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Non-Melanoma Skin Cancer in Young Adults Presenting at Three Academic Hospitals in Johannesburg: A 5-Year Audit

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ABSTRACT

Background: The incidence of Melanoma and Non-Melanoma Skin Cancers (NMSC) is increasing globally. The South African population is exposed to many risk factors associated with the development of skin cancer, particularly UVR exposure and HIV.

Aim: The aim of the study was to compare the prevalence and location of NMSC in Adolescent and Young Adults (AYA) versus the pattern in older adults.

Patients and Methods: An audit based on histopathology reports of patients who were above 15 years of age and were diagnosed with skin cancer at three academic hospitals in Johannesburg over a 5-year period was conducted. The project was approved by the Wits Human Research Ethics Committee (M200960). Categorical data was presented as total counts and percentages. The significance of the difference between categorical data was tested using the chi-square test and the two tailed Student t-test for continuous data. A value of $p < 0.05$ was considered statistically significant.

Results: A total of 385 records of patients from the 16 to 40 years and 198 (51.4%) were women. Of the 373 NMSC 148 (38.4%) were Squamous Cell Carcinoma (SCC), 133 (34.6%) basal cell carcinoma (BCC) and 56 (14.6%) Kaposi's sarcoma (KS) (n=56, 14.55%). Significant association was found between SCC and female sex ($p<0.001$) and BCC and male sex ($p<0.001$). HIV status was significantly associated with KS ($p<0.001$), BCC ($p=0.005$) and SCC ($p=0.006$). In the older adults 56.7% (605/1067) of skin cancers were BCC, 31.5% (336/1067) SCC and 2.5% (27/1067) KS.

Conclusion: Squamous cell carcinoma was the most common skin cancer in AYA whereas BCC was the leading tumour in older adults. Basal cell carcinoma was more prevalent in men while SCC was predominately diagnosed in women.

1. Introduction

Skin cancer is broadly classified into Melanoma and Non-Melanoma Skin Cancer (NMSC). The NMSC group includes Squamous Carcinoma (SCC), Basal Cell Carcinoma (BCC) and Kaposi Sarcoma (KS). The incidence of skin cancer is increasing and it is now become the commonest cancer in Canada the annual increase in costs related to skin cancer care is

higher than that of any other cancer[1,2]. In South Africa in 2015, an estimated ZAR 92.4 million was spent on the management of patients with skin cancer[3]. These costs will only increase with the increasing incidence of skin cancer.

At least 80% of skin cancers are NMSC, with BCC accounting for 70% of the NMSC and SCC accounting for 20%[4]. Basal cell carcinoma is twice as prevalent as SCC[5,6]. Most of the BCC and SCC arise from the head and neck region[7,8]. In individuals with darker skin, non-sun exposed areas are the most common location for SCC whereas in fair-skinned individuals, SCC commonly arises from sun-exposed areas[7]. The lower extremities are the most common sites for KS followed by the head and neck region[8,9].

The main risk factor for the development of all NMSCs and melanoma is chronic exposure to ultraviolet radiation (UVR)[10]. Individuals with oculocutaneous albinism type 2 (OCA2) have a one-thousand-fold higher risk of developing SCC compared to the general population[11]. Immunosuppression or altered immune states are a well-established risk factor for skin cancer. Immunosuppressive transplant treatment is associated with a fifty-fold increased risk of developing a SCC compared to the general population[11]. Individuals who are HIV positive have a two-fold risk of SCC as compared to HIV negative patients, with higher incidences being proportional to lower CD4+ T-cell counts[11]. Similarly, HIV positivity increases the risk of KS by 28.4-folds[12]. Kaposi sarcoma (KS) is more common in young adults, particularly in those with untreated HIV[9,13].

