

# A Clinicopathological Study of Skin Tumors from a Tertiary Care Centre in North India

## Abstract

**Background:** There is a huge spectrum of skin tumors which can be confused clinically with malignancies, particularly when they are pigmented or inflamed, and histopathological examination of a biopsy specimen is required to establish a definitive diagnosis and to facilitate appropriate intervention and follow up. **Aim:** To evaluate all skin tumors and categorize them according to their origin. **Methods:** The present study was conducted over a period of 4 years (July 1, 2013 to June 31, 2017) comprising of 1.5 years prospective and 2.5 years retrospective analysis in the departments of Dermatology and Pathology, at a tertiary hospital in North India. All specimens of skin tumors were analyzed grossly and microscopically. Immunohistochemistry was done wherever possible. **Results:** A total of 232 skin tumors were seen; of which 123 cases were benign (53.0%) and 109 cases were malignant (47.0%). The mean age of patients with benign and malignant skin tumors was  $40.3 \pm 19.9$  and  $60.8 \pm 14.8$  years, respectively. The most common site was face ( $n = 106$ ; 45.7%) followed by limbs ( $n = 44$ ; 19.0%). The male:female ratio of benign and malignant tumors was 1.01:1 and 1.31:1, respectively. Among the benign tumors, keratinocytic tumors were the commonest ( $n = 57$ ; 46.3%) followed by the melanocytic tumors ( $n = 37$ ; 30.1%) and appendageal tumors ( $n = 29$ ; 23.6%). The most common malignant skin tumors were the keratinocytic tumors ( $n = 87$ ; 79.8%) followed by 12 cases (11%) of hematolymphoid tumors and five cases (4.6%) each of melanocytic and appendageal tumors. **Limitations:** The lack of clinical and dermoscopic correlation and inclusion of retrospective data are the limitations of this study. **Conclusions:** Skin tumors affect people of all ages. The benign tumors are seen in the younger age group as compared to malignant tumors. Face is the most common site and keratinocytic tumors are the most common skin tumors in both benign and malignant categories.

**Keywords:** Histopathology, keratinocytic tumors, skin tumors

## Introduction

Skin tumors are so ubiquitous that they can affect people of all ages and they can be both benign and malignant.<sup>[1]</sup> Skin tumors have multifactorial causes related to the combination of several factors like genetic, chemical, hormonal, nutritional, viral, and environmental acting in concert within a susceptible individual. Tumors of skin arise from different components of skin such as surface epithelium, epidermal appendages, and dermis and are classified by WHO based upon their origin as keratinocytic, melanocytic, appendageal, and hematolymphoid tumors.<sup>[2]</sup>

Several tumor-like conditions are often confused clinically with malignancy, particularly when they are pigmented or inflamed, and a histopathological

examination of a biopsy specimen is frequently required to establish a definitive diagnosis.<sup>[1]</sup> This is important in ensuring that malignancies are not missed and to facilitate appropriate intervention and follow up. Thus, this study was undertaken to determine the pattern of cutaneous tumors including both benign and malignant skin tumors.

## Methods

This was a four-year study (1.5 years prospective and 2.5 years retrospective) from July 2013 and June 2017. The study was cleared by the ethics committee of our institute and informed consent was obtained from all patients. Skin biopsies with a clinical diagnosis of tumors of skin and its appendages were included in the study. Skin biopsies of soft tissue tumors were excluded from this study. Detailed history with

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reference to mode of onset, characteristics, and distribution of lesion was taken from patient. Also, clinical examination findings with particular reference to age, gender, and site of involvement was taken. For retrospective study, history and clinical findings were obtained from medical records. The histopathological examination (HPE) findings of the biopsy slide were recorded and analyzed. The tumors were classified according to the WHO classification.<sup>[2]</sup> The histopathological findings were correlated with the immunohistochemistry (IHC) findings.

