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DEPARTMENT OF DERMATOVENEREOLOGY

PATTERN AND MAGNITUDE OF CLINICAL & PATHOLOGIC CHARACTERSTICS OF BCC AT ALERT/AHRI CENTER, ADDIS ABABA, ETHIOPIA: A FIVE YEAR RETROSPECTIVE STUDY (2018 -2022 G.C)

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ADVISOR APPROVAL SHEET

This is to certify that the research thesis entitled "Magnitude And pattern of Clinical and Histopathological characterstics of cutaneous basal cell carcinoma , in ALERT hospital, Addis Ababa, Ethiopia, a five year retrospective study" is submitted in partial fulfillment of the requirements for the certificate of specialty in Dermatovenerology" to the Graduate Program of the College of health sciences of Addis Ababa University & will be carried out by Aderajew Birhan. Therefore, I recommend that the student has fulfilled the requirements and hence hereby can submit the thesis paper to the department.

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DECLARATION FORM OF PRINCIPAL INVESTIGATOR

I, the under Signed, hereby declare that this thesis is my original work and has not been presented for a degree in any other university and all sources of material used for this thesis have been duly acknowledged.

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Abbreviations/ Acronyms

AAU - Addis Ababa University

AHRI – Armauer Hansen Research Institute

ALERT - All African Leprosy Rehabilitation Training Center

E.C. – Ethiopian calendar

FDRE – Federal democratic republic of Ethiopia

FMoH - Federal Ministry of Health

G.C. – Gregorian calendar

H&E – Hematoxylin and Eosin

OPD- Out Patient Department

BCC- Basal cell carcinoma

NMSC- Non melanoma skin cancer

SCC- Squamous cell carcinoma

SPSS - Statistical Package for Social Science

Abstract

Background: basal cell carcinoma is the most common type of skin cancer in white population. In blacks it has lower incidence [1]. But knowledge and studies regarding the pattern and magnitude of cutaneous basal cell carcinoma in Africa and Ethiopia are few and lacking.

Objective: The primary goal of this research was to assess the pattern and magnitude of cutaneous basal cell carcinoma at ALERT hospital/AHRI, Adiss Ababa, Ethiopia.

Methods: A retrospective, cross-sectional research was undertaken from at ALERT Hospital/AHRI from May to Dec 2023 GC. All patients diagnosed with basal cell carcinoma from (January 2018- December 2022) at ALERT hospital/AHRI during the study period were included in the study. Data was collected by convenient sampling method using structured questionnaires. The collected data were checked for completeness, edited, coded, and entered into SPSS. Computerized data analysis was conducted by using Statistical Package for the Social Science (SPSS) version 27 software.

Results: We found 126 biopsy confirmed BCC cases. Of these, 74 cases (58.7%) from female patient with sex ratio (M: F) 1:1.42. The patients' mean age (SD) was 52.74 ±15.22 years (range 16-86 years old). The number of BCC cases diagnosed increased yearly from the start of our study period 2018 with the exception of 2019. 93 cases (73.8%) of the BCC patients came from urban areas. And also 61 cases (48.4%) BCC patients came from Addis Ababa city administration. The mean disease duration was 3.5 ±3.32 years (2 month to 18 years). 111cases (88.1%) were Primary BCC and 15(11.9%) were recurrent BCC. The most common tumor locations were 31 cases (24.6%) nose followed by 21 cases (16.7%) forehead and 16 cases (12.7%) Scalp. 111 cases (88 %) were on sun exposed areas of the body. Regarding clinical morphology, 46 cases (36.5%) were pigmented nodular, 30 cases (23.8%) non-pigmented nodular and 20 cases (15.9%) ulcerative lesions. Over all 98 cases (77.7%) of BCC patients had Nodular lesion, 43 cases (34.1%) of patient had ulceration of lesions and 58 cases (46%) of the lesions were clinically pigmented. 1 patient (0.9%) had XP and 5 patients (4.5 %) had retroviral infection. 84 cases (76.4%) were nodular subtype, the most common histologic subtype observed. Patients with superficial subtype BCC (52.50±16.59 years) had the youngest mean age at diagnosis. Overall, BCC with a non-aggressive biologic behavior type and single subtype were the dominant based on histologic features.

Conclusions: According to our findings, BCC is fairly prevalent. It generally showed a trend of increased cases of BBC diagnosed yearly. BCC incidence increased as age increased. Nodular, pigmented and ulceration lesions on sun exposed area of the body, BCC should be one of the differentials to be considered. Nodular BCC was the most common histologic subtype.

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1. Introduction

1.1. Background:

Basal cell carcinoma (BCC) is a skin cancer that arises from the basal cell layer of the epidermis. It is the most common type of skin cancer in the whole world and white people but is less common in people of color as much as 19-fold less than the Caucasians [1]. Europe, the United States, and Australia have the highest incidence of BCCs. People who live closer to the Equator have the highest incidence of BCC [2]. In the USA, above 3 million new cases per year, almost 75% of all NMSCs and almost 25% of all cancers diagnosed are BCCs. Incidence rates are steadily increasing 3% to 10% per year [3]. BCC (57%) is more common in older male individuals (>60 years of age) but is now seeing a disproportionate increase in BCC in women younger than age 40 years. The vast majority of BCCs were located on the head and neck. BCC tumors most typically develop on sun-exposed skin of lighter-skinned individuals [4]. Incidence rates of BCC are 5% in Hispanics, 4% in Asians, and 1.8% in blacks [5]. It is rare in dark skin because of the inherent photoprotection of melanin and melanosomal dispersion [6]. Bezabih et al, showed BCC was the least (17.6%) of NMSC and melanoma diagnosed between 1999 and 2000 at Tikur Anbessa Hospital, Addis Ababa, Ethiopia [7].

Age and gender (male) are found to be highly related with an increased risk of BCC. Incidence rates among the extremely elderly (those above 80 years of age) vary from 13 to 12,112 per 100,000 person-years, with males having the greatest rates. Numerous risk factors are linked to the development of BCC. It is widely acknowledged that sun exposure is the primary cause of BCC. Light-colored eyes, red or blond hair, and fair skin all stand out as risk factors because they are more vulnerable to UV radiation. Exposure to the sun during childhood and adolescence increases the risk much more than exposure to the sun later in life [2]. Using indoor tanning devices increased risk of early-onset BCC [62]. Psoralen plus ultraviolet A light (PUVA) therapy increases BCC and SCC risk with increasing exposure [8]. A slight increase in early-onset BCC (age ≤ 50) was associated with photosensitizing medication use (eg. Tetracycline, thiazide diuretics) [9],[60]. The treatment of acne vulgaris, tinea capitis, eczema, and cancers using therapeutic ionizing radiation increases the risk of BCC [10]. Chronic occupational exposure to ionizing radiation at low to moderate levels can increase the risk of BCC [11]. At a young age the deepest layer of the epidermis (basal) appears to be quite sensitive to malignant transformation induced by radiation, whereas lack of association with SCC shows the cells above the basal layer are resistant to radiation carcinogenesis [11]. Arsenic exposure causes multiple BCC tumors on non-sun exposed parts of the body (mainly the trunk) [12]. In transplant recipients (including hematopoietic stem cell transplant (HSCT) recipients) had an increasing incidence of BCC as the duration of immunosuppressive therapy increased. In renal transplant patients, risk factors increase by 7-16 times [13]. Total body irradiation (TBI) significantly increased the risk of BCC [14]. People with fair complexion, light/red hair color, light eye color, and poor ability to tan are at the highest risk of BCC. Melanocortin 1 receptor gene (MC1R) plays a major role in determining skin and hair color but MC1R gene variants are risk factors for

BCC, independent of the pigmentation phenotype [15]. Another risk factor for BCC development is personal and/or family history of skin cancer. A family history of skin cancer is associated with early-onset basal cell carcinoma independent of the MC1R genotype. The presence of multiple and/or early-onset BCC could be an underlying genetic condition, namely Gorlin, xeroderma pigmentosum, Bazex-Dupré-Christol, and Rombo syndromes [16].

UVR exposure, particularly the UV B spectrum (290–320 nm) which damages DNA and causes mutations in tumor suppressor genes (in about 50% of BCC cases), leading to genetic alterations and neoplasms is considered to be the main pathogenesis of BCC. Malignant activation of the sonic hedgehog (SHH) signaling pathway is the pivotal abnormality in all BCCs. Based on the genetic profiling of 293 BCCs, the majority of BCCs were found to have mutations in HH pathway genes: loss of PTCH1 (73%), 20% activation of Smoothened (SMO), and 8% loss of Suppressor of Fused (SUFU). Sporadic BCCs also commonly harbor mutations in TP53 (61%), PTCH1 (90%), and activating mutations in SMO protein (10%) [17] [60].

Translucency, ulceration, telangiectasias, and a rolling border are characteristics that are frequently observed. On the other hand, any lesion that does not heal should make skin cancer more likely. Various clinical subtypes, including as nodular, superficial, morpheaform, and pigmented BCCs as well as fibroepithelioma of Pinkus (FEP), may have various characteristics. The head and neck area is where BCC occurs most frequently (65%), followed by the torso (24%) and extremities (11%). The nose, cheeks, and forehead are the most often seen areas on the face, in that order [18], [60].

LABCC, or locally advanced BCC, is characterized by metastatic disease to lymph nodes and other organs or locally invasive BCC that is not responsive to conventional surgical and radiation therapy [19], [61].. Of all BCCs, LABCC makes up 0.8% and Metastatic BCC (MBCC) is responsible for 0.04%. The lungs (28%), bone marrow (24%), and lymph nodes (54%), are the most common sites of metastasis [19], [60].

Diagnosis of BCC needs a biopsy, either shave or punch biopsy. A punch biopsy may be useful for flat lesions of morpheaform BCC or recurrent BCC occurring in a scar [20], [60].

The histopathologic features vary somewhat with subtype, but most BCCs share some common histologic characteristics. The malignant basal cells have large nuclei(may not be atypical) and relatively little cytoplasm, mitotic figures are absent(usually) and slit-like retraction of stroma from tumor islands is present which is helpful in diagnosis [20]. Nodular BCC is the most common histologic subtype (53%) with 90% on the head and neck; superficial BCC (20%) with the trunk (46%) being the most common site. Aggressive histologic subtypes; infiltrating micronodular, metatypical, and morpheaform account for 21% of cases [21]. There are other rare histologic subtypes seen in BCC lesions [2]. The nodular and infundibulocystic variants are pigmented. Melanin accumulation in BCC is due to increased endothelin-1 signaling and ultraviolet B light-induced enhanced expression of the endothelin B receptor. The pigmented variant is common in sun-exposed parts of the body such as the head and neck [22].

Strong evidence is poor or lacking for prevention strategies. It is hypothesized that reducing UVR exposure through sun avoidance and sun protection practices will lower the incidence of BCC. Any oral NSAID use was found to reduce the incidence of BCC by 10%, according to a recent systematic review and meta-analysis. It has been demonstrated that sustained nicotinamide supplementation can lower the incidence of BCC by 20% in a high-risk group, which is characterized as having a history of two or more NMSC [23].

