



Spectrum of Skin Cancer in Kashmiri population: Seven year study in a tertiary care hospital

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Abstract:

Background: Cutaneous malignancies arise from skin and have the ability to invade or spread to other parts of the body, can cause significant morbidity and mortality especially if treatment is delayed. This study was done to determine the clinical and pathological pattern of skin cancer in the population of Kashmir.

Material and methods: Total number of 791 cases were collected and incorporated in the study. Before taking up of cases careful clinical and radiological findings were also taken into consideration. The tissue samples were Formalin-fixed paraffin-embedded (FFPE) followed by routine Hematoxylin and Eosin (H & E) staining.

Results: In our study we found that the most common cutaneous malignancy in Kashmiri population is squamous cell carcinoma which was reported in 63.59% (503) patients, this was followed by basal cell carcinoma which was reported in 23.64% (187) patients while malignant melanoma was reported in 12.76% (101) patients. Majority of the cases 89.76% (710) were above the age of 40 years while 10.24% (81) were below age 40 years. We observed in our study that cutaneous malignancies were more common in the male patients. The male to female ratio for squamous cell carcinoma was observed to be 1.92:1. The most common sites for squamous cell carcinoma were observed to be lower abdomen & inner thighs. Majority of the basal cell carcinomas presented in the head and neck region while Malignant Melanoma was more frequently reported on the backs, shoulders and the lower limbs.

Conclusion: Complete and in depth understanding of epidemiology of skin can provide basis for disease prevention. The various treatment options for skin cancer include surgery, radiation therapy, chemotherapy, and targeted therapy all of which are most effective when applied at the earliest stage.

Keywords: Skin cancer, Squamous cell carcinoma, Basal cell carcinoma, Malignant melanoma.

Introduction:

Skin cancers are malignancies that originate from the skin which is the thin layer of usually soft, flexible outer tissue covering the human body. They are due to the development of abnormal cells that have the ability to invade or spread to other parts of the body (1). There are three main types of skin

cancers (i) Basal cell carcinoma (BCC) (ii) Squamous cell carcinoma (SCC)

(iii) Malignant melanoma. The first two along with other rare type of skin cancers are known as non-melanoma skin cancer (NMSC). It is estimated that total number of new cases of Non-melanoma skin cancer both sexes, all ages for the year 2020 was 1,198,073 and the number of deaths in 2020, both

sexes, all ages was 63,731 this comprised 6.2% of all the malignancies reported in the year 2020 (2). The total number of new cases of melanoma skin cancer both sexes, all ages for the year 2020 was 324,635 and the number of deaths in 2020, both sexes, all ages was 57,043 (3).

Exposure to sunlight is considered as the most important risk factor for the development of skin cancer. More than 90% of cases are caused by exposure to ultraviolet radiation from the Sun (4) Exposure has increased, partly due to a thinner ozone layer (5) (6). Tanning beds are another common source of ultraviolet radiation (4) For melanomas and basal-cell cancers, exposure during childhood is particularly harmful (7) For squamous-cell skin cancers, total exposure, irrespective of when it occurs, is more important (4). Squamous cell carcinoma often develops from precursor lesions which are called actinic keratosis caused by UV-induced DNA damage that is associated with mutations in TP53 and other genes that also are frequently mutated in squamous cell carcinoma of the skin and with age progression the probability of developing squamous cell carcinoma increases. Between 20% and 30% of melanomas develop from moles (7) People with lighter skin are at higher risk (8) (9) as are those with poor immune function such as from medications or HIV/AIDS (5) (10).

Basal-cell cancer grows slowly and can damage the tissue around it but is unlikely to spread to distant areas or result in death (5). It often appears as a painless raised area of skin that may be shiny with small blood vessels running over it or may present as a raised area with an ulcer (8). Squamous-cell skin cancer is more likely to spread (5). It usually presents as a hard lump with a scaly top but may also form an ulcer (11). Melanomas are the most aggressive. Signs include a mole that has changed in size, shape, colour, has irregular edges, has more than one colour, is itchy or bleeds (12). Around 84% of the cases of melanoma present with localized disease, 9% with involvement of regional lymph nodes, and 4% present with distant metastases at diagnosis (13).