The incidence of NMSC is increasing globally and notably in young adults. The South African population is exposed to many risk factors associated with the development of skin cancer, particularly UVR exposure and HIV. The skin cancers with the strongest association with chronic UVR exposure is BCC followed by SCC, which combined account for approximately 90% of all NMSCs in South Africa[11]. The aim of the study was to evaluate the risk factors, sex distributions, physical characteristics and subtype prevalence of NMSC compared to melanoma in young adults aged 16-40 years in Johannesburg, from January 2011 to August 2017.

2. Patients and Methods

This was an audit based on histopathology records of patients who were diagnosed with skin cancer from the 1st January 2011 to 31st August 2017 at three academic hospitals in Johannesburg. The study population includes all individuals who were over the age of 15 years with melanoma or NMSC. The study received prior ethics approval (M200960).

Skin tumours were divided into five main groups for analysis: BCC, SCC, KS, melanoma and rare malignant skin others. The analysis of tumour body site includes primary and secondary skin cancer locations and subtypes. The body sites were categorised into head and neck, upper body, lower body and not specified. Risk factors were categorised based on frequency of occurrence as follows: HIV, chronic sun exposure, oculocutaneous albinism and other, which includes xeroderma pigmentosum, Gorlin syndrome and other rare risk factors.

Collected data were entered onto a Microsoft Excel (2019) spreadsheets and analysed with Python 3.7 Anaconda Distribution (Anaconda Inc., Berlin, Germany) using a variety of open-source data analysis libraries. Quantitative features such as age were summarized using the mean ± standard deviation (SD). Categorical data were presented as total count and percentages. The significance of the difference between categorical data was tested using the chi-square test. The two tailed Student t-test was used to compare continuous data. Statistical significance was set at a $p < 0.05$.

3. Results

For the group of patients aged 16 to 40 years, there were a total of 385 patients included in the study: 187 (48.6%) men and 198 (51.4%) women. The mean patient age was 33 ± 6 years (range: 16 -40 years) and the oldest was 40 years. The mean age of female patients was 32.9 + SD years and that of male patients was 32.3 + SD years.

Of the 385 patients in the 16 to 40 years group, 68 (17.7%) had multiple tumours. Of the patients with multiple tumours, 62 (91.2%) had a total of two tumours, 4(5.9%) had three, 1(1.5%) had four tumours (1.47%) and 1(1.5%) had six tumours (1.47%). Three hundred and seventy-three (96.9%) of all primary skin cancers were NMSC. Thirty-eight percent (148/385) were SCC, BCC 133 (34.6%) BCC and 56 (14.6%) were KS. Overall, BCC, SCC and KS make up 377 (90.4%) of all the primary NMSC tumours. Malignant melanoma was diagnosed in 12 (3.1%) of the cases.

The relationship between sex of the patients and the primary NMSC tumour type was found to be significant (p=0.024). Significant associations were found between SCC and female sex (p<0.001) and BCC and male sex (p<0.001). The distribution of the types of tumours according to sex is shown in (Figure 1).

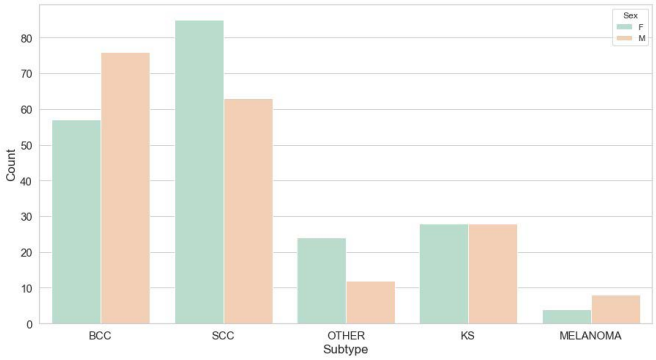

Figure 1: Distribution of skin cancer subtype according to sex.

