EPIDEMIOLOGICAL PATTERNS OF SKIN CANCER AMONG PATIENTS PRESENTING TO THE DEPARTMENT OF RADIATION ONCOLOGY AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL BETWEEN 2006 – 2011

BY

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By

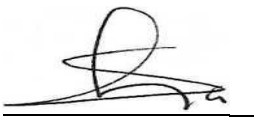
Sikudhani Shaban Muya

A research report submitted to the Faculty of Medicine in fulfillment of the requirements for a degree of Master of Medicine at the University of the Witwatersrand Johannesburg.

JUNE, 2020

DECLARATION

I **Sikudhani Muya**, I hereby declare that this report is my work, except where it is acknowledged. It is submitted as a partial fulfillment for the degree of master of medicine in Radiation Oncology University of Witwatersrand, Johannesburg. This thesis has been submitted for fellowship for Colleges of Medicines in Radiation Oncology South Africa in2014 as a requirement for final examination.



(Signature of candidate)

Signed at Johannesburg on 24th June of 2020

This study has received ethical approval from the University of Witwatersrand's Ethical Committee for Research on Human Subjects. PROTOCOL NUMBER M120851.

DEDICATION

To my daughter Ramla Ramadhan and my family.

PRESENTATION

Journal of continuing medical education

To Ocean Road Cancer Institute as a lecture

To the department as lecture

ABSTRACT

Purpose

To describe the epidemiological pattern of skin cancer among patients attending the Department of radiation oncology at Charlotte Maxeke Johannesburg Academic Hospital between 2006-2011.

Method and materials

207 patients with histologically diagnosed non melanoma skin cancer from January 2006 – December 2011 were retrospectively reviewed and analysed using SPSS. Trends in incidence of non melanoma skin cancers by race, age, gender, stage, and anatomical distribution in albino and general population were analyzed.

Results

Of the 207 patients analysed, 67.6 % (140) were males and 32.4 % (67) were females, there was no association between histology and gender.

White Population constituted 60.4% (125) of all the patients analysed, followed by black (combination of Blacks, Coloured, and Indians as the number of coloured and Indians was too small only 2 patients) population 39.6 % (82).

Squamous cell carcinoma was the most common histology found in blacks 92.6% (75 patients) while most whites had basal cell carcinoma 54.8 % (69 patients) and the difference was statistically significant.

The mean age at diagnosis was 61.3 years. The mean age for blacks was 52.96 years (52.96 ±15.8 years) and that for whites was 66.79 years (66.79 ±13.56 years). There was an association between histology and age.

The majority of whites presented with early stages of disease (stage 1 and 2) 88.0% (110 patients) while blacks presented with late stages of disease (stage 3 and 4) 46.3% (38 patients).

Head and neck was the most common site of lesions 65.2% (135 patients) for both whites and blacks but was more common in whites 72.8% (91 patients) while blacks had 53.7% (44 patients). Leg lesions were more common in blacks 30.5% (25 patients) and very few whites had leg lesions 8.0% (10 patients) and chest lesions 16% (35 lesions). There was an association between histology, race and anatomical distribution of non melanoma skin cancer.

Albino accounted for about 47.5 % (38 patients) of the black population with SCC being the commonest histology 29.5% (36 patients) followed by basal cell carcinoma 2.7% (2 patients), there was no association between albinism and stage of the disease and most of the lesions were on the head and neck region but there was no difference in the anatomical distribution of skin lesions between albinos and normal black population.

Conclusion

SCC is the most common histology of non melanoma skin cancer and more common in blacks than whites. BCC is the second most seen in whites, and the most frequently seen subtype was nodular BCC. Most whites presented with early stages of disease compared to blacks. There was an association between histology and age as well as race and anatomical distribution of lesions. There was no association between histology and gender.

Albinos present with SCC commonly than BCC with more lesions found on the head and neck. The findings are similar and comparable to most of the studies done in other parts of the world.

Prospective epidemiological studies are suggested in collaboration with dermatologists and plastic surgeons as most of the skin cancer patients are seen by them before referral to Radiation Oncologists.

Acknowledgment

I would like to express my sincere gratitude to the following people for their endless effort to help me with this work;

Dr. Bhavna Singh, my previous supervisor for helping me comes up with this idea of research Prof Vinay Sharma for his endless effort and facilitating my work when Dr. Singh was not available. Sister Danisile at skin clinic for simplifying my work on data collection.

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List of Acronyms, Abbreviations, and symbols

ARV	–	Antiretroviral drugs
BCC	-	Basal Cell Carcinoma
CMJAH	–	Charlotte Maxeke Johannesburg Academic Hospital
HIV	–	Human Immunodeficiency Virus
SHH	–	Sonic Hedgehog pathway
SCC	-	Squamous Cell Carcinoma
cSCC	–	Cutaneous Squamous Cell Carcinoma
NMSC	-	Non-Melanoma Skin Cancers

1. INTRODUCTION

1.1 Background

Non melanoma skin cancer is the most common malignancy in humans (1). Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the major histologies referred to as non melanoma skin cancer. Although there are other histologies such as adnexal skin cancer, but these are less common(2,3).