Decreasing exposure to ultraviolet radiation and the use of sunscreen appear to be effective methods of

preventing melanoma and squamous-cell skin cancer (7) (14). It is not clear if sunscreen affects the risk of basal-cell cancer (14). The various options available for treatment of skin cancer include combination of surgery, chemotherapy, radiation therapy and targeted therapy. Melanoma has one of the higher survival rates among cancers, with over 86% of people in the UK and more than 90% in the United States surviving more than 5 years (15) (16). In the best hands, five year cure rates for excision, curettage and cautery, and cryosurgery for basal cell carcinoma are in the order of 95% or better (17) (18) (19). Primitive SCC is often indolent tumours and with early and correct treatment they rarely develop metastases, with a 5-year survival rate of 90% (20). The evaluation of the clinical and histological characteristics of skin cancer at its earliest is the most fundamental step in acquiring relevant prognostic information, applying appropriate therapy and leads to a reduction in the incidence of metastases and recurrences.

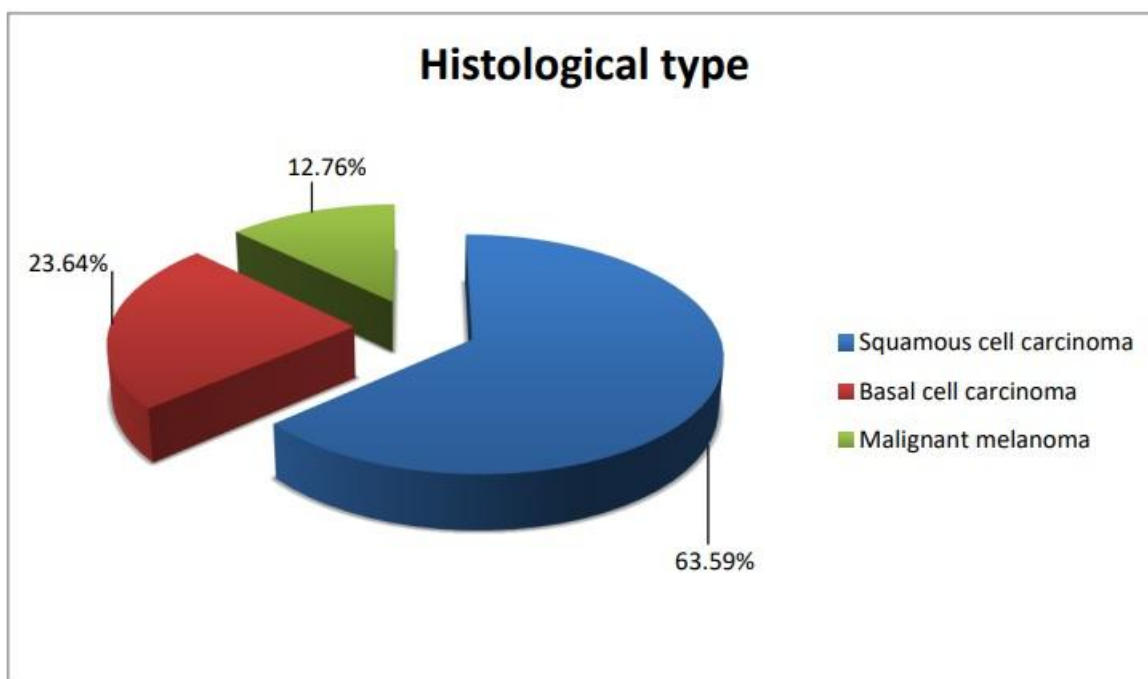
Material and Methods:

This was a retrospective study conducted in the department of Pathology, government medical college Srinagar, Kashmir which is a tertiary care referral hospital From January 2015 to December 2021. Total number of 791 cases were collected and incorporated in the study. Before taking up of cases complete history, clinical and radiological findings were taken into consideration. The tissue samples were Formalin-fixed paraffin-embedded (FFPE) followed by routine Hematoxylin and Eosin (H & E) staining. Sections were thoroughly studied with proper clinico radiological context. Categorization of the tumours was done on the basis of WHO classification.

Results:

In our study we found that the most common cutaneous malignancy in Kashmiri population is squamous cell carcinoma (Figure 1 & 2) which was reported in 63.59% (503) patients, this was followed by basal cell carcinoma (Figure 3 & 4) which was reported in 23.64% (187) patients while malignant melanoma (Figure 5 & 6) was reported in 12.76% (101) patients.

