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Original Research

Histopathological study of epidermal and adnexal tumour and tumour like lesions

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ABSTRACT
Background: There has been an alarming increase of skin cancer among fair skinned populations. Differences in trends and rates of skin cancer may be due to variation in skin types, geographical latitudes, occupational exposure, behaviour in terms of sun exposure and skin protection and differences in disease awareness and surveillance. Histopathology remains the gold standard for most dermatological diagnosis, but it has its limitations and very often a definite 'specific' diagnosis is not possible. Hence to establish this we examined histomorphology of epidermis and adnexae, histomorphology of tumor like lesions of epidermis and adnaxae and the epidemiology of tumors and tumor like lesions.
Material And Methods: The study was carried out in a tertiary care hospital at Kota, India. A properly completed surgical pathology requisition form containing the patient's identification, age, sex, essential clinical data and tissue submitted were noted. The WHO classification of skin tumours was followed. All the tumors arising from mucosa and genitalia were excluded from the study.
Results: Out of 484 cases, Epidermal tumors were most common (75%) followed by Adnexal tumors (20%) and Melanocytic tumors (5%). There is low incidence of Malignancy in all categories, with highest in Epidermal (5.78%). Male to female ratio was 2.3:1
Conclusion: Histopathological examination is essential for the accurate diagnosis and management of epidermal and adnexal tumors and tumor-like lesions. Clinicians should always consider histopathological evaluation for any suspicious skin lesion, especially those with non-specific clinical features.
Keywords: Epidermal tumors, Epidermis, Adnaxae, Malignancy

INTRODUCTION

Skinis the largest organ in human body. Skin is a complicated protective covering. It is divided into two seemingly separate but functionally interdependent layers, i.e. epidermis and dermis. The epidermal layer is composed of 90% of keratinocytes and the remaining 10% includes melanocytes, langerhans cells and neuroendocrine (merkel cells).[1]

There has been an alarming increase of skin cancer among fair skinned populations. Differences in trends and rates of skin cancer may be due to variation in skin types, geographical latitudes, occupational exposure, behaviour in terms of sun exposure and skin protection and differences in disease awareness and surveillance.[1]

Keratinocytictumours and tumor like lesions account for approximately 90% of all skin malignancies. Epidermal cysts are slowly growing, elevated, round, firm, intradermal or subcutaneous tumors that cease growing after having reached 1 to 5 cm in diameter. They occur most commonly on the face, scalp, neck, and trunk. Although most epidermal cysts arise spontaneously in hair bearing areas, occasionally they occur on the palms or sole or form as the result of trauma.[2-3]

Pilar or trichilemmal cysts are clinically indistinguishable from epidermal cysts but differ from them in frequency and distribution. They are less common than epidermal cysts, about 90% occur on the scalp. Furthermore, in contrast to epidermal cysts, pilar cysts are easily enucleated and appear as firm, smooth, white-walled cysts.

Three most frequent primary skin cancers are basal cell carcinoma (BCC), squamous cell carcinoma

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(SCC) and malignant melanoma. BCC and SCC, in combination, are referred to as non melanoma skin cancers (NMSCS). BCC is the commonest skin cancer worldwide, but various studies from India have reported SCC as the most prevalent skin malignancy.SCC commonly occurs on sun-damaged skin in white populations. It is the most frequent type of malignant tumor arising in scarred skin.[3]

Development of BCC has been correlated with prolonged, intensive uv exposure, with bcc occurring most commonly after the fifth decade of life. More than 90% of bcc develop in sun-exposed areas of the head and neck region regardless of the degree of pigmentation in an individual.

