THE PREVALENCE OF BASAL CELL CARCINOMA AND SQUAMOUS CELL CARCINOMA AT THE HELEN JOSEPH HOSPITAL

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DECLARATION

I, Karen Itumeleng Mosojane hereby declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Dermatology (in submissable format with the protocol and extended literature review), Department of Internal Medicine, University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

.....

.....24th .....day of .....Nov.....2022

DEDICATION

God all things are possible through you.

To my husband, Bakang Thuto Phala, thank you for the unconditional love, encouragement and support.

ACKNOWLEDGEMENT

I extend my gratitude to Professor Deepak Modi for his guidance and supervision in completing this work.

I would also like to thank the NHLS staff, Fadila, Thomas and Mandla, who made it possible for me to access the data.

ABSTRACT

Background

Basal cell carcinoma and squamous cell carcinoma account for the majority of nonmelanoma skin cancers. Although the diagnosis has a relatively low mortality in comparison to other malignancies, the patients incur significant morbidity and there is an immense financial burden on health care systems.

Objectives

To study the prevalence, demographic and histologic pattern of patients with basal cell carcinoma and squamous cell carcinoma at the Helen Joseph Hospital.

Methods

This was a retrospective study of adults who had histologically confirmed basal cell carcinoma and squamous cell carcinoma at Helen Joseph Hospital, Dermatology department for the duration of 1st June 2014 to 30th June 2019.

Results

Basal cell carcinoma

A total of 394 patients were included. The prevalence was 1.4% with a mean age of 69.4 years (standard deviation of 11.5). Males were 209 (53.0%) and 137 (34.8%) were female, gender was not documented in 48 (12.2%). The male to female ratio was 1.5:1. HIV negative patients were 62 (15.7%) and 5 (1.3%) were HIV positive.

Actinic keratosis was a risk factor for all the patients. A total of 393 (99.7%) patients were of Fitzpatrick's skin phototype I or II, 1 (0.3%) patient had oculocutaneous albinism and 4 (1.0%) patients were smokers. A previous diagnosis of skin cancer was observed in 87 (22.1%) patients.

The histologic subtypes that were diagnosed included nodular (69, 17.5%), metatypical/basosquamous and superficial both at 12 (3.1%) and ulcerated (11, 2.8%), however most patients (200, 50.7%) had a mixed subtype. Most of the lesions were located on the face 194 (49.2%) and upper limb 53 (13.5%).

Squamous cell carcinoma

Overall 85 patients were diagnosed with squamous cell carcinoma. The prevalence was 0.3%. The mean age was 68.7 years (standard deviation of 12.8). In the cohort, majority of our patients were male (61, 71.8%), 17 (20.0%) were female, and the male to female ratio was 3.6:1. Gender was not documented in 7(8.2%). There was no statistical significance between gender and age ($p>0.05$). HIV negative patients were 12 (14.1%) and 3 (3.5%) were HIV positive.

Almost all patients in this cohort were of a lighter skin phototype 83 (97.6%). Most patients had multiple risk factors, except 1 (1.2%) who had epidermodysplasia verruciformis as the only risk factor identified.

Moderately differentiated squamaous cell carcinoma was diagnosed in majority of the patients 59 (69.4%) and 3 (3.5%) patients had poorly differentiated squamous cell carcinoma. Most patients had an undocumented histologic variant 67 (85.9%). Squamous cell carcinoma occurred most commonly on the face 30 (35.3%), upper limb 16 (18.8%) and scalp 13 (15.2%)

Conclusion

Our findings are generally in line with other published reports. We noted that BCC has a higher prevalence than SCC. Both cancers were more common in elderly males. Fitzpatrick skin phototype 1 and 2, history of sun exposure, actinic keratosis and prior skin cancer are some of the risk factors that we elucidated. In our cohort these cancers occurred more frequently on sun exposed sites. Majority of our patients did not have a documented HIV status. There is lack of standardisation in history taking and documentation in our dermatology clinic, as well as histopathology reports which leads to important prognostic factors not being documented. These factors form a basis for patient treatment options and inform follow up plans.

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LIST OF ABBREVIATIONS

AK:	Actinic keratosis
BCC:	Basal cell carcinoma
BCNS:	Basal cell nevus syndrome
CEO:	Chief executive officer
EDV:	Epidermodysplasia verruciformis
HIV:	Human immunodeficiency virus
HJH:	Helen Joseph Hospital
HPV:	Human papillomavirus
HREC:	Human Research Ethics Committee
NMSC:	Non melanoma skin cancer
OCA:	Oculocutaneous albinism
PTCH:	Patched gene
SCC:	Squamous cell carcinoma
SCCis:	Squamous cell carcinoma in situ
SMO:	Smoothened receptor
UVA:	Ultraviolet A
UVB:	Ultraviolet B
UVR:	Ultraviolet radiation
XP:	Xeroderma pigmentosum

CHAPTER 1 – PROTOCOL WITH EXTENDED LITERATURE REVIEW

1.1. INTRODUCTION

According to the World Health Organization, cancer or malignancy refers to "a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs"[1]. Skin cancer is among the most frequently diagnosed malignancy[2,3]. Broadly, skin cancer is categorised into two groups; malignant melanoma and non melanoma[2-7]. Non melanoma skin cancer (NMSC) refers to all skin cancers that are not derived from melanocytes inclusive of basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (SCC)[8].

1.1.1. Historical background

The term "rodent ulcer" which describes the clinical presentation of BCC was first mentioned by Jacob in 1827 and Lebert in 1851[9-11]. Several authors in the years to follow documented their hypotheses about BCC arising from the epidermis, hair follicle and other adnexal structures[9-12]. Thereafter numerous discoveries were made on the histopathologic types and clinical course of BCC[9,11,12].

In 1775 Pott first described the link between chimney soot exposure and SCC of the scrotum[13,14]. Following this discovery, in the later decades and century, associations to arsenic, mineral oil, coal tar creosote and ultraviolet radiation (UVR) were discovered[13-19].

1.1.2. Epidemiology

Globally, between 2 and 3 million NMSC are diagnosed annually[2,3]. Worldwide majority of the NMSC are BCC and SCC[2-8,10]. Overall they both account for 99% of the cancers in the NMSC group[4,20]. Approximately 70-80% of all new skin cancers are BCC and 20-50% are SCC[6,21-23]. However in Sub-Saharan Africa, it has been documented that SCC is the leading type of skin malignancy and depending on geographic location BCC is still among the major types of NMSC[24,25].

1.1.3. Problem identification

Currently there is no published data about the prevalence of BCC and SCC at Helen Joseph Hospital (HJH) or Johannesburg, South Africa. However, in 2017, a retrospective study on the primary cutaneous malignancies in the Northern Cape province of South Africa concluded that indeed SCC and BCC still appear as the major NMSC[25]. Those published numbers may be much higher than stipulated because there may be under reporting of cases since cancer registries are not always compulsory and generally there are instances of NMSC being treated in the doctor's office[7,20,21,26,27].

Mortality from NMSC does occur, albeit at a low rate in comparison to other malignancies[20,21,26,27]. However NMSC are associated with significant morbidity since they tend to occur in easily visible areas such as the face, arms and legs[20,21,26,27]. Furthermore there is an immense economic burden to the treatment of this cancers[27-31].

Therefore given the paucity of data on the accurate prevalence of BCC and SCC, the patient morbidity and the economic costs incurred during treatment, this study is of utmost importance. It will help elucidate the burden of both these cancers. The information gathered can be used for planning of public health prevention strategies, be it primary, secondary or tertiary and proper allocation of limited medical resources. With the information we will be in a better position to convince the hospital management to avail treatment options to the dermatology clinic at HJH such as cryotherapy, 5-fluorouracil, aminolevulinic acid used for phototherapy and a cautery machine for cautery and electrodessication which according to the author's knowledge is currently not provided by the hospital.

1.2. LITERATURE REVIEW

A review of published literature in English was conducted using PubMed through the University of the Witwatersrand online portal. The search words used were basal cell carcinoma, cutaneous squamous cell carcinoma, epidemiology, risk factors, clinical presentation, diagnosis, histology, management and prevention.

1.2.1. BASAL CELL CARCINOMA

BCC is a slow growing, locally destructive cancer emanating from basal cells of the epidermis[4,20,26].

1. Epidemiology

   The precise incidence of BCC is not known. This is largely due to the fact that in most countries there are no uniform cancer registries recording data on BCC[7,20,21,26,27,32]. Be that as it may, published reports are in agreement that the estimates in incidence are increasing in the United States, Europe, Canada, Asia and Australia[33]. Cameron *et al* has estimated that yearly 2 million Americans develop BCC[33]. In Europe the increase in the rates of BCC has been reported to be around 5% annually[32]. Australia ranks top with the highest worldwide incidence rates of BCC, where 50% of Australians will have developed a BCC by the time they are 70 years old[10,32,34]. The incidence rates in Asia and South America are much lower, albeit still increasing[32]. Gallo *et al* has reported that BCC rates in parts of Africa are lower than in other parts of the world[34]. However in the South African context, data is scarce[34].

   BCC is known to commonly occur in the middle aged to elderly population[10,21,32,33] . There are much less reported cases of BCC in the black community as opposed to Caucasians[10,32]. Traditionally male gender is known to be a risk factor for developing BCC[10]. However there is increasing data about more females younger than 40 being diagnosed with BCC as opposed to their male counter parts in this age group[10,32]. This is thought to be due to the use of tanning beds and women having a higher health seeking behaviour[32].

2. Aetiopathogenesis

   Prior studies have implicated mutations in the patched (PTCH) gene and smoothened (SMO) receptor in the pathogenesis of both the basal cell nevus syndrome (BCNS)

and sporadic BCC[26,35-43]. Cytochrome P450, glutathione S-transferase and *p53* genes are also implicated in the aetiopathogenesis of BCC[10,26,35-43]. These mutations and over activation leads to uncontrolled cellular replication and growth, which is a fertile ground for malignant transformation.