Histological type	Percentage
Squamous cell carcinoma	63.59%
Basal cell carcinoma	23.64%
Malignant melanoma	12.76%



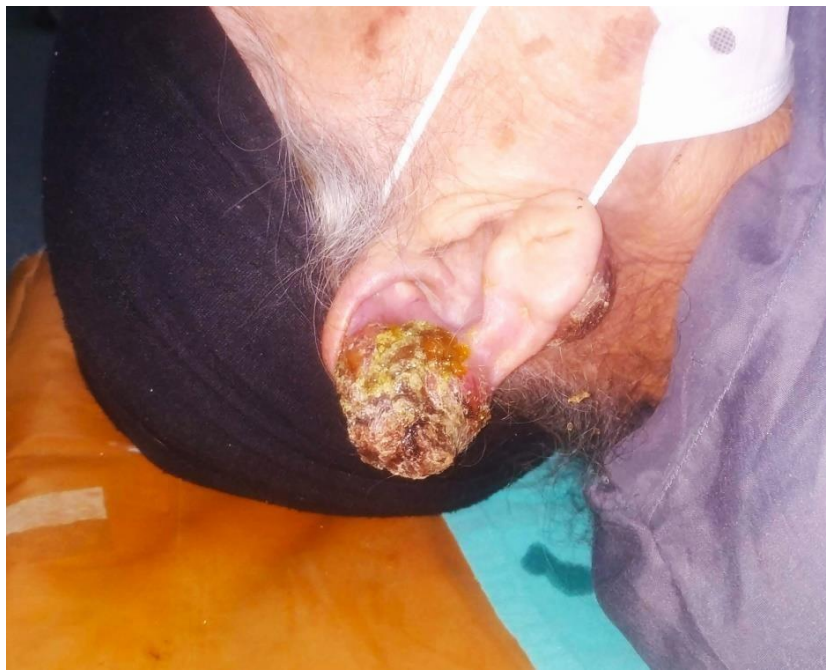


Figure 1 : Squamous cell carcinoma presenting as ulcer on external ear.

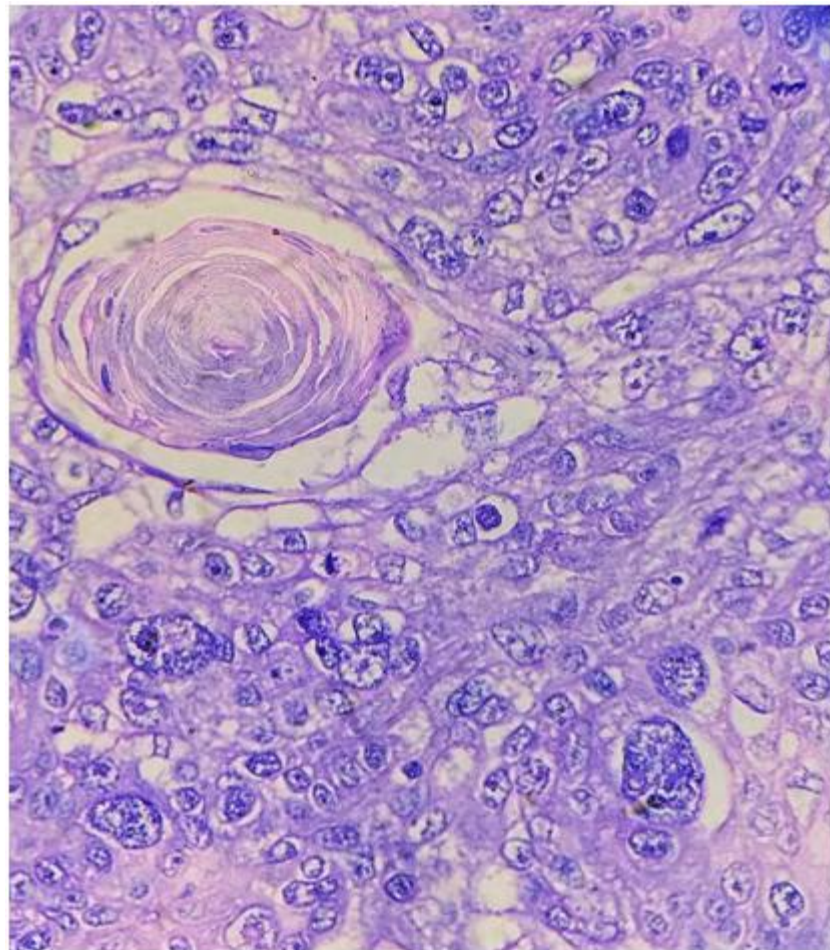


Figure 2 : Polygonal cells arranged in sheets with severe pleomorphism and having areas of keratinization.



Figure 3 : Basal cell carcinoma presenting as ulcer on infraorbital region.

