Original Article

Distribution and Clinicopathologic Characteristics of Squamous Cell Carcinoma of the Skin: An Analysis of 100 Cases

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Abstract

Background: The World Health Organization estimates that 2–3 million nonmelanocytic skin cancers occur annually worldwide and cutaneous squamous cell carcinoma (cSCC) is the most common of these tumors. This study analyzes the clinicopathological characteristics of SCC of the skin and the demographic profiles of the affected patients. **Materials and Methods:** A retrospective review of dermatological malignancies from January 2004 to December 2019 in the Department of Histopathology, National Hospital Abuja, was conducted. Data were exported from the department software in comma-separated value format and demographic and other clinicopathological characteristics were analyzed as categorical variables. Descriptive and inferential statistics, bi-variate correlation (Spearman ranking), and binary logistic regression analysis were applied between demographic variables: age and sex as independent variables, and clinicopathological variables: clinical presentation, anatomical site, and histological types. $P \leq 0.05$ is considered as statistically significant. **Results:** A total of 103 cases of cSCC were histologically confirmed during the study period, and these accounted for 25.8% of the dermatological malignancies within the period of the study. There were 59 (57.3%) males and 44 (42.7%) female patients with a male to female ratio 1.3:1. The mean age of the study participant was 35.9 ± 13 and the age range 4–81 years. The peak age incidence was within the third to fourth decade of life accounting for 69 (66.9%). **Conclusion:** cSCC was predominant in the head and neck region. Age was found to be a significant factor ($P < 0.05$), patients <50 years were 8 fold likely to develop SCC of the head and neck region (odds ratio = 7.731, 95% confidence interval = 1.257–47.560). Early preventive measures, early presentation, and proper evaluation could improve the outcome of SCC.

Keywords: Clinicopathological features skin, squamous cell carcinoma, topographical characteristics

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Introduction

Cutaneous squamous cell carcinoma (cSCC) is a malignancy of epidermal keratinocytes that displays variable degrees of differentiation and cytological features. Most SCCs of the skin result from prolonged exposure to ultraviolet and other radiation, either from sunlight or from tanning beds or lamps.[1]

It may also be associated with chronic immunosuppression, chronic ulcers, burn scars, sinus tracts, certain tars and oils arsenic, soot, distillation products[2] as well as infection.[3] The World Health Organization estimates that 2–3 million nonmelanocytic skin cancers (NMSCs) occur annually worldwide.[4] These are composed of basal cell carcinoma, Bowen's disease, and actinic keratosis (AK) apart from cSCC and constitute the largest number of skin malignancies among European populations.[5] Other reports estimate that 5.4 million NMSCs occur annually in the United States alone.[6] Recent estimates suggest that between 186,157 and 700,000 cSCCs are diagnosed annually in the United States.[7] A recent study relating the disease incidence to geographical latitude suggested an incidence of 5–499 per 1000 with a male predominance[8] further highlighting the role of environmental factors in the causation of the disease.

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The incidence of SCC in Nigeria reported previously from Lagos,[9] Ibadan[10] (Southwest), Kano[11] (Northwestern), and Calabar[12] (South-eastern) Nigeria makes it the most common of malignant skin diseases. Cutaneous SCC is believed to emanate from a multistep process involving mutation of certain genes notably the TP53, CDKN2A, NOTCH1 and NOTCH2, EGFR, and TERT as well as molecular pathways like RAS/RAF/MEK/ERK and PI3K/AKT/mTOR.[13] Cutaneous SCC typically manifests as a spectrum of progressively advanced malignancies, ranging from a precursor AK to SCC *in situ*, invasive cSCC, and finally metastatic SCC.[14] It may present as erythematous scaly thin papule or plaque or occasionally as thicker tumors with typical erythematous plaque, nodule, or ulcer. Most studies suggest the most common affected anatomical sites for SCC are the scalp, ear, lip, nose, and eyelid. It has been however reported as red raised patches or wart-like sores on or in the anus or genitalia.[15]

Risk factors are grouped into solar and nonsolar entities and their contributory role varies with race and geographic region. While sun exposure is a major etiological factor in Whites, chronic ulcers and inflammation appear to be the leading risk factor in Blacks.[16,17] Albinism and solar radiation are known risk factors for SCC in black Africans.[18] This study examines the clinicopathological characteristic of SCC as well as the demographic profiles of the affected patients.