The most important environmental cause for NMSC is UVR[10,20,26,39-44]. UVR leads to the formation of BCC through inactivating tumour suppressor genes such as *p53* and PTCH, activating proto-oncogenes and inducing free oxygen radicals[36,40.] This is evidenced by the fact that most NMSC occur in sun exposed areas of the body, in sun damaged skin and cases are higher in countries that have sunnier climates and people with fair skin such as Australia[26,40-44]. Ultraviolet B radiation (UVB) is implicated more in the causation of NMSC as compared to ultraviolet A (UVA) radiation[25,41,42]. BCC is associated with intermittent and childhood exposure to UVR, typically with a latency period of about 20-50 years before clinical onset[10,20,26,41,44-46].

3. Risk factors

Overall genetic, environmental and phenotypic factors put one at risk for developing BCC. These factors maybe modifiable through behavioural changes where as some are non modifiable. Numerous genetic conditions have been described in the literature as predisposing factors to the development of BCC[26,33,35,37,39,40]. Patients with BCNS, xeroderma pigmentosum (XP), Bazex-Dupre-Christol syndrome, oculocutaneous albinism (OCA) and Rombo syndrome are all at an increased risk for developing BCC[26,33,35,37,39,40]. Due to defects in the Hedgehog signalling pathway, patients with BCNS among other features, develop BCC from an early age[33,35]. XP precludes one from the ability to repair UVR induced mutations, making them susceptible to developing malignancies, including BCC[33]. Bazex-Dupre-Christol syndrome also confers a risk to developing BCC due to defects in the regulation of the cell cycle[33]. OCA patients are at an increased rate of developing cutaneous malignancies, including BCC, due to lack of the photoprotective melanin pigment[47]. The exact gene involved in Rombo syndrome has not yet been identified but the patients have a tendency to develop BCC[33].

The most important environmental risk factor, which can be modifiable is UVR[20,26,35,36,38,40,44,47]. Exposure may be secondary to proximity to the equator, participation in outdoor activities without adequate sun protection, sunbathing, use of tanning beds or medically indicated phototherapy[20,26,35,36,38,40,44,47]. Other implicated risk factors include a prior history of NMSC, as well as immunosuppression in organ

transplant recipients, human immunodeficiency virus (HIV), and secondary to the use of chronic immunosuppresive medications such as methotraxate in patients with rheumatoid and psoriatic arthritis[26,35,37,49,40,44,47]. Exposure to ionizing radiation and chemicals such as arsenic, vinyl chloride, polycyclic aromatic hydrocarbonates and alkalizing agents also increases one's risk of developing BCC[26,35,37,39,40,44,47]. Patients with lighter skin phototypes (Fitzpatrick skin type 1 and 2) who may have fair or red hair, blue or green eyes, a tendency to burn rather than tan and freckles are at a significantly increased risk of developing BCC[26,35,40,47].

4. Clinicohistopathologic subtypes

There are numerous clinicohistopathologic subtypes of BCC [40,48-52].

Nodular BCC

This is the most common subtype, accounting for 60-80% of all cases[35,40,48,52]. It usually occurs on the head and neck region[35,40,48,52]. The typical presentation is that of a pearly or translucent papule or nodule, with telangiectasia[35,37,39,40,48,49,52]. The lesion can then ulcerate and develop a rolled border "rodent ulcer"[35,37,40,48,49,52]. On dermoscopy, one appreciates arborizing vessels, large blue-grey ovoid nests, multiple blue-grey dots and a milky red background[37,48]. Histology will show nest-like infiltration by basaloid cells with peripheral palisading and a central haphazard arrangement, with retraction artefact between tumour cells and the surrounding stroma[35,40,48,49,52,53]. Differential diagnoses to consider include amelanotic melanoma, molluscum contagiosum, sebaceous hyperplasia, trichoblastoma, trichoepithelioma, keratoacanthoma, SCC and merkel cell carcinoma[35,40,53].

Superficial BCC

Approximately 10-30% of BCC are of the superficial variant[35,40,48]. It usually occurs on the trunk and limbs[35,40,48,49,51]. Clinically it presents as an erythematous scaly plaque, with clear borders, pearl shaped edge and superficial erosion[35,37,39,40,48,49,52,53]. The dermoscopic features are telangiectasia, structure-less hypopigmentation and hyperpigmentation, multiple erosions and a milky red background[48]. On histology there will be nests of basaloid cells subepidermally, usually confined to the papillary dermis[35,40,48]. This subtype may be confused with eczema, psoriasis, actinic keratosis and Bowen's disease[35,36,39,40,52,53].

Morpheaform (sclerosing, desmoplastic) BCC

This tumour accounts for around 5-10% of BCC and commonly occurs on the face and neck[35,40,48]. Presentation is as a depressed, waxy, scar-like plaque, with poorly defined borders often with ulceration[37,40,48,52,53]. Dermoscopy will reveal short, fine, telangiectasia, structure-less hypopigmentation and a white shiny area with a milky red background[46]. Histologically the nests and clusters of tumour cells are surrounded by thick fibrotic stroma[35,40,48]. Differential diagnoses to consider include a scar, a plaque of localised morphea, dermatofibrosarcoma protruberans and microcystic adnexal carcinoma[35,52,53].

Infiltrating/infiltrated BCC

The infiltrative subtype of BCC commonly occurs on the upper trunk and face[40]. It usually occurs with other subtypes, particularly the nodular type[45]. This tumour presents as a whitish, or pale pink, indurated, flat, poorly defined plaque with overlying erosions, crusts and ulceration[40,48] . Histologically there are thin, nest-like bundles of basaloid cells infiltrating in the dermal collagenous fibers with a peripheral palisading pattern[35,40,48].

Fibroepithelial BCC/ fibroepithelioma of Pinkus

This uncommon subtype usually affects women, as a solitary, pink or erythematous nodule on the back[40,48,49]. On histology there is trabecular, elongated and branched thin strands of basaloid cells extending into the dermis[40,48,49]. Differential diagnosis includes actinic keratosis, keratoacanthoma, seborrheic keratosis and SCC[40,49].

Pigmented BCC

The pigmented subtype of BCC occurs commonly in patients with darker skin phototypes, Fitzpatrick types III to VI[37,48,52,53]. It can occur as a dark brown to black nodular, superficial, multifocal or micronodular BCC[40,52]. Dermoscopy shows either spoke-wheel areas, in focus dots and concentric structures or pigment globules at the deeper layers of the dermis[37,48]. Histologic features are nests of basaloid cells, abundance of melanin and melanophages and moderate inflammatory infiltrate[40]. The differential diagnosis is malignant melanoma and melanocytic naevi[39,52].

Micronodular BCC

It commonly occurs on the back and with a nodular BCC on the same lesion[40,48]. The tumour usually presents as a firm nodule with well defined borders and may be

greyish in colour[53]. On histology there are small rounded nodules of basaloid cell with minimal palisading[35,40].

Other subtypes of BCC

The other subtypes of BCC include the basosquamous also called metatypical (histologically has both BCC and SCC features in different areas with a transition zone), cystic, infundibulocystic (usually occurs on the head and neck region and presents as pearly papules), giant (occurs on the trunk and it is usually associated with neglect, alcohol abuse and heavy smoking), clear cell, signet ring and granular[37,39,48,49,52].

5. Clinical course

   BCC is generally regarded as a slow, indolent, locally invasive malignancy[20,21,40,54-56]. Less than 1% of BCC metastasize, therefore overall this malignancy has a low mortality rate[20,21,40,54-56]. However the morbidity incurred by the affected patients is insurmountable largely due to the fact that it occurs on easily visible sites such as the face and extremities[20,21].

6. Diagnosis

   After inspecting a lesion that is suspicious of being a BCC, the clinician can use dermoscopy to help aid the diagnosis[35,48]. A dermatoscope makes it possible to non-invasively visualise the epidermis and dermis[35,48]. Definite diagnosis is made after histopathologic confirmation[35,48]. The specimen can be obtained through excisional, shave, incisional or punch biopsy[35,48]

7. Management

   Studies have reported that the most important factors to consider in the treatment of BCC are removing the tumour in its entirety, the chances of recurrence, preserving function and cosmesis as much as possible and patient preference[26,35]. Bearing this in mind, Samarasinghe and Madan have classified BCC as either high or low risk of recurrence and aggressiveness, which will guide the treatment options[26]. High risk BCC are 2cm or more on the L-area (trunk and extremities), 1cm or larger on area-M (cheeks, forehead, scalp), 1cm or more on area-H of the face (central face, eyelids, eyebrows, periorbital, nose, lips, preauricular, postauricular, ear, temple), occurring in the genitalia, hands and feet[35,37,48,57]. The morphoeic, infiltrative, micronodular and basosquamous clinicohistologic subtypes, recurrent lesions, lesions on sites of prior

radiation, lesions occurring in immunocompromised patients and perineural invasion are also all considered high risk[26,35,37,48,52,57].

Treatment

The available treatment modalities are also divided according to whether the BCC lesion is high or low risk[57,58].

The first line option for low risk BCC in non critical head and neck areas include standard surgical excision with 2-5mm margin and Mohs' micrographic surgery may be an alternative[37,57,58]. Second line options can be topical which are ideal for patients who are either not eligible for or decline surgery and have superficial BCC[37,57,58]. These are imiquimod 5% cream which is applied at night, five times a week, for six weeks or until there is a local reaction (erythema, scab formation and crusting) or fluorouracil 5% cream which is applied twice daily for two to four weeks or until there is a local reaction[37,57,58]. Intralesional modalities that have been used include interferon alfa-2b, fluorouracil and bleomycin[37,57,58]. For superficial BCC photodynamic therapy is an alternative[37,57,58].

Low risk BCC on the trunk and extremities are treated with topical, destructive methods or surgery[37,57,58]. The topical options are imiquimod 5% cream applied at night, five times a week, for six weeks or until there is a local reaction or fluorouracil 5% cream or solution applied twice daily for two to four weeks or until there is a local reaction[37,53,57,58]. The destructive therapies include curettage and electrodesiccation, laser ablation and cryotherapy[37,53,57, 58]. Standard surgical excision with a 4-5mm margin can also be attempted[37,53,57,58].

High risk BCC are best treated with Mohs' micrographic surgery[37,53,57,58]. For practical purposes, due to the fact that there are very few Mohs' micrographic surgeons, standard surgical excision with more than 5-15mm margin is an alternative[37,58,59]. Patient who are poor surgical candidates or decline surgery are offered primary radiation[37,53,58,59].