Two hundred and fifty-seven (55.5%) of the skin cancers were from the head and neck region, 104 (22.5%) from the upper extremities and 74 (16.0%). The location of the tumour was not specified in 28 (6.1%). The relationship between location and NMSC type was found to be significant (p<0.001). The distribution of subtype by location is shown in (Figure 2). The position of KS and SCC were found to be significantly associated with the lower body at p-values of 0.003 and 0.030, respectively. The site of occurrence of BCC was found to be significantly associated with the head and neck and the upper body at p-values of 0.001 and 0.014, respectively. Of note, SCC was not significantly associated with the head and neck or the upper body with p-values of 0.154 and 0.246, respectively.

There were 219 (56.9%) patients with recorded risk factors. Chronic sun exposure (n=52, 23.7%), HIV (n=72, 32.9%) and oculocutaneous albinism (n=70, 32.0%) accounted for 88.6% of the recorded risk factors. Other relatively rarer risk factors (n=25, 11.4%) include xeroderma pigmentosum, Gorlin syndrome and

previous skin cancer. There is a strong association between primary NMSC subtypes and risk factor (p<0.001). HIV was shown to be significantly associated with KS (p<0.001), BCC (p=0.005) and SCC (p=0.006). Chronic sun exposure was shown to be significantly associated with BCC (p=0.036) but not with SCC (p=0.245). Oculocutaneous albinism was also shown to be significantly associated with BCC (p=0.009) but not with SCC (p=0.104). The distribution of subtypes according to risk factor is shown in (Figure 3).

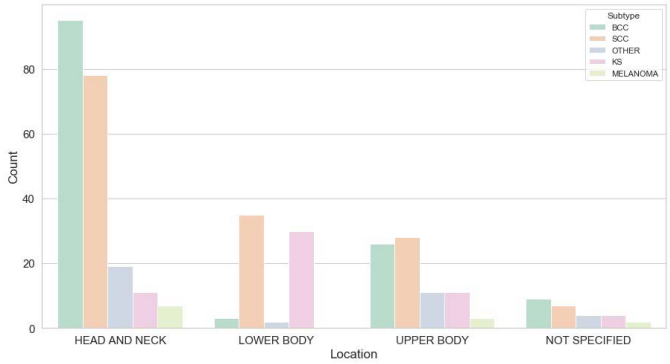

Figure 2: Distribution of skin cancer location according to subtype.

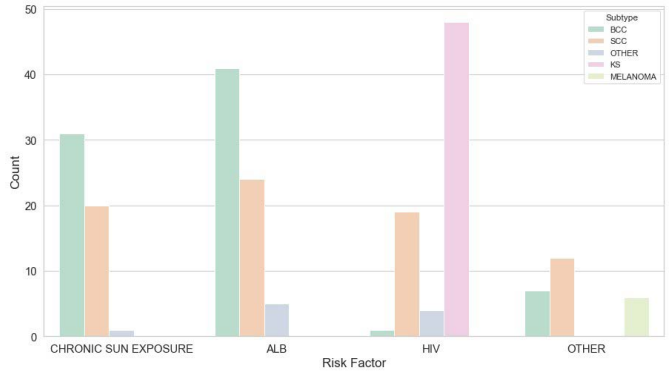

Figure 3: Distribution of skin cancer subtype according to risk factor.

In the group aged above 40 years, there were a total of 1 067 patients included in the study. The mean patient age was 78 years (SD±7 years) (range: 41 to 98 years). Six hundred and five (56.7%) of the tumours were BCC, SCC (n=336, 31.5%) and KS (n=27, 2.5%) and accounted for 90.7% of all the skin cancers recorded in this group. There were only 14 (1.3%) cases of malignant melanoma recorded. The absolute counts and proportions of each subtype in each of the two age groups is shown in (Table 1).

Table 1: Distribution of skin cancer subtype according to age group.