The incidence of non-melanoma skin cancers is on the rise (1,2). This may be contributed by environmental risk factors, sun exposure behaviors, and also as a result of expanded skin screening programs (1–4). Globally, about 2-3 million non melanoma skin cancers are diagnosed annually (5).

In South Africa basal cell carcinomas (BCC) and squamous cell carcinomas (SCC)are common, thus making South Africa rank number 2 for the highest incidences of skin malignancy after Australia with about 13000 new cases annually(6).

Risk factors for skin cancers include ultraviolet radiation exposure, genetic factors, gender, and fair complexion skin. Halder RM in the year 1988 found that the incidence of skin cancer is 232 per 100,000 population in Caucasians and 3.4 per 100,000 in dark skinned people annually, showing that Caucasians have 70 times more chances of developing skin cancer (6). About genetic disorders like albinism, Rippey, and Schmaman in the year 1972 looked at skin cancer histology like squamous cell carcinoma and basal cell carcinoma in dark skinned individuals and found that about 11% of SCC and 41% of BCC were in albinos (5). Skin cancers have been observed to be more common in males than females(1,4–9).

Non melanoma skin cancer (BCC and SCC) are seen in both fair skinned and dark skinned people. In fair skinned people, lesions occur on exposed hair bearing areas of the head and neck but rarely involve palms and soles (6). In dark skinned people, SCC may occur in sun protected sites such as the lower limbs (5)(6)(11), this is due to melanin which protects the skin from ultraviolet radiation from the sun. Other risk factors include infection with Human Papilloma Virus, transplant recipients on Immunosuppressive drugs, patients with Human Immunodeficiency Virus infection, people with multiple myeloma and lymphoma, areas of chronic skin damage and exposure to ionizing radiation (12). Mortality is usually higher in

dark skinned groups because the skin cancer they get is not due to excessive sun exposure (7)(13).

Different treatment modalities may be used to treat non melanoma skin cancer. The choice of treatment modality depends on the age of the patient, size, site, number of lesions, treatment intent (whether curative or palliative), cosmesis and functional results, as well as patient's preference. The different modalities include cryosurgery, curettage and electrodissection, chemotherapy, surgical excision, Moh's micrographic surgery, radiation therapy and targeted therapy for BCC patients with mutation in sonic hedgehog (SHH) pathway (1)(2)(4).

1.2 Rationale of the study

There are few studies on the epidemiological patterns of skin cancer done in Africa, and especially in Sub Saharan Africa. More specifically fewer studies have been done among the albino population.

This study described the different epidemiological patterns of non melanoma skin cancer seen at the Department of Radiation Oncology in the general population and albinos, hence adding to the body of knowledge in this area.

1.3 Literature review

Several studies have been done previously on the incidence, anatomical distribution, age and overall epidemiological pattern of skin cancer.

A. STUDIES ON INCIDENCE, GENDER AND AGE IN NMSC.

A prospective study done by Joseph Scotto, Thomas Fears and Joseph Fraumeni published in 1983 looked at the incidence of non-melanoma skin cancer in the United States. About 80% of skin cancers were BCC and for both cell types, males were at greater risk than females and it was more on sun exposed areas(14).

An observation study done in Japanese patients by Kikuchi et al (15) concluded that BCC does not commonly occur in African and Asian races, the ratio of male-female was 0.97, and the average age of the patients was 59 years.

A case control study done by Lannacone et al in 2012 concluded that sunlight exposure is associated with both BCC and SCC risk regardless of the pattern in which the exposure was

received (i.e. intermittent vs. continuous). The data also suggest that sunlight exposure at a younger age may be more important for SCC but not BCC(16).

The incidences of BCC and cSCC are increasing, with a disproportionate increase in cSCC relative to BCC. There is also a disproportionate increase in the incidence of both tumors in women, as well as a shift of anatomical distributions(17).

Steenbeck K.D and Balanda K.P conducted another study in Queensland Australia in 1984 and looked at the pattern of treated non melanoma skin cancer in Queensland the region with the highest incidence rates in the world, and it included total of1372 men and 702 women. The study found that the rates of skin cancer in men were double that of women and the incidence increases with age. The ratio of BCC to SCC was 3:1 (18).

An article in Continuous medical education by Gloster Hugh et al (19) revealed that SCC is the most common cutaneous malignancy among blacks and Asian Indians and second common in Caucasian while BCC is most common in Hispanics and second common in Blacks and Asian Indian.

Another study published in September 2009 done by Samhar Weshar et al (20) in King Hussein Medical Center Jordan reveals the male to female ratio was 1.5 to 1, the age of patients ranged between 23 and 90 years, 40.8 % were in the age group of 60-69 years.

A retrospective study done by Coebergh and Neumann in SE Netherlands examined a total of 650,000 persons from 1975-1988. They found the incidence of BCC and SCC was on the rise for males compared to females, and about 80% of the cases of BCC and SCC occurred on the head and neck (21).