Melanocytic lesions are important primarily because of malignant melanoma which is the single most common potentially lethal neoplasm of skin. There are a number of intraepidermal proliferative disorders that may be precursors of squamous cell carcinoma.[4]

Adnexaeextend from epidermis into the dermis and consist of specialized cells for hair growth, epithelial renewal (stem cells), and temperature regulation.Adnexaltumors includes a large spectrum of skin epithelial tumors including hamartoma, hyperplasia, benign, and malignant tumors that originate from or show differentiation toward adnexal epithelial structures, namely, pilosebaceous unit, eccrine, and apocrine.[4]

These tumors are derived from multipotential undifferentiated cells present within the epidermis of its appendageal structures and the histological features of a tumor are related to the activation of molecular pathways responsible for forming the mature adenexal structure. Most of the benign skin adnexal tumors present as asymptomatic papules or nodules and often difficult to diagnose clinically. However anatomical location, number and distribution of lesions provide important clue. They are however confirmed by histopathology, and immunohistochemistry may helps in confirmation of diagnosis.[4,5]

The distinction between benign and malignant neoplasm is rather more difficult to define when they occur in skin and histopathological study is required to establish diagnosis which is the most valuable means of diagnosis in dermatopathology inspite of its own limitations.[4,6]

Excision biopsy, incision biopsy, punch biopsy, curettage biopsy, shave biopsy and wedge biopsy are various type of biopsy techniquesdone for skin lesions.[7-8]

Indications of skin biopsy include

Excision of epidermal or dermal neoplasms, whether benign or malignant. Clear margins are required. An incisional biopsy for confirmation of diagnosis of a lesion too big for removal, which will be treated by alternative methods. An incisional biopsy of skin eruptions that are difficult to categorise. Fresh tissue incisional skin biopsies for immunopathological study.

Histopathology is highly specific and sensitive for many lesions and it remains the gold standard for most dermatological diagnosis, but it has its limitations and very often a definite ‘specific’ diagnosis is not possible. In these cases correlation of histopathological findings with clinical findings will make a diagnosis possible. Use of histochemistry and I.H.C whenever needed is an important objective.[9]

AIMS AND OBJECTIVES

1) To study histomorphology of epidermis and adnexae.
2) To study the histomorphology of tumor like lesions of epidermis and adnexae.
3) To study the epidemiology of tumors and tumor like lesions.

MATERIAL AND METHODS

The study wascarried out in the Department of Pathology, Government Medical Collegeand Associated group of Hospitals, Kota over a period of 1 year from January 2019 to December 2019. The study was carried out after obtaining proper approval from the Institutional Ethical Committee.

A properly completed surgical pathology requisition form containing the patient’s identification, age, sex, essential clinical data and tissue submitted were noted.

Inclusion criteria: All benign and malignant lesions of the epidermis and adnexae.

Exclusion criteria: Tumors of mucosa and genitalia were excluded from the study.

The WHO classification of skin tumours was followed. All the tumors arising from mucosa and genitalia were excluded from the study.

Then the specimen were allowed to fix in 10% buffered formalin for 12-14 hours at room temperature and the gross features like size, shape, colour, external surface, cut surface, consistency, color of cut section are noted. Sampling depended upon the size of specimen whether small or large.

Grossing

Biopsy measuring 3 mm or less : whole biopsy tissue was processed as such.

Biopsy measuring between 4-6 mm : tissue was cut through the center and both halves were processed.

Biopsy with a width of 7 mm or more : a 2-3 mm slice from the centre was processed for histology and remaining in formalin to be saved.

For all of the above we made sure that sections were embedded on edge.

For lesions which were clinically diagnosed as neoplastic and were large , margins were paintedand grossing done.