Materials and Methods

A retrospective review of dermatological malignancies of SCC from January 2004 to December 2019 in the Department of Histopathology National Hospital Abuja was carried out. Data were exported from the department software in comma-separated value format. The data analyzed demographic and other clinicopathological characteristics as categorical variables. Mean and standard deviation were determined for the quantitative variable. All variables were coded as binary dummy variables. For sex (male = 1, female = 2). Data presented as charts and frequency distribution generated for all categorical variables. Descriptive and inferential statistics; bi-variate correlation (Spearman ranking); and generalized linear regression models were used to evaluate incidence rates in relation to sex and age analysis was applied between demographic: Age and sex as independent variables, and clinicopathological: clinical presentation, anatomical site, variables, and histological types $P \leq 0.05$ is considered as statistically significant. SPSS version 23.0 (Chicago IL) for windows; for statistical analysis was used.

Results

A total of 103 cases of histologically confirmed SCC of the skin were reviewed. These accounted for 25.8% of the dermatological malignancies in the same period of the study. There were 59 (57.3%) males and 44 (42.7%) females patients identified with cases of SCC, with a male to female ratio 1.3:1. The overall mean age of the study participants was 35.9 ± 13 and the age range of 4–81 years respectively, the peak age incidence occurred within the third to fourth decade of life accounting for 69 (66.9%) as depicted in Figure 1. The average age of male patients ranges from 10 to 78 years (mean 37.8 ± 13.8), while female age ranged from 4 to 81 years (33 ± 11.9). With regard to the clinical presentation, 37 (35.9%) patients presented with pain, 24 (23.3%) had swellings, 16 (15.5%) experienced bleeding, 3 (2.9%) manifested with discharge while 12 (11.7%) had fever. Other symptoms were elicited in 11 (10.7%) patients. More than half of the patients fell within the age cohort of 21–30 and 31–40 years. Among the predominant age cohorts, swelling was the most common presentation accounting for 30% within the 21–30-year group, while pain is more frequent in the 31–40-year cohort with 33.3%. This is depicted in Table 1. Seventy-one percent of the SCC was observed in the head and neck region, followed by 17.5% in the trunk, 7.8% in the lower limb, and 2.9% in the upper limb [Table 2 and Figure 2].

Correlation and multivariate logistic regression

Spearman's ranking correlation shows a negative correlation between gender as predictor variable, clinical presentation as well as anatomical site as explanatory variable. However the correlation was not statistically significant ($R = -0.014$, $P = 0.891/R = 0.040$ $P = 0.690$), With regards to the age and clinicopathological variable, the correlation was found to be positive for anatomical location. Negative correlation was observed in the clinical presentation with age ($R = 0.84$, $P = 0.399$). Table 3 shows that patients younger than 50 years presenting with pain, are 3 times more likely to develop SCC of the skin than those older or equal to 50-year

Table 1: Distribution of clinical presentation by age of patients

Age	Pain (%)	Swelling (%)	Bleeding (%)	Discharge (%)	Fever (%)	Others (%)	Total
1-10	2 (100)	-	-	-	-	-	2
11-20	3 (60)	1 (20)	-	-	1 (20)	-	5
21-30	7 (21.2)	10 (30.3)	7 (21.2)	-	5 (15.2)	4 (12.1)	33
31-40	12 (33.3)	9 (25.0	6 (16.7)	2 (5.6)	3 (8.3)	4 (11.1)	36
41-50	6 (46.2)	1 (7.7)	1 (7.7)	-	2 (15.4)	3 (23.1)	13
51-60	4 (44.4)	2 (22.2)	1 (11.1)	1 (11.1)	1 (11.1)	-	9
≥70	3 (60.0)	1 (20.0)	1 (20.0)	-	-	-	5
Total	37 (35.9)	24 (23.3)	16 (15.5)	3 (2.9)	12 (11.7)	11 (10.7)	103