A retrospective study done in Germany by Katalinic and Kunze in 2003 looked at the epidemiology of cutaneous melanoma and non melanoma and found that the mean age of skin cancer in men was greater than that in women (56.6 years vs. 54.9years with $p<0.05$). The superficial spreading melanoma was the most frequent clinical type and that tumors were located in trunk among men and at legs and hips in women. As for non melanoma skin cancer, the age standardized incidence rates were 100.2 and 72.6 in 100000 men and women respectively, with more than 80% being BCC in this group(22).

A cohort study done by Kennedy C, Bajdik et al concluded that individuals with non melanoma skin cancer were slightly older and individuals with malignant melanoma slightly younger than individuals without any skin cancer and men were over-represented among patients with squamous cell carcinoma and nodular basal cell carcinoma(12).

B. STUDIES ON HISTOLOGIES AND ANATOMICAL DISTRIBUTION OF NMSC

A retrospective study done in Nigeria by Ochicha and Edino in 2004 looked at the patterns of skin cancer. The study included 125 histologically confirmed skin cancers and found that malignant skin cancer comprises 12.7% of all cancers. SCC was the most common, constituting 40% followed by melanoma comprising 34%, most of them occurring at the 6^{th}-7^{th} decade in life with a male to female ratio of 1.2:1(8).

Another study done by Graham Giles, Robin Marks and Peter Foley in 1988, looked at the incidence of non melanocytic skin cancer treated in Australia. The study included14800 patients and concluded that the rates of males were higher than that for females and that became more significant after the age of 60 years. The study also found that BCC was more common than any other non melanocytic skin cancer and both BCC and SCC were seen on sun exposed areas(23).

In their study, Lovatt and others in 2005 elucidated the relative effects of pattern of ultraviolet radiation exposure, site and histologic type of the first tumor, on the rate of increase in BCC numbers (2). The study which included 266 Caucasian patients found out that those patients with initial truncal BCC with superficial histology demonstrated significantly faster increases in BCC than other patients with other site and histology thereby concluding that site and histology defines subsets of patients with BCC.

Another study by Zanetti and Martinez done in the year 2006 compared risk pattern in non melanoma and melanoma of the skin. The study included 214 cases of malignant melanoma, 213 cases of BCC and 139 cases of SCC. They found that the body site of melanoma was mainly the trunk (50%) whereas BCC and SCC lesions were most frequently on the face and head (70%) for both types (24).

A case controlled study done in Florida looked at Pattern and timing of sunlight exposure and the risk of non melanoma skin cancer. The study suggested that sunlight exposure is associated with both BCC and SCC risk regardless of the pattern in which the exposure was

received (i.e. intermittent vs. continuous). The data also suggested that sunlight exposure at a younger age may be more important for SCC but not BCC and there was a need to further characterize sunlight exposure-response relationships in different types of NMSC (25).

A retrospective study done in Atlanta revealed that SCC is not rare on the legs of elderly African-American women(26).

A study done in Switzerland revealed that BCC has higher incidence and was observed more in the face for both genders, followed by neck, ears, and scalp with incidence more in males than females. SCC's highest incidence was on the face in both genders followed by neck, ears, and scalp and by the upper limbs and shoulders, with no specific gender preference(27).

C. STUDIES ON ALBINISM AND NMSC

A prospective study done in Soweto, South Africa by Kromberg, Castle and Zwane (1989) found that the prevalence and susceptibility of skin lesion and skin cancer in albinos increases with age. They also found that the distribution of the lesions is more in the head and neck than other parts. SCC was more frequent than BCC (11).

A study done in Nigeria by Ademiluyi et al (28) which looked at occurrence and recurrence of BCC of head and neck among Negroid and Albino Africans found that the Negroid patient present with cancer between 3rd and 4th decade while the albino presents a decade earlier. The commonest involved site was on forehead.

A retrospective study done in Bugando Medical Centre, Tanzania revealed that skin cancer is the most common, with SCC being the commonest followed by BCC(29).

Another study done in Eastern Nigeria done by Opara and Jiburum also shows that the commonest histology is SCC and commonly present at late stage(30).

An observation study done in Tanzania by Alexander and Ulrich on advanced skin cancer in Tanzanian albino from 1973 -1979 revealed that most of the lesions were on sun exposed area mostly head and neck regions. Few patients presented with nodal involvement and advanced stage(31).

A study done in Northern Nigeria by Ochicha et al revealed that SCC was the most common followed by Malignant melanoma and they commonly occur in the 6th and 7th decade of life and males were more affected(8).

A 10year retrospective histological review of skin cancer in African albino done in Moshi, Tanzania also revealed that SCC was common than BCC with a ratio of 1.2:1. SCC histology were of well differentiated while BCC was mainly Nodular(32).

1.4 OBJECTIVES

To describe the epidemiological pattern of skin cancers among patients attending to the Department of Radiation Oncology at Charlotte Maxeke Johannesburg Academic Hospital in terms of histology, race, sex, age, stage and albino population.

Specific objectives

- To describe the possible association between skin cancers histological types, race, sex, and age.
- To describe the different anatomical presentation of skin cancer among different races.
- To describe the pattern of skin cancer in the albino population in terms of incidence histology, stage and anatomic site.

