

**SPECTRUM OF SKIN TUMORS IN A TERTIARY CARE CENTRE IN NORTHERN INDIA**Sheenam Azad<sup>1</sup>, Seema Acharya<sup>2</sup>, Sandip Kudesia<sup>3</sup>, Sanjiv Kishore<sup>4</sup>, Anil Kumar Mehta<sup>5</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: BACKGROUND:** There is limited data on the spectrum of benign and malignant neoplasms of skin and subcutis in India. **AIM:** This study was undertaken in a tertiary care hospital of Uttarakhand to evaluate the frequency of various neoplasms affecting skin and subcutis in biopsy specimens. **MATERIAL AND METHODS:** A retrospective and prospective analysis of 660 skin biopsies was undertaken. The neoplasms were categorized as per International classification of World health Organization (WHO). **RESULTS:** Of all the skin biopsies analyzed, tumors were seen in 24.5% (162/660). Benign neoplasms were more frequently seen (72.8 %) than malignant neoplasms (27.2%). Benign to malignant ratio was 2.7:1. Amongst the benign neoplasms, soft tissue tumors including vascular, fibrous/ fibrohistiocytic, lipomatous and neural tumors constituted the largest group (61.2%) followed by appendageal tumors (22.0%), melanocytic naevi (12.3%) and keratinocytic tumors (5.1%). On the other hand, amongst the malignant neoplasms, keratinocytic tumors were the commonest (77.3%) followed by melanoma (9.1%) and appendageal tumors (9.1%). **CONCLUSION:** Soft tissue tumors of skin and subcutis form the largest group amongst the benign neoplasms and keratinocytic tumors are the commonest malignant skin tumors.

**KEYWORDS:** Keratinocytic, Melanocytic, Appendageal, Hematolymphoid, Soft tissue tumors.

**INTRODUCTION:** Skin tumors encompass a wide variety of benign and malignant neoplasms of skin and subcutis that are further classified as keratinocytic, melanocytic, appendageal, hematolymphoid, and soft tissue tumors.<sup>[1]</sup> The incidence of skin tumors varies geographically and is relatively well documented for malignant neoplasms like keratinocytic tumors {squamous cell carcinomas (SCC), and basal cell carcinomas (BCC)} and melanomas in different studies.<sup>[2-6]</sup> However, the frequency of occurrence of various benign skin tumors and other malignant skin tumors is poorly documented. Hence, this study was undertaken with the aim of evaluating the spectrum of all the benign as well as malignant neoplasms of skin and subcutis based on histopathological diagnosis using the International classification of World health Organization (WHO).<sup>[1]</sup>

**MATERIALS AND METHODS:** A retrospective and prospective analysis of 660 skin biopsies received in the Department of Pathology in a tertiary care teaching hospital in Uttarakhand was undertaken from January 2005 to April 2013. The study was approved by institutional review board and ethical committee. Cases from the previous years were retrieved from the departmental archives, reviewed and the clinical details were noted from histopathology requisition forms. Sections from formalin fixed, paraffin embedded blocks stained with Haematoxylin and Eosin stain were examined and analyzed independently by two histopathologists. Cases of benign and malignant neoplasms during the study period were further classified as per WHO classification of skin tumors.<sup>[1]</sup> Although there is recent evidence indicating that BCC should be included in the category adnexal neoplasms under the

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term trichoblastic carcinoma, we have followed the WHO working group classification which includes BCC in the keratinocytic tumors reflecting traditional categorization. For the purpose of this study, proliferating trichilemmal tumor is considered in malignant category as described in WHO manual although the International classification of diseases for oncology (ICD-O) considers it to be a borderline tumor.<sup>[7]</sup>

**RESULTS:** A total of 660 skin biopsies were received during the period under review. Out of these, there were 24.5% (n=162) cases of skin tumors. The sex distribution was M: F=1:1.05 (79 males; 83 females). The age range was 01-93 years. Of the 162 skin tumor biopsies, there were 118 (72.8 %) benign and 44 (27.2 %) malignant tumors giving benign to malignant ratio of 2.7:1. Soft tissue tumors constituted the largest group (45.1%) followed by keratinocytic tumors (24.7%) as shown in Table 1.