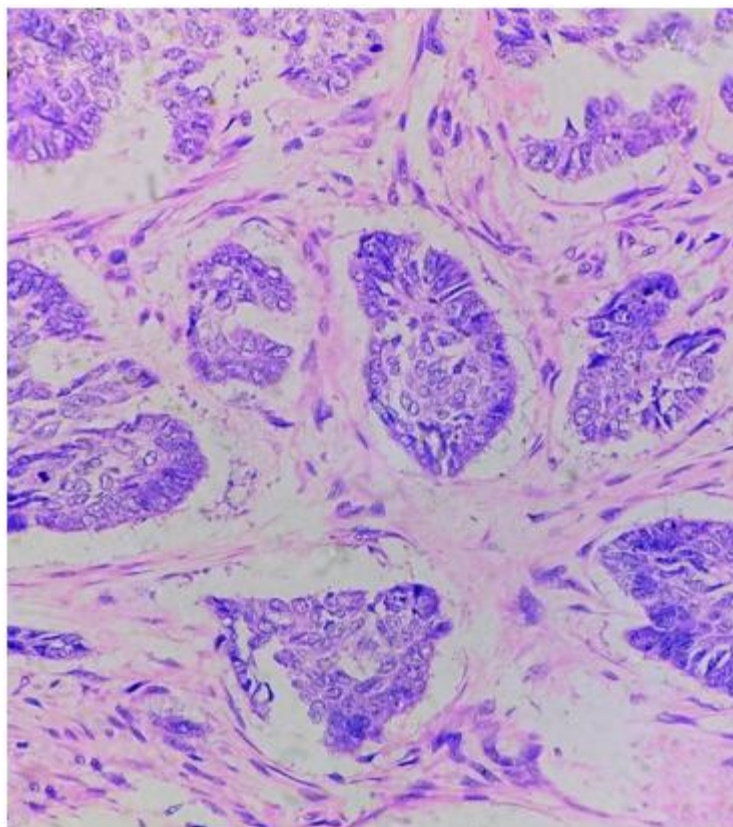


Figure 4 : Nests of basaloid cells with peripheral palisading associated with a fibromyxoid stroma

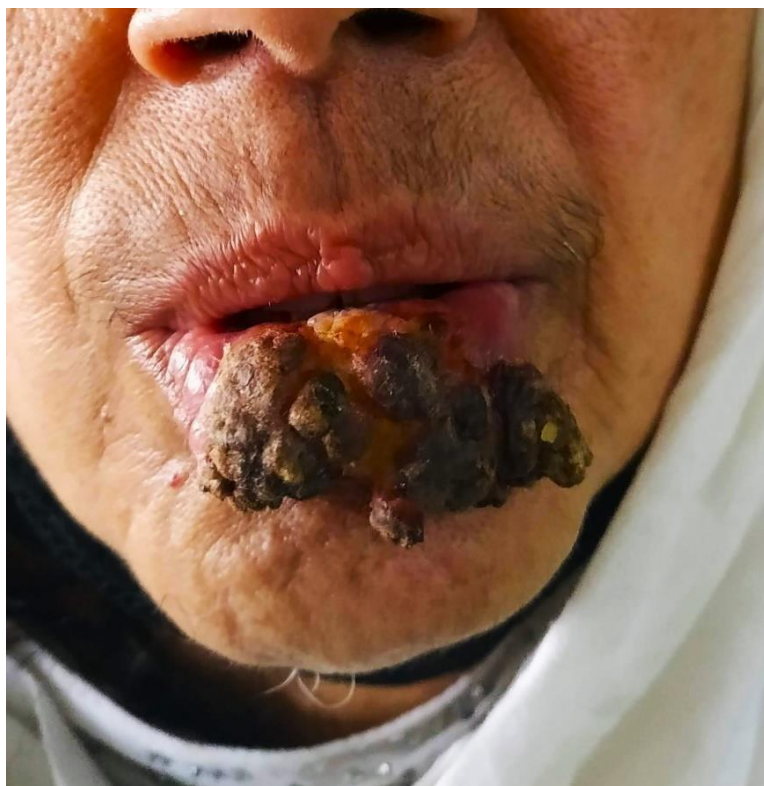


Figure 5 : Malignant melanoma presenting as raised polypoidal and hyper pigmented lesion on chin.