1.2 Statement of the problem

Basal cell carcinomas are slow-growing lesions with a relatively smaller risk of metastasis even though they are aggressive locally. The absence of pain or other disabling symptoms may not worry the patients enough to seek medical care early in the disease course. Even when they present to health care centers unless they encounter a health professional who has proper training in dermatology, they may not be diagnosed early and may visit several physicians before they are referred to a dermatologist a dermatopathologist, and surgeons for the appropriate management. And also the number of dermatologists in our country is not large enough to be accessible to our country's enormous population. There are a few studies done in Africa, Asia, the Middle East, and other populations of color that show the incidence of BCC to be lower than in whites still we need to do our research which will help us to know the pattern and magnitude of BCC and clinical and histologic characteristics of BBC patients. This research will help us know how incidence, patients at risk, type and number of BCC lesions, which syndromes should we follow, clinical features, and histologic subtypes of BCC. BCC can present as any non-healing lesion, so it should be biopsied to rule it out. New cases of BCC have increased dramatically worldwide in the past ten years as a result of better diagnosis, heightened awareness, and the use of ancillary diagnostic aids. This indicates that although not common, these tumors are still prevalent and their incidence is rising [3]. Therefore, physicians should keep in mind their possibility whenever encountering similar cases. As BCCs are relatively common, the prevalence is also unknown and there are only very few studies despite its importance. Literature on the African population is almost nonexistent and no study has been done in Ethiopia. To fill the gap and add on this deficient data, it would be of help to carry out a study in our country and compare it with the available works of literature.

1.3. Significance of the study

The present study helps to assess the pattern and magnitude of clinical and pathologic features of BCC in ALERT hospital/AHRI. It compares the patterns seen in Ethiopia with those of other African literatures and the patterns in the West looking for similarities and differences. As there has been no study done in Ethiopia so far on the pattern and magnitude of clinical and pathologic features of BCCs, this study will give an insight into how which histologic subtypes are the most common and their most common locations, age, and sex of the patient, duration of illness and area from the patient comes from in our country. This will be helpful for clinicians to be informed about the burden and features of this malignancy in our country and to keep these in mind when faced with similar lesions clinically. The present study can also encourage other researchers to carry out further studies in the field utilizing it as a base.

2. Literature review

Cutaneous Basal Cell Carcinoma is the commonest skin cancer in the world and especially white people [1]. It is the 2nd commonest skin cancer in Black, Asians and Indians [1]. Even though it is not as common as it is in white skinned individuals, it can be a significant cause of morbidity in black skinned individuals as well. There are multiple studies done in white population on the pattern and magnitude of clinical and pathologic characteristics of BCCs and fewer studies done in dark skinned populations and even fewer in our continent and almost none in our country. We will review some literatures in different parts of the world studying their pattern.

1. EUROPE

A. ROMANIA

A retrospective, five years (1 January 2003 -1 January 2008) at Clinical County Hospital of Emergency, Craiova. They found 647 cases, with slightly higher in females (51.49% vs. 48.51%) 37.13% coming from urban and, and 62.87% from rural environment. Medium average age for women was slightly older than males (56.6 vs. 55.5 years). 49.9% and 40.83% of patients in the age categories of 51-70 years and above 70 years of age respectively.

About tumor location, they found, that 89.90% were on the head and neck. From the face; Nasal region (30.58%); followed by the genial region (13.66%); orbital region (10.24%); auricular region (7.54%); frontal region (5.83%); infraorbital region (5.69%); temporal region (5.41) and some others with less frequencies. Histologically, solid BCC (44.95%) was the most common subtype; followed by adenoid (20.91%); keratotic (9.10%); pigmented (8.39%); basosquamous (6.83%); superficial type (5.26%) and others with less frequencies [24].

B. POLAND

A Retrospective (from 1999 to 2019) study was carried out at seven oncology and dermatology centers in Poland by using histopathological databases of these centers for the record. They recorded 13,913 NMSCs occurred in 10,083 patients. BCC represented 85.2% of all cases. Annual growth (5–7%) in incidence rates was observed between 2005 and 2014. The mean age of men was 70.9±11.4 years and that of women was 71.4 ± 11.9 years. Similar incidence rate was seen in males and females. Nodular (including the nodular and ulcerative subtype) BCC was the most frequent BCC subtype for both men and women (44.0%); superficial (30.5%),

infiltrative (14.1%), mixed superficial with nodular (3.4%) and mixed with aggressive subtype (1.1%), basosquamous (3.4%), adenoid (0.5%), pigmented (0.4%), micronodular (0.3%) and other (2.5%). Superficial BCCs were more common in women than in men, Infiltrative subtype incidence showed a 3x increase between 2010 and 2019. The incidence of superficial BCC increased by 1% annually, while nodular subtype declined. Patients with superficial BCC were slightly younger (67.7 ± 11.5 years) than other subtypes (69.3 ± 12.7 years). Moreover, women with superficial BCC were younger than men with the same BCC subtype (67.0 ± 13.7 years vs. 68.6 ± 12.2 years). Patients with basosquamous BCC (72.2 ± 11.3 years), nodular BCC (69.4 ± 12.7 years), and infiltrative BCC (71.1±12.3years) were on average older than patients with other subtypes. The distribution of the lesions were; face (73%), trunk (15%), upper extremities (4%), lower extremities (3%), scalp (2%), and neck (3%).On the face: nose (29.7%); eye (16.2%), cheek (15.8%), temple (12.0%), forehead (11.4%), earlobe (9.1%), lips (3.2%)and others with lower frequencies The superficial BCC subtype was more common in photo-protected areas, whereas the nodular BCC subtype occurred on the face [25].

C. NETHERLANDS

Retrospective study between 1985 and 1996 diagnosed and/or treated Departments of Dermatology, Pathology and Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands. Of the 1711 patients, 54% were male and 46% were female. A total of 2990 tumors were registered: 1704 in male patients and 1286 in female patients. The patient group was divided into 97% non-transplant recipients and 3% transplant recipients. Of the first group, 74% had one tumor, 22% had 2–5 tumors, 3% had 6–10 tumors, and 1% had more than 10 tumors. The transplant recipients, of whom 79% were male and 21% were female, had a total of 136 BCC. 58% had one BCC, 31% had 2–5 BCC, 6 % had 6–10 BCC, and 6% had more than 10 BCC.

The nodular BCC was by far the most frequently occurring type, followed by the superficial type. The nodular BCC occurred significantly more often in males and the superficial type more often in females. Infiltrative BCC was also significantly more prevalent in females. The other subtypes were seen equally among the sexes. 69% of all BCC were observed in the head and neck region, 21% on the trunk,3% on the arms, and 5% on the legs. The overall mean age of females at diagnosis of a BCC was significantly lower as compared with males. The mean age of patients at diagnosis of a superficial BCC was significantly lower as compared with the mean age of patients with nodular BCC [57.5 vs. 65.5 y]. Furthermore, the mean age of females with a superficial BCC was significantly lower as compared with males [26].

D. FRANCE

A retrospective study at Laboratoire d'Histopathologie Cutane´e, Clinique Dermatologique des Hoˆpitaux Universitaires de Strasbourg, 1 Place de l'Hoˆpital, France during 1967–96. The study showed 13,457 cases in 10245 patients (M ⁄ F ratio 0.92) of mean age 65±14.44 years (range 6–107). Among patients having multiple BCCs, 1089 had two tumors, 305 had three, 120 had four, 54 had five and 114 had six or more. 83.1% of cases were located on the head, trunk (11.5%), upper limb (3.2%), lower limb (2%) and genitalia (0.2%) and unknown (1.6%). The distribution of histopathological subtypes confirmed the predominance of nodular BCC (78.7%), superficial BCC (15.1%) and morphoeiform BCC (6.2%) and indeterminate in (9%).

Superficial BCCs showed the most striking differences according to gender, predominating on the head and neck in women (44.8% vs.34.7% in men), but on the trunk in men (49.9% vs.42% in women). Men had more nodular BCCs than women (79.9%vs.77.5%); whereas women had more morphoeiform types (7.2% vs. 5.2%). The superficial types represented 14.9% of BCCs in men and 15.3% in women. The M⁄F ratio was 1.02 in nodular BCCs, 0.96 in superficial BCCs and 0.73 in morphoeiform BCCs. The mean age of excision was 66.3±13.9 years in patients with BCC of the nodular subtype, 63±14.2 years in superficial BCC and 65.8 ± 14.2 years in morphoeiform type [27].

2. ASIA

A. Pakistan

A one year prospective study was carried out at the Department of Ophthalmology, Postgraduate Medical Institute, Hayatabad Medical Complex, and Peshawar from September 2001 to August 2002. A total of 30 patients were recruited in the study out of which 17 (57%) were male and 13 (43%) were female. The mean age of the sample patients was 55 years. Clinically the nodular ulcerative type was the most common presentation (36.7%) followed by the nodular type (33.3%) and nodular pigmented (30%).The lower lid was the most frequently affected side (63.3%) followed by the medial canthus (23.33%). The upper lid and lateral canthus were the least involved (6.67%) each area. On histological examination the most common type was nodular (56.67%), basosquamous subtype (13.33%), multifocal (10%), pigmented and adenoid (6.67%) each. Morphoea and the cystic type were the least common (3.33%) each [28].

F. INDONESIA

This was a descriptive retrospective study at General Hospital of Dr. Moh. Hoesin Palembang, between January 2014 and December 2016 based on demographic and clinicohistophatologic data of BCC patients. In this study, they found 193 cases of BCC (0, 02%) from January 2014 - December 2016.Predominantly affected were male patients 104 cases (53.9%) and 89 cases (46.1%) in female. The mean age of BCC is 61.74±11.76. Distribution of BCC were predominantly on the face, mainly the nasal region with 98 cases (50.8%), 11 cases (5.7%) on the neck, 2 cases (1%) on the trunk, and 3 cases (1.5%) on extremities. Regarding the histologic subtype, nodular around 172 cases (89.1%), 10 cases (5.2%) micronodular, 9 cases (4.7%) infiltrative, 1 case (0.5%) superficial and 1 case (0.5%) basosquamous [29].

G. INDIA

A hospital based study was conducted at a tertiary care hospital situated in Punjab. A total of 36 cases of BCC with absolute number of cases 9, 11, and 16 diagnosed per year with in 2011, 2012, and 2013. In regards to gender, males were 36.1% (13/36) and females were 63.9% (23/36) with M: F ratio being 0.57: 1. The age of the patients ranged from 29 - 92 years and mean age was 60.9±14.2 years (65.92 ± 14.35 years for males and 57.96 ± 13.54 years in case of females). The mean duration of disease was 4.7 years (5 months to 15 years). None had features associated syndromes. Out of 36 patients, one (2.8%) had been previously treated for breast and endometrial carcinoma. Majority of patients (88.9%) had a solitary lesion and two (5.6%) had 2 lesions. Majority of cases (97.2%) had lesions confined to head and neck area. The distribution of lesions was as follows; nose (50%), cheeks (22.2%), ear and preauricular area (13.9%), lower eyelid (13.9%), temporal area (5.6%), upper lip (2.8%), forehead (2.8%), scalp (2.8%), and mons pubis (2.8%). The most common morphological subtype of BCC was nodular/noduloulcerative growth (77.8%). A significant percentage of BCC was clinically pigmented (22.2%). The most common histopathological variant was nodular subtype (77.8%) with 16.7% being pigmented, followed by micronodular (19.4%), basosquamous (8.3%), micronodular (2.8%), morpheaform (2.8%), keratotic (2.8%), adenoid (2.8%) and BCC with adnexal differentiation (2.8%) [30].