Medical therapy in the form of hedgehog inhibitors, is indicated for patients with locally advanced BCC, metastatic BCC, patients who are not surgical and radiation therapy candidates and those with BCNS[37,58,59]. The two medications are Vismodegib 150mg/day orally and Sonidegib 200mg/day orally[58,59].

8. Prevention

Prevention of BCC can be primary, secondary or tertiary[32]. It is very important because of the morbidity that these patients face as well as the financial costs involved as disease progresses. Primary prevention entails reducing the chances of a patient developing their first BCC[32]. Due to the fact that some BCC risk factors are non-modifiable, such as Fitzpatrick skin phototypes 1 and 2 and genodermatoses, it is imperative that the modifiable factors are targeted. Educating patients on photoprotection cannot be overemphasised[32,37.60]. Studies have reported that encouraging patients from an early age to use broad spectrum sunscreen is imperative[32.60]. Other photoprotective measures include avoiding sun exposure during peak hours, using hats and sunglasses and wearing long sleeved clothing when one is outdoors[60]. Verkouteren *et al* and Fagan *et al* describe how some countries have adopted policies such as tax free sunscreen and banning indoor tanning salons in an effort to prevent BCC[32,60]. In addition to the use of sunscreen, chemoprotection has also been reported to be advantageous when topical and oral retinoids are used in patients with BCNS and XP[32].

Secondary prevention involves screening, diagnosing and treating the initial presentation of a BCC at an early stage, although studies differ on the cost effectiveness of this approach[32]. Chemoprevention in the form of 500mg of oral nicotinamide twice daily has shown positive results in preventing the development of a second BCC[60]. Sunprotective measures are also still encouraged at this stage.

Tertiary prevention is aimed at patients with advanced BCC[32]. The goal is to reduce morbidity, prevent mortality and increase patient quality of life with hedgehog inhibitors, Mohs' micrographic surgery and radiation therapy[32].

1.2.2. SQUAMOUS CELL CARCINOMA

Epidermal keratinocytes are also the precursor cells of SCC, however in contrast to BCC incidence of metastasis of up to 16% has been reported and it accounts for 20% of skin cancer related deaths[20,59].

1. Epidemiology

As is the case with BCC, reporting the exact numbers of SCC is a challenge due to the lack of standardized recording tools in some countries[22,28]. Being the second most common NMSC worldwide, SCC accounts for about 1 million cases annually in the United States leading to around 9000 deaths, approximating renal and oropharyngeal carcinomas and melanoma[6,21-23,61]. Waldman and Schmults state that the lifetime risk of developing SCC in white patients in the United States is 14-20%[61]. This number is estimated to increase

yearly by up to 200%[61]. Similarly in South Korea and Germany SCC rates have also been noted to be on the increase over the past years[62]. In South Africa, an increase in keratinocytic carcinomas was observed, both for Caucasians and the black population[63]. Contrary to this Australia has observed a plateau and a decline in some areas in the incidence of SCC[64]. This has been attributed to their robust public health preventative measures[64].

The incidence of SCC, just like BCC, increases with advancing age[22,28,61-64]. In Australia, Germany, the United States and South Africa SCC is much more common in males than females[61-64]. Although known to be a disease of fair skinned individuals, there are cases of SCC occurring in darkly pigmented patients, albeit at lower numbers[28,63].

2. Aetiopathogenesis

   One of the most significant environmental aetiologic factors, is chronic UVR exposure which may be therapeutically indicated, in the case of phototherapy, occupational related or due to activities such as sunbathing and tanning[2,4,19,20,26,45,46,65-67]. The latter two activities are amenable to behavioural modification.

   The genes that are commonly found to be mutated in the pathogenesis of SCC include tumour suppressor genes *p53* and *NOTCH1*, cell cycle control protein *CDKN2A, WNT, Ras* (involved in cellular signal transduction), *p16INK4, NF-κB* and *c-Myc*[22,26,28,66,67]. This means that any mutations during the cell cycle, which may be brought about by UVR among other things will go unchecked and not corrected, leading to uncontrolled growth and replication, hence malignancy.

3. Risk factors

   The risk of SCC is higher in men as compared to women and it further increases with advancing age[2,19,20,]. Phenotypically, lighter skin phototypes (Fitzpatrick skin type 1 and 2, fair skin, red hair, blue eyes and increasing number of melanocytic naevi) are associated with an increased risk of developing SCC[19,22,26]. Immunosuppresion as a result of medical conditions such as HIV, leukaemia, lymphoma and organ transplantation also put one at risk of developing SCC[4,19,22,26,65].

There are some genetic conditions that may put one at risk of developing SCC including OCA, XP, epidermodysplasia verruciformis (EDV) and dystrophic junctional epidermolysis bullosa[19,65]. This is because of increased photosensitivity due to varying degrees of lack of melanin in patients with OCA and inability to repair UV induced mutations in the case of XP[19]. There is evidence implicating human papilloma virus (HPV) as a risk factor in the development of SCC[26,28,65-68]. Patients with EDV harbour strains of HPV that makes them susceptible to developing SCC[19]. The clinical manifestations of dystrophic junctional epidermolysis bullosa include blistering, chronic wounds, inflammation and scarring; this increases the risk of developing SCC[69].

Other dermatologic conditions that lead to chronic inflammation and scarring such as Marjolin ulcers, burns, sites of prior radiation therapy, porokeratosis, discoid lupus erythematosus, lupus vulgaris, granuloma annulare, lymphogranuloma venereum, osteomyelitis and hidradenitis suppurativa are also risk factors for the development of SCC as well as precancerous actinic keratosis[4,19,26,65,66,70-72]. Exposure to carcinogens including arsenic, topical nitrogen mustard, vinyl chloride, polycyclic aromatic hydrocarbonates, nitrosamines, alkylating agents and ionizing radiation can also lead to SCC[22,26,65].

4. Clinical features

SCC usually occurs on sun exposed sites such as the face, neck, scalp and the extremities[28,65,66]. The clinical presentation is highly variable and it may occur along with precursor lesions of actinic keratosis or squamous cell carcinoma in situ[65]. Usually SCC presents as a papule, plaque or indurated nodule with a smooth, scaly, crusted, hyperkeratotic, verrucous or ulcerated surface[65,66]. The lesions may be skin coloured, erythematous or brown, asymptomatic, pruritic or tender[66,67].

5. Diagnosis

Physical examination and dermoscopy are important in making a diagnosis of SCC. On dermoscopy linear irregular vessels, elongated hairpin vessels, dotted vessels or a combination of these can be visualised[22,23,26,28]. An excisional, shave or punch biopsy should be done for confirmation[26,66].

6. Histologic grading

   The Broder's classification categorises SCC into grade I to IV correlating to the degree of differentiation[4,22,65,73-75] . These are well differentiated (less 25% of undifferentiated cells), moderately differentiated (less than 50% undifferentiated cells), poorly differentiated (less than 75% undifferentiated cells) and anaplastic/pleomorphic (more than 75% undifferentiated cells)[4,22,65,73-75]. The grading is informed by nuclear pleomorphism, degree of architectural atypia and keratinisation[65,73].

7. Histologic variants

   Generic/simplex/conventional SCC

   Histologically, atypical keratinocytes develop in the epidermis and invade the dermis[4,73]. The tumour cells are enlarged, hyperchromatic, with pleomorphic nuclei and prominent atypical mitotic activity[4,73]. Keratin pearls and intercellular bridges are seen[4,73]. In ulcerated lesions lymphoplasmacytic and neutrophilic inflammation is present[4].

   Adenoid/acantholytic SCC/adenoacanthoma

   On histology tumour cells are arranged in cords and nests with clefts produced by acantholysis of cells[4,73]. The acantholysis results in various morphologic patterns such as pseudoglandular, pseudoalveolar or pseudovascular spaces[59]. The histologic differentials to consider are adenoid BCC, eccrine carcinoma, metastatic adenocarcinoma and angiosarcoma[65].

   Adenosquamous SCC

   This is a rare unusually aggresive variant characterised by a mixed squamous and true glandular differentiation[4,65,74]. The atypical squamoid cells are arranged as small to large interconnecting nests forming keratocysts[65,74]. There is intercellular bridging, keratin pearl formation, parakeratotic differentiation and an adenomatous component[4]. Histologically the differential diagnosis is acantholytic SCC and metastatic and primary mucoepidermoid carcinoma[65,74].

   Desmoplastic SCC

   It is a rare tumour with high malignant potential characterised by aggregates of moderate or poorly differentiated keratinocytes surrounded by desmoplastic stroma[4,65,74]. The desmoplastic components makes up more than 30% of the

tumour volume[4,65,74]. Desmoplastic SCC usually has peri-neural invasion and metastases[4,65,74]. Syringoma, desmoplastic trichoepithelioma, microcystic adnexal carcinoma, morpheaform BCC and desmoplastic melanoma should be considered as differential diagnoses[65].

Spindle cell/pleomorphic/sarcomatoid SCC

This SCC variant usually occurs on sites of prior trauma or radiotherapy and it is associated with Marjolin's ulcer[4,73,74]. It is composed of haphazard growth of spindle shaped cells in the dermis that intermingle with strands of collagen in a whorled fashion[4,65,73]. Mitotic activity and pleomorphic giant cells are present[4,65,73]. The surrounding stroma may be myxoid or pleomorphic[4]. The desmoplasia represents less than 30% of the tumour volume[4,64]. The differential diagnosis is leimyosarcoma, spindle cell/desmoplastic melanoma, atypical fibroxanthoma, malignant fibrous histiocytoma and undifferentiated pleomorphic sarcoma[65,73].

Pigmented SCC

It usually occurs on the oral and conjuctival mucosa in dark skinned persons[4]. It is composed of lobules, nests and cords of atypical squamous cells with keratinisation[65]. Numerous darkly pigmented melanocytes are intermixed within the tumour cells[59,75]. The histologic differentials to consider are seborrheic keratosis, melanoacanthoma, pigmented trichoblastoma, pigmented pilomatricoma, pigmented BCC and melanoma[65,74].