2. METHODOLOGY

2.1 Study design and setting

This was a descriptive study conducted as a retrospective record review.

The study was conducted in the Department of Radiation Oncology at Charlotte Maxeke Johannesburg Academic Hospital in South Africa. This is a tertiary referral hospital for the Gauteng Province.

Using information gathered from patient's files (data that were originally collected for non-research purposes) relevant information from files were recorded on a proforma. All patients with non melanoma skin cancers (SCC and BCC) seen at the department of radiation oncology from January 2006 – December 2011 who met inclusions criteria were included.

2.2 Study population

Patients who presented to CMJAH with histologically confirmed non melanoma (SCC and BCC) skin cancer who met inclusion criteria were included in this study.

The details of patients were retrieved from patient's files kept in the medical records department.

All skin clinic register books were checked. Information taken included socio demographic data, race and if albino or not, clinical presentation, anatomical sites, tumor stage, histopathological types and grade, presence of metastasis (nodal, number of distant metastases), risk factors, performance status, and treatment modalities. The anatomical sites were categorized as head and neck, trunk, arms, hands, legs and feet and number of lesions per anatomical site.

2.3 Sampling and sample size

Through a patient registration book at a skin clinic in the Department, all patients registered with non-melanoma skin cancer, their file numbers were recorded in a plain paper by the investigator. The files were then traced at the medical records and all-important data were extracted and recorded on the data capture sheet. A total of 300 patients files were reviewed and sorted according to the inclusion criteria, 2 patients were excluded due to their ages (16 and 17years) and the other 91 patients were excluded because of different reasons including mixed histologies (some had Non Melanoma mixed with Melanoma) as well as missing data

(anatomical sites distribution or number of lesions and size of lesions). Hence a total of 207 patients with all the relevant information were obtained and included in the study.

2.4 Inclusion criteria

Patients included in the study were;

All histological diagnosis of BCC and SCC at first presentation as seen in the Department of Radiation Oncology, Charlotte Maxeke Johannesburg Academic Hospital from 2006 – 2011.

- Age more than 18 years.
- Males and females.

2.4Exclusion criteria

Patients excluded in the study were;

- All patients with incomplete data in the files
- Histology other than BCC and SCC
- Patients less than 18 years of age.

2.5 Statistical analysis

Data extraction forms were carefully reviewed for completeness and consistency. In case of any missing information, patient records or medical register were rechecked and information from patient files were traced back.

Data from data extraction forms were then entered and coded into a Microsoft excel sheet database which was then exported to SPSS for cleaning and statistical analysis.

Continuous variables were summarized by means, median, and range.

Categorical variables were summarized by frequencies, percentages for general description.

Fisher's Exact Test, Pearson Chi-square and P-value were used to test for significance associations and differences between the predictor and outcome variables in the categorical variables.

2.5 Ethical considerations

Ethics clearance was obtained from the Human Sciences Research and Ethics Committee of the University of the Witwatersrand with ethical clearance certificate number M120851 and permission to conduct the study and use data from patient's records in the hospital was also obtained from the CEO.

The research involved no added risk to the subjects, it involves secondary data analysis, research data was applied to the patients that had already consented for treatment and it didn't affect the rights and welfare of the subjects.

2.6 Study limitations

This was a retrospective study and some of the important information was not recorded well and hence there was some missing information (as in the past before 2011 the Red Cap data capture was not yet introduced in the department for some cancers). Among the data that were missing in files includes anatomical location, size of lesions or number of lesions of skin cancer. Also, most of the skin cancer patients only present to the Department of Radiation Oncology when there are indications for Radiation therapy, otherwise, they will be seen and treated at Dermatology and Plastic surgery Departments and hence this study reflects the small number of skin cancer patients in Radiation Oncology Unit, therefore the results only reflect patients who received radiation therapy.

2.7 Quality control

The data obtained was coded to ensure the anonymity of patients, and was also edited before any statistical analysis to be carried out on them. No patient identifiers were extracted or analyzed and all care taken into account to ensure that only the principal investigator had access to raw patient records through the creation of a password protected Microsoft excel sheet data flow sheets. The patient's numbers used to extract the raw patient's data to the excel sheets was not transcribed into the SPSS database for statistical analysis; instead, each record packet was assigned a new study number. As such only the principal investigator was able to link the primary data with the secondary data. The data shall be used for the sole purpose of writing this study and for scientific publications only.

3. RESULTS;

Table 1: Two hundred and seven patients were included in the study.

Variable		Frequency (n)	Percentage (%)
Age (years)	**20-40**	27	13
	41-60	63	30.4
	61-80	98	47.3
	>81	19	9.2
Sex	**Male**	140	67.6
	Female	67	32.4
Race	***Black combined**	82	39.6
	White	125	60.4
Albino	**Yes**	38	18.4
	No	169	81.6
ECOG (Performance status)	**0**	11	5.3
	1	138	66.7
	2	48	23.2
	3	10	4.8

Table 1: Socio demographic characteristics of the study population (n=207)

The mean age was 61.3 years for the whole study group. The mean age for the black population was (52.96±15.8 years) and for the white population (66.79 ±13.56 years).

