

Clinicopathological study of skin tumors

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ABSTRACT

Background: The diagnosis of skin tumors can cause difficulties due to their wide variety of overlapping differentiation and complicated nomenclature. Histopathological study is the most valuable means of diagnosis. Keeping in view these facts, an attempt is made to study the different varieties of tumors of the skin. **Aims and Objectives:** (1) The aim of this study was to study the histomorphology of different skin tumors with ancillary technique necessary and to correlate with the clinical features. (2) To find the proportion of various skin tumors. (3) To classify and identify various skin tumors and study its variation according to age, sex, site, etc., which will bear an impact on patient management and prognosis.

Materials and Methods: This observational study included all cases of skin tumors received in the Department of Pathology, Kottayam Medical College, during a period of 1 year. Biopsy samples were collected, fixed in 10% formalin, processed and embedded in paraffin blocks, and stained with hematoxylin and eosin (H and E). The stained sections were studied under a microscope and histopathological diagnosis was correlated with clinical diagnosis.

Results: Out of the 227 cases of skin tumors, 102 (44.9%) were male and 125 (55.1%) were female. The incidence of skin tumors peaks in individuals older than 60 years of age. The most common sites affected were face (40%). Keratinocytic tumors constituted the largest proportion of tumors (43%), followed by melanocytic tumors (31%), soft-tissue tumors (13%), appendage tumors (11%), neural (1%), and hematomolymphoid tumors (1%).

Conclusion: Out of the 227 cases in the present study, the clinical diagnosis of only 169 cases was correlating with the histopathological diagnosis. This emphasizes the role of microscopy in the correct diagnosis of skin tumors.

Key words: Keratinocytic tumors; Melanocytic tumors; Soft-tissue tumors; Appendage tumors; Neural and hematomolymphoid tumors

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INTRODUCTION

The skin is the largest organ in the body. Over the areas exposed to the greatest friction, the skin gives mechanical protection to the underlying tissues. Unique character of the skin is due to its complex histomorphological features. It has two seemingly separate but functionally interdependent layers, the epidermis and dermis. The epidermal layer is composed mainly of keratinocytes (>90%), with scattered Langerhans cells, melanocytes and neuroendocrine (merkel cells). The epidermis is formed by stratified squamous which has five different layers: 1. Basal cell layer (stratum basalis), 2. Stratum spinosum (malpighian layer), 3. Stratum granulosum, 4. Stratum lucidum, and 5. Stratum corneum (keratin layer). The dermis has bundles of collagen and

elastic fibers embedded in an acellular ground substance, together with scattered inactive fibroblasts that synthesize the collagen, elastic fibers, and matrix. The dermis also contains the vascular supply and nerve innervation of the skin. Dermis has two layers, a superficial papillary dermis just beneath the epidermis and a deeper reticular dermis which borders the subcutis. There are also specialized structures such as hair follicles, sweat glands and sebaceous glands which are called the skin appendages.^{1,2}

Skin tumors form a small, but significant proportion of patients with cancer. Skin tumors are an ideal subject for study in the clinical and morphological point of view and it can affect people of all ages. An alarming increase of skin cancer has been identified among fair-skinned

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populations.¹ These differences in trends of skin cancer may be due to variations in skin types, geographical latitudes, occupational exposure, behavior in terms of sun exposure and skin protection and differences in disease awareness and surveillance. Skin tumors may have various clinical presentations. Histopathology is the most valuable means of diagnosis of skin tumors.

In the World Health Organization (WHO) skin tumors are classified into keratinocytic tumors, melanocytic tumors, appendageal tumors, hematolymphoid tumors, soft-tissue tumors, and neural tumors. Keratinocytic tumors are derived from epidermal and adnexal keratinocytes and constitute the largest spectrum among skin lesions. Keratinocytic tumors range from benign acanthomas to malignant squamous cell carcinomas (SCCs) which may show aggressive growth and metastatic potential.¹ Melanocytic tumors are the second largest group of skin tumors. Benign melanocytic tumors and malignant melanomas are two important entities included under melanocytic tumors. Intermittent high doses of ultraviolet radiation in combination with endogenous factors including genetic susceptibility are the major environmental risk factor. Cutaneous appendages can give rise to a bewildering number of neoplasms, more than accounted. Adnexal tumors are rare and there is paucity of literature on their clinicopathological features. Benign adnexal tumors can mimic malignant lesion and usually manifest in younger age group. Adnexal carcinomas are characterized by a wider range from those in which actinic damage is the norm, such as the common basal cell carcinoma (BCC) to those that seem to have little relationship to sun exposure.¹