Verrucous carcinoma

It was first described by Ackerman in 1948 when it occurred in the oral cavity[76]. Over the years different authors have had conflicting views when it came to classification and terminology. Some have used Buschke-Lowenstein tumour, carcinoma cuniculatum/epithelioma cuniculatum/papillomatosis cutis and oral florid verrucosis/florid papillomatosis/verruca acuminate as synonyms of the same entity occurring in different areas of the body[4,65,73]. However recent data classifies verrucous carcinoma as a rare variant of SCC, distinct to Buschke-Lowenstein tumour evidenced by lack of HPV cytopathic changes and carcinoma cuniculatum[76-80]. Clinically verrucous carcinoma can affect the skin and mucosae as a slow growing, locally invasive but rarely metastasising tumour[76-80]. On histology it is deeply endophytic, broad and with a pushing base[78]. The cells are well differentiated and atypia is either absent or confined to

one or two layers at the base of the tumour[78]. The histologic differential diagnoses include Buschke-Lowenstein tumour, carcinoma cuniculatum, verruca vulgaris, condyloma acuminatum, keratoacanthoma and prurigo nodularis[65,78].

Clear cell/hydropic/pale cell SCC

It has three categories, which are type I (keratinising), type II (nonkeratinising) and type III (pleomorphic)[65,74]. Type I lesions have sheets or islands of clear cells with peripherally displaced nuclei or central nuclei with bubbly cytoplasmic appearance and focal areas of keratinisation and keratin pearls[65,74]. In type II the tumour is localised to the dermis, the cytoplasm has a finely reticulated clear appearance and arranged in parallel or anastomosing cords separated by a fibrotic stroma with a heavy inflammatory infiltrate[65,74]. There is no keratinisation but there may be central necrosis[65,74]. The type III category has extensive ulceration, pleomorphism with foci of acantholysis, dyskeratosis, keratinisation, peri-neural and lymphovascular invasion[65,74]. The differential diagnosis is clear cell acanthoma, clear cell hidradenoma, tricholemmoma, trichilemmal carcinoma, clear cell BCC, balloon cell nevus and metastatic renal cell carcinoma[65,74].

Signet ring SCC

This variant of SCC is extremely rare[65,74]. It is composed of a number of signet ring cells, clear cytoplasm and peripherally located nucleus[65,74]. The differential diagnosis is BCC, melanoma, histiocytoid carcinoma of the eyelid, lobular carcinoma of the breast, thyroid carcinoma and metastatic adenocarcinoma[65,74].

Other variants include papillary SCC, follicular SCC, squamoid eccrine ductal carcinoma and small cell SCC[65,74]. Currently there is no consensus as to whether Bowen's disease and keratoacanthoma should be considered as variants of SCC. pre-malignant lesions or entities on their own.

8. Management

Most importantly, an SCC lesion should be classified as either low or high risk. High risk SCC has a higher chance of recurrence and metastasis. The depth of invasion, histologic features, location, horizontal size, perineural involvement, recurrence, incomplete excision, multiple tumours and patient characteristics are all taken into account when making this distinction[59]. High risk tumours are

more than 2cm in diameter and 4mm in thickness, with perineural and lymphovascular involvement, poorly differentiated, previously treated, occurring on the ear, forehead, temple, scalp, lip and anogenital region, arising from a scar and in an immunocompromised patient[22,65,66,73-75, 81]. Desmoplastic, acantholytic, adenosquamous and spindle cell variants of SCC are all considered high risk[22,65,74-75,81].

Staging

There are a number of different staging systems that different authors and centres use. These include the 2002 TNM staging by the American Joint Committee on Cancer, the revised American Joint Committee on Cancer and International Union Against Cancer (**Figure 1**), Brigham and Women's Hospital Tumor staging (**Figure 2**), National Comprehensive Cancer Network guidelines (**Figure 3**) and European Organization for Research and Treatment of Cancer guidelines[22,59,65].

Figure 1: The revised American Joint Committee on Cancer and International Union Against Cancer TNM Staging for Squamous Cell Carcinoma of the head and Neck

Table 3 Eighth Edition of the TNM Staging Manual of the AJCC for Cutaneous Epidermal Carcinoma (SCC) of the Head and Neck and Nonmelanoma Skin Cancer Other Than Merkel Cell Carcinoma of the Head and Neck.

AJCC TNM Staging Manual for Squamous Cell Carcinoma of the Head and Neck (Eighth Edition)		
T	TX	Primary tumor cannot be assessed (after curettage...)
	T0	No evidence of primary tumor
	Tis	Carcinoma in situ
	T1	Greatest dimension up to 2 cm
	T2	Greatest tumor dimension > 2 cm but < de 4 cm
	T3	Greatest tumor dimension ≥ 4 cm or minimal erosion of the bone or perineural invasion or deep invasion[a]
	T4	Tumor with extensive cortical or medullary bone involvement **(T4a)**, invasion of the base of the cranium or invasion through the foramen of the base of the cranium **(T4b)**
N	NX:	Nearby lymph nodes cannot be assessed (prior resection for another reason, body habitus...)
	N0	No involvement of nearby lymph nodes as determined clinically/radiologically
	N1	**Metastasis in an isolated ipsilateral lymph node ≤ 3 cm in greatest dimension, ENE (−)**
	N2	**N2a: metastasis in an isolated ipsilateral lymph node 3-6 cm in greatest dimension, ENE (−)** N2b: metastasis in multiple ipsilateral lymph nodes less than 6 cm, ENE (−) N2c: metastasis in bilateral or contralateral lymph nodes, less than 6 cm, ENE (−)
	N3	**N3a: metastasis in a lymph node greater than 6 cm, ENE (−)** **N3b: metastasis in any lymph node(s) and ENE (+)**
M	M0	Absence of distant metastasis
	M1	Distant metastasis

AJCC TNM Staging System for SCC of Head and Neck (Eighth Edition)			
T1	N0	M0	Stage I
T2	N0	M0	Stage II
T3	N0, N1	M0	Stage III
T1	N1	M0	Stage III
T2	N1	M0	Stage III
T1-T3	N2	M0	Stage IV
Any T	N3	M0	Stage IV
T4	Any N	M0	Stage IV
Any T	Any N	M1	Stage IV

Sites on the lower lip are included, eyelid carcinoma is excluded. Tumors of the vulva, pens, perineal region, and other sites other than the head and neck are excluded.
In boldface, aspects most relevant to staging.
Abbreviations: ENE extranodal or extracapsular extension defined as extension through the lymph node capsule in the surrounding connective tissue with or without stromal reaction; SCC squamous cell carcinoma; SLNB sentinel lymph node biopsy.
[a] Deep invasion defined as thickness greater than 6 mm or invasion deeper than subcutaneous fat. For a tumor to be T3, perineural invasion should be present in nerves greater than 0.1 mm, deeper than the dermis, or clinical and radiological involvement of affected

Figure 2: The Brigham and Women's Hospital Tumor staging

TABLE 1.

Brigham and Women's Hospital (BWH) Tumor Staging System

Designation	Description
T1	0 high-risk factors
T2a	1 high-risk factor
T2b	2-3 high-risk factors
T3*	4 or more high-risk factors or bone invasion

High-risk factors include tumor diameter ≥ 2 cm, poorly differentiated, perineural invasion of ≥ 0.1 mm, or tumor invasion beyond fat (excluding bone invasion, which upgrades tumor to stage T3). Our patient's stage is denoted by *.

Figure 3: Features identified by the National Comprehensive Cancer Network as risk factors for recurrence of cutaneous squamous cell carcinoma

History and Presentation:
- Location/size*
  - High-risk areas
  - Medium-risk areas $\geq$ 10 mm
- Poorly defined borders
- Site of prior radiotherapy or chronic inflammatory process
- Immunosuppression
- Recurrent tumour
- Rapidly growing tumour
- Neurologic symptoms

Pathology
- Poorly differentiated
- Adenoid (acantholytic), adenosquamous (showing mucin production), desmoplastic, or metaplastic (carcinosarcomatous) subtypes†
- Depth: $\geq$ 2mm or Clark levels IV or V
- Perineural, lymphatic, or vascular invasion

* Location/size: High-risk area = 'mask regions' of face: central face, chin, ear, eyebrow, eyelid, lip, mandible, nose, periorbital, preauricular, postauricular, temple.
Medium-risk area = cheeks, forehead, scalp.

† Area H constitutes high risk based on location, independent of size. Narrow excision margins due to anatomic and functional constraints are associated with increased clearance and maximal tissue conservation. For tumors < 6 mm in size, without other high risk features, other treatment modalities may be considered if at least 4-mm clinically tumor-free margins can be obtained without significant anatomic or functional distortions.

Treatment

As first line, standard surgical excision with a minimum margin of at least 4mm around the tumour border for low risk SCC and a minimum margin of 6mm for high risk SCC is offered to patients[28,59,66,75,81-83]. Ideally, Mohs' micrographic surgery is the preferred modality for high risk SCC, however due to the fact that it is not easily accessible, most patients are managed with standard surgical excision[28,59,66,75,81-83]. In the hands of an experienced physician, curettage and cautery is an option for small tumours that are less than 1cm and are low risk [28,59,66,75,81-83]. When treating small, low risk SCC, where surgery is impractical and the procedure is performed by an experienced physician cryotherapy can be an alternative[28,59,66,75, 81-83]. Radiotherapy is indicated for older patients who are not legible for surgery or those with non resectable tumours[28,59,66,75, 81-83]. Other treatment options that do not have enough supporting evidence published include topical imiquimod, intralesional interferon alpha, intralesional 5-fluorouracil and photodynamic therapy[28,59,66,75, 81-83].

Currently the available treatment modadilities for metastatic SCC are surgical removal of the tumour where feasible, lymph node dissection, with or without adjuvant radiation therapy and with or without concurrent systemic therapy with either 5-fluorouracil or cisplatin[75,83].

9. Prevention

Prevention is imperative due to the fact that SCC has a significant risk of metastasis and mortality. The goal of primary prevention is to decrease known exposures or modifiable factors that put one at risk for developing SCC. Behavioural modifications include avoiding sun exposure during peak hours, avoiding recreational sunbathing and sun tanning, using broad spectrum sunscreen when outdoors, wearing long sleeved clothing, hats and sunglasses[84].