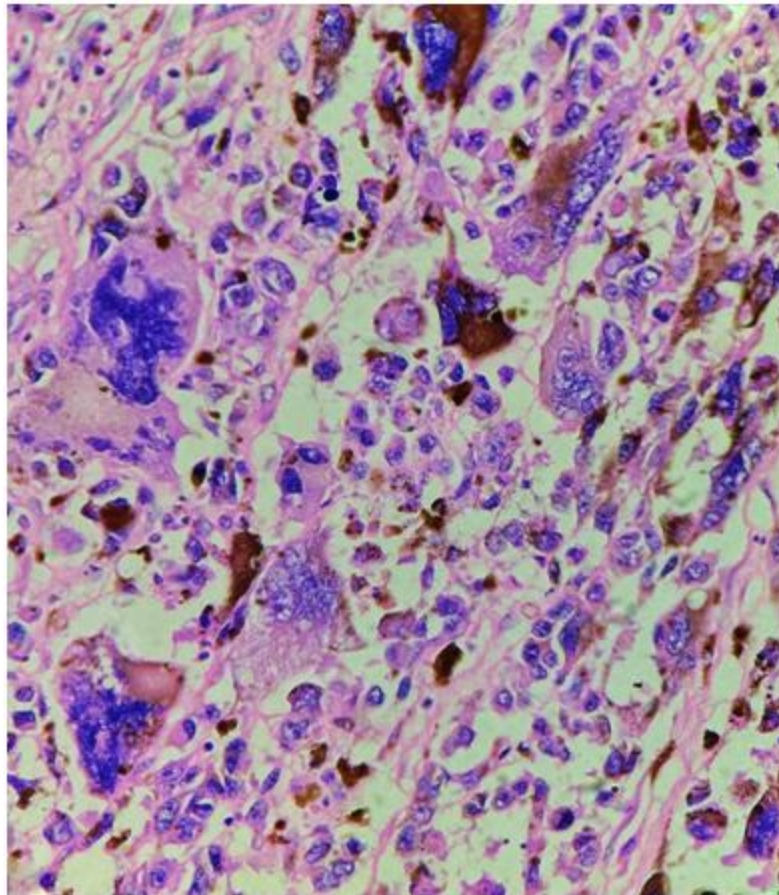


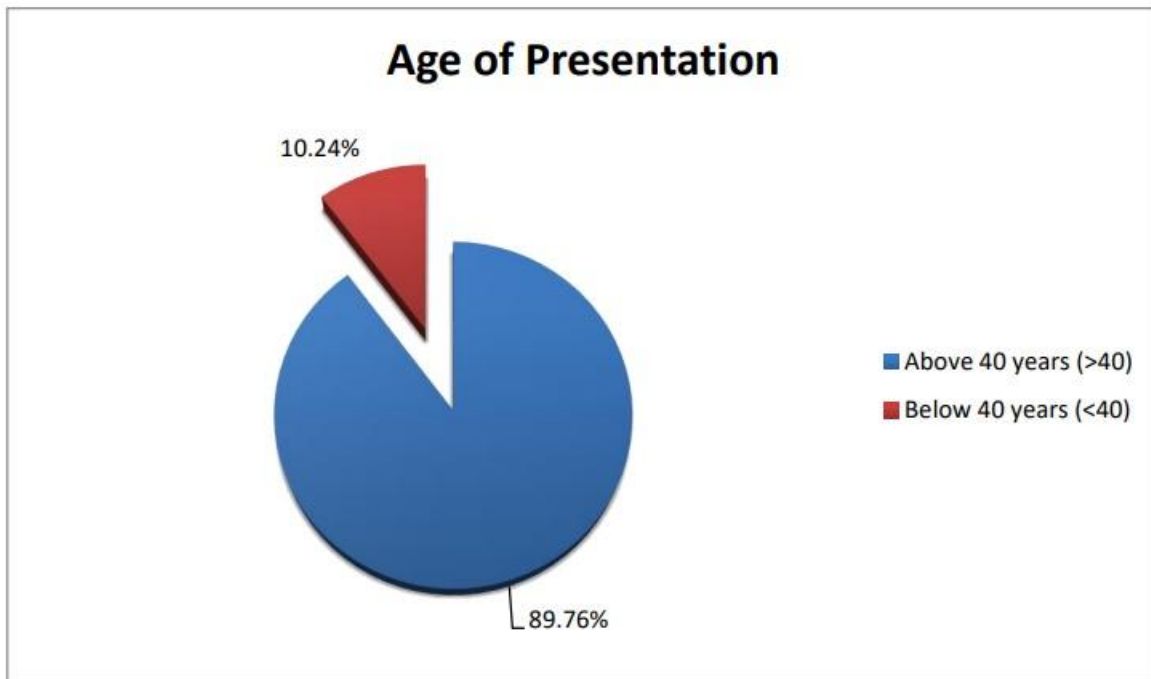
Figure 6 : large irregular cells with severe pleomorphism, prominent nucleoli and pigmentation.