## Results

Of the total 232 skin tumors included in the study, 53% tumors were benign and 47% were malignant. Maximum numbers of benign tumors were seen in the 3<sup>rd</sup> decade (26.9%) whereas malignant tumors were most numerous in the 7<sup>th</sup> decade (26.6%). Thus, benign tumors were seen four decades earlier as compared to malignant tumors, and this difference was statistically significant. The mean age of patients with benign and malignant skin tumors was 40.3 and 60.8 years, respectively [Figure 1]. Males (124 cases) were more affected than females (108 cases) with a Male:Female ratio being 1.15:1. The Male:Female ratio of benign and malignant tumors was 1.01:1 and 1.31:1, respectively. The most common site of skin tumors is face in 106 cases (45.7%) followed by limbs in 44 (19.0%) cases in both the benign and malignant categories.

Keratinocytic tumors formed the largest group constituting 144 cases (62.0%). Melanocytic tumors were the second commonest comprising 42 cases (18.1%) followed by appendageal tumors constituting 34 cases (14.7%). Among the benign tumors, the keratinocytic tumors were the commonest ( $n = 57$ ; 46.3%) followed by the melanocytic tumors ( $n = 37$ ; 30.1%) and appendageal tumors ( $n = 29$ ; 23.6%). Most common malignant skin tumors were keratinocytic tumors ( $n = 87$ ; 79.8%) followed by 12 cases of hematolymphoid tumors (11%) and 5 cases each of melanocytic and appendageal tumors (4.6%) [Table 1].

In our study, verrucas (20.1%) were the most common benign keratinocytic tumor followed by seborrheic keratosis (19.5%). Verruca were seen equally and most commonly on face (34.5%) and extremities (34.5%). The most common variant of seborrheic keratosis encountered by us was the acanthotic variant [Figure 2] in 14 (50%) followed by the hyperkeratotic variant in six (21.4%), the irritated variant in four (14.3%), and the pigmented variant in three (10.7%) cases.

Malignant tumors formed the bulk of keratinocytic tumors of which basal cell carcinoma (BCC) was the commonest constituting 48 cases (33.3%) followed by 34 cases (23.6%) of squamous cell carcinoma (SCC) [Table 1]. The most common variant of BCC was the nodular variant ( $n = 20$ ; 41.7%) followed by the basosquamous variant

( $n = 12$ ; 25%) [Table 2]. Regarding the extent of BCC, three cases (6.2%) were observed confined to the papillary dermis while the majority of cases were observed in the reticular dermis ( $n = 38$ , 79.2%). Two cases (4.2%) were involving the subcutaneous tissue and five (10.4%) were infiltrating the underlying skeletal muscles bundles.

A majority of cases were moderately differentiated SCC ( $n = 21$ ; 61.8%) followed by well-differentiated SCC ( $n = 11$ ; 32.3%). Well-differentiated SCC had many keratin pearls. Of the 2 cases of poorly differentiated SCC, IHC was done on one case and showed strong positivity of CK5/6 in the tumor cells.

Most common melanocytic tumor was intradermal nevus ( $n = 31$ , 73.8%). IHC was used in two cases of intradermal nevus, which were S100 positive.

Five cases of malignant melanoma (11.9%) were also diagnosed which had marked nuclear atypia, prominent nucleoli, and melanin pigmentation. Two cases were of Clarks level V and one case belonged to level III and IV each, and in one case the Clarks level could not be ascertained, as it was superficial. IHC was used in three of these cases of malignant melanoma, which were HMB45 and Melan A positive. Among appendageal tumors, tumors with follicular differentiation were the commonest. The most common benign appendageal tumor was pilomatricoma (38.3%) [Table 1]. Of the 12 cases of hematolymphoid tumors, three cases were of leukemia cutis. All of them were known cases of acute leukemia and presented with nodular lesions.

Rest all cases were of Non-Hodgkin's lymphoma (NHL), including one case each of mycosis fungoides, cutaneous T cell lymphoma, and lymphomatoid granulomatosis. The NHL were classified based on their IHC characteristics, and two cases which were not classified further.