Tumour type	16-40 years n (%)	40+ years n (%)
SCC	148(38.4%)	336(31.5%)
BCC	133(34.6%)	605(56.7%)
KS	56(14.6%)	27(2.5%)
Melanoma	12(3.1%)	14(1.3%)
Other	36(9.4%)	85(8%)
Total	385(100)	1067 (100)

The rare skin tumours made up 17/385 (4.4%) of skin cancers in the 16 to 40 years compared to 124/1067 (11.6%) in older adults. The most reported rare tumours in the 16 to 40 years were basosquamous followed by porocarcinoma at 35.3% and 29.4%, respectively. The two most common tumours in the patients who were above 40 years of age were basosquamous cancer and trichilemmal carcinoma at 37.9% and 22.6%, respectively (Table 2).

Table 2: Distribution of rare skin cancer subtype according to age group.

Tumour type	16-40 years n (%)	40+ years n (%)
Basosquamous	6(35.3%)	47(37.9%)
Porocarcinoma	5(29.4%)	7(5.6%)
Trichilemmal carcinoma	0(0%)	28(22.6%)
Adenocarcinoma	1(5.9%)	8(6.5%)
Merkel cell carcinoma	1(5.9%)	6(4.8%)
Poorly differentiated cancers	4(23.5%)	16(12.9%)
Adnexal carcinoma	0(0%)	2(1.6%)
Angiosarcoma	0(0%)	4(3.2%)
Dermatofibrosarcoma protuberans	0(0%)	3(2.4%)
Primary cutaneous lymphoma	0(0%)	1(8.1%)
Acantholytic squamous cell carcinoma	0	1
Metastases	0(0%)	2(1.6%)
Total	17(100%)	124 (100%)

4. Discussion

In keeping with international literature, the older adults of this cohort make up most patients with skin cancer when compared to younger adults (n=1067 compared with n=385). In both patient groups, NMSC accounts for most of the skin cancer. NMSC accounts for 96.89% of skin cancers in young adults and 98.69% of skin cancer in older adults. In both groups, the most prevalent NMSCs are SCC and BCC, which is comparable with the results of studies conducted by Byfield et al.[14] and Garcovich et al.[4].

In older adults, BCC is the most common group, accounting for 56.70% of all skin cancers. SCC in this group accounts for 31.49%. This is in line with the findings reported by Christenson et al.[6]. SCC is the largest group of skin cancers in this study's cohort of young adults. This contrasts with BCC being the most common NMSC in young adults reported by Christenson et al.[6] and Pearce et al.[5]. SCC accounts for 38.44% of all skin cancers, followed closely by BCC, which accounts for 34.55%. This may be explained by the fact that HIV, as described by Wright et al.[11], is a major risk factor for SCC. HIV is much more prevalent in this South African cohort when compared to the cohorts of the studies conducted by Christenson et al.[6]. and Pearce et al.[5], which focused on populations in the United States of America and the United Kingdom, respectively.

Both the number and proportion of KS in young adults (n=56, 14.55%) is higher than that of older adults (n=27, 2.53%). Research conducted by Chalya et al.[9]. and Luu et al.[13]. corroborate these findings, with both authors concluding that the incidence and prevalence of KS declines with age. This is likely due to the higher burden of HIV and particularly untreated HIV, in younger adults in South Africa.

The incidence of melanoma cases in both groups was found to be almost identical and in both cases much less substantial than NMSC counts. The younger group consisted of 12 cases compared to the older group which consisted of 14 cases of

melanoma. This contrasts with the results of a study conducted by Byfield et al.[14], who showed that melanoma was much more prevalent in older adults.

Although most patients in this study's cohort presented with SCC located in the head and neck region, it was not associated with any statically significance. Furthermore, SCC was not significantly associated with the upper body. Both findings contrast with research conducted by Subramaniam et al.[8] and Norval et al.[7], who found these areas to be associated with a high degree of significance. This study did demonstrate a strong association of SCC with the lower body, which is comparable to the results of a 10-year population-based cohort study conducted in Minnesota by Muzic et al.[15]. This result is again, however, in contrast to the findings of Subramaniam et al.[8]. and Norval et al.[7]. Body site associations in patients with BCC found in this study were consistent with the results found by Subramaniam et al.[8]. and Muzic et al.[15]. BCC was found to be significantly associated with the head and neck region. However, in this study, it was found that there was also a large association between BCC and the upper body. Our results were also consistent with previous studies as to the lower body being the least common location[7].

