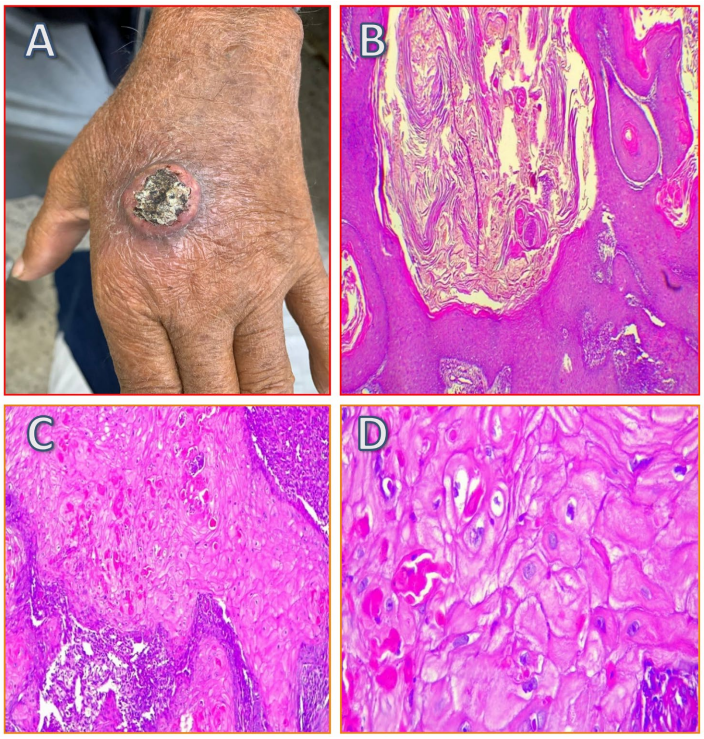

Figure 4. Keratoacanthoma on the dorsum of the hand. (A) clinical photograph. (B), (C), and (D) histopathological photographs. A crater filled with keratin (B), pale, glassy-appearing cytoplasm with neutrophil abscesses (C) and dyskeratotic cells and minimal atypia (D).

Regarding the histopathological features of BD, the eye-liner sign was found in 50% and acantholysis in 37.5% of lesions, as shown in Table 8 and Figure 5.

Table 8. The histopathological features of lesions of BD.

HISTOTLOPATHOLOGICAL FEATURE	NUMBER OF LESIONS	PERCENTAGE
CONFLUENT PARAKERATOSIS	5	62.5
DYKERATOSIS	4	50
ABNORMAL MITOSIS	2	25
NESTING	2	25
ACANTHOLYSIS	3	37.5
EYE LINER SIGN	4	50
BASAL CELL COMPRESSED	2	25
MELANIN INCONTINANCE	2	25
LYMPHOCYTIC INFILTRATION	6	75
PERIFOLLICULAR	2	25
PERIVASCULAR	2	25

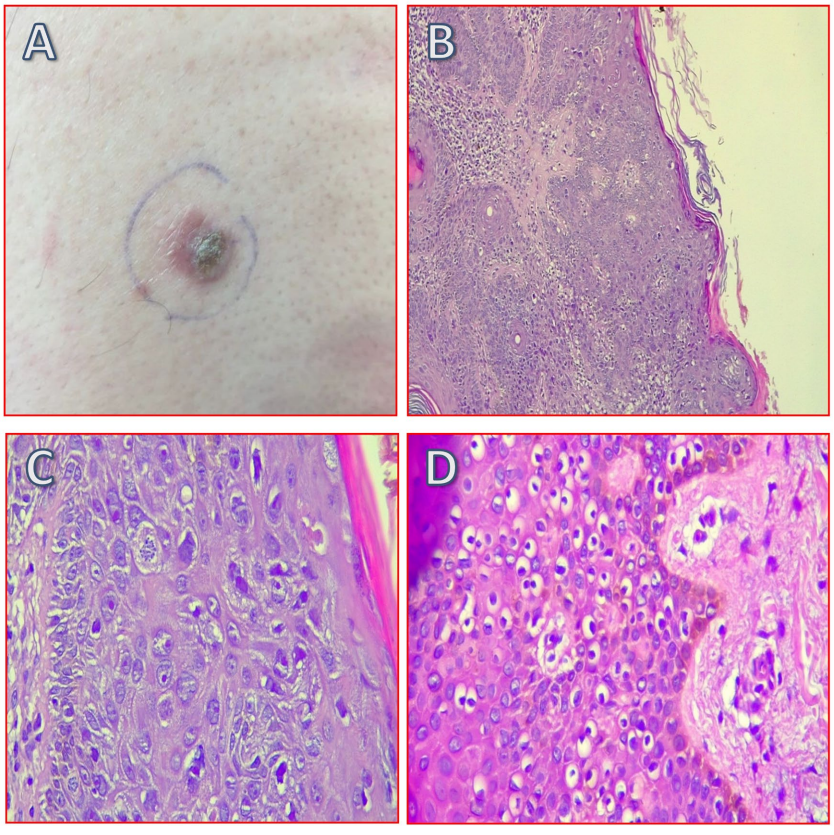

Figure 5. Clinical features (A) and histopathological features (B), (C), and (D) of Bowen's disease. Irregular epidermal hyperplasia with atypical pleomorphic keratinocytes throughout the entire epidermal thickness (wind-blown) (B), the eye liner sign (C), and dyskeratotic cells and abnormal mitosis (D).

4. Discussion

There are many studies dealing with SCC, KA, and BD from all over the world. However, the time of study and the number of patients varied.

This study presents an 8-year retrospective analysis of SCC, KA, and BD cases, focusing on clinicopathological characteristics and histological subtypes. Compared to other studies [6] [8] with shorter durations and larger patient numbers, our relatively small sample (n = 55) can be attributed to the overlap with the COVID-19 pandemic and the exclusion of cases without available histological slides. Additionally, patients with advanced SCC were often referred to the surgical department directly, limiting our dataset to earlier or more superficial presentations.