The clinical presentation of patients with squamous cell carcinoma

Table 2: Distribution of anatomical site by age

Age	Trunk (%)	Head and neck (%)	Upper limb (%)	Lower limb (%)	Total
1-10	0	2 (100)	0	0	2
11-20	1 (20)	3 (60)	1 (20)	0	5
21-30	9 (27.3)	20 (60.6)	1 (3.0)	3 (9.1)	33
31-40	4 (11.1)	30 (83.3)	0	2 (5.6)	36
41-50	1 (7.7)	12 (92.3)	0	0	13
51-60	1 (11.1)	5 (55.6)	1 (11.1)	2 (22.2)	9
>70	2 (40)	2 (40)	0	1 (20)	5
Total	18 (17.5)	74 (71.8)	3 (2.9)	8 (7.8)	103

The distribution of squamous cell carcinoma according to anatomical regions of the body

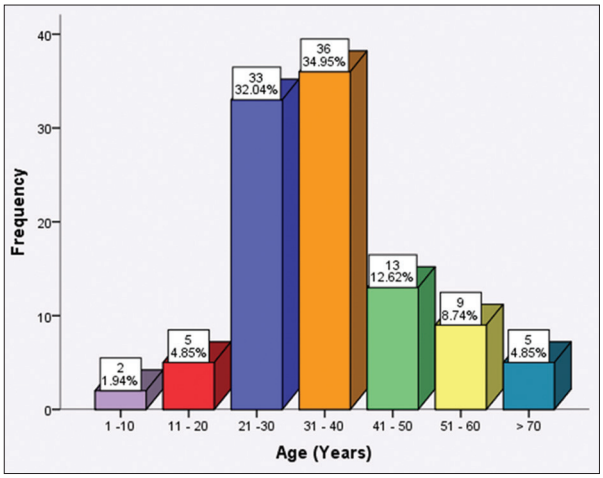

Figure 1: The age distribution of squamous cell carcinoma in National Hospital Abuja over the study period

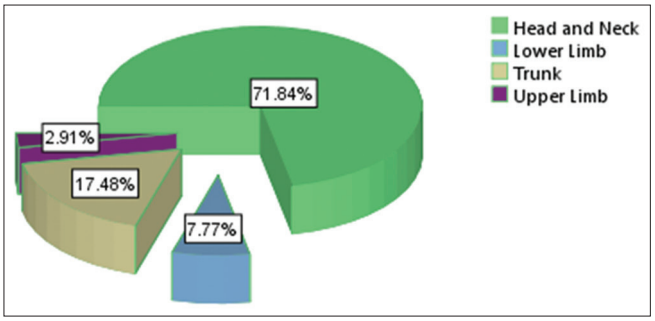

Figure 2: The distribution of body regions affected by squamous cell carcinoma

age (odds ratio [OR] = 2.5, 95% CI = 4.394–1.508). Concerning gender, however, there was no significant variation between males and females. Multivariate logistic regression of the site of lesion shows that age was a significant factor ($P < 0.05$), thus patients younger than 50 years were approximately 8 fold likely to develop SCC of the Head and Neck region (OR = 7.731, 95% CI = 1.257–47.560). Trunk and upper limb, on the other hand, were not statistically significant in relation to sex, and age of patients [Table 4].

Discussion

SCC accounted for 25.8% of the dermatological malignancies encountered in this center during the study period. Similar studies done elsewhere reported varying figures. Thus in Ibadan, southwestern Nigeria SCC accounted for 40.5%,[10] while Calabar in southeastern Nigeria, SCC accounted for 36%,[19] Ahachi *et al*. in Makurdi obtained 44.3%,[20] Ochicha *et al*. in Kano, (Northern Nigeria) reported 40.5% incidence of SCC,[11] Forae and Olu-Eddo obtained 25% in Benin,[21] while in Tanzania[22] and Tunisia[23] cSCC was reported to account for 40%, and 31% respectively. In Spain, the incidence of SCC was according to a report 38.16 (95% CI, 29.82–46.49) cases per 100,000 person-years.[24] Studies estimated that SCC is generally falling in Australia, stable in the United States, and rising in Germany.[17]

The overall mean age of the study participant was 35.9 in our study and the age range 4–81 years. This is lower than the findings of Asuquo in Ibadan who obtained 44.8 and Forae in Benin with 47 years.[25] Furthermore reports from Ile-Ife located in a similar geographical location as Ibadan provided 39.3 years mean age. This study reveals that an overwhelming 70% of the SCC occurred in the head and neck region. This concurs with a recent report from Germany where Amaral *et al*. reported 80% of patients had SCC localized in the head and neck area.[20] This is however in sharp contrast with the report from Makurdi (north central Nigeria), stating that SCC was found to predominate in the lower limb region.[25]