We observed that skin cancer in Kashmiri population was more common in individuals with age above 40 years. Majority of the cases 89.76% (710) were above the age of 40 years while 10.24%

(81) were below age 40 years. The mean age of presentation for Squamous cell carcinoma was 58 years, youngest patient being 16 years old and

oldest being 85 years old. The mean age of presentation for Basal cell carcinoma was 54 years, youngest patient being 21 years old and oldest being 80 years old. The mean age of presentation for malignant melanoma was 59 years, youngest patient being 28 years old and oldest being 81 years old.

Age of Presentation	Percentage
Above 40 years (>40)	89.76%
Below 40 years (<40)	10.24%

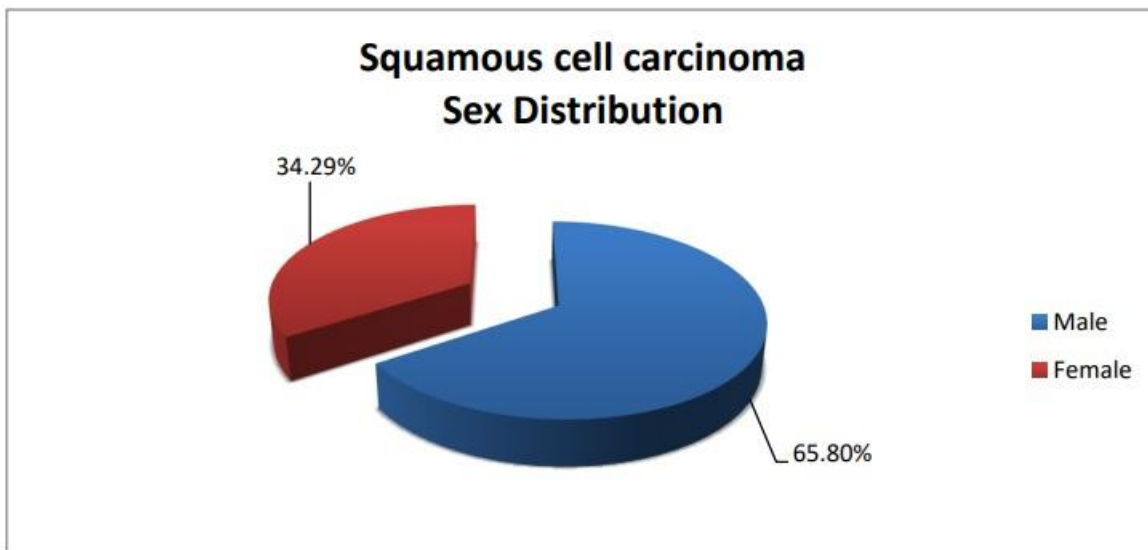


We observed in our study that cutaneous malignancies were more common in the male patients. The male to female ratio for squamous cell carcinoma was observed to be 1.92:1. Out of total 503 patients having squamous cell carcinoma 65.80% (331) patients were male and 34.29% (172) patients were female.

The male to female ratio for Basal cell carcinoma was 1.25:1. Out of total 187 patients having basal cell carcinoma 55.61% (104) patients were male and 44.39% (83) patients were female.

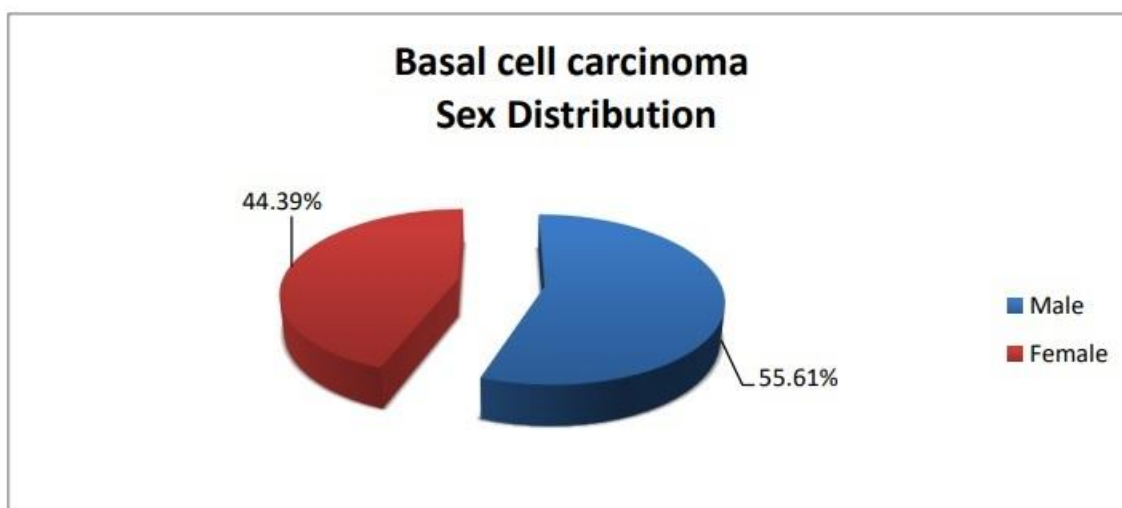
The male to female ratio for Malignant melanoma was 1.24:1. Out of total 101 patients having malignant melanoma 55.45% (56) patients were male and 44.55% (45) patients were female.