## Discussion

Skin can be often affected by neoplasms both benign and malignant. Benign epithelial neoplasms are common and usually biologically inconsequential, although they may represent significant sources of psychologic discomfort for the patient. They are often confused clinically with malignancy, particularly when they are pigmented or inflamed, and histologic examination of a biopsy specimen is frequently required to establish a definitive diagnosis and to facilitate appropriate intervention and follow up.<sup>[1]</sup>

In the present study skin tumors, both benign and malignant, from each of the 4 major WHO categories were identified histologically across all age groups. A total of 232 skin tumors were analyzed, out of which 123 cases (53.0%) were benign and 109 cases (47.0%) were malignant. This is in concordance with the studies conducted by Bari *et al.* and Har-Shai Y *et al.*<sup>[3,4]</sup> Bari *et al.* reported benign and malignant tumors as 51.2% and 48.8%, respectively,

**Table 1: Distribution of Skin Tumors According to Tumor Differentiation**

Distribution of skin tumors			
According to Tumor Differentiation	Benign (n=123) (%)	Malignant (n=109) (%)	Total (n=232) (%)
Keratinocytic	57 (46.3)	87 (79.8)	144 (62)
Melanocytic	37 (30.1)	5 (4.6)	42 (18.1)
Appendageal	29 (23.6)	5 (4.6)	34 (14.7)
Hematolymphoid	-	12 (11)	12 (5.2)
Keratinocytic tumors	Benign (n=57)	Malignant (n=87)	Total (n=144) (%)
Verrucae	29 (20.1)	-	29 (20.1)
Seborrheic keratosis	28 (19.5)	-	28 (19.5)
Bowen disease	-	5	5 (3.5)
Squamous cell carcinoma	-	34	34 (23.6)
Basal cell carcinoma	-	48	48 (33.3)
Appendageal tumors	Benign (n=29)	Malignant (n=5)	Total (n=34) (%)
Apocrine/eccrine			
Syringoma	4	-	4 (11.8)
Hidradenoma papilliferum	1	-	1 (2.9)
Nodular hidradenoma	1	-	1 (2.9)
Poroma	4	-	4 (11.8)
Syringocystadenoma papilliferum	2	-	2 (5.9)
Porocarcinoma	-	2	2 (5.9)
Follicular			
Pilomatricoma	13	-	13 (38.3)
Trichoepithelioma	1	-	1 (2.9)
Proliferating tricholemmal tumor	-	2	2 (5.9)
Sebaceous			
Sebaceoma	1	-	1 (2.9)
Sebaceous adenoma	2	-	2 (5.9)
Sebaceous carcinoma	-	1	1 (2.9)
Melanocytic tumors	Benign (n=29)	Malignant (n=5)	Total (n=34) (%)
Intradermal nevus	31	-	31 (73.8)
Compound nevus	5	-	5 (11.9)
Giant hairy nevus	1	-	1 (2.4)
Malignant melanoma	0	5	5 (11.9)
Hematolymphoid tumors	Benign (n=0)	Malignant (n=12)	Total (n=12) (%)
Leukemia cutis	0	3	3 (25.1)
Mycosis fungoides	0	1	1 (8.3)
Cutaneous T-cell lymphoma-gamma delta subtype	0	1	1 (8.3)
Lymphomatoidgranulomatosis	0	1	1 (8.3)
Blastic plasmacytoid dendritic cell neoplasm	0	1	1 (8.3)
Non-Hodgkin's lymphoma, B cell type	0	2	2 (16.7)
Non-Hodgkin's lymphoma, T cell type	0	1	1 (8.3)
Non-Hodgkin's lymphoma, NOS	0	2	2 (16.7)

**Table 2: Subtypes of basal cell carcinoma**

Basal cell carcinoma	No. of cases	%age
Nodular variant	20	41.7
Basosquamous variant	12	25
Infiltrating variant	5	10.4
Nodulocystic variant	5	10.4
Superficial spreading variant	3	6.2
Pigmented variant	2	4.2
Adenoid variant	1	2.1

while Har-Shai *et al.* found 64.4% tumors in benign and premalignant category and 31.6% tumors as malignant.<sup>[3,4]</sup>