Secondary prevention entails diagnosing and treating precursor lesions such as actinic keratosis and early SCC. Nemer and Council advocate for chemoprevention in patients with severe photodamage, numerous actinic keratosis, prior NMSC, organ transplant recipient, chronic immunosuppressive state due to medications, HIV, hematologic malignancies, genetic disorders that put one at risk of developing NMSC such as XP, OCA, Rombo syndrome, EDV and chronic arsenic exposure[85]. Patients with actinic keratosis can be offered chemoprevention in form of photodynamic therapy, topical Imiquimod, 5-

fluorouracil, diclofenac sodium and ingenol mebutate[85]. Oral nicotinamide at 500mg twice daily has been proven to reduce new actinic keratoses as well as the number of NMSC[85]. Although studies have shown a decrease in NMSC in organ transplant recipients on oral retinoids such as acitretinin, use is limited due to side effects such as mucocutaneous xerosis and hypercholesterolemia[85].

The aim of tertiary prevention is treat advanced SCC and prevent morbidity and mortality.

1.2.3. STUDY OBJECTIVES

1. To calculate the overall number and percentages of adult patients with a histologically confirmed diagnosis of BCC and SCC at HJH, dermatology outpatient clinic during the period 1st June 2014 to 30th June 2019.
2. To calculate the prevalence of BCC and SCC at the HJH, dermatology outpatient clinic for the period 1st June 2014 to 30th June 2019.
3. To describe the epidemiology of BCC and SCC according to:
   i. Age
   ii. Gender
   iii. HIV status
   iv. Risk factors
   v. Anatomic location
   vi. Histopathologic subtype

   The information was obtained from histopathology reports and Dermatology outpatient clinic files.

1.2.4. METHODOLOGY

1. Study design

   This was a retrospective study of adult cases of histologically confirmed BCC and SCC in patients attended at HJH, Dermatology department for the duration of 1st June 2014 to 30th June 2019.

   The histopathology results were obtained as an excel file from the national health laboratory service, central data warehouse department. The patient's age, gender, diagnosis, tumour subtype, histologic grading and differentiation (for SCC) and anatomic site were extracted. The histologic grading of SCC was categorised as poor, moderate or well. The category undocumented accounted for those not stated as well as those that were reported as keratinizing, invasive or microinvasive. In patients presenting with more than one lesion, each lesion was recorded according to the tumour location. Those with both a BCC and SCC at the same time were recorded under each heading. Patients presenting with a subsequent BCC or SCC were recorded as thus on each occasion. The dermatology outpatient clinic files were used to find the patient's HIV status and risk factors. Identifiable information was anonymised before data capturing.

2. Study population

   All patients seen at dermatology outpatient clinic at HJH from 1st June 2014 to 30th June 2019 were assessed. Those with a histologic diagnosis of BCC and SCC were preliminarily included and their clinic files were reviewed.

3. Study site

   This was the dermatology outpatient department, HJH situated in Auckland Park, Johannesburg. HJH is a 700 bed teaching hospital. The dermatology clinic runs twice a week, on a Monday and Thursday. We receive referrals from neighbouring hospitals such Rahima Moosa, Yusuf Dadoo and Leratong, as well as clinics in the Roodepoort area. During the 5 year study period we saw a total of 28 215 patients in our clinic. In 2014 from 1st June to 31st December 2176 patient were seen. The year 2015 had 5685 patients and 2016 had 6254. We saw 5788 patients in 2017 with 5950 accounting for clinic visits in 2018. The duration of 1st January 2019 until 30th June 2019 had only 2362 patients. Anecdotally patients of all races are seen in our clinic from the age of 14 years

and above. During our study period, a total of 2454 biopsies were done. In our clinic biopsies are performed when the clinical diagnosis is a tumour, benign or malignant, inflammatory condition that are not responding to topical therapies and need systemic treatment modalities, as well as infectious diseases.

4. Inclusion criteria

   All adults (18 years old and above) with histologically confirmed BCC and SCC seen at Dermatology department, HJH during the time period of 1st June 2014 to 30th June 2019.

5. Exclusion criteria

   i. Histopathological diagnoses that were inconclusive.

6. Data variables

   The following variables were extracted from the laboratory reports and dermatology clinic outpatient files:

   i. Demographic data: age, gender, HIV status, risk factors
   ii. Diagnosis of BCC and SCC, subtype, anatomic site of tumour

   The data collection sheet is attached in the appendices.

7. Data processing and analysis

   The extracted data was stored in a Microsoft excel file in a password protected laptop known only to the principal investigator. The data was cleaned and checked for any missing variables. Any patient identifiable information was not recorded. Each patient was given a unique study identification number. Data analysis was performed using Stata version 16.1. The Pearson chi-square test was used to calculate an association between age and gender, gender and HIV status as well as gender and subtype of tumour. The standard significance level of 0.05 was used throughout the analysis. The results are presented using tables showing absolute numbers/frequencies and percentages.

1.2.5. ETHICAL APPROVAL

The research proposal was submitted and approved by the Human Research Ethics Committee of the University of the Witwatersrand. Permission was obtained from the CEO of HJH.

1.2.6. LIMITATIONS OF THE STUDY

This was a retrospective study that relied on the completeness of pathology reports and Dermatology outpatient clinic files. Some details which were missing which would have been of value included duration of lesions, symptoms, family history of cancers, a thorough review of risk factors, HIV status, tumour subtype, histologic variant and grading as well as treatment rendered. The study also had selection bias since it took place in one hospital and lacked great variability in terms of Fitzpatrick skin phototype. Patients with both a BCC and SCC at the same time were recorded under each heading. Those presenting with a subsequent BCC or SCC were recorded as thus on each occasion. Although this gives a correct picture of the burden of cancers it can lead to over-representation of our total patients seen during the study period. Therefore caution should be exercised before generalising the results.

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CHAPTER 2 – SUBMISSIBLE ARTICLE

Title: The Prevalence of Basal cell carcinoma and Squamous cell carcinoma at the Helen Joseph Hospital.

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ABSTRACT

Background

Basal cell carcinoma and squamous cell carcinoma account for the majority of nonmelanoma skin cancers. Although the diagnosis has a relatively low mortality in comparison to other malignancies, the patients incur significant morbidity and there is an immense financial burden on health care systems.

Objectives

To study the prevalence, demographic and histologic pattern of patients with basal cell carcinoma and squamous cell carcinoma at the Helen Joseph Hospital.

Methods

This was a retrospective study of adults who had histologically confirmed basal cell carcinoma and squamous cell carcinoma at Helen Joseph Hospital, Dermatology department for the duration of 1st June 2014 to 30th June 2019.

Results

Basal cell carcinoma

A total of 394 patients were included. The prevalence was 1.4% with a mean age of 69.4 years (standard deviation of 11.5). Males were 209 (53.0%) and 137 (34.8%) were female, gender was not documented in 48 (12.2%). The male to female ratio was 1.5:1. HIV negative patients were 62 (15.7%) and 5 (1.3%) were HIV positive.

Actinic keratosis was a risk factor for all the patients. A total of 393 (99.7%) patients were of Fitzpatrick's skin phototype I or II, 1 (0.3%) patient had oculocutaneous albinism and 4 (1.0%) patients were smokers. A previous diagnosis of skin cancer was observed in 87 (22.1%) patients.

The histologic subtypes that were diagnosed included nodular (69, 17.5%), metatypical/basosquamous and superficial both at 12 (3.1%) and ulcerated (11, 2.8%), however most patients (200, 50.7%) had a mixed subtype. Most of the lesions were located on the face 194 (49.2%) and upper limb 53 (13.5%).

Squamous cell carcinoma

Overall 85 patients were diagnosed with squamous cell carcinoma. The prevalence was 0.3%. The mean age was 68.7 years (standard deviation of 12.8). In the cohort, majority of our patients were male (61, 71.8%) and only 17 (20.0%) were female, and the male to female ratio was 3.6:1. Gender was not documented in 7(8.2%). There was no statistical significance between gender and age ($p>0.05$). HIV negative patients were 12 (14.1%) and 3 (3.5%) were HIV positive.

Almost all patients in this cohort were of a lighter skin phototype 83 (97.6%). Most patients had multiple risk factors, except 1 (1.2%) who had epidermodysplasia verruciformis as the only risk factor identified.

Moderately differentiated squamaous cell carcinoma was diagnosed in majority of the patients 59 (69.4%) and 3 (3.5%) patients had poorly differentiated squamous cell carcinoma. Most patients had an undocumented histologic variant 67 (85.9%). Squamous cell carcinoma occurred most commonly on the face 30 (35.3%), upper limb 16 (18.8%) and scalp 13 (15.2%)

Conclusion

Our findings are generally in line with other published reports. We noted that BCC has a higher prevalence than SCC. Both cancers were more common in elderly males. Fitzpatrick skin phototype 1 and 2, history of sun exposure, actinic keratosis and prior skin cancer are some of the risk factors that we elucidated. In our cohort these cancers occurred more frequently on sun exposed sites. Majority of our patients did not have a documented HIV status. There is lack of standardisation in history taking and documentation in our dermatology clinic, as well as histopathology reports which leads to important prognostic factors not being documented. These factors form a basis for patient treatment options and inform follow up plans.

2.2 INTRODUCTION

According to the World Health Organization, cancer or malignancy refers to "a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs"[1]. Skin cancer is among the most frequently diagnosed malignancy[2,3]. Broadly, skin cancer is categorised into two groups; malignant melanoma and non melanoma[2-7]. Non melanoma skin cancer (NMSC) refers to all skin cancers that are not derived from melanocytes[8]. Globally, between 2 and 3 million NMSC are diagnosed annually[2,3]. Worldwide majority of the NMSC are basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (SCC)[2-10]. They both account for 99% of the cancers in the NMSC group[4,11]. Approximately 70-80% of all new skin cancers are BCC and 20-50% are SCC[6,12,13]. However in Sub-Saharan Africa, it has been reported that SCC is the leading type of skin malignancy and depending on geographic location BCC is still among the major types of NMSC[14,15].

BCC is a slow growing, indolent, locally destructive cancer derived from basal cells of the epidermis[4,11,12,16-22,24-26]. Less than 1% of BCC metastasize, therefore overall this malignancy has a low mortality rate[11,12,22,24-26]. However the morbidity incurred by the affected patients is insurmountable largely due to the fact that it occurs on easily visible sites such as the face and extremities[11,12]. SCC is also derived from epidermal keratinocytes, however in contrast to BCC incidence of metastasis of up to 16% has been reported and it accounts for 20% of skin cancer related deaths[11,25]. The other skin cancers that cause significant mortality are melanoma and merkel cell carcinoma [11,25]. Of utmost importance is the fact that there is an immense economic burden to the treatment of both of these cancers[17-20].