- *Black combined (blacks, Indians, and Coloured)

Table 2: Risk factors for non melanoma skin cancers (n=207)

Variable		Frequency (n)	Percentage (%)
Sun Exposure	**Yes**	190	91.8
Previous scar	**Yes**	9	1.0
Previous burns	**Yes**	3	87.7
Previous existing chronic ulcer	**Yes**	9	4.3
Xeroderma-pigmentosum	**Yes**	0	0
HIV status	**Nonreactive**	19	9.2
	Reactive	17	8.2
	Unknown	171	82.6
HAART status	**Yes**	12	5.8
	No	24	11.6
	Unknown	171	82.6

Table 3: Clinical pathological characteristics of the study population (n=207)

Variable		Frequency (n)	Percentage (%)
Histology	**BCC**	75	36.2
	SCC	132	63.7
Basal cell carcinoma subtype	**Nodular BCC**	31	15.0
	Superficial BCC	1	0.5
	Morphoeaform BCC	13	6.3
	Infiltrative BCC	10	4.8
	Baso-squamous	11	5.3
	Not specified	15	7.2
	Not applicable	126	60.9
Stage of skin cancer	**1**	41	19.8
	2	113	54.6
	3	51	24.6
	4	2	1
Lymph node involvement	**Yes**	51	24.6
	No	156	75.4
Sites of lymph node involved	**Inguinal lymph nodes**	22	10.6
	Axillary lymph nodes	6	2.9
	Cervical lymph nodes	22	10.6

Table 4: Anatomical sites of non melanoma skin cancers (n=207)

Variable		Frequency (n)	Percentage (%)
Head and neck lesions	**Yes**	135	65.2
Head and neck-number of lesion	**1**	97	46.9
	2	21	10.1
	3	11	5.3
	4	3	1.4
	5	3	1.4
Chest lesion	**Yes**	13	6.3
Number of chest lesions	**1**	11	5.3
	3	2	1
Arm lesions	**Yes**	11	5.3
Number of arm lesions	**1**	10	4.8
	3	1	0.5
Hands lesion	**Yes**	6	2.9
Number of Hand Lesions	**1**	6	2.9
Leg Lesions	**Yes**	35	19.6
Number of Leg Lesions	**1**	32	15.5
	2	2	1
	3	1	0.5
Feet Lesions	**Yes**	1	0.5
Site of Distant Metastasis	**Bone**	2	1
	Brain	1	0.5

Table 5: Association between race and histology of non melanoma skin cancer

		Race	
		Black combined n(%)	**White n (%)**
Histology	**BCC**	6 (7.4)	69 (54.8)
	SCC	75 (92.6)	57 (45.2)
	Total	**81 (100)**	**126 (100)**

Chi-square p value <0.001)

Tables 5 show that most blacks had SCC and most of the whites had BCC and the association was statistically significant (p<0.001).

Table 6: Association between histology of non melanoma skin cancer and gender

		Gender	
		Male n (%)	**Female n (%)**
Histology	**BCC**	47 (33.6)	28 (41.8)
	SCC	93 (66.4)	39 (58.2)
	Total	**140 (100)**	**67 (100)**

Chi-square p value =0.39

Tables 6 show that there was no histological difference according to gender.

Table 7: Association between histology of non melanoma skin cancer and age

		Age(years)	
		< 60 years n (%)	**> 60 years n (%)**
Histology	**BCC**	21 (23.3)	54 (46.2)
	SCC	69 (76.7)	63 (53.9.)
	Total	**90 (100)**	**117 (100)**

Fisher's Exact Test p value <0.001

Tables 7 shows that patients who were less than 60 years old mostly had SCC and those more than 60 years old were equally affected by both SCC and BCC and the association was statistically significant (p<0.001)

Table 8: Association between race and head & neck skin lesions.

		RACE - GROUP	
		***BLACK COMBINED** n (%)	**WHITES** n (%)
H/N LES	YES	44 (53.7)	91 (72.8)
	NO	38 (46.3)	34 (27.2)
	Total	**82 (100)**	**125 (100)**

Chi-square p value = 0.005

Table 8 shows that head and neck lesions were more common among whites compared to blacks and the association was statistically significant (p= 0.005).

Table 9: The association between race and occurrence of leg lesions.

		Leg lesions	
		Yes n (%)	**No** n (%)
Race	**Black**	25 (30.5)	57 (69.5)
	White	10 (27.6)	115 (66.9)
	Total	**35 (100)**	**172 (100)**

Chi-square p value =<0.001

Table 9 show leg lesions were more common among blacks compared to whites and the association was statistically significant (p =<0.001).

Table 10: The association between histology of non melanoma skin cancer and albinism.

		Albino	
		Yes n (%)	**No** n (%)
Histology	**BCC**	2 (5.3)	73 (43.2)
	SCC	36 (94.7)	86 (50.9)
	Total	**38 (100)**	**169 (100)**

Fishers Exact test p value <0.001

According to Table 10, SCC was the commonest histology (94.7%) among albinos and that was statistically significant (P value <0.001)**.**

Table 11: The association between head & neck skin lesions and albinism.