3. NORTHAMERICA

A. USA

1. A retrospective, population-based (Olmstead County) cohort was identified through the Rochester Epidemiology Project (REP), study period was from January 2, 2000, to December 31, 2010. 3,621 incident BCCs were diagnosed in 3,325 patients. The mean age at diagnosis was 63.4 years and male patients represented 50.2% cases. Incidence rate increased with age for women and at a faster rate for men, with a peak among patients aged 80–89 years. The incidence of BCC in patients younger than 40 years was higher among women than among men. Subsequent BCC diagnosis was at the age of 65.2 years. The most common locations of BCCs for both sexes were the head and neck followed by the torso. The extremities were the least frequent site, but BCCs occurred in the extremities more commonly among women than men. The most common histologic subtype was nodular BCC (n=1,764; 53.1%), followed by superficial (n=679; 20.4%). Men had a statistically greater percentage of the nodular subtype (66.5%) compared to women (56.5%). Conversely, women had a statistically greater percentage of the superficial subtype (28.2%) compared to men (19.1%). A total of 686 tumors (20.6%) were an aggressive subtype or had an aggressive component. There were 68 recurrences (2.0%), with a median of 3.7 years between initial BCC diagnosis and recurrence. The incidence of BCC increased among residents older than 18 years between the 1976–1984 and 2000–2010 periods. The overall age- and sex-adjusted incidence rate increased significantly from 222 to 321.2 per 100,000 persons. The increased incidence of BCC affected both sexes in virtually all age groups [31].

2. They presented the results of a retrospective case series of 17 self-identified black and/or African American patients treated with Mohs Micrographic Surgery (MMS) within a 10-year period (2007 and 2017) at their academic institution. The mean age at diagnosis was approximately 61 years of age, and the majority of patients (82%) were female. 50% of lesions (n = 9) were located in the high-risk area H, while only 11% of lesions (n = 2) were located within the lower risk area L. 70% of the tumors (n = 14) were solely on the head and neck. For most patients, it took more than a year to receive a diagnosis of BCC, with 33% (n = 6) 3 years after first noticing a lesion. 61% of the tumors (n = 11) were pigmented, and 17% of the tumors

(n = 3) were infiltrative. All the identified BCCs, except for one were primary tumors. None had syndromes predisposing to BCCs or had identifiable risk factors for BCCs [32].

4. SOUTH AMERICA

A. BRAZIL

1. This was a cross-sectional study conducted at the Dermatology Outpatient Clinic of the University Hospital of Taubaté from January 1 2008 to December 31 2009 with a confirmed diagnosis of basal cell carcinoma. The study included 239 patients; 138 (57.7%) subjects were male and 101 (42.3%) were female. The mean age of the sample was 68±12.2 years (34-88 years). Most 173 cases (72.3%) patients were older than 60 years. Only 3 (1.2%) cases were detected in subjects under 40 years old and 57 (23.8%) cases were seen in individuals aged between 40 and 60 years. With regard to histological subtypes, the nodular/nodular-ulcerative subtype accounted for 83 (34.7%) cases and superficial subtype with 40 (16.7%) cases. In 179 (74.9%) patients the tumor was located in the head and neck, especially the nose with 51 (28.4%) cases and frontotemporal region with 44 (24.5%) cases; followed by trunk (10.5%) and upper (9.6%) and lower limbs (4.2%). The mean age of onset of superficial BCC was 63.0±11.9 years, while for other subtypes it was 69.0±13.0 years [33].

5. AFRICA

A. Nigeria

A six-year retrospective study at the Ear, Nose and Throat and Plastic and Reconstructive clinics of Lagos University Teaching Hospital with a clinical diagnosis of BCC of the head and neck. The histology reports confirmed basal cell carcinoma in the 60 patients studied. Of these, 45 were males and 15 females. 44 (73.28 %) were Negroid while 16 (26.72 %) were albinoid. The age distribution of the Patients, shows negroids presenting between 3rd and 4th decades while the albinos presented a decade earlier. The commonest site was the nose (48%) followed by forehead (20%) of. Three cases involving the inner canthus (5%) were found. The scalp and the temple were the least common sites. 32 (53.3 %) of the cases were found to be already ulcerated at presentation. Other clinical types observed were: nodular type 13 (21.67 %); pigmented type 8 (13.3 %); and the atrophic scar type 7 (11.67 %) [34].

B.EGYPT

Retrospective study between from January 2015 to December 2019 at Dermatopathology unit of Department of Dermatology and Venereology, Al-Hussein University Hospital, Cairo, Egypt. A total of 80 patients with a total of 105 histologically proven primary BCCs were assessed. As regards the age of the patients, it ranged from 22-84 years with a mean age of 59.7 ± 13.4 years. As regard sex, they were 46 males (57.5%) and 34 females (42.5%). The mean disease duration in all studied patients was 3.1 ± 3.7 (0.25-20 years). 69 patients (86.25%) had single BCC and 11 patients (13.75%) had multiple BCCs. There were 69 lesions (65.7%) in the single BCC subgroup and 36 lesions (34.3%) in the multiple BCC subgroup.

There were 80 lesions (76.2%) in the head, 17 lesions (16.2%) in the trunk and 8 lesions (7.6%) in the extremities. Concerning the clinical types of BCC, there were 41lesions (39%) of ulcerative type, 39 lesions (37.1%) of nodular non pigmented type, 13 lesions (12.4%) of nodular pigmented type, 9 lesions (8.6%) of superficial type and 3 lesions (2.9%) of advanced type. As regards the histological subtypes, 52 lesions (49.5%) were nodular, 11 lesions (15.9%) were pigmented, 9 lesions (8.6%) were adenoid, 9 lesions (8.6%) were superficial, 8 lesions (7.67%) were infiltrative, 7 lesions (6.7%) were micro-nodular, 6 lesions (5.7%) were nodulocystic and 3 lesions (4.3%) were basosquamous [35].

C.SUDAN

This descriptive cross-sectional study was conducted in three main pathology centers in Khartoum State, Sudan, namely the National Health Laboratory (NHL) which a reference laboratory, Omdurman Teaching Hospital (OTH) (A tertiary hospital) and Soba University Hospital (SUH) that a tertiary hospital belongs to Khartoum University, in four years' duration (from the first of January 2010 to the 31 of December 2013). The total numbers of cases were 84 cases were included in this study. A mean age at diagnosis was 56 ±1.75 years. The most common incidence was among the age group 51 - 60 years 40 (46.4%) and 13 (15.5%) were >70 years. Regarding gender distribution 53 cases (63.1%) were females and 31cases (36.9%) were males with a female to male ratio 1.7:1.Total percentage of females <50 years were 21 (39.6%) while males in this age group were 10 (32.3%).

Most cases were seen in the face (89.3%), particularly the nose comprising (31%) of those in the face, followed by trunk (6%). Other sites including the and lower limbs represents (4.8%). Concerning histopathological variants, (54.8%) were nodular variant while infiltrative represents (11.9%), followed by superficial variant (8.3%) and other variants constitute lesser frequencies. About one third (35.7%) of basal cell carcinoma cases were histologically pigmented. Regarding clinical information 4.8% of cases showed the history of recurrence and 2.4% were known cases of Albinism. One case (1.2%) was clinically diagnosed as Xeroderma pigmentosa [36].

E. Ethiopia

A retrospective cross sectional study was conducted between 1999-2000 on patient records of January 1985 and December 1998 within Tikur Anbessa teaching hospital, (pathology Department, Medical faculty, Addis Ababa University). Of the 1087 skin biopsies preformed during the stated period of time, 228 patients with skin cancers were reviewed in this study. The mean ages were 47.6±16.7 years; 50.6±17.9 years for males and 52.9±14.0 years for females. The male to female ratio was 1.2:1 for BCC. The percentage of patients who were older than 40 years of age were 32/38 (84.2%), for BCC, as age of patients increased there was an increase in see and BCC frequencies. BCC was the least common encountered cancer 38/228 (16.7%), and was seen most frequently on the face in 15/38 (39.5%), with the other cases distributed fairly evenly between the remaining sites of the body [7].

6. OCEANIC

A. AUSTRALIA

1. A case series of BCC from a prospective population-based register study collecting information on all excised and histologically confirmed skin cancers in Townsville, north Australia between 1997 and 1999. During the 3-year study period there were a total of 5044 patients with at least one excised histologically confirmed BCC recorded. Most patients (58.6%) were male and the mean ± SD age at first excision of a BCC was 58.3 ± 15.6 years. Most patients (64.6%) had only one BCC, while 6.5% had five or more BCCs excised. Histologically, Nodular BCCs were (48.1%), superficial BCCs (26.2%), infiltrative BCCs (14.2%) and micronodular BCCs (7.8%).

Age-specific incidence rates for different subtypes of BCC rose steadily with age, except for superficial BCC. Patients with at least one superficial BCC were younger (54.7 ± 15.9 years) than other patients (60.6 ± 15.4 years), and females with at least one superficial BCC were younger than respective male patients (52 ± 16 vs. 56.7 ± 15.5). Patients with at least one nodular BCC (62.2% vs. 54.8%) or with at least one infiltrative BCC (62.4% vs. 57.7%) were more likely to be male. Those differences were also apparent in the incidence rates, with a male/female ratio of 1.8: 1 for nodular and infiltrative BCC. For superficial BCC the male/female ratio was notably lower, at 1.3: 1.

In both sexes, body-site distribution for nodular, infiltrative and micronodular BCC was dominated by the face, while superficial BCCs were most frequent on the posterior trunk in males and on the upper extremities in females. For all histological subtypes and both genders relative tumor density was highest for the face, followed by the neck. An exception to this occurred with superficial BCC in males, where the posterior trunk was second, followed by the neck [37].

3. Objective of the study

3.1. General objective

- To evaluate the pattern and magnitude of clinical and pathological characteristics of basal cell carcinoma in ALERT/AHRI, Addis Ababa, Ethiopia, among all biopsy confirmed BCC cases in ALERT/AHRI pathology laboratory, between January 2018 and December 2022 G.C.

3.2. Specific objectives

- To determine the pattern and magnitude of clinical characteristics of patients with biopsy confirmed BCC during the five year period.
- To study the pattern (spectrum) of histologic subtypes between the years 2018 and 2022 G.C.
- To determine the magnitude of BCC from all skin biopsies specimens obtained during the five year period.

4. Methods and Materials

4.1. Study area

The study was conducted at All African Leprosy Rehabilitation Training Center (ALERT) and Armauer Hansen Research Institute (AHRI). ALERT is located in an area locally called Zenebework, Kolfe Keraniyo sub city of Addis Ababa. It was initially established as a treatment center for Hansen's disease (leprosy) and it focuses on rehabilitation of leprosy patients, training programs for leprosy personnel from around the world and leprosy control. The hospital is the main dermatologic center in the country that functions as the referral dermatology institute in and around Addis Ababa, but also gives specialized services in the field of internal medicine, orthopedics, physiotherapy, reconstructive and plastic surgery and ophthalmology.