Amongst the benign category, maximum numbers of cases (38%, 45/118) were seen in the age group 21-40 yrs. There were 52.5% females (62/118) and 47.5% males (56/118) giving a male to female ratio of 1:1.1. Soft tissue tumors constituted the largest group 61.2 %, followed by appendageal tumors 22.0 %, melanocytic tumors (Naevi) 12.3 % and keratinocytic tumors (verruca, papilloma, acanthomas etc.) 5.1%. In contrast, amongst the malignant neoplasms, majority of the cases, (70.5%, 31/44) were observed after the age of 40 years. Male: female ratio was 1:1. Keratinocytic tumors were the commonest (77.3%), followed by melanoma and appendageal tumors. The findings are depicted in Table 2 and 3.

**DISCUSSION:** Skin diseases are common throughout the world including rural and urban areas. Various lesions afflicting the skin range from non-specific dermatoses and inflammatory diseases to neoplastic changes of various components of the skin. The neoplasms include a wide variety of benign and malignant neoplasms of skin and subcutis that are further classified as keratinocytic, melanocytic, appendageal, hematomatous, and soft tissue tumors.

Barring some studies,<sup>[2, 8, 9]</sup> there is a paucity of data on the spectrum of benign & malignant neoplasms of skin and subcutis which prompted us to undertake the present study. In this study, nearly one-fourth of the total skin biopsies (162/660) examined histopathologically were tumors. This included 17.9% benign and 6.7% malignant neoplasms. Similar findings have been reported in a study by Bin Yap from the island of Borneo in Malaysia in 2009.<sup>[10]</sup>

Further evaluation of skin tumors revealed that 72.8 % neoplasms were benign and 27.2% were malignant. This observation is in accordance with a study by Park et al. in 2006 on skin tumors wherein 70.8% were benign tumors, 20.8% were malignant tumors, and 8.4% were premalignant lesions.<sup>[8]</sup>

**BENIGN NEOPLASMS:** The soft tissue tumors were the commonest benign neoplasms in our study. It is known that most soft tissue tumors are benign, outnumbering malignant ones by about 100 to 1. The common benign tumors are lipomas, fibrous histiocytomas, vascular or smooth muscle lesions including angioleiomyomas and nerve sheath tumors (schwannoma, neurofibroma). Neural tumors represent a small but important part of the cutaneous soft tissue neoplasms.<sup>[1]</sup>

A study on skin tumors from Korea by Ha and Kim in 1996 reported that the most common tumor was epidermal cyst followed by lipoma, cavernous hemangioma, neurofibroma, pilomatricoma, and seborrheic keratosis.<sup>[9]</sup> The present study also showed lipomas and vascular

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tumors to be the most common benign soft tissue neoplasms followed by fibrous and fibrohistiocytic tumors.

Appendageal tumors are tumors having differentiation towards one or more of the adnexal structures of the skin. These tumors formed the second major group in our study constituting 22% of the benign neoplasms. Depending on their presumed origin, they are categorized into lesions with apocrine, eccrine, follicular or sebaceous differentiation.<sup>[1]</sup> Nair observed that eccrine tumors were the most common followed by tumors with trichilemmal differentiation. He reported a female preponderance and the maximum numbers of cases were seen in the age group 11-20 years.<sup>[11]</sup> In accordance with previous studies,<sup>[11-13]</sup> maximum numbers of cases (42%) of appendageal tumors in present study were also seen in the age group less than 20 years indicating that adnexal tumors are disorders of the young. However, no significant gender difference was observed. Further, tumors with sebaceous differentiation constituted the largest group (34.6%) followed by tumors with eccrine differentiation and tumors with follicular differentiation in equal proportions (26.9% each). This difference could possibly be due to variation in susceptibility of different population groups in diverse geographical regions.

Benign melanocytic skin tumors include a large variety of naevi with distinct clinical, morphological and genetic profiles.<sup>[1]</sup> In this study, naevi comprised only 12.3 % of benign neoplasms. These were common in the younger age groups and no case was seen above 60 years of age.

Keratinocytic tumors are derived from epidermal and adnexal keratinocytes. These comprise a large spectrum of lesions ranging from benign proliferations (acanthomas) to malignant squamous cell carcinomas.<sup>[1]</sup> In the present study, only six cases of benign keratinocytic tumors were observed, most of them were in older age groups and no gender difference was seen (M:F= 1:1).