Keratinocytic tumors are derived from epidermal and adnexal keratinocytes and comprise a large spectrum of lesions ranging from benign proliferations to malignant squamous and basal cell tumors. Among the benign keratinocytic tumors, verrucae were the most common tumors in our study followed by seborrheic keratosis. Verrucae were most common in the age group of 11–20 years with male preponderance in our study. This is in concordance with the study conducted by Bari *et al.* who report verruca as the most common benign keratinocytic tumor in 32.85% cases.<sup>[4]</sup> Literature reports extremities as the most common site of verrucae but in our study, they

were most common and equally distributed over the face and extremities (34.5% each).<sup>[4,5]</sup> Verrucae is included in the WHO classification of skin tumors, in the broad category of keratinocytic/epidermal tumors, and further subcategorized under carcinoma precursors/benign stimulants.<sup>[2]</sup> Although verrucae have an infective etiology, they were included in this study on the basis of their inclusion in the WHO classification and various other authors have also included verrucae in their studies on skin tumors.<sup>[2,4]</sup>

Benign melanocytic tumors were also more common in younger age group and majority were seen on face. Most common benign melanocytic tumor was intradermal nevus which showed female preponderance with a M:F ratio of 1:2.7. This is in concordance with the studies conducted by Bari *et al.* They observed benign melanocytic tumors to be 9.4% of all the benign tumors.<sup>[4]</sup>

Among the benign appendageal tumors, pilomatricoma was the commonest ( $n = 13$ ; 38.3%, Figure 3). This observation is in concordance with the study conducted by Kaur K *et al.* who reported pilomatricoma in 28.2% cases.<sup>[6]</sup> Parate *et al.* found eccrine acrospiroma to be most common, while Saha *et al.* reported syringomas to be most common benign appendageal tumors.<sup>[7,8]</sup>

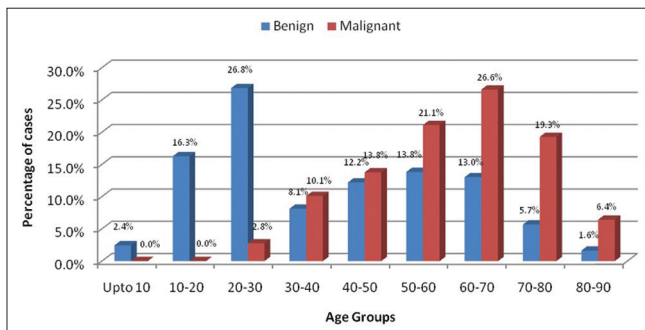


Figure 1: Age distribution of skin tumors

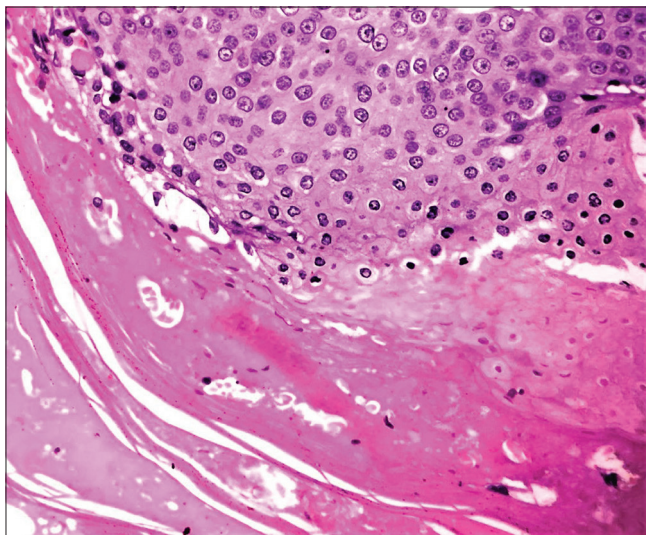


Figure 3: Pilomatricoma showing the basaloid cells and shadow cells. (H and E, X400)