The histopathology records of the patients in this study were obtained from the pathology laboratory of AHRI. The AHRI (Armauer Hansen Research Institute) was established as a biomedical research institute located next to the All Africa Leprosy Rehabilitation and Training Hospital (ALERT). It was founded in 1970 through the initiative of the Norwegian and Swedish Save the Children organizations seconded by the Ministry of Health of Ethiopia. The Institute got its name from the Norwegian physician, Gerhard Henrik Armauer Hansen, who first described the leprosy bacillus (Mycobacterium leprae). The Pathology laboratory which is one of a number of units in AHRI provides diagnostic laboratory services on histopathology and FNA for patients coming from ALERT hospital. In addition, it is serving as research as well as training facility for students.

4.2. Study period

The study was conducted from May 2023 – Sep 2023 GC.

4.3. Source population

All the patients that visited ALERT Hospital and all biopsies examined at AHRI pathology laboratory for histopathologic evaluation between January 2018 and December 2022 G.C .

4.4. Study population

All patients with histopathologically confirmed diagnosis of BCC in ALERT Hospital /AHRI pathology laboratory between January 2018 and December 2022 G.C.

4.5. Study design

A five year hospital based retrospective cross-sectional study conducted to assess the pattern and magnitude of clinical and pathologic characteristics of BCC cases that were diagnosed during the period of January 2018 to December 2022 G.C in ALERT Hospital /AHRI pathology laboratory.

4.6. Eligibility criteria

4.6.1. Inclusion criteria

- All histopathologically confirmed BCC cases in during the period of January 2018 to December 2022 G.C.

4.6.2. Exclusion criteria

- Cases of biopsy reports that had been re-evaluated and diagnoses changed.
- Cases of histologically diagnosed BCC with incomplete record.

4.7. Sample size determination and sampling technique.

The sample size for this study was all the biopsy confirmed cases of cutaneous BCC at ALERT Hospital/AHRI pathologic laboratory from January 2018-December 2022 G.C.

4.8. Study variables

4.8.1. Variables of interest

- Basal Cell Carcinoma histologic subtype
- Age
- Sex
- Distribution(site)
- Number of BCC lesions
- Environment (urban vs. rural)
- Duration of lesions
- Associated Syndrome/ comorbidity
- Regional state (residence)
- Recurrent or primary BCC
- Lesion morphology
- Case registration year
- Biologic behavior of histologic subtype

4.8.2. Operational definition

- **BCC** - a NMSC that arises from basal cells [48].

- **Histologic subtype**
- ✓ **Nodular BCC** – 'presents microscopically as large nests or islands of malignant basaloid cells with central, haphazard cell arrangement and peripheral palisading, tumor-stroma clefting, mucoid/myxoid stroma with spindle cells, with/without amyloid deposits. It several subtypes, keratotic (with mature keratin deposits found central in the tumor islands), cystic/nodulocystic (cystic degeneration) and adenoid (with cribriform arrangement of tumor nests)' [47], [48].
- ✓ **Superficial BCC**- 'develops as small islands or lobules of malignant basaloid cells with peripheral palisading, localized in the superficial dermis, with a connection to the epidermis and within a myxoid stroma, associated with a lichenoid, band-like, inflammatory infiltrate' [47], [48], [52].
- ✓ **Micronodular BCC** – 'is characterized by small islands or nests of malignant tumor cells which infiltrate deep into the dermis, sometimes even into the subcutaneous tissue; the tumor has a satellite-like arrangement of discrete nodules with irregular contours, lined by a thin margin of stroma and separated by normal dermal collagen' [47], [48], [53].
- ✓ **Infiltrating BCC** - is a subtype composed mainly of chords or thin nests of tumor cells (with a thickness of >5-8 cells) which infiltrate deeply, with angulated edges and have an irregular, permeating invasion pattern at the tumor edge. It frequently overlaps with morphoeic/sclerosing BCC and can be found with a nodular component' [47], [48], [49], [53].
- ✓ **Sclerosing/morphoeic BCC** - 'is comprised of very thin strands/chords of tumor cells (with a thickness of 1-5 cells, and also with angulated ends) found in a collagenous type of stroma, with seldom tumor-stroma clefting. It infiltrates deeply and differs from the infiltrating subtype of BCC by the stromal characteristics, the latter lacking the highly collagenous stroma' [47], [48], [52].
- ✓ **Basosquamous carcinoma (metatypical BCC)** – 'is a subtype characterized by the presence of both BCC and SCC tumor features, with transition areas between the two. The tumor nests are comprised of basaloid cells, which are intermingled with atypical squamous cells with eosinophilic cytoplasm which are dispersed or have a focal distribution; the stroma is oftentimes highly cellular, with a fibrotic appearance' [47], [48], [54].
- ✓ **Pigmented BCC** – 'is a variant of nodular or superficial BCC, which contains melanin pigment derived from an increased number of dendritic melanocytes with in the malignant tumor nests' [47], [48], [55].
- ✓ **Metaplastic carcinoma** - **'**is characterized by a malignant proliferation of basaloid cells found within a sarcomatous stroma with variable histology' [47], [48].
- ✓ **BCC with adnexal differentiation – '**a subtype of BCC exhibiting differentiation towards follicular, eccrine, apocrine or sebaceous glands' [47], [48], [56].
- ✓ **Fibroepithelial BCC** – 'is a distinct variant composed of thin strands of anastomosing basaloid cells with reticular pattern of development, linked to the epidermis and within a fibroblastic stroma' [47], [48], [57].

- **Environment**
- ✓ **Urban** – cities or towns who are densely populated /is any incorporated place with at least 2,500 inhabitants [61].
- ✓ **Rural** - any incorporated place with fewer than 2,500 inhabitants that is located outside of a UA [61].

- **Associated Syndrome/ comorbidity**- condition characterized by a set of associated symptoms [60].

- **Regional state**- The regional state where patient is residing (referring the regional states of FDRE).

- **Primary/ recurrent BCC**

✓ **Recurrent** - refers to cancer that has come back after treatment and a period of time during which there is no trace of the cancer [3], [5], [59].

✓ **Primary** - newly formed BCC for the first time in previously healthy skin [3], [5], [59].

- **Lesion morphology** - form or structure of an individual skin lesion [60].

- **Biologic behavior**

✓ **Aggressive** - micronodular, basosquamous, infiltrative and sclersoing /morphoeic subtype or mixed type including the one of the mentioned subtypes [49], [58].

✓ Non aggressive - all subtypes except the ones mentioned in aggressive types [49], [58].

4.9. Data collection tools and procedures

After obtaining ethical clearance, data was collected from histopathology records of patients visiting ALERT center by using a structured data extraction sheet. The histopathology records of patients diagnosed with cutaneous Basal cell carcinoma during the time period; January 2018 to December 2022 was retrieved and evaluated from AHRI. For any incomplete data their corresponding medical chart records was evaluated. The biopsy specimens had been processed in 10% formalin-fixed, paraffin-embedded tissue sections and stained with hematoxylin and eosin and were examined under a light microscope. The histopathologic examination was carried out in AHRI pathology laboratory and the data was also be retrieved from there. The tumors was be analyzed based on their histologic subtype type and lesion morphology, anatomic distribution, age, sex, environment, census region, number of lesions, primary or recurrent, and duration of lesion before diagnosis.

4.10. Data processing and analysis

Data entering, coding and cleaning and statistical analysis was done using SPSS (Statistical Package for Social science) version 27. Frequency distributions, percentages, tables and charts were used to show descriptive results and Cross tabulations was done to show correlation between study variables. Finally, the study finding was presented using diagrams, tables and figures below**.**

4.11. Data quality management

A pretested data extraction sheet was used. Trained data collectors were involved in data collection. The principal investigator closely supervised and actively participated in the data collection process. Data was checked for completeness, clarity and consistency after being filled each day.

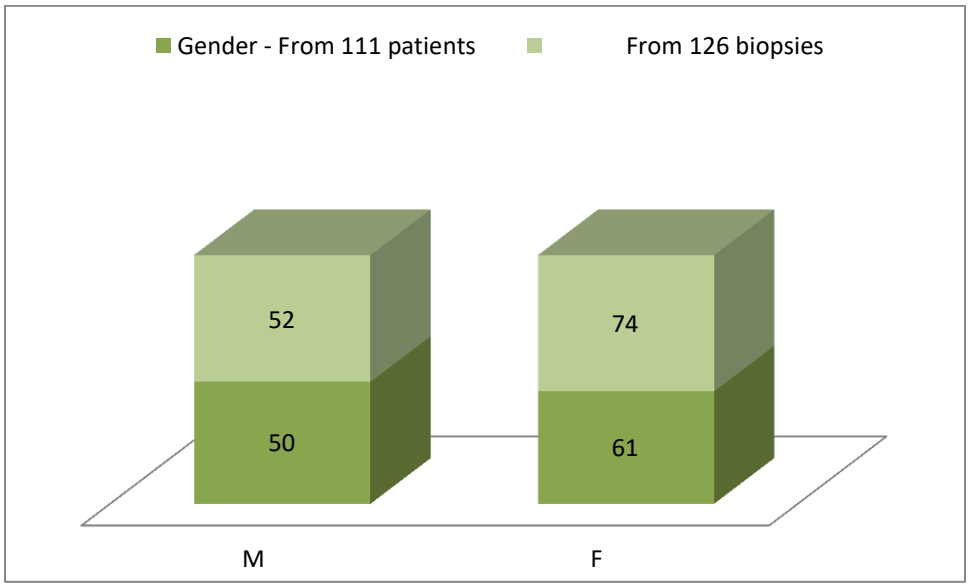
4.12. Ethical considerations

Prior to starting the research, Ethical Clearance was obtained from Institutional Review Board (IRB) of Addis Ababa University. Permission to review patient charts and histopathologic records and Ethical clearance was also obtained from AHRI/AHRI Ethical Review Committee. Any identifying information of the patients was not taken. The data collected was not disclosed and will remain confidential as it was only passed between the investigators listed on this protocol.