The distribution of KS that were found were consistent with the literature. A review undertaken by Chalya et al.[9]. demonstrated cutaneous KS to be associated significantly with the lower limbs, accounting for almost half of all cases. This is in keeping with the results of this study, which demonstrated that the lower limb was the most frequent anatomical site of KS. The results of Chalya et al.[9]. and Bogaert et al.[16] showed the next most common body sites to be the head and neck region, followed by the upper limbs. This is consistent with the findings of this study, although a statistically significant association could not be demonstrated.

Risk factors identified for BCC in young adults in this research are chronic sun exposure, OCA2 and the male sex. The risk factors identified for SCC in this research are HIV and the female sex. These findings are in keeping with the international literature[3,11]. Olsen et al.[17]. and Modenese et al.[18]. describes the greatest risk factor for BCC being sun exposure in childhood and adolescence. These studies also describe the greatest risk factor for SCC being cumulative sun exposure, therefore shifting age of diagnosis to later in life.

Individuals with OCA2 have a decreased amount of eumelanin, an important protective factor against all types of skin cancer[19]. Due to this they are more likely to get recurrent sunburns and repeated sun damage. Our research found that BCC was more common in OCA2 individuals than SCC. This contrasts with Hong et al.[20]. who describes SCC being the most common NMSC in OCA2 individuals. However, Hong et al.[20]. quotes these statistics from four articles from 1980, 1985, 1990 and 1995, which only considered 62 histopathologically diagnosed individuals. It was found that HIV is significantly associated with the development of KS, BCC and SCC. KS was the most common NMSC in this group, which is corroborated by research conducted by Cesarman et al.[21]. Wright et al.[11]. demonstrated that SCC is more common than BCC in individuals with HIV. This finding is in line with the results of this study.

The occurrence of BCC was found to be higher in males than in females. This is in keeping with the results of Apalla et al.[22]. who showed males having a two-fold increased risk of developing BCC when compared to females. The occurrence of SCC was found to be higher in females than in males. This is not in keeping with the current literature. Apalla et al.[22]. showed that males were at a three-fold increased risk of developing SCC when compared to females. Kaposi sarcoma was found to be equal in males and females. This is in keeping with the findings of Wang et al.[23]. and Forae et al.[24], who found that KS incidence is equal in males and females in Sub-Saharan Africa.

5. Limitations of the Study

Only histologically confirmed skin cancer cases were included. Some skin cancers may have been diagnosed based on clinical features, resulting in underestimation of the true incidence. It is possible that risk factors were not recorded in the database, which may affect the validity of associations found in this study. The data was sourced from an already existing database and so sampling errors and selection biases cannot be ruled out. There was a small study population and a relatively short study period of only 5 years. This study will only consider data from the public healthcare sector and does not consider data from the private healthcare sector. This study is limited to three Johannesburg hospitals and so the results may not be generalizable to the entire Gauteng or South African population. There may be several confounding factors which cannot be controlled or accounted for.

6. Conclusion

The incidence of skin cancer is increasing worldwide and notably in the young adult population. Populations living in Southern Africa are exposed to a significant number of risk factors for skin cancer and it is important, therefore, to investigate these trends. This retrospective descriptive analysis found a few associations between subtype, age, sex, risk factors and body site. SCC was found to be associated with female sex, HIV and the lower body site. BCC was found to be associated with male sex, HIV, chronic sun exposure, OCA2 and HIV. It was commonly found in sun-exposed areas. KS was associated with younger individuals, no sex and HIV and was commonly found in the lower limbs. These results give important insight into the characteristics of NMSC and melanoma in young and older adults.

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