Lymphomas may involve the skin as the primary and only site of involvement or may spread to the skin as a secondary site of disease. Some of the cutaneous lymphomas morphologically resemble their counterparts in lymph node, but can differ in terms of phenotype, genotype and clinical behavior, suggesting that they represent an independent entity.³ Vascular tumors, lymphatic tumors, smooth muscle tumors, skeletal muscle tumors and neural tumors constitute a small proportion of skin tumor. Most soft-tissue tumors are benign ones.⁴

The diagnosis of skin tumors can pose unique difficulties due to their wide variety of overlapping differentiation and complicated nomenclature. The distinction between benign and malignant neoplasm is rather difficult to define when they occur in skin and histopathological study is the most valuable means of diagnosis.⁵ Keeping in view these facts, an attempt is made to study the different varieties of tumors of skin with the following objectives.

Aims and objectives

1. To study the histomorphology of different skin tumors with ancillary technique necessary and to correlate with the clinical features.
2. To find out the proportion of various skin tumors.
3. To classify and identify various skin tumors and study its variation according to age, sex, site, etc., which will bear an impact on patient management and prognosis.

MATERIALS AND METHODS

This observational study included all cases of skin tumors received in the department of pathology, Kottayam Medical College during a period of 1 year. Biopsy samples were collected. Nature of specimen was noted. Specimens were fixed in 10% formalin for 12–36 h and the gross features were examined. Extent of sampling depended on the size of tumor as follows. Specimens measuring 3 mm or less were submitted in toto. Specimens measuring 4–6 mm were through the center and both halves submitted for processing. Specimens measuring 7 mm or more, a 2–3 mm slice from the center were cut and submitted for processing. For larger malignant lesions, 2–4 sections from tumor and 4 or more sections from surgical margins were taken.

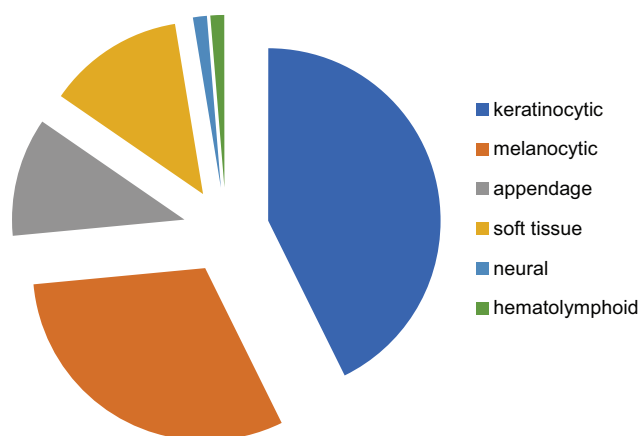
Further, tissue was processed and embedded in paraffin blocks. Sections of 3–5 micron thickness were taken, incubated, cleared with three changes of xylene and stained with hematoxylin and eosin (H and E). Stained sections were studied under a microscope and histopathological diagnosis was correlated with clinical diagnosis. Immunohistochemistry and special stains were used in the case of diagnostic dilemma. Special stains included in the study were massons fontana alkaline silver technique and bleaching method using potassium permanganate for melanin, toluidine blue staining for confirming mast cell. Immunohistochemical stains included in the study were P40, P63, BerEP4, HMB 45, Melan A, S100, LCA, CD20, CD3 (Lymphoma) etc. The data were entered in Microsoft Excel and further analysis will be done using software SPSS version 16.0. The proportion of patients with skin tumors was analyzed and classified according to the WHO classification of skin tumors 2006.^{6,7}

RESULTS

Out of the 227 cases of skin tumors, 102 (44.9%) were males and 125 (55.1%) were females with a male-to-female ratio of 1:1.22. The incidence of skin tumors peaks in individuals older than 60 years of age, accounted for 74.8% of cases. Benign lesions accounted for 62.6% of cases and malignant lesions accounted for 37.4% of cases. The most common sites affected were face (40%), followed by limbs (25.6%) and trunk (15%).

Most of the lesions presented as nodules (54%) (Table 1).