5. Results

5.1. Social and demographic characteristics of BCC patients

This study describes a 5-year (January 2018 to December 2022) retrospective study of the pattern and magnitude of BCC at ALERT Specialized Hospital, department of Dermatovenerology and Armauer Hansen Institute, Addis Ababa, Ethiopia. Initially, 155 cases of BCC were collected, however, 29 cases were excluded due to various reasons like incorrect coding, double specimens from one patient (biopsy and surgery), and change of diagnosis; thus, 126 biopsy-confirmed cases from 111 patients were analyzed.
Our research showed, that from 126 biopsy-confirmed BCC cases, 52 cases (41.3%) were from male patients and 74 cases (58.7%) were from female patients an M: F ratio of 1:1.42; From 111 patients, 61 patients (55.45%) were female and 50 patients (45.05%) were male and M: F ratio of 1:1.22 **(Column Chart 1).**



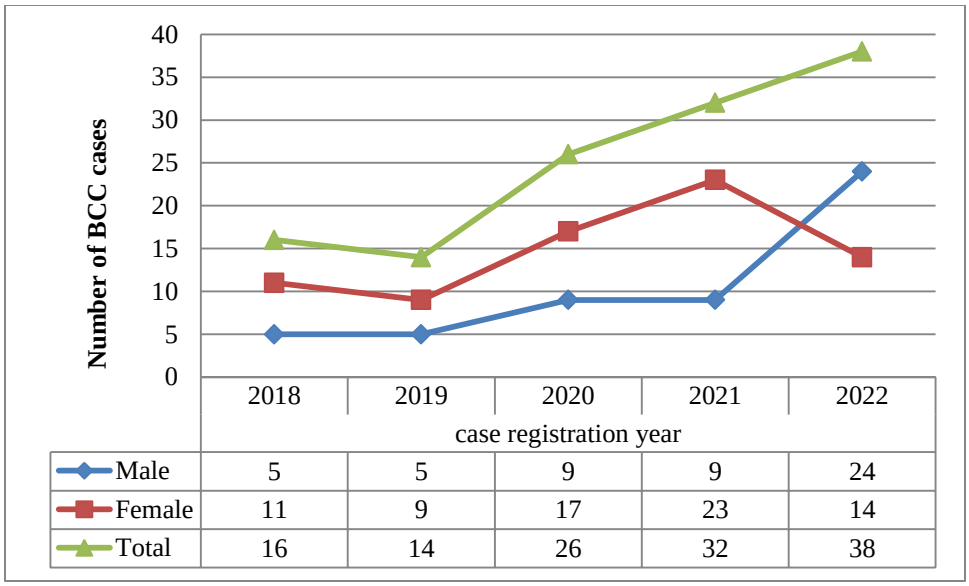
Column Chart 1: Gender distribution of BCC patients

We also found the mean age of BCC patients was 52.74 ±15.22 years (range 16-86 years old). The average age for females was 52.86±15.11 and for males 52.56±15.56 years. The median age was 52.50 years old. As you can see in Table 1 below, age categories with the highest incidence of BCC were age groups of 50-59 years and 60-69 years each having incidence of 32 cases (25.4%). For females, 23 cases (31.1%) were between 50-59 years of age, and 17 cases (23%) were 60-69 years of age; for males, 15 cases (28.8%) were between the age of 60-69 years and 12 cases (23.1%) were between 30-39 years old. Only 26 cases (20.6%) of BCC patients were under the age of 40 with men representing slightly increased incidence (26.9% vs. 16.2%).

Table 1: Social and Demographic characteristics BCC patients

Social and demographic characteristics		*Sex(count/percentages)*		
		Male	*Female*	*Total*
Age(years)	Mean age	52.56±15.5	52.86±15.1	52.74±15.2
	Median age		52.50	
Age category (years)	0-20 years	0(0.0%)	1(1.4%)	1(0.8%)
	20-29 years	2(3.8%)	5(6.8%)	7(5.6%)
	30-39 years	12(23.1%)	6(8.1%)	18(14.3%)
	40-49 years	6(11.5%)	12(16.2%)	18(14.3%)
	50-59 years	9(17.3%)	23(31.1%)	32(25.4%)
	60-69 years	15(28.8%)	17(23.0%)	32(25.4%)
	≥ 70 years	8(15.4%)	10(13.5%)	18(14.3%)
	< 40 years	14(26.9%)	12(16.2%)	26(20.6%)
	≥ 40 years	38(73.1%)	62(83.8%)	100(79.4%)
Environment	Urban	37(71.2%)	56(75.7%)	93(73.8%)
	Rural	15(28.8%)	18(24.3%)	33(26.2%)

From our study, we noticed the number of BCC cases diagnosed increased yearly from the start of our study period in 2018 except for 2019 which saw a slight decrease. 16 cases (12.7%), 14 cases (11.1%), 26 cases (20.6%), 32 cases (25.4%), 38 cases (30.2%) were diagnosed in 2018,2019,2020,2021 and 2022 G.C respectively. Females were in higher percentages (64.3% - 71.9%) than males (28.1%-35.7%) for the first four years of the study but in 2022 G.C males were diagnosed more (63.2% vs. 36.8%) Line Chart 1. The total number of biopsies examined at AHRI pathology laboratory were as follows; 3272 cases (2018), 1533 cases (2019), 1203 cases (2020), 1413 cases (2021), and 1548 cases (2022). When we saw the percentage of BCC from all the biopsies done each year, we found it to be 0.5% (2018), 0.9% (2019), 2.16% (2020), 2.26% (2021) and 2.45% (2022) (Table 2).

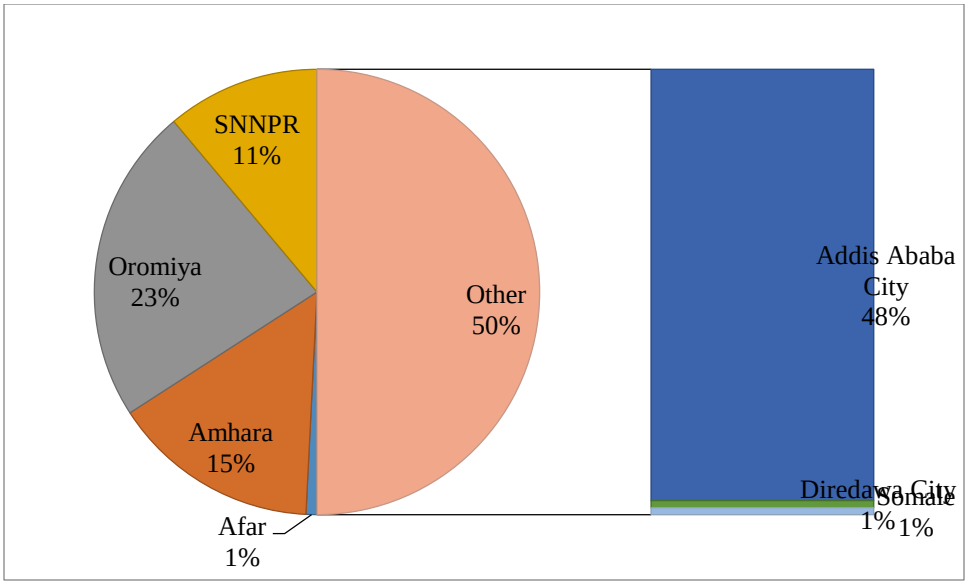


Line Chart 1: Number of BCC cases Diagnosed per year during the study period

Table 2: Proportion of BCC cases/ Total no. of Biopsies

		Total number of biopsies	*Proportion of BCC cases*
Case Registration year	2018	3272	0.5%
	2019	1533	0.9%
	2020	1203	2.16%
	2021	1413	2.26%
	2022	1540	2.45%

Our research revealed that 93 cases (73.8%) of the BCC patients came from urban areas and 33 cases (26.2%) from rural areas, with urban to rural ratio of 2.8: 1. And also 61 cases (48.4%) came from Addis Ababa city administration; 29 cases (23%) were from Oromiya Regional state, 19 cases (15.1%) were from Amhara regional state and 14 cases (11.1%) came from SNNPR state. (Pie Chart 1)



Pie Chart 1: BCC patients Residency (FDRE regional states)

5.2. Clinical characteristics of BCC tumors

Our study revealed the duration of the disease from the first appearance of the tumor to presentation to the ALERT dermatologic department ranged from 2 months to 18 years with mean and median durations of 3.5 ±3.32 and 2.00 years respectively. For females, the mean duration was 3.2±3.26 years, and for males was a 3.92±3.39 year. 52.4% of patients had disease duration of less than 2 years and more female patients presented earlier than male patients (34.1% vs.18.3%), 28.6% had duration of more than 4 years (Table 3).

Clinical characteristics of BCC		*Sex(count/percentage)*		
		Male	*Female*	*Total*
Duration	Mean	3.92±3.39	3.21±3.26	3.50±3.32
	Median	2.00 years		
	Range	0.166 -18 years		
Duration category				
	Less than 2 years	23(44.2%)	43(58.1%)	66(52.4%)
	2-4 years	13(25.0%)	11(14.9%)	24(19.0%)
	At and above 4 years	16(30.8%)	20(27.0%)	36(28.6%)

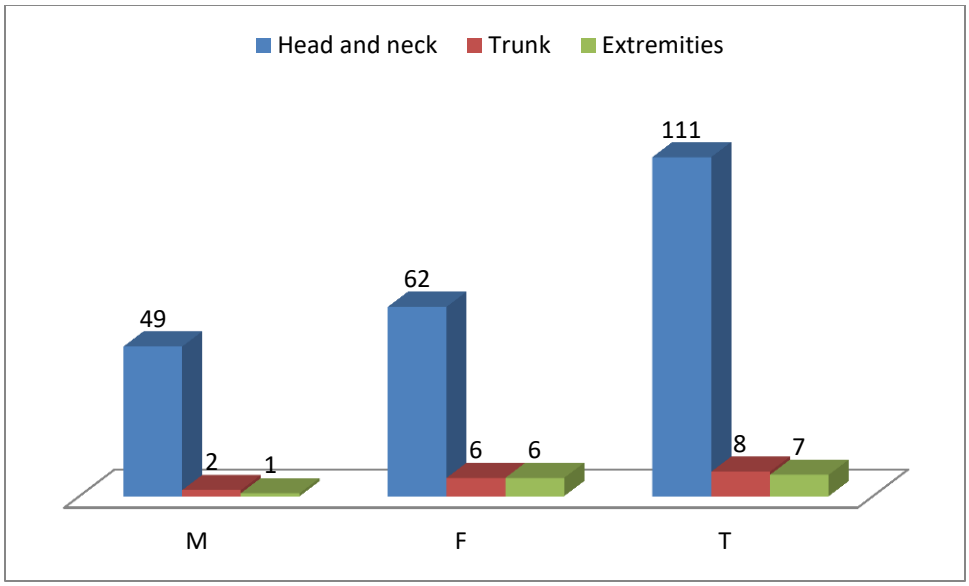
Table 3: Disease duration of BCC patients

As presented below in Table 5, 111cases (88.1%) were Primary BCC tumors and 15 cases (11.9%) were recurrent BCC tumors.

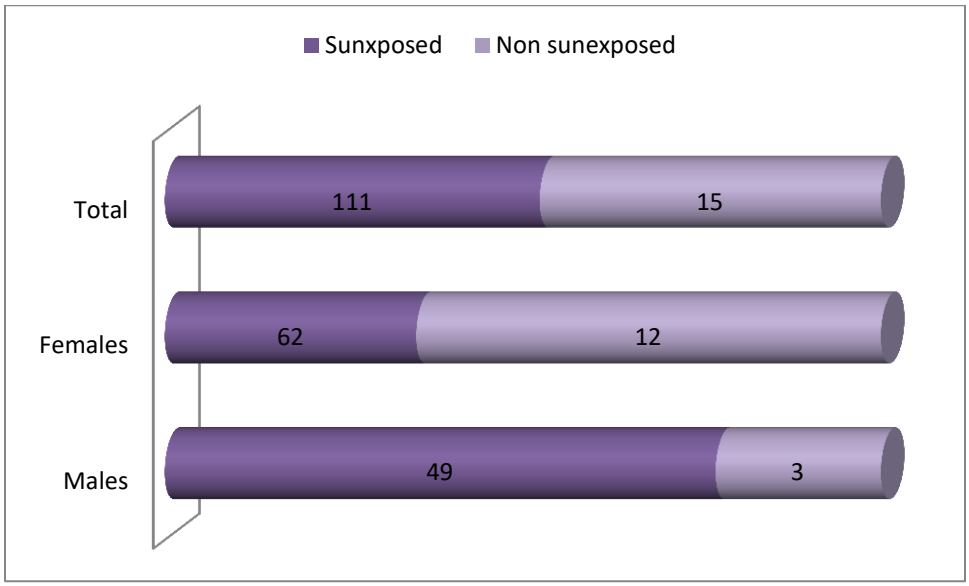
The most common area for tumor location was found to be the nose 31 cases (24.6%), followed by the forehead 21cases (16.7%), Scalp 16 cases (12.7%), and eyelids and cheeks each with 9 cases (7.1%) tumors. For male patients; the nose 14 cases (26.9%), scalp 10 cases (19.2%) followed by forehead 7(13.5%), and cheek 4 cases (7.7%) were the most common tumor locations. For female patients; the nose 17 cases (23%) and forehead 14 cases (18.9%) followed by eyelids and scalp 6 cases (8.1% each) were the most common anatomic areas of tumor location. Scalp, face, and neck were tumor locations in 111 cases (88.1%) of the cases, followed by 8 cases (6.3%) on the trunk and 7 cases (5.6%) on the extremities (Column Chart 2). 111 cases (88.1%) of BCCs were in sun-exposed areas of the body (57% female and 43% male) while 15 cases (12%) of BCC were located in non-sun-exposed areas of the body (Cylinder Bar Chart 1).