		Head and neck lesions	
		Yes n (%)	**No n (%)**
Albino	**Yes**	29 (2.7)	9 (12.5)
	No	106 (97.3)	63(87.5)
	Total	**135 (100)**	**72 (100)**

Fishers Exact test p value=0.133

There was no difference in the distribution of skin lesions in head and neck between albinos and normal population (p=0.133)

Table 12: The association between leg lesions and albinism.

		ALBINO	
		Yes n (%)	**No n (%)**
LEG LESION	**Yes**	6 (15.8)	29 (17.2)
	No	32 (84.2)	140 (82.8)
	Total	**38 (100)**	**169 (100)**

Chi-square p value=0.839

Table 12 shows that there was no difference in the distribution of skin lesions in legs between albinos and normal people (p=0.839)

Table 13: The association stage of skin cancer and albinism.

		Albino		
		Yes n (%)	**No n(%)**	**Total n (%)**
Stages	**I & II**	19 (50.0)	135 (79.9)	154 (74.4)
	III & IV	19 (50.0)	34 (20.1)	53 (25.6)
	Total	**38 (100)**	**53 (100)**	**207 (100)**

Chi-square p value<0.001

Table 13 showed that distribution of skin cancer of early stages and late stages was equal among patients with albinism; however, among those without albinism most (79.9%) had early stages skin lesions ($p < 0.001$)

Table 14: The association between race and stage

		Race		
		Black combined n (%)	**Whites n(%)**	**Total(%)**
Stage	**Stage I and II**	44 (53.7)	110 (88.0)	154 (74.4)
	Stage III and IV	38 (46.3)	15 (12.0)	53 (25.6)
	Total	**82 (100)**	**125 (100) (100)**	**207**

Chi-square p value <0.001

Table 14 shows that the majority of whites had early staged lesions (88%) while blacks had more advanced staged lesions (46.3%) and the difference was statistically significant (p<0.001)

Table 15: The association between race and lymph node involvement.

		Lymph node involvement		
		Yes n (%)	**No n (%)**	**Total(%)**
Race	**Black combined**	36 (43.9)	46 (56.1)	82 (100%)
	White	15 (12.0)	110 (88.0)	125 (100%)
	Total	**51 (100)**	**156 (100)**	**207 (100%)**

Chi-square p value <0.001

According to Table 15, majority of blacks had more lymph nodes involvement as compared to whites (p<0.001).

Table 16: The association between HIV status and non melanoma skin cancer stage.

		Stages		
		I & II (%)	**III &IV(%)**	**Total(%)**
HIV	**Reactive**	9 (45.0)	10 (62.5)	19 (52.8)
	Non-Reactive	11 (55.0)	6 (37.5)	17 (47.2)
	Total	**20 (100)**	**16 (100)**	**36 (100.0**

Chi-square p value =0.07

Table 16 shows that there was no difference in the distribution of early and late skin cancer stages according to HIV status (p=0.07).

Table 17: The association between sun exposure and histology.

		Histology		
		BCC (%)	**SCC (%)**	**Total (%)**
Sun Exposure	**Yes**	75 (100)	105 (87.1)	190 (91.8)
	No	0 (0)	17 (13.9)	17 (8.2)
	Total	**75 (100)**	**122 (100)**	**207 (100)**

Fisher's Exact Test p value <0 .001

Tables 17 showed all patients who had BCC had a history of sun exposure and 86.1 % of patients with SCC had a history of sun exposure (p<0 .001) and hence there was a significant association between histology and history of sun exposure.

Table 18: Mean ages of different races

Age group	**Number**	**Mean age in years**	**Std Deviation**
Race			
1	**90**	**52.96**	**15.79**
2	**117**	**66.79**	**13.56**

Anova Test p value = <0.0001

***Age groups are <60 years =1 and >60 yeas =2, and Races 1= Blacks and 2 =Whites.**

There were statistically significant differences between group means. The younger age group in the black population than in whites and the difference is statistically different. The mean age for the black population was 52.96 while that of the white population was 66.79.

The analysis of other independent variables was not included in the results because they were not statistically associated with the occurrence of non melanoma skin cancer in this study

SCC was the most common histology constituting about 63.8 % (132) followed by BCC 36.2 % (75 patients). The majority of SCC patients were blacks 92.6% (75 patients) while white

patients had BCC 54.8% (69 patients) and the association was statistically significant (Table 5). There was no histological difference according to gender (Table 6).

All patients who had BCC had a history of sun exposure while only 86.1 % (105 patients) of SCC had a history of sun exposure, which means SCC has other risk factors other than sun exposure.

There was no statistically significant association between histology and other risk factors like previous scar, chronic ulcer, xeroderma pigmentosum as well as previous burns

The mean age was 61.3 years for the whole study group. The mean age for the black population was (52.96±15.8years) and for the white population (66.79 ±13.56 years). (Table1) .There was statistically significant differences between group means. The younger age group in the black population than in whites and the difference was statistically significant.