**MALIGNANT NEOPLASMS:** Malignant neoplasms comprised slightly more than one-fourth of the total skin tumors. The mean age of this group was 55.8 years. No appreciable gender difference was observed (M: F=1.1:1). A study by Heidari and Najafi also mentions a similar trend in age distribution with increase in incidence by the age group 50-59 years and rising sharply thereafter. They observed a definite male predominance.<sup>[3]</sup> On the other hand, Pinedo et al. reported a higher proportion of cases in women (58.6%) as compared to men (41.4%).<sup>[4]</sup> Bahamdan and Morad found that the mean age was 61.0 years with a male: female ratio of 1.6:1.<sup>[14]</sup>

Keratinocytic tumors comprised the largest group (more than three-fourth of the malignant neoplasms). The WHO manual on skin tumors states that keratinocytic tumors account for approximately 90% or more of all skin malignancies, of which, approximately 70% are BCC.<sup>[1]</sup> In the present study, SCC (43%) was more common than BCC (34%). This observation is in concordance with other studies reported from India;<sup>[5, 15]</sup> whereas; many other studies done in Caucasian population have reported a higher incidence of BCC.<sup>[2, 6, 7, 16]</sup> The same may be explained by the fact that the most common predisposing factor in the pathogenesis of BCC is light skin color in association with exposure to strong sunlight.<sup>[17]</sup> Female preponderance was observed in the cases of BCC (M:F=1:2). Few studies have also reported the same;<sup>[2, 4]</sup> although some studies observed male predominance.<sup>[6, 16, 18]</sup> Cases of SCC did not show any gender difference in the present study (M: F=1.1:1).

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Melanoma is predominantly a disease of fair skinned people living in higher altitude because exposure to sunlight is an important risk factor for this disease. Non-white patients tend to present later, with more advanced tumors.<sup>[19]</sup> Although less common than the BCC and SCC of the skin, they are much more frequently fatal due to their intrinsic tendency for lymphatic and haematogenic metastasis.<sup>[1]</sup> In the current study, melanoma comprised 9% of all the malignant skin tumors and males outnumbered females (M:F=3:1). Our results correlated with the report by Holterhues et al. who found that melanomas comprised 11% of all skin malignancies. However, in their study majority of patients were females with median age of 53 years.<sup>[2]</sup> This observation can be explained by the fact that in our study, malignant melanocytic tumors constituted only a small fraction. A study carried out in a larger group comprising only malignant skin tumors would probably give a more valid data that can be reliably compared with other studies.

Adenxal carcinomas are a rare and diverse group of neoplasms with variable differentiation. Their incidence increases with age, with a peak in the eighth decade. Males and females are equally affected below fifty years of age but male predominance is observed with increasing age.<sup>[20]</sup> All the four cases of malignant appendageal tumors (three of follicular differentiation; one of sebaceous differentiation) observed in the study were also elderly males.

Sarcomas of cutaneous origin are relatively rare and are far outnumbered by carcinomas, melanomas and benign mesenchymal neoplasms of skin and subcutis.<sup>[1]</sup> This is also reflected in the present study and only a single case was seen during the entire period.

Among the hematology lymphoid tumors, only one case of indeterminate cell histiocytosis (ICH) was reported. ICH is a proliferative cutaneous disorder of the so called "indeterminate cells" (IC). The disease is very rare, usually occurs during adulthood with few exceptions and both sexes are equally affected.<sup>[1]</sup>

Though our study presents a comprehensive overview of all WHO skin tumors groups, some underreporting may have occurred because some skin tumors may have been treated without being confirmed by histopathological examination. Moreover, for certain tumor types, stratified trend analysis was not possible because of the limited number of cases.

**CONCLUSION:** Soft tissue tumors of skin and subcutis form the largest group amongst the benign neoplasms and keratinocytic tumors are the commonest malignant skin tumors.

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| Groups of skin tumors                     | Benign     | Malignant | Total (%)       |
|---|------------|-----------|-----------------|
| 1. Keratinocytic Tumors                   | 6          | 34        | 40 (24.7)       |
| 2. Melanocytic Tumors                     | 14         | 4         | 18(11.1)        |
| 3. Appendageal Tumors                     | 26         | 4         | 30(18.5)        |
| a. Tumors with eccrine differentiation    | 7          | 0         | 7               |
| b. Tumors with apocrine differentiation   | 3          | 0         | 3               |
| c. Tumors with follicular differentiation | 7          | 3         | 10              |
| d. Tumors with sebaceous differentiation  | 9          | 1         | 10              |
| 4. Hematolymphoid Tumors                  | 0          | 1         | 01(0.6)         |
| 5. Soft tissue Tumors                     | 72         | 1         | 73(45.1)        |
| a. Vascular                               | 25         | 0         | 25              |
| b. Fibrous/Fibrohistiocytic               | 14         | 1         | 15              |
| c. Lipoma                                 | 26         | 0         | 26              |
| d. Neural                                 | 7          | 0         | 7               |
| <b>Total</b>                              | <b>118</b> | <b>44</b> | <b>162(100)</b> |