Keratinocytic tumors constituted the largest proportion of tumors (43%), followed by melanocytic tumors (31%), soft-tissue tumors (13%), appendage tumors (11%), neural (1%), and hematolymphoid tumors (1%) (Table 2).



Among the keratinocytic tumors, SCC constituted the largest number of cases (39.2%), followed by BCC (18%), verrucae vulgaris (VV), seborrheic keratosis (SK), verrucous carcinoma (VC), Bowens disease, and keratoacanthoma (KA) (Figures 1 and 2).

Among melanocytic tumors, benign nevoid lesions constituted 86% of cases, and malignant melanoma constituted 14% of cases. Out of 71 cases of benign nevoid lesions, intradermal nevus accounted for 59.15%, followed by compound nevus (17%) (Figures 1 and 2).

Among the 24 cases of appendage tumors, the most number of cases were nodular hidradenoma (24%), followed by pilomatricoma (16%) trichofolliculoma, sebaceoma, eccrine spiradenoma, and syringoma (Figures 1 and 2).

Among the 29 cases of soft-tissue tumors, hemangioma accounted for most number of cases (65.5%), followed by dermatofibroma (15.7%), dermatofibrosarcoma protuberance (DFSP) (6.9%). There were three cases of neural tumors all were granular cell tumor. There were three cases of hematolymphoid tumor. One was a case of non-Hodgkin's lymphoma (NHL), other was a case of cutaneous mastocytosis and the third one was a case of juvenile xanthogranuloma (Figure 3).

Benign lesion was common in younger age groups with a mean age of 37 years. Malignant lesion was common in older age groups with a mean age of 65 years. There was a mean age difference of 28 years, which was found to be statistically significant assessed through an independent t-test with a $P < 0.005$.

Table 1: Distribution of skin tumors according to the clinical presentation

Clinical presentation	No of cases	%
Nodule	125	54.9
Ulceroproliferative	41	18.1
Pigmented	28	12.3
Verrucous	13	5.7
Ulcer	11	4.9
Papule	9	4

Table 2: Frequency of distribution of various keratinocytic skin tumors

Distribution	No of cases	%
SCC	38	39.2
BCC	18	18.6
VC	7	7.2
VV	9	9.3
KA	2	2.1
SK	16	16.5
Bowens	7	7.2

BCC: Basal cell carcinoma, SCC: Squamous cell carcinomas, VV: Verrucae vulgaris, SK: Seborrheic keratosis, VC: Verrucous carcinoma, KA: Keratoacanthoma

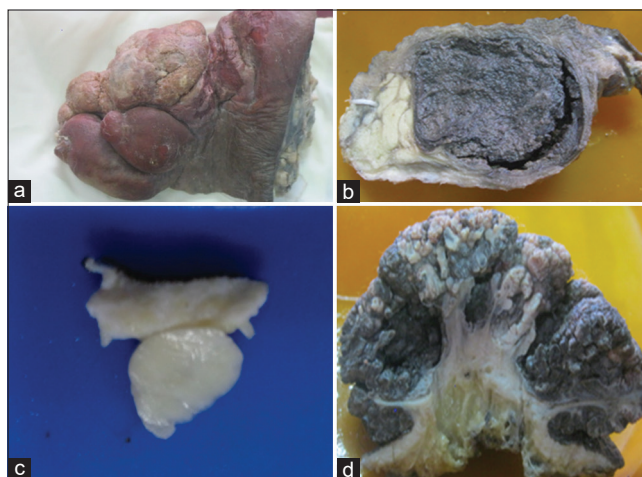


Figure 1: (a) Squamous cell carcinoma-large ulceroproliferative growth plantar aspect of foot. (b) malignant melanoma-irregular black lesion thigh. (c) trichofolliculoma-light brown glistening nodular lesion scalp. (d) condyloma acuminatum – warty dark brown growth on the surface of the skin

DISCUSSION

Out of 227 cases, 62.6% were benign and 37.4% were malignant. The ratio of benign to malignant tumors in the present study was 1.67:1. In the study done by Shaikh,⁸ the ratio of benign (46) to malignant tumors (89) was 1:1.93.