Patients who were less than 60 years old mostly had SCC and those more than 60 years old were equally affected by both SCC and BCC and the association was statistically significant. (Table 7)

Majority of white patients presented with early stage (stage 1 and 2) disease 88.0 % (110 patients) while black patients presented with late stage (stage 3 and 4) disease with 46.3% (38 patients) having more lymph node involvements. The difference is statistically significant. (Table 14 and15).

There was no association between HIV infection and stage of the disease. This may be due to the small number of patients with known HIV status in the study (Table 16).

Head and neck was the most common area with skin lesions and the lesions were more common among whites compared to blacks and the association was statistically significant (Table 8). Leg lesions were more common among blacks compared to whites and the association was statistically significant (Table 9).

Albinos were 18.4% (38 patients) among the black population. SCC was the most common histology constituting of 94.7% (36 patients) followed by BCC 5.3% (2 patients). The majority had head and neck lesions 76.3% (29 patients) followed by leg lesion 15.8% (6 patients) though most of the patients had multiple sites of lesions. (Tables 1, 10, 11 and 12).

The distribution of skin cancer stages among albino patients was equal (Table 13), this may be due to the number of albino patients included in the study.

4. DISCUSSION

4.1 BCC

I.BCC with race and Age

Non melanoma skin cancer is the commonest cutaneous malignancy with BCC being the most common in Caucasians while SCC was seen mainly in blacks (1),(6),(33). In this study, BCC was the second most common histology with the majority of patients being whites 54.8% (69 patients) and only 7.4% (6 patients) blacks. Equivalent results were also seen in studies done in India, Japan, and Nigeria (8,33,34). In this study, BCC appears to be more prevalent after the 6th decade of life, 46.2% (54 patients) which has also been seen in other studies (12),(19)(22)(35).

ii. BCC with Gender and Anatomical location of lesions

This study shows that the majority of males were diagnosed to have non-melanoma skin cancer than females, with BCC accounting to33% (47 male patients) and 41.8% (28 female patients) though the study shows that the association was not statistically significant.

Studies have shown different incidence of skin cancer according to gender, with the majority of the studies showing that men are more affected than women (6,13,36,37).

This study showed there was no association between gender and anatomical location of lesions, and hence it doesn't correlate with other studies conducted worldwide.

Studies have shown that BCC commonly occurs on sun exposed areas of the head and neck, regardless of the degree of pigmentation of the skin (36,37) which correlates with this study.

4.2. SCC

i. SCC race and Age

Studies have shown that SCC is the most common cutaneous malignancy in the black race and was the second most common among Caucasians (19,34,35). The findings are similar to this study wherein SCC was the commonest histology in blacks 92.6 % (75 patients) while in whites it accounts for about 45.2 % (57 patients).

This study has also shown that SCC was more common in younger age. The majority of patients had SCC,75.6 % (68 patients) diagnosis at the age of less than 60 years, though it was still seen at an older age as some patients were diagnosed with SCC after the 6th decade

of life 46.2 % (54 patients). The findings are similar to other studies done elsewhere e (19,26,35).

ii. SCC with gender and Anatomical site

Most studies on NMSC have shown that males are more affected than females (19,34,35), this study has also shown that a large number of males are affected though it is not statistically significant.

It has also been shown that whites had more head and neck lesions 67.4 % (91 patients) while blacks had 32.6 % (44 patients) with head and neck lesions. Similar findings have been seen in other studies (5,18).

4.3. Albinos

In this study, we found that most of albinos had SCC 29.5 % (36patients) and only 2.7 % (2 patients) had BCC. These findings were similar to other studies published (22,29,32,38). It also revealed that most of the lesions were on head and neck followed by leg lesion 2.7% (29 patients) and 17.1%(6 patients) respectively, similar findings were seen by other studies (11,30,39,40).

The study has also revealed that the distribution of skin cancer of early stages and late stages was equal among albinos.

Not much has been documented in literature about HIV infection among albinos with skin cancer. In this study, about 10 out of 38 albino patients were HIV reactive and only 50% of them were already on ARV's, this might explain on high morbidity of the disease among this group of patients.

4.4 Risk factors for NMSC

This study shows that the most common risk factor for both histology BCC and SCC was sun exposure 100% (75 patients) and 86.1% (105 patients) respectively. Similar findings were seen in other studies (5,12,41,42).

5. CONCLUSION AND RECOMMENDATIONS

SCC is the most common histology of Non melanoma skin cancer and more common in black than white patients that were seen at the Department of Radiation Oncology. BCC is the second most commonly seen in whites and the most frequently seen subtype was nodular BCC. Most whites had early staged disease while blacks had advanced disease and more lymph nodes involvement. There was no association between histology and gender, but there was between histology and age as well as between race and anatomical distribution of lesions.

All patients who had BCC had a history of sun exposure while some patients with SCC had no history of sun exposure.

There was no difference in the distribution of early and late skin cancer stages according to HIV status.

Albinos present with SCC commonly than BCC, with more lesions seen on the head and neck. They have equal distribution of early and late stages of disease.

The findings are similar and comparable to most of the studies done in other parts of the world.