**Table 1: Distribution of benign and malignant neoplasms of skin and subcutis (n= 162)**

| Benign Neoplasm                 | 0-20 yrs  | 21-40 yrs | 41-60 yrs | 61 & above | Total (%)       | Males     | Females   | Ratio        |
|---------------------------------|-----------|-----------|-----------|------------|-----------------|-----------|-----------|--------------|
| 1. Keratinocytic Tumors         | 1         | 0         | 2         | 3          | 6 (5.1)         | 3         | 3         | 1:1          |
| 2. Melanocytic Tumors (Naevi)   | 2         | 8         | 4         | 0          | 14 (12.3)       | 6         | 8         | 1:1.3        |
| 3. Appendageal Tumors           | 11        | 7         | 6         | 2          | 26 (22.0)       | 14        | 12        | 1.16:1       |
| 4. Hematolymphoid Tumors        | 0         | 0         | 0         | 0          | 0 (0)           | 0         | 0         | -            |
| 5. Soft tissue Tumors           | 14        | 30        | 17        | 11         | 72 (61.2)       | 33        | 39        | 1:1.18       |
| a. Vascular                     | 8         | 11        | 4         | 2          | 25 (21.2)       | 6         | 19        |              |
| b. Fibrous/<br>Fibrohistiocytic | 1         | 7         | 4         | 2          | 14 (12.3)       | 8         | 6         |              |
| c. Lipoma                       | 2         | 9         | 9         | 6          | 26 (22.0)       | 14        | 12        |              |
| d. Neural                       | 3         | 3         | 0         | 1          | 7 (5.9)         | 5         | 2         |              |
| <b>Total</b>                    | <b>28</b> | <b>45</b> | <b>29</b> | <b>16</b>  | <b>118(100)</b> | <b>56</b> | <b>62</b> | <b>1:1.1</b> |

**Table 2: Age and gender distribution of benign neoplasms (n= 118)**

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| Malignant Neoplasm               | 0-20 yrs | 21-40 yrs | 41-60 yrs | 61 & above | Total (%)       | Males     | Females   | Ratio        |
|----------------------------------|----------|-----------|-----------|------------|-----------------|-----------|-----------|--------------|
| 1. Keratinocytic Tumors          | 3        | 5         | 11        | 15         | 34 (77.3)       | 15        | 19        | 1:1.3        |
| Basal Cell Carcinoma             | 1        | 0         | 5         | 9          | 15 (34.1)       | 5         | 10        | 1:2          |
| Squamous Cell Carcinoma          | 2        | 5         | 6         | 6          | 19 (43.2)       | 10        | 9         | 1.1:1        |
| 2. Melanocytic Tumors (Melanoma) | 2        | 1         | 0         | 1          | 4 (9.1)         | 3         | 1         | 3:1          |
| 3. Appendageal Tumors            | 0        | 0         | 0         | 4          | 4 (9.1)         | 4         | 0         | 4:0          |
| 4. Hematolymphoid Tumors         | 1        | 0         | 0         | 0          | 1 (2.3)         | 1         | 0         | 1:0          |
| 5. Soft tissue Tumors            | 0        | 1         | 0         | 0          | 1 (2.3)         | 0         | 1         | 0:1          |
| a. Vascular                      | -        | -         | -         | -          | (0)             | 0         | 0         |              |
| b. Fibrous/<br>Fibrohistiocytic  | -        | 1         | -         | -          | 1(2.3)          | 0         | 1         | 0:1          |
| c. Lipoma                        | -        | -         | -         | -          | (0)             | 0         | 0         |              |
| d. Neural                        | -        | -         | -         | -          | (0)             | 0         | 0         |              |
| <b>Total</b>                     | <b>6</b> | <b>7</b>  | <b>11</b> | <b>20</b>  | <b>44 (100)</b> | <b>23</b> | <b>21</b> | <b>1.1:1</b> |

Table 3: Age and gender distribution of Malignant neoplasms (n= 44)

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