Table 4: Anatomic Distribution of BCC cases

Clinical characteristics of BCC		*Sex(count/percentage)*		
		Male	*Female*	*Total*
Anatomic Distribution of BCC tumours	Face	2(3.8%)	3(4.1%)	5(4.0%)
	Ear	1(1.9%)	0(0.0%)	1(0.8%)
	Lips	3(5.8%)	3(4.1%)	6(4.8%)
	Eyelids	3(5.8%)	6(8.1%)	9(7.1%)
	Forehead	7(13.5%)	14(18.9%)	21(16.7%)
	Cheeks	4(7.7%)	5(6.8%)	9(7.1%)
	Temple	1(1.9%)	4(5.4%)	5(4.0%)
	Malar area	2(3.8%)	3(4.1%)	5(4.0%)
	Scalp	10(19.2%)	6(8.1%)	16(12.7%)
	Neck	2(3.8%)	0(0.0%)	2(1.6%)
	Trunk	0(0.0%)	3(4.1%)	3(2.4%)
	Lower extremities	1(1.9%)	6(8.1%)	7(5.6%)
	Submandibular	0(0.0%)	1(1.4%)	1(0.8%)
	Axilla	0(0.0%)	1(1.4%)	1(0.8%)
	Pelvic area	2(3.8%)	2(2.7%)	4(3.2%)

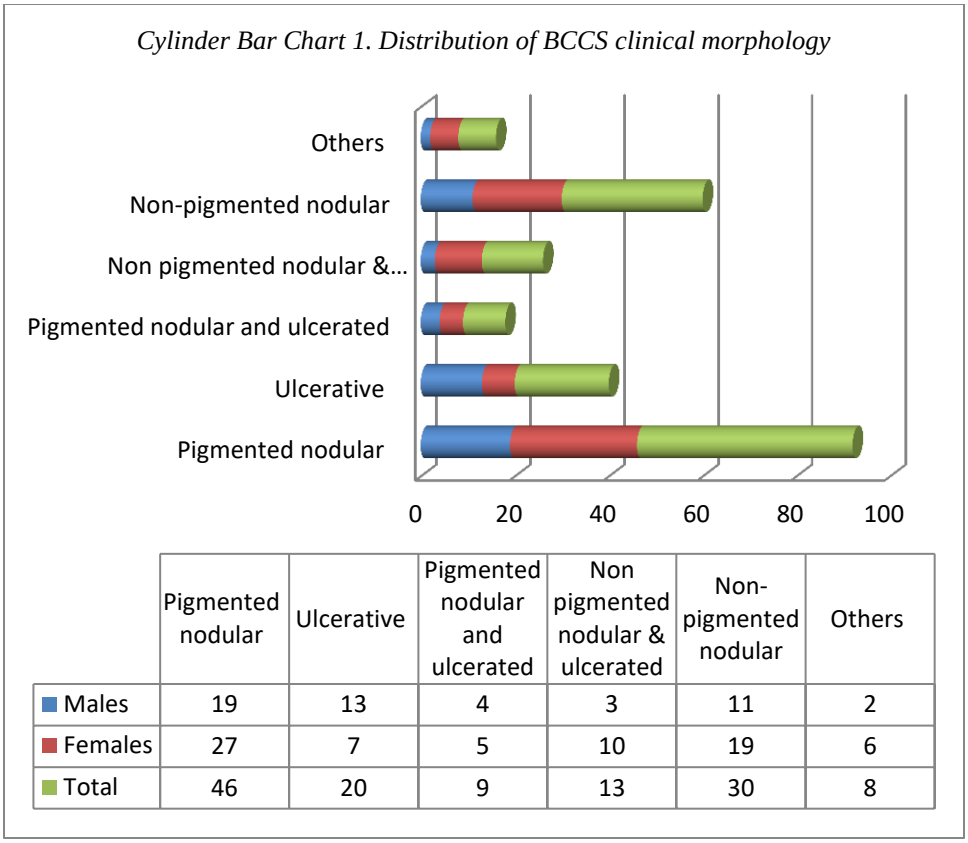


Column Chart 2: Distribution of BCC based on anatomic regions



Cylinder Bar Chart 1: Anatomic Distribution of BCC based on Sun exposure

As illustrated in Bar Chart 1 below, we found that when it comes to the clinical morphology of BCC; pigmented nodular 46 cases (36.5%), non-pigmented nodular 30 cases (23.8%), ulcerative 20 cases (15.9%), non-pigmented nodular & ulcerated 13 cases (10.3%) and pigmented nodular & ulcerated lesions were seen in 9 cases (7.1%) of the cases. Overall, 98 cases (77.7%) of BCC patients had Nodular lesions; 43 cases (34.1%) of patients had ulceration of lesions and 58 cases (46%) of the lesions were pigmented.



	Pigmented nodular	Ulcerative	Pigmented nodular and ulcerated	Non pigmented nodular & ulcerated	Non-pigmented nodular	Others
Males	19	13	4	3	11	2
Females	27	7	5	10	19	6
Total	46	20	9	13	30	8

Bar Chart 1: Clinical Morphology of BCC lesions

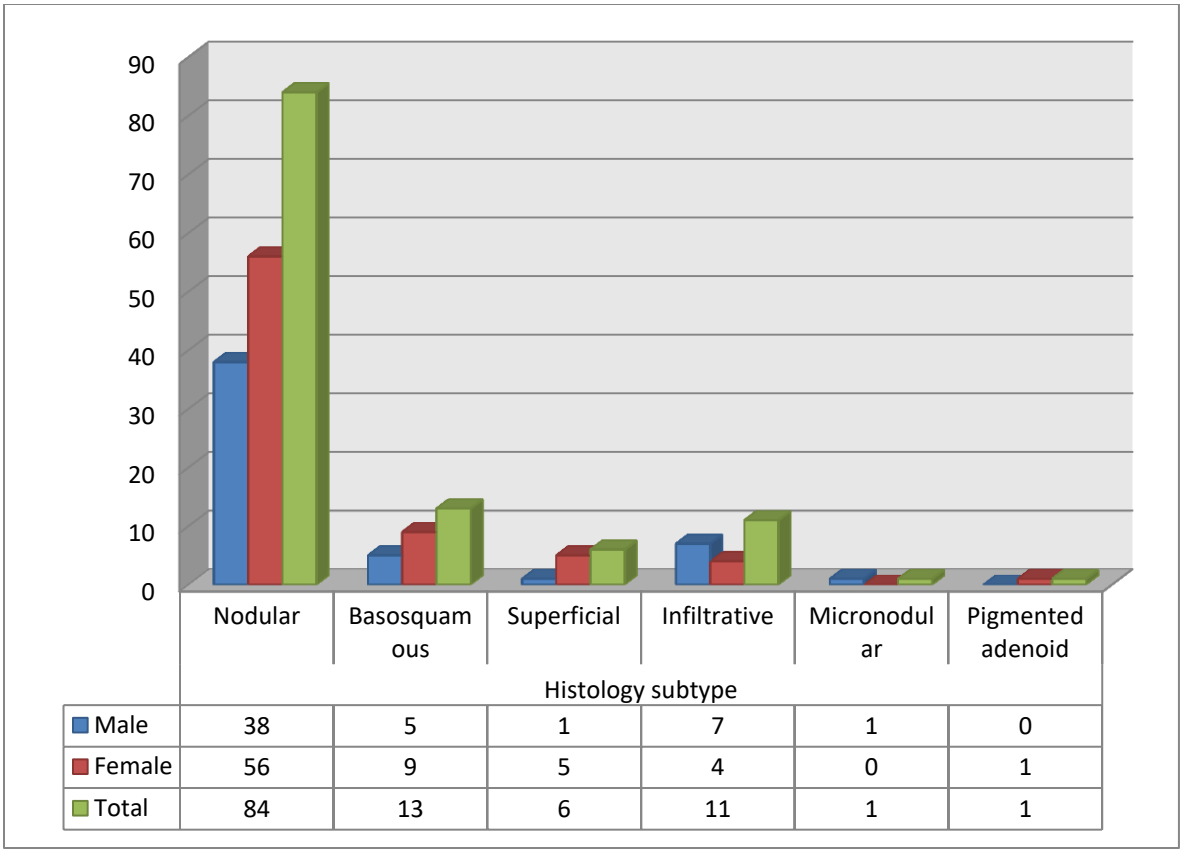
Also, 106 cases (96.36%) of the patients had no known associated syndromes, 1 case (0.9%) patient had XP and 5 cases (4.5%) had a retroviral (HIV/AIDS) infection (Table 5**Error! Reference source not found.**).

Table 5: Clinical characteristics of BCC lesions

Clinical characteristics of BCC		*Sex(count/percentage)*		
		Male	*Female*	*Total*
Number of Lesions	1	51(98.1%)	66(93.6%)	117(96.0%)
	2	0(0.0%)	4(6.4%)	4(3.2%)
	3 or more	1(1.9%)	0(0.0%)	1(0.8%)
Type of BCC				
	Primary	46(88.5%)	65(87.8%)	111(88.1%)
	Recurrent	6(11.5%)	9(12.2%)	15(11.9%)
Associated syndromes	None	50(100%)	55(90.2%)	111(94.6%)
	Xeroderma pigmenteosum	0(0.0%)	1(1.6%)	1(0.9%)
	Retroviral(HIV/AIDS)	0(0.0%)	5(8.2%)	5(4.5%)

5.3. Histopathologic subtypes and variants of BCC

Of the histologic subtypes mostly seen in our research, 84 cases (74.6%) were nodular subtypes followed by 13 cases (10.3%) basosquamous subtype, 11 cases (8.7%) infiltrative subtype, and 6 cases (4.8%) superficial subtype. The nodular subtype is the most common histologic subtype for both sexes. In 7 cases (13.5%) infiltrative subtype is the second most common subtype for male patients while in 9 cases (10.8%) basosquamous subtype was the second most common subtype for female patients (Bar Chart 2). Patients with superficial subtype BCC (52.50±16.59 years) had the youngest mean age at diagnosis while the micronodular subtype (65 years) had the oldest (Table 6).