Prospective epidemiological studies are suggested in collaboration with dermatologists and plastic surgeons as most of the skin cancer patients are seen by them before referral to Radiation Oncologists.

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6. Appendices

Appendix A

The American Joint Committee on Cancer (AJCC) Staging for Non-Melanoma skin cancer, 7th Edition.

1. Classification of Carcinoma of the Skin

Primary Tumor (T)	
T_X	Primary tumor cannot be assessed
T_0	No evidence of primary tumor
T_{is}	Carcinoma in situ
T_1	Tumor 2 cm or less in greatest dimension
T_2	Tumor more than 2 cm, but not more than 5 cm, in greatest dimension
T_3	Tumor more than 5 cm in greatest dimension
T_4	Tumor invades deep extradermal structures (i.e., cartilage, skeletal muscle, or bone)
Note: In case of multiple simultaneous tumors, the tumor with the highest T category will be classified and the number of separate tumors will be indicated in parentheses; for example, T_2 (5).	

Regional Lymph Nodes (N)	
N_X	Regional lymph nodes cannot be assessed
N_0	No regional lymph node metastasis
N_1	Regional lymph node metastasis

Distant Metastasis (M)	
M_X	Distant metastasis cannot be assessed
M_0	No distant metastasis
M_1	Distant metastasis

Stage Grouping			
Stage 0	T_{is}	N_0	M_0
Stage I	T_1	N_0	M_0
Stage II	T_2	N_0	M_0

Appendix B

Ethical clearance

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Sikudhani Muya

CLEARANCE CERTIFICATE	**M120851**
PROJECT	Epidemiological Pattern of Skin Cancer among Patients Presenting to the Department of Radiation Oncology at Charlotte Maxeke Johannesburg Academic Hospital
INVESTIGATORS	Dr Sikudhani Muya
DEPARTMENT	Department of Radiation Oncology Chartlotte Maxeke Johannesburg Academic Hospital
DATE CONSIDERED	31/08/2012
DECISION OF THE COMMITTEE*	Approved unconditionally Changed Supervisor 07/10/2015

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 31/08/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof Vinay Sharma

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX C: DATA CAPTURE

1. Code number
2. Place of residence

3. Race
    1. Black
    2. Coloured
    3. Indian
    4. White
    5. Others…….. specify
4. albino
    1. Yes
    2. No

5. Age
6. Sex
    1. Male
    2. Female

7. ECOG status
    0.
    1.
    2.
    3.
    4.
8. Occupational risk

Sun exposed (outdoor)

    1. Yes
    2. No

9. Previous scar

1. Yes

2. No

10. Previous burns

1. Yes

2. No

11. Previous existing chronic ulcer

1. yes

2. no

12. xeroderma pigmentosum

1. Yes

2. No

13. Previous trauma

1. Yes

2. No

14.HIV status

1. Nonreactive
2. Reactive
3. Unknown

15. on ARV's

1. Yes

2. No

3. Not applicable

16. Histology

1. Basal cell carcinoma

2. Squamous cell carcinoma

3. Both BCC and SCC in different sites

17. Basal cell carcinoma subtype;

1. Nodular BCC
2. Superficial BCC

3. Morphoeaform BCC
4. Infiltrative BCC
5. Basosquam
6. BCC not specified.
7. Not applicable

18. Stage of skin cancer

Refer to TNM staging for melanoma and non melanoma skin cancer (Appendix 1)

1. Stage I
2. Stage II
3. Stage III
4. Stage IV

19. Lymph node involvement

1. Yes
2. No

20. Sites of lymph node involved

1. Inguinal nodes
2. Axillary lymph nodes
3. Cervical lymph nodes
4. Not applicable

21. Site and number of lesions

Head and neck

1. Yes
2. No

22. Head and neck number of lesion

0
1
2
3
4
5

23. Scalp

1. Yes

2. No

24. Number of scalp lesions

0

1

2

3

4

5

25. Trunk

1. Yes

2. No

26. Number of trunk lesions

0

1

2

3

4

5

27. Chest lesion

1. Yes

2. No

28. Number of chest lesions

0.

1.

2

3

4

5

29. Arm lesions

1. Yes
2. No

30. Number of arm lesions

0.
1.
2.
3.
4.
5.

31. Hands lesion

1. Yes
2. No

32. Number of hands lesions

0.
1.
2.
3.
4.
5.

33. Legs lesion

1. Yes
2. No

34. Number of legs lesions

0.
1.
2.
3.
4.
5.

35. Feet lesions

1. Yes
2. No

36. Number of feet lesions

0.
1.
2.
3.
4.
5.

37. Any distance metastasis

1. Yes
2. No

38. Sites of metastasis

1. Lung
2. Bones
3. Liver
4. Brain
5. Not applicable

39. Radiation received

1. Yes
2. No

40. Intent of radiation

1. Radical
2. Palliative
3. Not applicable

41. Indication of radiation

1. Close or positive margin
2. Lymph node status and extracapsular extension
3. Inoperable or gross disease

4. Palliative

5. Not applicable

42. Radiosensitizer given

1. Yes

2. No