In the present study out of 85 cases of malignant tumors, 38 cases were SCC, 18 cases were BCC, 10 cases were malignant melanoma, seven cases were VC, seven cases were Bowen's disease, two cases were DFSP, two cases

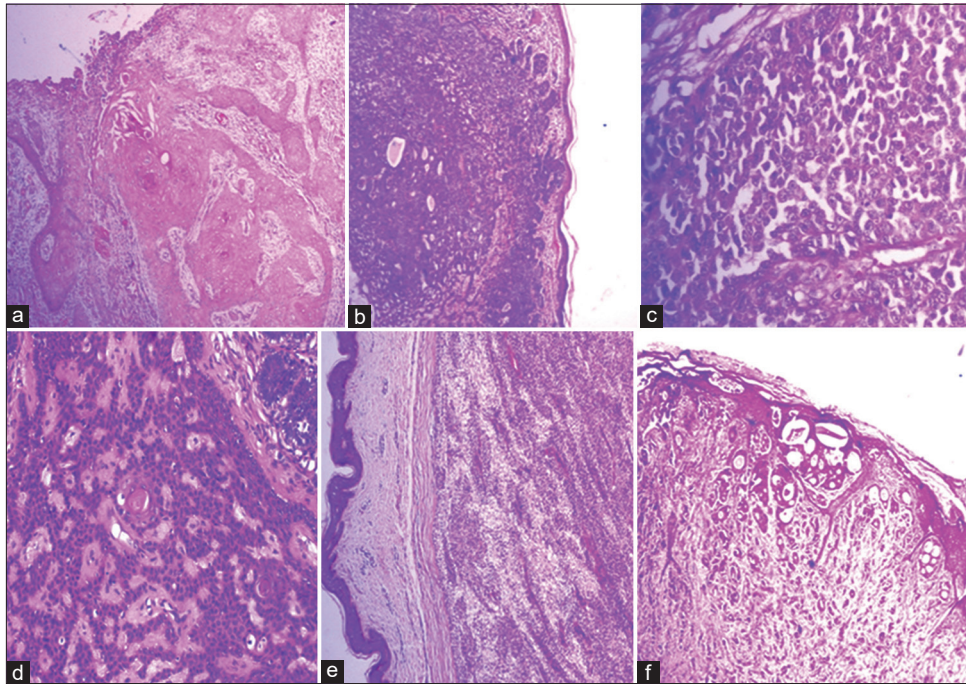


Figure 2: (a) Squamous cell carcinoma-infiltrating neoplastic cells arranged in nests, (b) basal cell carcinoma – basaloid squamous cells in sheets and nests, (c) malignant melanoma – neoplastic cells arranged in sheets, (d) trichoepithelioma – circumscribed basaloid neoplasm in deep dermis arranged in nests, racemose, cribriform, reticulate patterns, (e) nodular hidradenoma – circumscribed nodular neoplasm showing clear cells, cuboidal cells, and squamous cells in sheets, and (f) apocrine carcinoma – an infiltrating neoplasm arranged in tubular pattern, in cribriform pattern, and in cords