The modal age group was the third to fourth decade of life (66.9%). Age was found to be a significant factor ($P < 0.05$). Thus patients of age <50 years were approximately 8 times likely to develop SCC of the head and neck region (OR = 7.731, 95% CI = 1.257–47.560) than other age groups. Muzic *et al*., on the other hand, reported the 50–59-year age group as the predominantly affected cohort with an almost 2 fold increase in incidence compared to other age groups (1.55 to be exact).[26]

Although a significant majority of cSCCs is successfully eradicated by surgical excision, a subset of cSCC possesses features associated with a higher likelihood of recurrence, metastasis, and death.[27] This tendency to poor outcomes gives the tumor a special public health importance. Indeed a study approximated the mortality from cSCC to that of oropharyngeal and renal carcinomas as well as melanomas.[3] The potential to metastasize, as proposed by a study, is dependent on tumor size, Clark's level, degree of differentiation, the presence of small

Table 3: Multivariate logistic regression analysis of age, gender, and clinical presentation

Clinical presentation versus age and gender	*P*	OR	95% CI (lower bound-upper bound)
Pain			
<50	0.000	2.574	4.394-1.508
≥50		1	
Male	0.866	1.125	0.285-4.441
Female		1	
Swelling			
<50	0.000	4.755	6.598-3.426
≥50		1	
Male	0.452	1.749	0.407-7.505
Female		1	
Bleeding			
<50	0.000	2.678	3.565-2.012
≥50		1	
Male	0.790	1.239	0.257-5.960
Female		1	
Discharge			
<50	0.000	1.339	7.149-2.507
≥50		1	
Male	0.722	1.652	0.103-26.401
Female		1	
Fever			
<50	0.000	3.518	3.518-3.518
≥50			
Male	0.421	2.015	0.365-11.120
Female		1	

The relationship between age gender and clinical presentation in squamous cell carcinomas encountered. OR: Odds ratio, CI: Confidence interval

Table 4: Multivariate logistic regression analysis of age, gender, and anatomical site of lesions

Anatomical site versus age, and gender	*P*	OR	95% CI (lower bound-upper bound)
Trunk			
<50	0.188	3.994	0.508-31.398
≥50		1	
Male	0.454	2.058	0.311-13.606
Female		1	
Head and neck			
<50	0.027	7.731	1.257-47.560
≥50		1	
Male	0.076	4.746	0.848-26.568
Female		1	
Upper limb			
<50	0.634	2.081	0.102-42.464
≥50		1	
Male	0.337	4.325	0.217-86.111
Female		1	

The relationship between age, gender, and anatomical location of squamous cell carcinoma in affected patients. OR: Odds ratio, CI: Confidence interval

tumor nests, infiltrative tumor strands, single-cell infiltration, perineural invasion, acantholysis, and recurrence. According to that study location, ulceration, inflammation, and Breslow depth did not correlate with the development of metastasis.

Mortality and metastasis from cutaneous SCC are acknowledged to be low but significant in some communities. A study reported a metastatic rate of 3.7% and a disease-specific death of 2.1%.[28]

This according to the workers may be associated with tumor size beyond 2 cm, invasion beyond the fat layer, poor differentiation, perineural invasion and ear, temple, or anogenital location.[29] Furthermore, the presence of cSCC is reputed to heighten the likelihood of death from other concurrent malignancies.[30]

Conclusion and Recommendation

The increasing incidence and the predisposition to poor outcomes of SCC should generate more attention of workers on the potentials of the disease as an emerging public health problem. In this study, SCC was predominant in the Head and Neck region. Age was found to be a significant factor, patients of <50 years were approximately 8 fold likely to develop SCC in the head and neck region. Hence, SCC deleterious effects may be mitigated by early prevention approaches, early presentation, and surgical evaluation of chronic ulcers. There is a need to intensify awareness and public enlightenment on sun protection and skin cancer programs for reducing this largely preventable cancer. Subsequently devising other preventive, therapeutic, and palliative strategies should be a priority.

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Conflicts of interest

There are no conflicts of interest.

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