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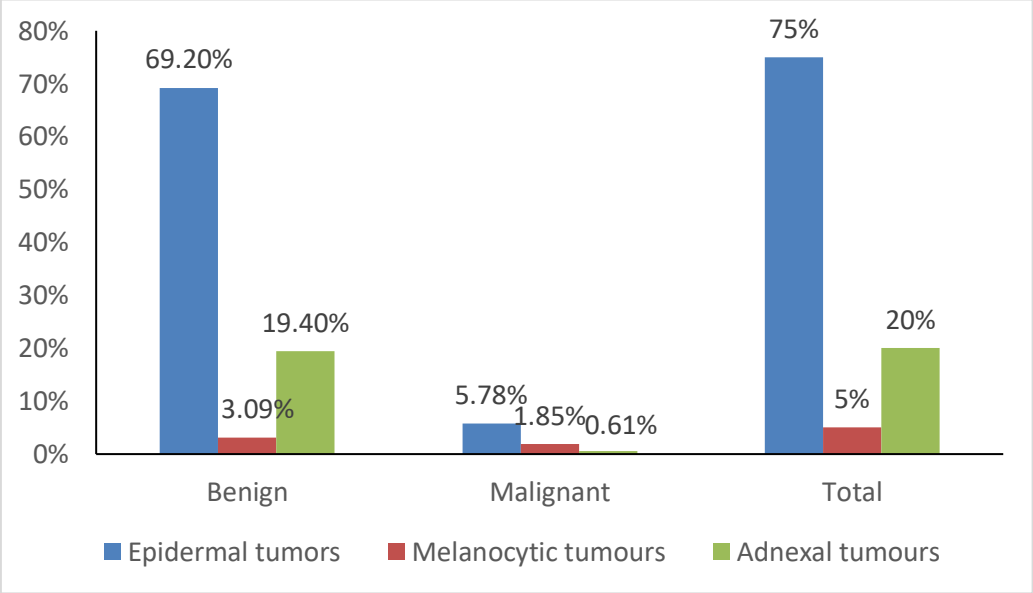
Cutting of the blocks: Cutting of the blocks is done by the microtome knife at the thickness of 4-5 micron. Before cutting icing of the blocks is done then sectioning ribbon is prepared and floated on floatation bath and pick-up section on albumin smeared slides then keep slides in hot air oven at 65ºC for 30 minutes and then the slides are subjected to routine H & E staining and special stains wherever required.The procedure is as follows –

Statistical Analysis: Data entry was done utilizing MS Excel. A statistical analysis was performed using GraphPad Prism 10. Relevant descriptive statistics were analyzed and plotted as frequency and percentage.

RESULTS

The present study was done for over a period of 1 years from January 2019 to December 2019 & includes 484cases of skin lesions in the Department of Pathology, Govt. Medical College Kota. The observations made are depicted in tables below:

Graph 1: Distribution and incidence of benign and malignant tumors of epidermis and adnexal



In the present study out of 484 cases,Epidermal tumors are most common (363/75%)followed by Adnexal tumors (97/20%) and Melanocytic tumors (24/5%). There is low incidence of Malignancy in all categories, with highest in Epidermal (5.78%), followed by Melanocytic (1.85%) & Adnexal (0.61%).

Table: 1 Sex-wise distributions of Epidermal lesions-

		No.	%	Male	Female
Epidermal Lesions	**Benign**				
	Epidermal cyst	269	55.5%	191	78
	Fibroepithelial polyp	11	2.2%	5	6
	Dermoid cyst	15	3%	9	6
	Corn	12	2.4%	6	6
	Squamous papilloma	1	0.20%	00	1
	Keratoacanthoma	5	1%	4	1
	Seborrheic Keratosis	2	0.41%	00	2
	Warty lesions	18	3.71%	14	4
	Linear epidermal nevus	2	0.41%	2	00
	Total Benign	**335**	**69.2%**		110
	Chi square 14.44; P value = 0.07 (NS)				
Keratinous Lesions	**Malignant**				
	Squamous cell carcinoma	14	2.8%	12	2
	Verrucous carcinoma	2	0.41%	1	1
	Basal cell carcinoma	12	2.47%	9	3
	Total Malignant	**28**	**5.78%**		
	Total	**363**	**75%**	**253**	**110**
	Chi square 1.48; P value = 0.48 (NS)				

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In the present study out of 484 cases, 363(75%) are Epidermal tumors of which epidermal cyst is the most common benign lesion- 269(55.5%), followed by warty dyskeratosis- 18(3.71%), dermoid cyst- 15(3%), fibroepithelial polyp- 11(2.2%), cornu- 12(2.4%), keratoacanthoma- 5(1%), linear epidermal nevus- 2(0.41%), Seborrheic Keratosis 2(0.41%) and squamous papilloma- 1(0.20%). Out of 28 malignant Epidermal Neoplasm, squamous cell carcinoma was most common- 14(2.8%) followed by basal cell carcinoma- 12(2.4%) and verrucous carcinoma- 2 (0.41%). (P>0.07, NS) (Table 1)