A majority of malignant tumors were keratinocytic tumors out of which BCC was the commonest followed by SCC in our study. In dark-skinned individuals, SCC is the most common cutaneous neoplasm, accounting for 30 to 65% of the cases whereas in lighter skin, SCC ranks second to BCC, representing 15–25% of the cutaneous malignancies.<sup>[9,10]</sup> In studies of nonmelanoma skin cancer from Indian subcontinent, Baruah *et al.* and Adinarayan *et al.* report SCC more frequently than BCC.<sup>[11,12]</sup> However, in a recent study, Khullar G *et al.* interestingly found BCC to be more common than SCC in a 10-year retrospective analysis.<sup>[13]</sup> In another study from Saudi Arabia, BCC was found to be more common than SCC.<sup>[14]</sup> In our study, the maximum number of cases of BCC [Figure 4] were seen in the 6<sup>th</sup> and 7<sup>th</sup> decade and the most common variant was the nodular variant [Figure 5] followed by basosquamous variant. Hakverdi, Adinarayan,

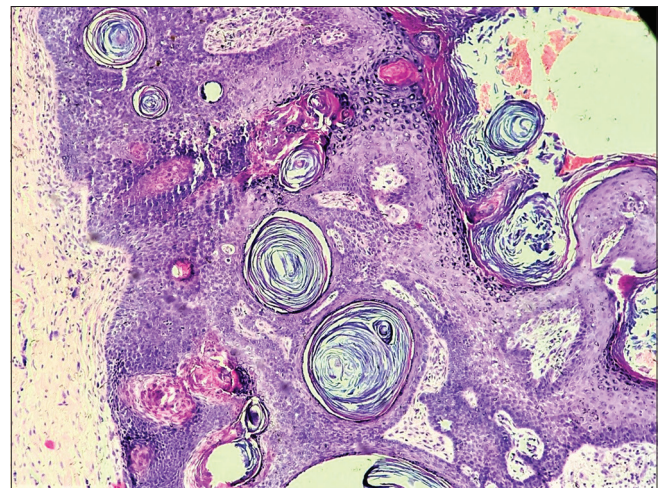


Figure 2: Seborrheic keratosis (acanthotic variant) showing acanthosis and hyperkeratosis of epidermis with presence of numerous horn cysts. (H and E, 400x)