Currently there is no published data about the prevalence of BCC and SCC at Helen Joseph Hospital (HJH) or Johannesburg. In 2017, a retrospective study on the primary cutaneous malignancies in the Northern Cape province of South Africa concluded that indeed SCC and BCC still appear as the major NMSC[15]. Therefore the prevalence forms a baseline to which informed decisions about primary, secondary and tertiary prevention of BCC and SCC can be based on. As well as guiding the proper allocation of resources towards management of both these cancers at HJH.

2.3 AIMS

To calculate the prevalence, describe the patient demographics including age, gender, HIV status, risk factors, and features and location of the tumour in patients with a histologic diagnosis of BCC and SCC at HJH, dermatology outpatient clinic during the period 1st June 2014 to 30th June 2019.

2.4 MATERIALS AND METHODS

This was a retrospective study of adult cases of histologically confirmed BCC and SCC in patients attended at HJH, Dermatology department, outpatient clinic for the duration of 1st June 2014 to 30th June 2019. The histopathology results were obtained as an excel file from the national health laboratory service, central data warehouse department. The patient's age, gender, diagnosis, histologic features and tumour anatomic site were extracted. In patients presenting with more than one lesion, each lesion was recorded according to the tumour location. Those with both a BCC and SCC at the same time were recorded under each heading. Patients presenting with a subsequent BCC or SCC were included on each occasion. The histologic grading of SCC was categorised as poor, moderate or well differentiated. The category undocumented accounted for those not stated, as well as those that were reported as keratinizing, invasive or microinvasive. The dermatology outpatient clinic files were used to find the patient's HIV status and risk factors. Identifiable information was anonymised before data capturing and each patient was given a unique study identification number.

2.5 DATA PROCESSING AND ANALYSIS

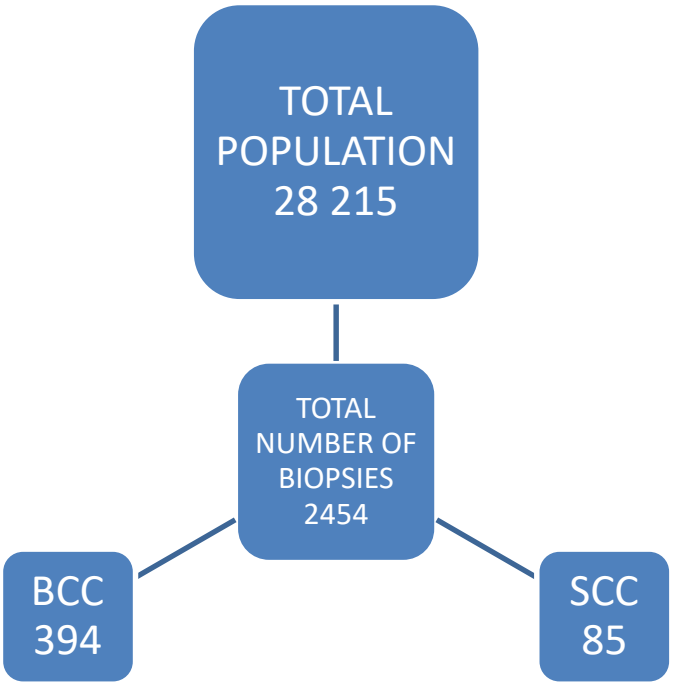
The extracted data was stored in a Microsoft excel file in a password protected laptop known only to the principal investigator. The data was cleaned and checked for any missing variables. Any patient identifiable information was not recorded. Data analysis was performed using Stata version 16.1. The Pearson chi-square test was used to calculate an association between age and gender, gender and HIV status as well as gender and subtype. The standard significance level of 0.05 was used throughout the analysis. The results are presented using tables showing absolute numbers/frequencies and percentages.

2.6 ETHICAL APPROVAL

The research proposal was submitted and approved by the Human Research Ethics Committee of the University of the Witwatersrand. Permission was obtained from the CEO of HJH and the Head of the Division of Dermatology.

2.7 RESULTS

Figure 4: Total number of patients in the study



During the study period, 28 215 patients were seen at the dermatology outpatient clinic. A total of 2454 biopsies were done.

Basal cell carcinoma

Prevalence of BCC

BCC was diagnosed in 394 patients during the 5 year study period. Therefore the prevalence of BCC in our clinic was 1.4%.

Table 1: Demographic findings of patients with BCC

VARIABLE	CATEGORY	N	%
GENDER	MALE	209	53.0
	FEMALE	137	34.8
	UNDOCUMENTED	48	12.2
	TOTAL	394	100
AGE (YEARS)	31-40	8	2.0
	41-50	18	4.6
	51-60	56	14.2
	61-70	113	28.7
	71-80	142	36.0
	81-90	54	13.7
	91-96	3	0.8
	TOTAL	394	100
HIV STATUS	NEGATIVE	62	15.7
	POSITIVE	5	1.3
	UNDOCUMENTED	327	83.0
	TOTAL	394	100

GENDER	**MALE**		**FEMALE**		**UNDOCUMENTED**	
AGE (YEARS)	N	%	N	%	N	%
31-40	5	2.4	3	2.2	0	0
41-50	12	5.7	6	4.4	0	0
51-60	32	15.3	19	13.9	5	10.4
61-70	61	29.2	37	27.0	15	31.3
71-80	78	37.3	54	39.4	10	20.8
81-90	19	9.1	17	12.4	18	37.5
91-96	2	1.0	1	0.7	0	0
TOTAL	209	100	137	100	48	100

GENDER	**MALE**		**FEMALE**		**UNDOCUMENTED**	
HIV STATUS	N	%	N	%	N	%
NEGATIVE	38	18.2	13	9.5	11	22.9
POSITIVE	3	1.4	2	1.5	0	0
UNDOCUMENTED	168	80.4	122	89.0	37	77.1
TOTAL	209	100	137	100	48	100

In our BCC cohort of 394 patients, the mean age was 69.4, standard deviation 11.5. The youngest patient was 31 and the oldest was 96. Majority of our patients (209, 53%) were male and 48, (12.2%) did not have a documented gender. The male to female ratio was 1.5:1. There was a statistically significant association between age and gender (P-value=0.00). This means that indeed there is a relationship between age and gender. A large proportion of our patients had an undocumented HIV status (male 168, 80.4% and female 122, 89%). There was no statistical significance between gender and HIV status (P-value = 0.114).

Table 2: Risk factors of patients with BCC

RISK FACTOR	N	%
AK, light skin	285	72.3
AK, light skin, EDV	1	0.2
AK, light skin, prev BCC	56	14.2
AK, light skin, prev lentigo maligna	2	0.5
AK, light skin, prev BCC and SCC	19	4.8
AK, light skin, prev BCC and SCC, prolonged sun exposure	1	0.2
AK, light skin, prev BCC x2	2	0.5
AK, light skin, prev BCC x3	1	0.2
AK, light skin, prev BCC, prolonged sun exposure	1	0.2
AK, light skin, prev SCC , prolonged sun exposure	3	0.8
AK, light skin, prev SCCis, prolonged sun exposure	1	0.2
AK, light skin, prolonged sun exposure, prev BCC and SCC	1	0.2
AK, light skin, prolonged sun exposure	13	3.3
AK, light skin, prolonged sun exposure, smoker	3	1.2
AK, light skin, smoker	4	1.0

AK, OCA	1	0.2
TOTAL	394	100

Abbreviations: AK= actinic keratosis BCC= basal cell carcinoma EDV= epidermodysplasia verruciformis OCA= oculocutaneous albinism Prev= previous SCC= squamous cell carcinoma SCCis= squamous cell carcinoma in situ

All of the patients enrolled had at least two documented risk factors, one of which was actinic keratosis. A total of 393 (99.7%) patients were of Fitzpatrick's skin phototype 1 or 2 and only 1 (0.3%) patient had OCA. Almost three quarters (285, 72.3%) had actinic keratosis and a lighter skin phototype. In addition to being of a lighter skin phototype and presenting with actinic keratosis, 4 (1.0%) patients were also smokers. A previous diagnosis of skin cancer was observed in 87 (22.1%) patients. These were BCC, SCC, squamous cell carcinoma in situ (SCCis) and lentigo maligna, and some patients were presenting with a recurrent BCC. History of prolonged sun exposure was documented in only 22 (5.6%) of the patients.

Table 3: Histologic subtype of BCC

SUBTYPE	**N**	**%**	**MALE**		**FEMALE**		**UNDOCUMENTED**	
			N	**%**	**N**	**%**	**N**	**%**
Mixed	200	50.7	113	54.0	67	48.9	20	41.7
Nodular	69	17.5	22	10.5	28	20.4	19	39.6
Metatypical/basosquamous	12	3.1	9	4.3	3	2.2	0	0
Superficial	12	3.1	7	3.3	4	2.9	1	2.1
Ulcerated	11	2.8	8	3.8	3	2.2	0	0
Micronodular	9	2.2	6	2.9	3	2.2	0	0
Solid	6	1.5	4	1.9	2	1.5	0	0
Adenoid	3	0.8	3	1.5	0	0	0	0
Morpheic	3	0.8	3	1.5	0	0	0	0
Infiltrating	2	0.5	1	0.5	1	0.7	0	0
Macronodular	1	0.3	0	0	1	0.7	0	0
Undocumented	66	16.7	33	15.8	25	18.2	8	16.6
TOTAL	394	100	209	100	137	100	48	100

Most patients had a mixed BCC 200, (50.7%). This comprised of different histologic subtypes of nodular, micronodular, macronodular, superficial, metatypical/basosquamous, pigmented, ulcerated, morpheic, infiltrating, solid and adenoid subtypes. The nodular subtype of BCC was the second most common (69, 17.5%). A significant proportion of patient had an undocumented

histologic subtype of BCC 66, (16.7%). There was an association between gender and histologic subtype (P-value = 0.025). This means that there is a relationship between gender and histologic subtype.