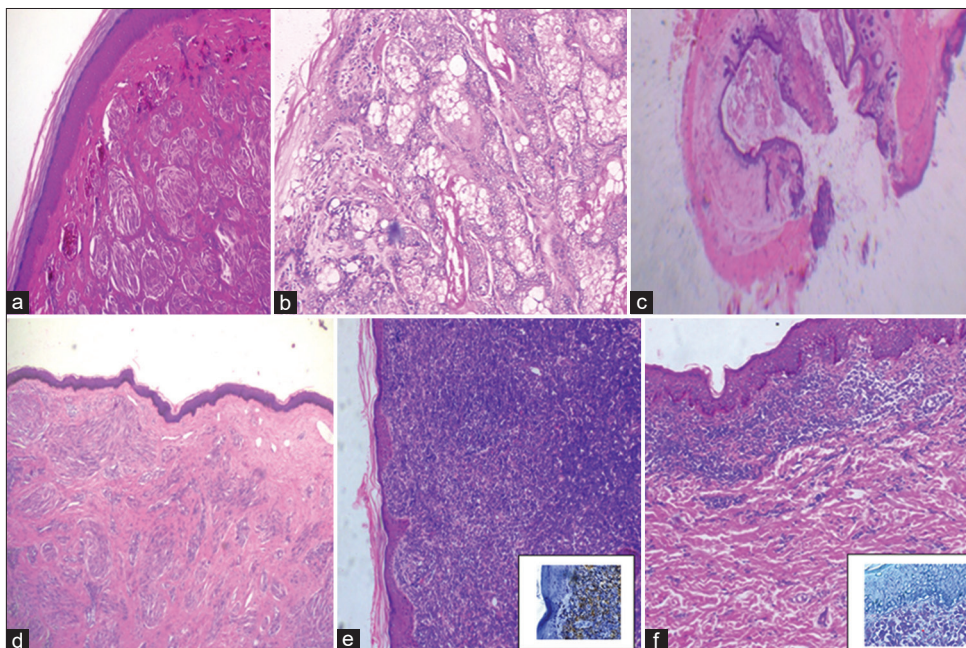


Figure 3: (a) Spitz nevus – intradermal neoplasm composed of cells arranged in nests, (b) sebaceoma – lobular arrangement of mature and immature sebaceous cells, (c) trichofolliculoma – dilated infundibulocystic units and vellus hair follicles, (d) pleomorphic fibroma – dermal proliferation of spindle cells admixed with collagen, (e) cutaneous B-cell lymphoma – dense infiltration of dermis by neoplastic lymphocytes (inset CD20 positivity in neoplastic cells), and (f) mastocytosis – band like infiltrate of mast cells in the papillary dermis (inset-toluidine blue positivity in neoplastic cells)

were hematolymphoid tumors, and one case was apocrine carcinoma. In the present study, SCC accounted for the

most number of cases (38 cases, 44%) of malignant tumors followed by BCC (18 cases, 21%).

In the study by Budharaja et al., SCC (49.02%) was the most common type, followed by malignant melanoma (29.41%), BCC (17.65%), and adnexal carcinoma (0.98%).⁹ In the study by Chakravorthy and Dutta-Choudhuri, SCC (64.3%) was the most common type, followed by BCC (16.5%), malignant melanoma (8.69%), and adnexal carcinoma (2.6%). In the study by Deo et al., also SCC was the most common type (55.8%), followed by malignant melanoma (26.1%) and BCC (18.1%).¹⁰

In the present study, SCC constituted a maximum number of cases (45 cases), out of which seven cases were *in situ* SCC. This is the most common neoplasm in our country as observed in the studies done by Budharaja et al., Deo et al., and Chakravorthy and Dutta-Choudhuri.⁹⁻¹¹ In this study, 31 cases were males and 14 were females. In the study done by Shaikh, the majority of the patients were males (39 patients). Out of 38 cases, three cases were SCC arising in KA and one was a case of basosquamous carcinoma.^{8,12}

VC: It is a low-grade variant of SCC. In the present study, seven cases were encountered. The majority of cases occurred in males (75%). Most cases were seen on penis. These findings were similar to the observations made by Shaikh.⁸ There were 18 cases of BCC (18.6%), out of which 11 cases were females and seven cases were males. Three cases were diagnosed as pigmented variant of BCC and four cases were adenoid variant. All observations were comparable with similar Indian studies.^{13,14}

Sixteen cases of SK were obtained during the present study period. Out of which three cases were irritated SK; two were hyperkeratotic variant, one case of inflamed variant, and one case of pigmented variant. Male-to-female ratio is 1:1. In a study done by Shaikh, there were five cases of SK, all are acanthotic variant.⁸

Two cases of KAs were studied, both were elderly males. One was on limb and other is on scalp. This was concordance with the study done by Schwartz.¹⁵

In the present study, VV constituted about 9.5% of cases (9 cases). Out of the nine cases, seven were males and two were females. Limbs were the commonly affected sites. The youngest age group affected was a 19-year-old female. Kilkenny et al., found no difference in the overall frequency of warts between males and females.¹⁶

In this study, there were 10 cases of malignant melanoma, two were spindle cell variant and one was a case of amelanotic variant. All were elderly with a slight male predominance with male to female ratio 1.2:1, which was consistent with the findings of Chakravorthy and Dutta-Choudhuri, Mukhopadhyay et al., and Katalinic

et al. The most common sites affected were extremities, similar observations were noted by Mukhopadhyay et al. In the present study, majority of cases (70%) occurred in the age range of 60–79 years. Similar observations were made by Katalinic et al., (38.8%) and Mukhopadhyay et al., (45.5%).^{9,17,18}