Squamous cell carcinoma	
Male	Female
65.80%	34.29%
1.92	1

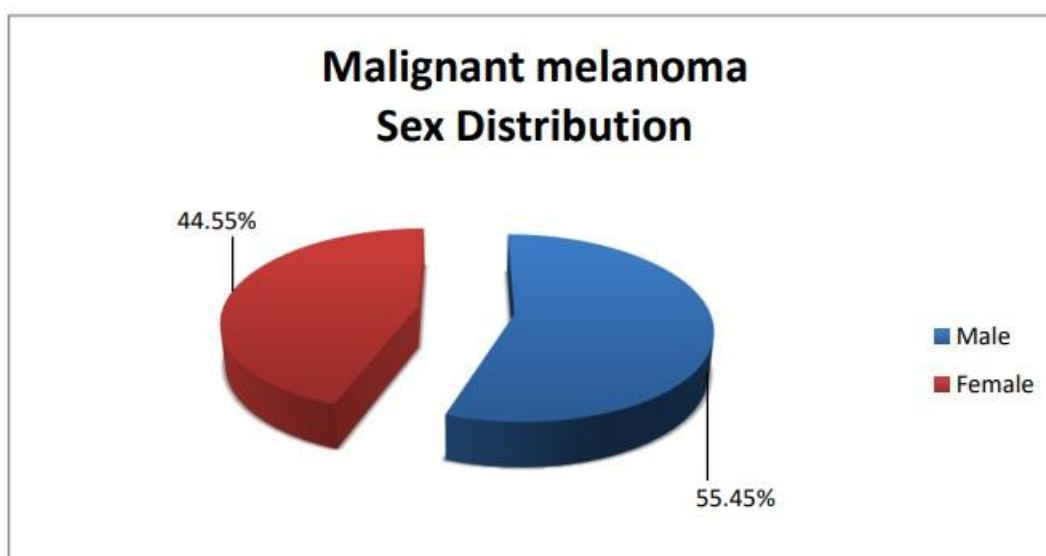


Basal cell carcinoma

Male	Female
55.61%	44.39%
1.25	1



Malignant melanoma	
Male	Female
55.45%	44.55%
1.24	1



The most common sites for squamous cell carcinoma were observed to be lower abdomen, inner thighs, face, neck, scalp, extensor surface of forearms, dorsal surface of hands, and shins. Majority of the basal cell carcinomas presented in the head and neck region, followed by trunk and lower limbs while Malignant Melanoma was more frequently reported on the backs, shoulders and the lower limbs.

Summary:

The aim of this study was to report the age/gender distribution, clinical features, and histopathological types of cutaneous cancers in the population of Kashmir.

Squamous cell carcinoma is the most common type of cutaneous malignancy that we observed in our study (63.59%).The most common site observed was lower abdomen and inner thighs and is possibly due to the use of a kanger, which a ceramic pot covered

Squamous cell carcinoma presented as plaque, nodule or ulcer with erythema. Basal cell carcinoma presented as a pink or flesh coloured papule or nodule with arborizing and branching vessels on surface. Malignant melanoma presented as flat, elevated, nodular and polypoidal pigmented lesion.

with wicker-work, carried as a source of warmth during cold weather. This malignancy arises from epidermal keratinocytes and displays variable degree of differentiation and cytological features. Precursor lesion known as actinic keratosis is a well-known risk factor. Other risk factors include ultraviolet radiation, immunosuppression, albinism (lack of pigmentation in skin), ingestion of arsenicals, burn scars, chronic ulcers, chronic inflammation, human papillomavirus infection, exposure to industrial carcinogens - tars and oils and xeroderma pigmentosum (21).