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Table 4: Anatomic location of BCC

SITE	PATIENTS		LESIONS	
	N	%	N	%
Abdomen	1	0.3	1	0.2
Abdomen, back	1	0.3	2	0.4
Back	14	3.5	14	3.2
Back, chest	4	1.0	8	1.8
Back, face	4	1.0	8	1.8
Back, lower limb	1	0.3	2	0.4
Back, upper limb	1	0.3	2	0.4
Cheek, lower limb	1	0.3	2	0.4
Chest	18	4.5	18	4.1
Chest, face	5	1.3	10	2.3
Chest, lower limb	2	0.5	4	0.9
Chest, upper limb	1	0.3	2	0.4
Face	194	49.2	194	43.9
Face, lower limb	4	1.0	8	1.8
Face, lower limb, upper limb	1	0.3	3	0.7
Face, neck	7	1.8	14	3.2
Face, neck, scalp	1	0.3	3	0.7
Face, scalp	2	0.5	4	0.9
Face, upper limb	4	1.0	8	1.8
Lower limb	26	6.6	26	5.9
Lower limb, neck	2	0.5	4	0.9
Lower limb, scalp	1	0.2	2	0.4
Lower limb, upper limb	1	0.2	2	0.4
Neck	22	5.6	22	5.0
Neck, upper limb	2	0.5	4	0.9
Scalp	17	4.3	17	3.8
Scalp, upper limb	1	0.3	2	0.4
Upper limb	53	13.5	53	12.0
Undocumented	3	0.8	3	0.7
TOTAL	394	100	442	100

In terms of tumour location, most of the lesions were located on the face 194 (49.2%), upper limb 53 (13.5), lower limb 26, (6.6%) and chest 18 (4.5). The abdomen accounted for only 0.3% of the tumour location. A total of 41 (10.4%) patients had at least two tumour locations.

Squamous cell carcinoma

Prevalence of SCC

Of the total of 28 215 patients seen in the dermatology outpatient clinic, during the period 1st June 2014 to 30th June 2019, SCC was diagnosed in 85 patients. Therefore the prevalence of SCC was 0.3% in our clinic.

Table 5: Demographic findings of patients with SCC

VARIABLE	**CATEGORY**	**N**	**%**
GENDER	MALE	61	71.8
	FEMALE	17	20.0
	UNDOCUMENTED	7	8.2
	TOTAL	85	100
AGE (YEARS)	34-49	6	7.0
	50-60	15	17.7
	61-70	27	31.8
	71-80	19	22.3
	81-90	17	20.0
	91-95	1	1.2
	TOTAL	85	100
HIV STATUS	NEGATIVE	12	14.1
	POSITIVE	3	3.5
	UNDOCUMENTED	70	82.4
	TOTAL	85	100

GENDER	**MALE**		**FEMALE**		**UNDOCUMENTED**	
	N	%	N	%	N	%
AGE (YEARS)						
34-49	5	8.2	1	5.9	0	0
50-60	12	19.7	2	11.8	1	14.3
61-70	23	37.7	2	11.8	2	28.6
71-80	13	21.3	5	29.4	1	14.3
81-90	8	13.1	6	35.3	2	28.6
91-95	0	0	1	5.9	1	14.3

TOTAL	61	100	17	100	7	100
GENDER	**MALE**		**FEMALE**		**UNDOCUMENTED**	
	N	%	N	%	N	%
HIV STATUS						
NEGATIVE	9	14.8	3	17.6	0	0
POSITIVE	2	3.2	1	5.9	0	0
UNDOCUMENTED	50	82.0	13	76.5	7	100
TOTAL	61	100	17	100	7	100

The mean age of patients diagnosed with SCC was 68.7 years (standard deviation of 12.8). The range was 34 years to 95 years. Majority of our patients were male (61, 71.8%) and only 17 (20.0%) were female. The male to female ratio was 3.6:1. There was no association between age and gender (P-value = 0.241). The peak age was 61-70 years for males and 81-90 for females. Only 15 (17.6) patients out of the total of 85 had a documented HIV status, 12 (14.1%) were HIV negative and 3 (3.5%) were HIV positive. There was no statistical significance between gender and HIV (P-value = 0.733)

Table 6: Risk factors of patients with SCC

RISK FACTOR	N	%
AK, light skin	52	61.1
AK, light skin, prev BCC	8	9.4
AK, light skin, prev BCC and SCC	10	11.7
AK, light skin, prev BCC x2	1	1.2
AK, light skin, prev BCC, prolonged sun exposure	2	2.4
AK, light skin, prev SCC	4	4.7
AK, light skin, prev SCCis	1	1.2
AK, light skin, prev chemoradiation, prev SCC	1	1.2
AK, light skin, prolonged sun exposure	3	3.5
AK, OCA	1	1.2
Chronic wound, light skin	1	1.2
EDV	1	1.2
TOTAL	85	100

Abbreviations: AK= actinic keratosis BCC= basal cell carcinoma EDV= epidermodysplasia verruciformis OCA= oculocutaneous albinism Prev= previous SCC= squamous cell carcinoma SCCis= squamous cell carcinoma in situ

Almost all patients in this cohort were of a lighter skin phototype 83 (97.6%), 1 (1.2%) patient had OCA and another was of a darker skin phototype. Actinic keratosis and lighter skin phototypes were identified as risk factors in 52 (61.1%) of the patients. A total of 27 (31.8%) patients had a prior NMSC diagnosis, and 1 (1.2%) patient had undergone chemoradiation. Prolonged sun exposure as a risk factor was documented in only 5 (5.9%) patients.

Table 7: Histologic grading of SCC

GRADING	N	%
Well differentiated	7	8.2
Moderately differentiated	59	69.4
Poorly differentiated SCC	3	3.5
Undocumented	16	18.8
TOTAL	85	100

The most common histologic grading was moderately differentiated SCC (59, 69.4%). Grading was not documented for 16 (18.8%) of patients.

Table 8: Histologic variants of SCC

VARIANT	N	%
Basaloid	1	1.1
Focal acantholytic	5	5.9
Keratoacanthoma-like	5	5.9
Undocumented	74	87.1
TOTAL	85	100

Majority of the patients with SCC had an undocumented histologic variant (74, 87.1%). Focal acantholytic and keratoacanthoma-like were each diagnosed in 5 (5.9%) patients. The basaloid variant accounted for 1 (1.1%) of the cases.

Table 9: Anatomic location of SCC

TUMOUR LOCATION	PATIENTS		LESIONS	
	N	%	N	%
Anus	1	1.2	1	1.1
Back	4	4.7	4	4.5
Chest	2	2.4	2	2.2
Chest, face	1	1.2	2	2.2
Chest, upper limb	1	1.2	2	2.2
Face	30	35.3	30	33.7
Face, neck	1	1.2	2	2.2
Face, scalp	1	1.2	2	2.2
Lower limb	9	10.6	9	10.1
Neck	6	7.0	6	6.7
Scalp	13	15.2	13	14.6
Upper limb	16	18.8	16	18.0
TOTAL	85	100	89	100

Most SCC commonly occurred on the face (30, 35.3%). The scalp and the upper limb were each affected in 13 (15.2%) and 16 (18.8%) of the patients respectively. Multiple tumour locations were encountered in 4 (4.7%) patients.

DISCUSSION

This study is the first to present the prevalence of BCC and SCC in a tertiary teaching hospital in Johannesburg, South Africa.

Basal cell carcinoma

The prevalence of BCC in this study was 1.4%. This is much lower than what was previously reported by York et al in the Northern Cape, South Africa where BCC accounted for 27.8% of the cases they reviewed[15]. This might be because they looked at the most common cutaneous malignancies in the entire Northern Cape population where as our study was conducted in only one facility and only focusing on BCC and SCC in the department of dermatology as the at risk population.

In our cohort, the mean age was 69.4 years (standard deviation 11.4) and the range was 31 years to 96 years. This differs slightly to what was reported by other authors in South Africa, Iran, Bosnia and Herzegovina, Poland and the United States of America [12,21,27-31]. In South Africa the mean age was 63 years, in Iran it was 63 years in males and 60.9 in females, this was reported as 66.4 years in Bosnia and Herzegovina, 66.15 years in Poland and 65 years and 67 years in females and males in the United States of America[12,21,28,-30]. However the consensus is that the risk of developing BCC does increase with advancing age[12,21,27-31].

In line with previous similar studies, patients were predominantly male (209, 53% male to female 137, 34.8%, ratio 1.5:1) and this is attributed to greater occupational and recreational exposure to UVR as well as different ways of dressing[21,29,30]. These findings differ to the female predominance reported in Poland and the United States, which is most probably secondary to the use of tanning beds and leisure UVR exposure[12,21,30].

The current study depicted a peak age for both genders of 71-80 years, differing to what was published by Kasumagic-Halilovic and colleagues[21]. They reported an earlier peak age of 61-70 years, perhaps related to the common practice of sun tanning in Bosnia and Herzegovina[21]. We did not find a statistically significant difference between gender and age, as was the case in Bosnia and Herzegovina[21].

HIV is a known risk factor for NMSC presumably due to the inherent immunosuppresion and photosensitization by the virus and some antiretroviral drugs, however only 67 (17%) of our patients had a documented HIV status, with 62, (15.7%) being HIV negative and 5, (1.3%) HIV positive. This is far below the 90-90-90 target set by the Joint United Nations Programme on HIV and AIDS for the year 2020[32,33]. The organisation had set a target of 90% of those infected with HIV should be diagnosed, 90% of those diagnosed should be on antiretroviral treatment and 90% of those on treatment should be virologically suppressed by the year 2020[32,33]. Not

surprisingly there was no statistical significance between gender and HIV status because majority of our patients did not have a known HIV status.

Almost all patients (393, 99.7%) enrolled in the study were of a Fitzpatrick's skin phototype 1 or 2 which is a well documented risk factor for BCC. This is in line to what has been previously reported in the literature[21,33].