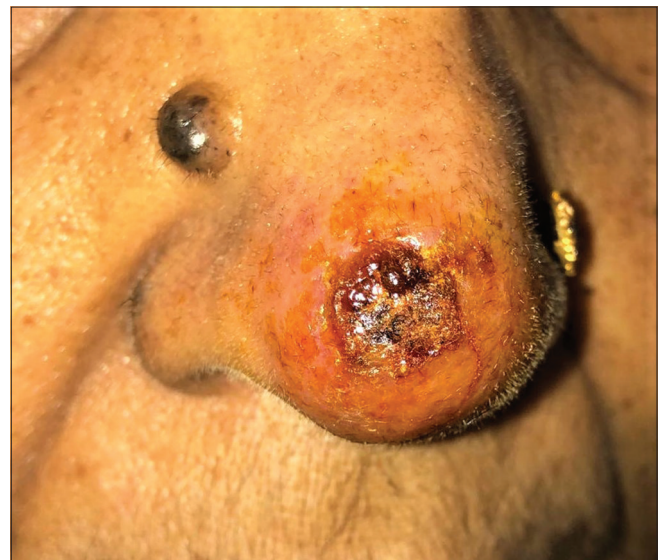


Figure 4: 65 old female with basal cell carcinoma over nose

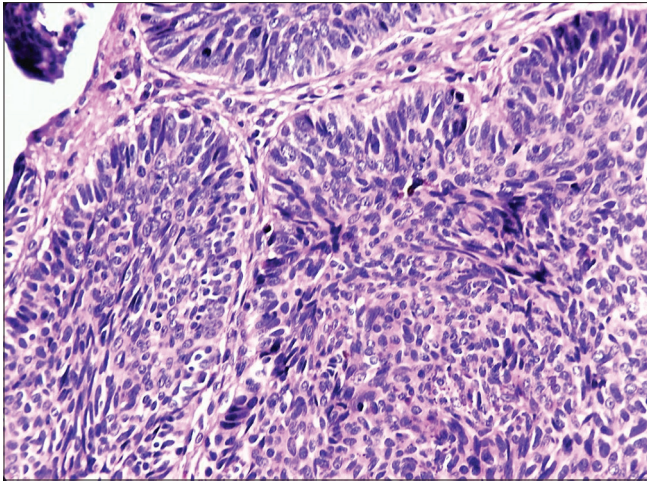


Figure 5: Basal cell carcinoma (nodular variant) showing lobules of basaloid cells with peripheral palisading of nuclei. (H and E, X400)



Figure 6: 60-year-old female with Squamous cell carcinoma

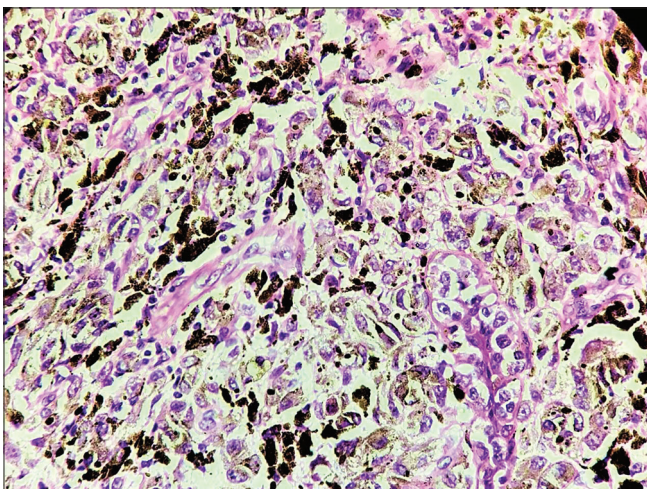


Figure 7: Malignant melanoma showing cytologic atypia, prominent nucleoli and melanin pigment. (H and E, X400)

and Baruah too report nodular variant as the most common histologic subtype of BCC in their studies.<sup>[11,12,14]</sup> Majority

of SCC cases [Figure 6] in our study were moderately differentiated.

In the present study, malignant melanoma was seen in 11% cases. This is similar to Indian studies where malignant melanoma accounted for 8.85% to 29.4% of all skin cancers<sup>[4,15,16]</sup> Four cases of malignant melanoma were reported over the extremities and 1 case on face [Figure 7]. Foot was the most common site in Indian studies as well.<sup>[15-17]</sup>

Of the five cases of malignant melanoma, two cases were of Clarks level V and one case belonged to level III and IV each. One of the cases was received as a superficial biopsy strip, so its Clarks level could not be ascertained. On IHC, they were HMB45 and Melan A positive. Clark's level III was the most common type in study by Panda S *et al.*<sup>[17]</sup> All tumors with biopsy suggestive of malignancy were sent to the oncology department for complete excision.

Malignant appendageal tumors constituted 14.7% of all appendageal tumors, of which 5.9% cases each of porocarcinoma and proliferating tricholemmal tumor and 2.9% cases of sebaceous carcinoma were observed in our study. Bari *et al.*<sup>[4]</sup> reported 33.3% malignant appendageal tumors, of which 13.3% were sebaceous carcinoma and 20% proliferating tricholemmal tumor.

Hematolymphoid tumors constituted 5.2% of all skin tumors of which Non-Hodgkin's lymphoma was the most common. Male preponderance was noted with the mean age being 61.9 years. In a six-year study of 35 cases of cutaneous T cell lymphomas by Khader *et al.*,<sup>[18]</sup> the authors report similar male preponderance and a mean age of onset of 52.66 years. Majority of cases in their study were of T cell Lymphoma (94.3%).

## Conclusions

Skin tumors affect people of all ages. The benign tumors are seen in younger age group as compared to malignant tumors. Face is the most common site and keratinocytic tumors are the most common skin tumors in both benign and malignant categories.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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