	Nodular	Basosquamous	Superficial	Infiltrative	Micronodular	Pigmented adenoid
Male	38	5	1	7	1	0
Female	56	9	5	4	0	1
Total	84	13	6	11	1	1

Bar Chart 2: Distribution of histologic subtypes of BCC

Histopathologic characteristics of BCC		*Mean age ± SD at diagnosis(in years)*
Histology subtype	Nodular	52.56±14.51
	Infiltrative	52.64±17.12
	Basosquamus	53.00±20.19
	Superficial	52.50±16.59
	Micronodular	65
	Pigmented Adenoid	56

Table 6: Mean age at diagnosis of Histologic subtypes

As shown in Table 7 below 100 cases (79.4%) are non-aggressive and 26 cases (20.6%) is biologically aggressive. Overall, BCC with a non-aggressive type and single subtype were the dominant based on histologic features. Most subtypes were nodular for the single non-aggressive type and infiltrative and basosquamous for aggressive types.

Histopathologic characteristics of BCC		*Sex(count/percentage)*			*Mean age at diagnosis*
		Male	*Female*	*Total*	
Biologic behavour					
	Aggressive	13(25.0%)	13(17.6%)	26(20.6%)	53.77±17.32
	Non-aggressive	39(75.0%)	61(82.4%)	100(79.4%	52.47±14.71
No. BCC subtypes					
	Single type	52(41.7%)	74(57.3%)	126(100%)	
	Mixed type	0(0.0%)	0(0.0%)	0(0.0%)	

Table 7: Histologic variants of BCC

6. Discussion

6.1. Analysis based on social and demographic characteristics of BCC patients

From 126 biopsy confirmed BCC cases from 111 patients, 50 patients (45.04%) were male, 61 patients (54.95%) were from female patients, with a M: F ratio of 1:1.22. These results were similar to those of publications by Mateoiu et al. [24], Gupta et al. [32], Suleiman et al. [36], and Kumar et al.[30] described female predominance. However, most including Bastiaens et al.[26], Scrivener et al.[27], Muzic et al.[31], Hussain et.al.[28], Maradong et al.[29], Ferreira et al.[33], Ademiluyi et al.[34], Al-Bayomi et al.[35] consistently shown increased incidence of Basal cell carcinoma in male patients. The possible reasons for our findings could be; that the trend of increasing incidence of BCC in female patients [3] and females having more health-seeking behavior could be another reason [66]. However additional studies about occupation, sun exposure habits, genetics, immunosuppression, and other possible risk factors need to be assessed to know the exact reasons.

In our study, the Mean ages of the patients were 52.74 ±15.22 years (16-86 years). Most of our patients were in age categories 50-59 and 60-69 years each had a 25.4% incidence and only 20.7% of patients were younger than 40 years of age. When we compared our findings with other studies; A study from our country done by Bezabih et al. revealed that mean ages were 47.6±16.7 years (50.6 ±17.9 years for males and 52.9 ±14.0 years for females); the percentage of patients who were older than 40 years of age were 32/38 (84.2%) which were lower than our findings except for the mean age for females which is comparable to ours and proportion of patients over 40 years which was slightly higher than ours [7]; Hussain et.al. found a mean age of patients was 55 years [28] And Suleiman et al. reported a mean age 56 ±1.75 years The most common incidence was among the age group 51 - 60 years 40 (46.4%) and 13 (15.5%) were >70 years which is comparable to our findings [36]. Whereas most researchers showed higher mean age including, Al-Bayomi et al. mentioned a mean age of 59.7 ± 13.4 years [35],Scrivener et al. reported mean age 65±14.44 years (range 6–107) [27]; Maradong et al. found a mean age of 61.74±11.76 [29]; Kumar et al. found a mean age 60.9±14.2 years (65.92 ± 14.35 years for males and 57.96 ± 13.54 years in case of females) [30]; Muzic et.al found a mean age of 63.4 years [31]; Gupta et al. showed a mean age 61 years of age[32]; Ferreira et al. recorded a mean age of 68±12.2 years [33]; Ciążyńska et al. reported the mean age of men was 70.9±11.4 years and that of women was 71.4 ± 11.9 years [25]. The reason for these findings could be related with old age increased cumulative sun exposure and accumulated mutations in cancer causing diseases [12]. Why the mean age was lower than most studies could be another reason could be our life expectancy is lower (67.1 years old) [45], than other countries which might explain some of the discrepancies. Also, older individuals in our country usually don't know the exact year they were born rather the time period and when asked about it they give an approximation rather than exact

date. And socio-economic and cultural factors regarding sun exposure, occupation, genetics and other risk factors of BCC could be one factor, all of which need additional study to verify.

We found that the majority of our BCC patients 73.8% came from urban areas and 26.2%were from rural areas, with urban to rural ratio of 2.8: 1. Similar to our findings Zargaran et al. reported among his patients 68.02% were from urban and 31.98% were from rural regions [39]; Cocuz et al. revealed 51% were from urban areas, and 49% were from rural areas [41]. While others had different outcome than ours including Mateoiu et al. found 37.13% came from urban and, and 62.87% from rural areas [24]; Hakimi et al. shown more cases of BCC among residents of rural (60.78%) rather than urban region (39.13%) [46]. On one hand, the urban population usually has more access to healthcare centers, therefore, resulting in more registered cases of BCC in urban areas. The type of occupation was not recorded for the patients which might be a factor and other cultural, social, and economic factors also could play a role producing the necessary risk factors (sun exposure, immunosuppression, genetic disease, radiation exposure) for the development of BCC and will need a study to determine the exact reasons for this finding.

In this study, 48.4% came from Addis Ababa city administration; 23% were from Oromiya Region state, 15.1% were from Amhara region state and 11.1% came from SNNPR state. As expected the study center's location is an important factor in determining patients from which areas seek treatment. ALERT Hospital is located in Addis Ababa, Ethiopia, and the majority of the patients came from Addis Ababa (48.4%) and the surrounding Oromiya region (23%). Whether any other factors other than proximity to the Alert hospital have any role in incidence rate differences will need further study.
The number of BCC cases increased yearly from the start of our study period in 2018 except for 2019 which saw a slight decrease in the number of Cutaneous BCC cases diagnosed. That aligns with other studies from different parts of the world including Cocuz et al. [41], Ciążyńska et al. [25], Jurčiukonytė et al. [45], and Muzic et.al [31] that showed variable degrees of increment in the cases of bcc diagnosis in their respective study years. The reasons for this could be better diagnosis and management of BCC patients by health professionals and increased access to health care services. Whether the increasing trend of BCC patients ALERT/AHRI center translates into increased incidence in general population needs a study.

6.2. Analysis Based on clinical features of BCC

The duration from the first appearance of the tumor to presentation to the ALERT dermatologic department ranged from 2 months to 18 years with a mean duration of 3.5 ±3.32 years and a median duration of 2 years. Kumar et al. reported a disease duration ranging from 5 months to as long as 15 years, with the mean duration being 4.7 years [30], which was slightly longer than ours. Kasumagic-Halilovic et al. reported duration of the disease ranged from 1to120 months (18 months for both genders on average) [42], which were shorter than ours. Comparable duration had been reported by El-Khalawany et al. with a mean duration of BCC was 3.9± 3.8 years [43] and Al-Bayomi et al. with a mean duration of 3.1 ± 3.7 years with a minimum duration of 0.25

year and maximum duration of 20 years [35]. The slow-growing nature of the disease, the lack of knowledge about skin cancer by the patients and health professionals, and the absence of dermatologists other than in urban areas may contribute to the long duration of illness before basal cell carcinoma is ultimately diagnosed.
In our study, 111 (88.1%) were Primary lesions and 15(11.9%) were recurrent lesions. Bartos et al.[44], Suleiman et al.[36], Bartoŝ et al.[40] and Kasumagic-Halilovic et al.[42] and reported overall recurrence rates of 4.1%, 4.8%,4.9%, and 9.7% respectively which was lower than ours. Most cases of recurrence were caused by incomplete excision. Why the rate of recurrence was higher than in other studies needs investigation but skill, experience of the surgeon, the margin of excision used, BCC histologic subtype, and anatomic location of tumors may be possible factors.

The most common area for BCC tumor location was found to be the Nose (24.6%) followed by Forehead (16.7%) and Scalp (12.7%).111 cases (88 %) were on sun-exposed areas of the body. Similar findings to our research include Mateoiu et al.[24]; Ciążyńska et al.[25]; Ferreira [33]; Scrivener et al.[27]; Suleiman et al.[36]; Maradong et al.[29]; Kumar et al.[30] and Al-Bayomi et al.[35] who found that sun-exposed areas of the body and nose were the most common BCC tumor locations. This is easily explained by the fact that BCC is strongly associated with UV exposure [2] and head face & neck areas are directly exposed to sunlight and UV radiation.
When it comes to the clinical morphology of BCC; pigmented nodular (36.5%) followed by non-pigmented nodular (23.8%) and ulcerative (15.9%) lesions were most commonly seen. 77.1 % of patients had nodular lesions, 34.1% of patients had ulceration of lesions and 46% of the lesions were clinically pigmented. Hussain et al. reported the nodular ulcerative type was the commonest presentation (36.7%) followed by the nodular type (33.3%) and nodular pigmented (30%) [28]. Al-Bayomi et al. showed 41 lesions (39%) of ulcerative type, 39 lesions (37.1%) of nodular non-pigmented type, 13 lesions (12.4%) of nodular pigmented type, 9 lesions (8.6%) of superficial type and 3 lesions (2.9%) of advanced type [35]. The studies reveal more or less similar picture that nodule, pigmentation and ulcerations are the main clinical morphologies seen in BCC lesions.

In Terms of number of BCC lesions on a patient, from 126 biopsies taken ,117 were single lesions (95.9%), 4 patients with 2 lesions (3.27%) and 1 patient with 3 lesions (0.8%).Similar to our study, most publications including Scrivener et al.[27], Kumar et al. [30], Al-Bayomi et al.[35], Raasch et al.[38] demonstrated the majority of their patients presented with a single lesion, even though the percentage of patients with multiple BCC lesions in our study was smaller than others.

Patients with younger onset of age, and multiple lesions of BCC tend to have multiple risk factors like inherited BCC-associated syndromes like XP, arsenic exposure, and immunosuppression [16] all of which we clinically see less often in our clinical setup and confirmed in our study were we found only 6/111 patients had associated immunosuppression (RVI) or genetic syndrome like XP, which may explain why few number of patients we have with multiple lesions. Our patients have Fitzpatrick’s skin type III to VI and BCC incidence is

lower in dark skin because of the inherent photoprotection of melanin and melanosomal dispersion [6].

6.3. Analysis based on histologic subtypes and variants of BCC

The histologic subtypes seen in our research were 84 cases (76.4%) nodular subtype followed by 13 cases (10.3%) basosquamous subtype, 11 cases (8.7%) infiltrative subtype, 6 cases (4.8%) superficial subtype and other subtypes with lesser frequencies of BCC cases. Similar to our study Ciążyńska et al.[25], Kumar et al.[30], Ferreira et al.[33], Al-Bayomi et al.[35], Hussain et al.[28] and Maradong et al. [29] all reported nodular subtype was the most common subtype of BCC. Also, we found 25 cases (19.8%) of the BCC patients showed pigmentation on histology; Kumar et al.[30], Al-Bayomi et al.[35] and Suleiman et al. [36] also showed BCC pigmentation on histology in 16.7%, 15.9%, and 35.7% of the tumors which was lower than ours in the first two studies and higher in the case of the last study compared to ours. We also found that patients with Superficial BCC had the youngest mean age (52.50±16.59 years) at diagnosis while micronodular BCC had the oldest patient (65 years). Like our study Ciążyńska et al. [25], Raasch et al.[38] and Muzic et al.[31] described patients with superficial BCC had the youngest age at diagnosis.