The mean patient age in this study (59 years) was lower than that reported by Ciuciulete *et al.* (74.2 years) and Corpas *et al.* (77.6 years), but higher than that in Naz *et al.* (51 years). This may reflect geographic and occupational differences, as many of our patients were outdoor workers with chronic UV exposure and minimal sun protection. Male predominance (74.5%) was noted, consistent with studies from Ciuciulete and Corpas, and likely due to greater occupational sun exposure and lifestyle factors. Cultural practices, such as conservative clothing among women, may also contribute to reduced exposure. In an Iraqi study Al-Hamamy *et al.* found that the 7th decade was the most commonly affected age group [2].

Regarding the location of the lesions in Ciuciulete *et al.*, the most common location was the head and neck (76% of patients), and the second most common location was the lower limbs (68%); there were about 4.9% of cases in the groin, while in the Corpas *et al.* study the face was affected in 26.9% of patients, the scalp in 24.4%, the ear in 15.1%, and the lower lip in 5% [6] [7].

In the present study, the head was the most common site involved (83.3%), with the scalp as the most common area of the head affected, followed by the forehead and then the nose. This warrants a public health awareness program for lesions on the head and neck especially for people who accustomly exposed to sunlight. The lips were involved in 11%. The genitalia were affected in 2.77% of total cases. This distribution is expected due to exposure to sunlight. Involvement of the genitalia could be due to HPV infection.

Histologically, the degree of differentiation of SCC was mentioned in a number of studies. In the study of Ciuciulete *et al.*, well-differentiated SCC constituted 49% of cases, moderately differentiated 36.9%, and poorly differentiated 13.6%. Naz *et al.* mentioned that well-differentiated constituted 22.2%, moderately differentiated 72.2%, and poorly differentiated 5.6%. In the study of Corpas *et al.*, well-differentiated constituted 68.1%, moderately differentiated 29.4%, and poorly differentiated 2.5%. Al-Hamami *et al.* found that the well-differentiated type was the most common variant, followed by moderately differentiated and then poorly differentiated [3].

In the present study, moderately differentiated were the majority (77.8%), followed by well-differentiated (16.7%), then poorly differentiated (5.6%).

This difference between the present study and Ciuciulete *et al.* in the percentage of poor differentiation could be explained by the fact that, in our hospital, patients with advanced SCC usually consult the surgical department directly.

In the study by Corpas *et al.*, perineural invasion was found in 5.9% of cases, and perivascular invasion in 0.8%. In the study by Naz *et al.*, lymphovascular invasion was 0% in patients older than 40 years and 5.3% in patients younger than 40 years. In our study, there was no perineural invasion, while 11.1% of cases exhibited perifollicular invasion. The absence of perineural invasion in the present study could be attributed to the fact that few of our biopsies showed poor differentiation, a factor important in perineural invasion. Also, some of our biopsies were not deep enough to include deep dermal or subcutaneous nerves.

In the Ciuciulete *et al.* study, the acantholytic type was seen in (9.7%) of biopsies, and the spindle cell type in (1.9%) [6]. Al-Hamami *et al.* found acantholysis in only one biopsy [3]. While in the present study, the acantholytic type constituted (19.4%) of cases, and spindle cells were found in one patient (2.7%).

In the present study, the most frequent architecture of SCC was nesting (69.4%), followed by strands (36.1%). This was also stated by Schmitz *et al.* [12].

Pearl horns and squamous eddies were found in the majority of lesions; this is expected to be more common in well-differentiated SCC, as mentioned by Schmitz *et al.* [12] Cellular atypia, such as abnormal mitosis, dyskeratosis, and 2 nucleoli, was found in many biopsies. This was also mentioned by Schmitz *et al.* [12].

Regarding KA, Aung *et al.* found that a crater filled with keratin was found in 100% of cases and glassy keratinocytes in 86.7%, apoptotic keratinocytes in 90%, and neutrophilic abscesses in 36.7% [13]. In the present study, a crater filled with keratin and a glassy eosinophilic appearance were found in all cases, and neutrophilic clusters within tumor masses were seen in 45.5%. It is interesting to note that eosinophils were present in all biopsies and neutrophils were found much more than in SCC; also, this is mentioned by the Schmitz *et al.* study [12].

In lesions of BD, abnormal mitosis and dyskeratosis were important features found in all biopsies. Confluent parakeratosis was found in 62.5% of lesions; nesting was seen in 25%; acantholysis in 37.5%. These findings were also mentioned by Schmitz *et al.* [12]. The basal layer was seen as a single-cell layer pushed by the tumor cells (eye-liner sign) in 50% of cases, and in 25% the basal cells were compressed. Perifollicular invasion was found in about 25% of cases. The importance of the eye-liner sign in BD was stressed by Schmitz *et al.* [12].

The major findings in the present study regarding SCC is that cases were moderately differentiated with no perineural invasion. While lesions of BD and KA were promptly diagnosed depending on their histopathological features.

The predominance of lesions on the head region, particularly among older males, highlights the need for targeted public health initiatives focusing on sun protection and early skin cancer detection in this demographic, especially in regions with high UV exposure.

This study has several limitations that should be acknowledged. The relatively small sample size (n = 55) may limit the generalizability of the findings to the broader population. Additionally, the data collection period overlapped with the COVID-19 pandemic, which may have contributed to underreporting or delays in diagnosis and treatment. The retrospective nature of part of the study may also introduce potential biases related to incomplete clinical documentation. Future studies with larger, multicenter cohorts and prospective designs are recommended to validate and expand upon these findings.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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