Squamous cell carcinoma exhibits tumour progression and has the potential to metastasize in the body. Less than 5% of these tumours metastasize to regional nodes; these lesions are generally deeply invasive and involve the subcutis

(21). Definitive diagnosis is made by shave, punch or excisional biopsies followed by histopathological examination. Squamous cell carcinomas not invading through the basement membrane of the dermoepidermal junction are termed as in situ carcinoma. Invasive squamous cell carcinoma shows variable degrees of differentiation, ranging from well differentiated tumours composed of polygonal cells arranged in orderly lobules and having numerous large areas of keratinization, to neoplasms consisting of highly anaplastic cells that exhibit only abortive, single-cell keratinization – dyskeratosis (21). Prognosis depends on lesion size, depth of invasion, differentiation and perineural invasion lymphovascular invasion and immunosuppression. Surgical excision is the primary treatment modality for cutaneous squamous cell carcinoma, with Mohs micrographic surgery being the preferred excisional technique. Radiation therapy is reserved for squamous cell carcinoma in older patients or those who will not tolerate surgery, or when it was not possible to obtain clear margins surgically.

Basal cell carcinoma is the second most common type of cutaneous malignancy that we observed in our study (23.64%). Most common site of presentation was the head and neck region. These tumours arise from the interfollicular or follicular epithelium. Basal cell carcinoma is usually a slow-growing tumour that rarely metastasizes. BCC can be locally aggressive leading to destruction and disfigurement of local tissues when treatment is inadequate or delayed. Risk factors include UV exposure, Nevoid basal cell carcinoma syndrome and immunosuppression (21). Histologically, the tumour cells resemble those in the normal basal cell layer of the epidermis and the malignancy exhibits nests of basaloid cells with peripheral palisading associated with a fibromyxoid stroma. Prognostic factors include Histological type with lower risk types being : nodular, superficial, pigmented, infundibulocystic, fibroepithelial and higher risk types being : basosquamous, sclerosing

/ morpheaform, keloidal, infiltrating, BCC with sarcomatoid differentiation and micronodular variants. Other prognostic factors include presence of perineural and lymphovascular invasion, status of surgical margins and tumor size. Mohs micrographic surgery technique is one of the most often used options for assessment of margins of surgery specimens followed by by histopathological examination.

In our study Malignant melanoma was reported in the 12.76% patients. Most common site of presentation was back and lower limbs. Malignant melanocytic tumours arise from melanocytes in the skin. Melanocytes are cells derived from neural crest and can be found principally in the basal epidermis, in hair follicles, along mucosal surfaces, meninges and in the choroidal layer of the eye. Melanoma is the most deadly of all skin cancers and is strongly linked to acquired mutations caused by exposure to UV radiation in sunlight (22). Other risk factors include lightly pigmented individuals, family and personal history of melanoma, increased mole count, dysplastic nevi and immunosuppression. Individual melanoma cells are usually considerably larger than normal melanocytes or cells found in melanocytic nevi, having large nuclei with irregular contours, chromatin that is characteristically clumped at the periphery of the nuclear membrane, and prominent red (eosinophilic) nucleoli (23). The most important warning signs, sometimes called the ABCDEs of melanoma, are (1) asymmetry; (2) irregular borders; and (3) variegated colour, (4) increasing diameter, and (5) evolution or change over time, especially if rapid (23). Prognostic factors include the following variables: (1) tumour depth (the Breslow thickness); (2) number of mitoses; (3) evidence of tumour regression (presumably due to the host immune response); (4) ulceration of overlying skin; (5) the presence and number of tumour infiltrating lymphocytes; (6) gender; and (7) location : central body or extremity (23). Treatment options include wide surgical

excision with safety skin margins according to Breslow depth. Chemotherapy and radiotherapy is used in difficult cases with extensive local invasion or metastasis. Checkpoint inhibitors (PD1 / PDL1 inhibitors, CTLA4 blockade) along with targeted therapy (BRAF and MEK inhibitors, KIT inhibitors) are the latest modalities of treatment.

Conclusion:

Our study provides insight into the incidence, age of presentation, gender distribution, symptoms and histological patterns of cutaneous malignancies in the population of Kashmir. We conclude that a thorough understanding of epidemiology of skin cancer can

provide basis for disease prevention. The various treatment options for skin cancer include surgery, radiation therapy, chemotherapy, and targeted therapy all of which are most effective when applied at the earliest stage.

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