The presence of actinic keratosis was documented in all the patients but only 22 patients (5.6%) had a history of prolonged sun exposure. UVR exposure is a well studied aetiologic and risk factor in the pathogenesis of BCC[21,30,32]. Due to the retrospective nature of the study, a previous history of sun exposure might not have been elicited from all patients seen, and exposure was not further quantified as to if it was recreational or leisurely. Other BCC risk factors documented in our study were OCA and EDV, each occurring in one patient. This is in contrast to a similar study in Bosnia and Herzegovina which did not yield any known syndromes that predispose to the development of BCC[21]. There is paucity of data about both oculocutaneous albinism and epidermodysplasia verruciformis in the literature in Bosnia and Herzegovina. Currently no direct cause and effect relationship has been found between smoking and BCC however 4 (1.0%) patients were smokers in our cohort[34]. Literature has shown that patients who have frequent BCC might harbour an inherited cancer susceptibility[35]. In our study 87 (22.1%) of the patients had a previous skin cancer, which included BCC, SCC and lentigo maligna, and some patients were presenting with a recurrent malignancy.

In patients who had a single subtype of BCC diagnosed, nodular (69, 17.5%) was the most frequent followed by metatypical/basosquamous and superficial, both at (12. 3.1%) and ulcerated (11, 2.8%) however most patients (200, 50.7%) had a mixed subtype. In line with our findings, nodular BCC has consistently been reported to be the most commonly diagnosed single subtype with varying combinations of the other subtypes[12,21,28,33]. Similar to other publications the face (194, 49.2%) was the most affected anatomic location[12,21,28,29,33]. In descending order of frequency the upper limb 53 (13.5%), lower limb 26 (6.6%), neck 22 (5.6%), chest 18 (4.5%) and scalp 17 (4.3%) followed. This is in agreement with what other authors have reported as BCC are more common in sun exposed sites[12,21,28,29,33]. A total of 41 (10.4%) patients had at least two tumour locations, this is not unheard of in the literature and it poses a concern for recurrence and the development of new BCC[21].

Squamous cell carcinoma

Compared to similar studies in Africa, from the 1st June 2014 to 30th June 2019 we report a prevalence of SCC of 0.3% which is lower than what has been reported by other authors[14,15,29,36,37]. This might be due to the fact that we had a smaller sample size and our study was only limited to one clinic.

The mean age was 68.7 years (standard deviation of 12.8), range 34 years to 95 years. This differs greatly with other studies from different geographical locations[14,15,29,38-41]. It may be a reflection of different climates and sun protection practices. In accordance with other reports in the literature, majority of our patients were male at 61 (71.8%) as opposed to 17 (20.0%) females, male to female ratio was 3.6:1, and gender was undocumented in 7 (8.2%) patients[29,38-41,49,50]. The peak age was 61-70 years for males and 81-90 for females which is similar to Venables et al[38,40]. Being male and elderly is a well documented risk factor for the development of SCC[29,39-41].

Of the total 85 patients included, only 15 (17.6) patients had a documented HIV status, 12 (14.1%) were HIV negative and 3 (3.5%) were HIV positive. The importance of HIV status when dealing with SCC lies in the fact that it confers a significant risk for the development of new SCC in general, as well as the occurrence of multiple tumours with lower CD4 counts and higher viral loads[15,32,42-44].

As was expected almost all patients in this cohort were of a lighter skin phototype 83 (97.6%), and only 1 (1.2%) was of darker skin. In accordance with our findings Fitzpatrick skin phototypes 1 and 2 are well documented risk factors for the development of SCC, however making the diagnosis in patients with darker skin phototypes is of utmost importance due to the increased morbidity and mortality in this population group[45,46].

In our study 1 (1.2%) patient had OCA and another had EDV, these are known risk factors for developing SCC[36,47,48]. A total of 27 (31.8%) patients had a prior NMSC diagnosis, 1 (1.2%) patient had undergone chemoradiation and another had a personal history of a chronic wound which all confers a higher chance of a high risk SCC[14,27]. Prolonged sun exposure as a risk factor was documented in only 5 (5.9%) patients. Due to the retrospective nature of this study this may not be a true representation of the actual numbers. The clinicians may have not elicited the history of sun exposure or documentation was not done.

Moderately differentiated SCC was diagnosed in majority of the patients (59, 69.4%) and 3 (3.5%) patients had poorly differentiated SCC. The histologic differentiation of SCC is of paramount significance because it determines the success of treatment as well the prognosis of the patient[49-55]. It is well documented in the literature that poorly differentiated tumours can be incompletely excised during surgery, are at risk of local recurrence as well as distant metastasis and therefore increase the patient's risk for mortality[49-55]. In our cohort focal acantholytic and keratoacanthoma-like variants were each diagnosed in 5 (5.9%) patients and basaloid variant accounted for 1 (1.1%) of the cases. Majority of the patients had an undocumented histologic variant (74, 87.1%). In addition to tumour differentiation, studies have shown that some SCC variants like desmoplastic, acantholytic and adenoid should be considered high risk and associated with a poor prognosis[50,55].

Lastly SCC occurred most commonly on sun exposed sites, the face (30, 35.3%), upper limb (16, 18.8%) and scalp (13, 15.2). This is similar to what has been reported internationally[56-58]. Multiple tumour locations were encountered in 4 (4.7%) patients. Aside from the known association of UVR exposure and SCC, the location of the tumour is also regarded as a prognostic factor. The face, particularly, temple, lip, ear, the scalp, genitalia and acral sites are known high risk areas[50,51,54,55].

CONCLUSION

This study shows the magnitude of BCC and SCC at a tertiary hospital in Johannesburg. We noted that BCC has a higher prevalence than SCC, in keeping with worldwide publications. As per other reports, both BCC and SCC were more common in elderly males. Majority of our patients did not have a documented HIV status, although studies have shown that HIV is a risk factor for SCC. In line with previous reports, Fitzpatrick skin phototype 1 and 2, history of sun exposure, actinic keratosis, prior NMSC, smoking, OCA and EDV are some of the risk factors that were elucidated in our report. In our cohort these cancers occurred more frequently on sun exposed sites, as was previously reported by other authors. It is evident that there is lack of standardisation in terms of history taking and documentation in our dermatology clinic, as well as histopathology reports which leads to important prognostic factors such as risk factors, HIV status, tumour subtype, grading and differentiation not being documented. These factors form a basis for patient treatment options and inform follow up plans.

RECOMMENDATIONS

This study highlights the dire need for proper history taking, physical examination and documentation by physicians. We call for standardised reporting methods to improve decisions made about patient management and to improve the accuracy of databases. Emphasis is placed on the need to promote prevention through patient education and early identification of at risk patients in order to improve diagnostic and management strategies.

LIMITATIONS OF THE STUDY

This retrospective study relied on the completeness of pathology reports and Dermatology clinic outpatient files. Some details which were missing which would have been of value included duration of lesions, symptoms, family history of malignancies, a thorough review of risk factors, HIV status, tumour subtype, histologic variant and grading as well as treatment rendered. The study also took place in one department and in one hospital. It lacked great variability in terms of Fitzpatrick skin phototype. The denominator used to calculate the prevalence was the total number of patients seen during the study period, in the department of dermatology. Ideally the denominator should have been the total number of patients seen at HJH during the study period. Patients presenting with both a BCC and an SCC were counted as a single entry under each heading. Although this gives a correct picture of the burden of cancers it can lead to over-representation of our total patients seen during the study period. Therefore caution should be exercised before generalising the results to a wider population.

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APPENDICES

3.1 DATA COLLECTION SHEET

UNIQUE PATIENT ID:_____ DATE:_____

AGE:_____ GENDER:_____

HIV STATUS:_____

DIAGNOSIS:_____

RISK FACTORS:_____

HISTOLOGIC SUBTYPE:_____

GRADING:_____

TUMOUR LOCATION:_____

3.2 WITS HREC ethics clearance

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr KI Mosojane

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M200140

NAME: (Principal Investigator)	Dr KI Mosojane
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Internal Medicine - Dermatology Charlotte Maxeke Johannesurg Academic Hospital
PROJECT TITLE:	The prevalence of Basal Cell Carcinoma and Squamous Cell Carcinoma at The Helen Joseph Hospital
DATE CONSIDERED:	31/01/2020
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor D Modi
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/02/21

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I agree to submit a yearly progress report. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **January** and will therefore reports and re-certification will be due early in the month of **January** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

22/02/2020
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

3.3. Helen Joseph Hospital Ethics

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Gauteng Department of Health
Helen Joseph Hospital
Enquiries: Dr. M. Mukansi
Research Committee: Chairperson
Tel :(011) 489-0306/1087
Fax :(011) 489 1038
E mail:Murimisi.mukansi@wits.ac.za

21 November 2019

To whom it may concern

Subject: HELEN JOSEPH HOSPITAL RESEARCH COMMITTEE APPLICATION

PROTOCOL TITLE: The prevalence of basal Cell carcinoma and squamous cell carcinoma at the Helen Joseph Hospital

Protocol Ref No: Dr Karen Itumeleng Mosojane

Ethics Clearance: Pending

Principal investigator: Dr Karen Itumeleng Mosojne

Department:Dermatology

Committee Recommendations
The Committee is giving you Conditional access while awaiting the final ethical clearance certificate from the University of Witwatersrand HREC.

It is the duty of the researcher to collect the data to the relevant department after the Research Committee approved the study.

Dr. M. Mukansi
Chairperson of HJH Ethic and Research Committee

3.4 HELEN JOSEPH HOSPITAL RESEARCH COMMITTEE AND CEO PERMISSION

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Gauteng Department of Health
Helen Joseph Hospital
Enquiries: Dr. R. Ncha
Chief Executive Officer
Tel :(011) 489-0306/1087
Fax :(011) 726-5425
E mail: Relebohile Ncha@gauteng.gov.za
Date: 25 August 2022

Dear DR Karen Mosojane

STUDY: The Prevalence of Basal Cell Carcinoma and Squamous Cell Carcinoma at the Helen Joseph Hospital.

RESEARCHERS: DR Karen Mosojane

GP_202208_063

The above the study was discussed at the Research Committee meeting. We recommend that permission be granted for Helen Joseph Hospital to be used as a site for the above research,
The researcher is expected to the following:

- Upon completion of the study, copy thereof should be submitted to Helen Joseph Hospital.
- It is the researcher's duty to collect the data from the relevant department after the Research Committee approved the study.

Please liaise with the HOD and Unit Manager or Sister in Charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the feedback of your study on completion of the research.
Thank you

Dr. M.D Mukansi
Helen Joseph Hospital
Research Chairperson

Approved

Dr. R. Ncha
Helen Joseph Hospital
CHIEF EXECUTIVE OFFICER
DATE: 01/09/22