Out of 60 cases of benign nevoid lesions, 42 cases were intradermal nevus, 12 cases were compound nevus, two cases each of junctional and verrucous epidermal nevus, and one case each of blue nevus, spitz nevus, congenital melanocytic nevus. Shoko and Tetsunori has analyzed 531 cases of nevus out of which 15 were junctional, 134 cases were compound, and 382 cases were dermal. In the present study, females constituted the most number of cases with male to female ratio is 5:1. The most common age group affected in the present study was below 30 years of age.¹⁹

Among the 24 cases of appendage tumors, most number of cases were nodular hidradenoma (6 cases, 24%), followed by pilomatricoma (4 cases, 16%), two cases each of trichofolliculoma, sebaceoma, eccrine spiradenoma, syringoma and one case each of eccrine poroma, apocrine hidrocystoma, eccrine acrospiroma, hidradenoma papilliferum, proliferating trichilemmal tumor, and apocrine carcinoma. Out of the 24 cases, 23 were benign and only one case was malignant. In the study by Reddy et al., benign tumors formed the majority.²⁰

Out of the 24 cases of appendage tumors, 15 were females and nine were males. This was similar to the study done by Shaikh and Marrogi et al.^{8,21}

In the present study, three cases of hematology lymphoid tumors were included, one was a case of cutaneous mastocytosis in a 9-month-old male child who presented with multiple papular lesions over trunk. Second was a case of NHL in a 77-year-old lady. She presented as a nodular lesion over arm and diagnosis was later confirmed by immunohistochemistry. Third case was that of juvenile xanthogranuloma in a 3-year-old female child. In a study done by George et al., in Christian Medical College, Vellore, 33 cases of cutaneous lymphoma were studied -31 had NHL and two had Hodgkin's disease. Out of 31 NHL cases, 20 patients with cutaneous T-cell lymphoma, seven patients with cutaneous B-cell lymphoma, one with anaplastic large cell lymphoma, and three cases were unclassifiable. Mycosis fungoides was the most common cutaneous T-cell lymphoma.²²

Among the 29 cases of soft-tissue tumors in this study, hemangioma accounted for the most number of cases (65.5%), followed by dermatofibroma (15.7%) and DFSP

(6.9%). Out of 19 cases of hemangioma, 10 were males and nine were females. Younger age groups were commonly affected. In dermatofibroma and DFSP, male to the female ratio was found to be equal. In the study done by Tae Young et al., young females were commonly affected.²³

Limitations of the study

The descriptive nature of the study makes the generalization of the results obtained to the larger population difficult.

Ancillary test like immunohistochemistry and cytochemistry were done only in selected number of cases.

CONCLUSION

Out of the 227 cases of skin tumors obtained, females (55.1%) were the predominant population, with male-to-female ratio of 1:1.22. The incidence of skin tumors peaks in individuals older than 60 years of age (74.8%). Benign lesions accounted for 62.6% of cases and malignant lesions accounted for 37.4% of cases. The most common sites affected being face (40%) and most of the lesions presented as nodules (54%). There was a mean age difference of 28 years between the occurrence of benign and malignant lesions, which was found to be statistically significant assessed through independent t-test with a $P < 0.005$. Out of 227 cases, keratinocytic tumors constituted the largest proportion of tumors (43%), followed by melanocytic tumors (31%), soft-tissue tumors (13%), appendage tumors (11%), neural (1%), and hematolymphoid tumors (1%). SCC constituted the largest number of cases (39.2%), among the keratinocytic tumors. Among melanocytic tumors, benign nevoid lesions constitute 86% of cases and malignant melanoma constituted 14% of cases. Out of the 24 cases of appendage tumors, 24% of cases were hidradenoma, followed by pilomatricoma (16%) trichofolliculoma, sebaceoma, eccrine spiradenoma, and syringoma. Among the 29 cases of soft-tissue tumors, hemangioma accounted for most number of cases (65.5%). There were three cases of neural tumors and three cases of hematolymphoid tumor. Out of the 227 cases in the present study, the clinical diagnosis of only 169 cases was correlating with the histopathological diagnosis. This emphasizes the role of histopathology in the correct diagnosis of skin tumors and remains the gold standard.

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Authors' Contributions:

NU- Definition of intellectual content, literature survey, prepared the first draft of manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation, and submission of the article; **LV**- Guidance, coordination, and manuscript revision

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