We also found that 20.6% of histology subtypes had aggressive biological behavior similar figure was reported by Muzic et al. [31]. Our study only showed single type histology in all of our patients.

7. Conclusion

According to our findings, basal cell carcinoma is a less commonly encountered malignancy. BCC predominantly occurred in female patients in our study. The incidence increased as the patient's age increased, 80% of BCCs occurred above the age of 40 years. The median duration before diagnosis was 2 years. Nodular skin lesion with or without pigmentation and with or without ulceration is the most common clinical morphology found. And the majority of the patients had single BCC lesions. The majority of the patients had no associated syndromes. However, 4.5% had HIV infection and 0.9% had XP. We found the majority of BCCs were primary BCCs (88.1%). The most common location of BCC was on sun-exposed areas of the skin, especially, the face and scalp. The nose is the single most common site for BCC. The most common type of histologic variant seen in our study was the nodular subtype. All the BCC cases had single-type histology. The majority of BCCs had nonaggressive biological behavior.

8. Recommendations

To reduce the incidence and morbidity associated with a late diagnosis of basal cell carcinoma, we recommend efforts to increase public awareness/health education about basal cell carcinoma. Prospective studies with the involvement of specialists (dermatopathologists and dermatosurgeons) to find the risk factors and treatment outcomes of Basal cell carcinoma. To increase the awareness among public health professionals to pick basal cell carcinoma early and minimize the morbidity associated with a late diagnosis. We suggest that the present data collection methods be revised by providing training to healthcare professionals to improve their understanding of how to properly record the information about detected lesions. We recommend changing the traditional paper-based patient data recording method to a computerized one, where all the necessary information regarding the patient can be preserved and personal biases in recording medical information would improve.

9. Strengths and Limitations of the study

9.1. Strengths

It is the first study on cutaneous BCC (on its own) done in our country. We gathered the socio-demographic and clinical characteristics of BCC patients in Ethiopia, which will help health professionals diagnose early and minimize morbidity. It can be used as a stepping stone to do research regarding the risk factors of BCC and treatment outcomes of different management options. It can also be used to generate information regarding BCC for raising public awareness about cutaneous BCC.

9.2. Limitations

The fundamental drawback of this study is the retrospective nature and the data collected depended on the written histologic and clinical records. This is a hospital-based study which makes it impossible to extrapolate the study to the general population. The histologic and clinical data have been recorded by different health professionals which makes it difficult because of the lack of uniformity of data recorded. Insufficient data regarding the information of skin phenotype, family history, size of the lesions, rate of exposure to sunshine, occupation, physical and chemical protective usages, depth of invasion, treatment margin and follow-up information, etc. made it difficult to obtain accurate reports and reach clear reasons for the studied cases.

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APPENDIX I: QUESTIONNAIRE (Q) and Informed Consent – English version

Questionnaire that was used to assess the pattern and magnitude of the clinical and pathological characteristics of cutaneous basal cell carcinoma at ALERT Hospital/AHRI pathology laboratory, Addis Ababa, Ethiopia.

1. **Informed consent**

   I, the undersigned individual, I am oriented about the objective of the study. I have informed that all of my information will be kept confidential and used only for this study. Your signature below indicates that you have read /or listened, and understand the information provided for you about the study. Before you sign, please understand purpose of the study, procedure, risks and benefits of participation, right to refuse or withdraw, confidentiality and privacy and who to contact if you have any question. I have read /or listened to the description of the study and I understand what procedures are and what will happen to me in the study. Based on the above information I agree to participate in the research

   Signature: _____ Date: _____

   if you have any question, you can ask the principal investigator Mobile: +251924517741

Medical record number = ____

Part 1 - Socio-demographic data of the patient

1) Age (years) = _____
2) Sex
   A. Male
   B. Female
3) Environment
   A. Urban
   B. Rural
4) Ethiopian census Region
   A. Tigray
   B. Afar
   C. Amhara
   D. Oromiya
   E. Benshangul
   F. SNNPR
   G. Gambela

H. Addis Ababa
I. Diredawa
J. Somalia

5) Case registration year =____

Part 2. Clinical characteristics of BCC tumors

6) Location of the tumor(s) =____
   A. Face
   B. Ear
   C. Nose
   D. Lips
   E. Eyelid
   F. Forehead
   G. Cheek
   H. Temple
   I. Malar
   J. Scalp
   K. Neck
   L. Trunk
   M. Upper Extremities
   N. Pelvic Area
   O. Lower Extremities
   P. Others, specify____
7) Clinical morphology of lesion
   A. Nodular, pigmented
   B. Nodular,non pigmented
   C. Sclerosing
   D. Keratotic
   E. Superficial
   D. Ulcerative
   F. Other, specify
8) Number of lesions =____
   A. 1
   B. 2
   C. 3 or more

9). BCC type
   A. Primary
   B. Recurrent

10). Associated syndrome

D. None
E. Xeroderma pigmentosum
F. Gorlin syndrome
G. Rombo syndrome
H. Bazex-Dupre-Christol syndrome
I. Other, Specify = _____

Part 3. Histopathologic characterstics of BCC

11). Histologic subtype =____

J. Nodular
K. Superficial
L. Morphiaform
M. Infiltative
N. Infundibulocystic
O. Fibroepithelioma of pinkus
P. Pigmented
Q. Mixed, specify:
R. Other, specify: ____
S. Unclassified, specify: ____

12). Number of Histology subtypes/lesion

A. Single type
B. Multiple type

13). Biologic behavior

T. Aggressive
U. Non aggressive

APPENDIX II: - መጠየቅ እና በመረጃ የተደገፈ ስምምነት የአማርኛ ቅጂ

አዲስአበባ ዩኒቨርሲቲ የቆዳ እና አባላዘር ህክምና ትምርት ክፍል

የ ቆዳ ካንሠር (basal cell carcinoma) ክሊኒካዊ እና ፓቶሎጂያዊ ባህሪያት ንድፍ እና መጠን

መለያ ጥናት ውጤት መሙያ ፎርም ከጥር 2018 እስከ ታህሣሥ 2022 እ.ኤ.አ

1.በመረጃ የተደገፈ ስምምነት

እኔ፣ የተፈረመበት ግለሰብ፣ እኔ የጥናቱ አላማ ላይ አተኩራለሁ. ሁሉም መረጃዎቼ በሚስጥር እንደሚጠበቁ እና ለዚህ ጥናት ብቻ እንደሚውሉ አሳውቄያለሁ. ከዚህ በታች ያለው ፊርማዎ እንዳነበቡ/ወይም እንዳዳመጡ እና ስለ ጥናቱ የቀረበልዎትን መረጃ እንደተረዱ ያሳያል. ከመፈረምዎ በፊት፣ እባክዎን የጥናት፣ የአሰራር ሂደት፣ ስጋቶች እና የተሳትፎ ጥቅሞች፣ የመከልከል ወይም የመውጣት መብት፣ ሚስጥራዊነት እና ግላዊነት እና ማንኛውም ጥያቄ ካለዎት ማንን ማግኘት እንደሚችሉ ይረዱ.

የጥናቱን መግለጫ አንብቤአለሁ/ወይም አዳመጥኩ እና በጥናቱ ውስጥ ምን አይነት ሂደቶች እንዳሉ እና ምን እንደሚደርስብኝ ተረድቻለሁ. ከላይ ባለው መረጃ መሰረት በጥናቱ ለመሳተፍ እስማማለሁ

ፊርማ: _____ ቀን: _____

ማንኛውም ጥያቄ ካለህ ዋናውን መርማሪ ሞባይል መጠየቅ ትችላለህ፡ +251924517741

i. የታካሚዎች ማህበራዊ እና ስነ-ሕዝብ ባህሪያት

1. ካርድ ቁጥር=_____
2. እድሜ=____
3. **ጾታ**
   - ሀ. ወንድ
   - ለ.ሴት

3.አካባቢ

- ሀ.ከተማ
- ለ.ገጠር

4.ክልል

- ሀ.ትግራይ
- ለ.አፋር
- ሐ.አማራ
- መ.ኦሮምያ

ሠ.ቤንሻንጉል

ረ.ደቡብ

ሰ.ጋምቤላ

ሸ.አዲስአበባ

ቀ. ድሬዳዋ

በ.ሶማሌ

iii. **የ BCC ቁስል ክሊኒካዊ ባህሪያት**

1. **ካንሠሩ የወጣበት የሠውነት ክፍል**

ሀ. ፊት

ለ.ጀሮ

ሐ.አፍንጫ

መ.ከንፈር

ሠ.የአይን ሽፋን

ረ. ግንባር

ሰ.ቴምፕል

ሸ.ጉንጭ

ቀ.ራስ

በ.አንገት

ተ.ትረንክ

ቸ.እጅ,(አፐር ኤክስትሪሚቲስ)

ነ.ብልት አካባቢ

ኘ.እግር(ሎወር ኤክስትሪሚቲ)

አ. ሌላ የሠውነት ክፍል_____

2. የካንሠር ቁስል ቅርጽ

ሀ. ጥቁር እብጠት

ለ. ያልጠቆረ እብጠት

ሐ. ጠባሣ መሣይ(ስክሎረሢንግ)

መ.ኬራቶቲክ(ክንታሮት መሣይ)

ሠ.ሡፐርፊሻል

ረ. ሌላ አይነት, ግለጽ_____

3. **የካንሠር እጢወች ብዛት**

ሀ.1

ለ.2

ሐ. 3 ወይም ከዛ በላይ

4. **የካንሠር አይነት**

ሀ. የመጀመሪያ

ለ. ተመልሶ የመጣ

5. **ተያያዥ ህመም**

ሀ. የለም

ለ. ዜሮደርማ ፒግመንቶሠም

ሐ. ጎርሊን ሲንድሮም

መ.ሮምቦ ሲንድረም

ሠ.ባዜክስ ዱፕሬ ክሪስቶል ሲንድረም

ረ. ሌላ, ግለጽ_____

III. **የቢሲሲ (BCC) የስነ ደዌ አይነት ሂስቶፓቶሎጂካል ባህሪያት**

1. **የቢሲሲ (BCC) የስነ ደዌ ንዑስ ዓይነቶች**

ሀ. የለም

ለ.ሡፐርፊሻል

ሐ.ሞሮፊያፎርም

መ.ኢንፍልትሬቲብ

ሠ.ኢንፈንዲቡሎሲስቲክ

ረ.ፋይብሮኢፒቴሊዉማ ኦፍ ፒንከስ

ሰ.ድብልቅ_____

ሸ. ፒግመንትድ

ቀ.ሌላ,_____

በ. ያልተመደበ

2. **የካንሠሩ ጸባይ**

ሀ.አደገኛ አይነት

ለ.አደገኛ ያልሆነ

3. **የሂስቶሎጂ ንዑስ ዓይነቶች ብዛት**

A.ነጠላ ዓይነት

B.ብዙ ዓይነት