In the present study out of 363 cases of Epidermal tumors , all cases (Benign & Malignant) are more common in males (253/69.7%) as compared to females (110/30.3%). Male to female ratio is 2.3:1. Malignant Epidermal tumors are more common in 61-80 years number of cases are 13(46.4%), followed by 41-60 years 10(35.7%) cases, 21-40 years and 81-100 years each of 2(7.14%) cases and only 1(3.5%) case in 0-20 years of age. (P>0.07, NS) (Table 1)

Table: 2 Sex-wise distributions of Melanocystic lesions-

Melanocytic lesions	**Benign -**	**No.**	**%**	**Male**	**Female**
	Intradermal Nevus	12	2.27%	3	9
	Common blue Nevus	1	0.20%	00	1
	Compound Nevus	1	0.20%	00	1
	Dysplastic Nevus	1	0.20%	1	00
	Malignant				
	Malignant melanoma	9	1.8%	5	4
	Total	**24**	**4.9%**	**9**	**15**
	Chi square = 4.92, p value = 0.29 (NS)				

In the present study out of 484 cases 24 cases are of Melanocytic tumors, out of 24 cases 15(62%) are benign nevus and 9(38%) cases a Malignant Melanoma. In the present study of 484 cases, 24(4.9%) cases are of melanocytic tumors out of which 15 (62.5%) cases are seen in females and 9 (37.5%) cases are seen in males. Female to male ratio is 1.6:1. (p=0.29; NS) (Table 2)

Table: 3 Sex-wise distributions of Various lesions-

		No.	**%**	**Male**	**Female**
Malignant adnexal neoplasm	Malignant Acrospiroma	1	33.3%	1	00
	Malignant adnexal neoplasm	1	33.3%	00	1
	Trichilemmal carcinoma	1	33.3%	00	1
	Total	3	100%	1	2
Eccrine and apocrine lesions-	**Benign**				
	Eccrine poroma	9	9.6%	7	2
	Eccrine hyracytoma	1	1.06%	1	00
	Hidradenoma	3	3.19%	2	1
	Syringocystadenomapapilliferum	3	3.19%	1	2
	Cylindroma	1	1.06%	00	1
	Syringoma	1	1.06%	1	00
	Spriradenoma	1	1.06%	1	00
	Low grade adnexal tumor	1	1.06%	00	1
	Sebaceous nevus	4	4.3%	3	1
Follicular Lesions-	**Benign**				
	Trchilemmal cyst	51	54.2%	20	31
	Pilomatricoma	13	13.8%	7	6
	Trichoadenoma	1	1.06%	1	00
	Trichoepithelioma/ Trichoblastoma	2	2.12%	1	1
	Trichofolliculoma	2	2.12%	2	00
	Proliferating Trichilemmal tumor	1	1.06%	00	1
	Total	**94**	**(100%)**	46	48

In the present study the incidence of Malignant adnexal neoplasm are more in females 2(66.7%) as compared to males 1(33.3%) with female to male ratio of 2:1.In the present study most common benign Eccrine/ Apocrine lesion was Eccrine poroma (9.6%) and most common Follicular lesion was Trichilemmal cyst (54.2%). Malignant adnexal Neoplasm are rare in our studies 3.1% of all adnexal tumors and tumor like lesions. (Table 3)

Trichilemmal Cysts form more than half of the cases (54.2%), followed by Pilomatricoma (13.8%) & Eccrine Poroma (9.6%).In the present study both

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genders are almost equally involved in benign adnexal leions. Male to Female ratio is 1:1.04. (Table 3)

Table: 4 Age-wise distribution of benign Epidermal lesions-

		Age Group in Years				
		0-20	**21-40**	**41-60**	**61-80**	**81-100**
Epidermal Lesion	**Benign**					
	Epidermal cyst	36	126	74	33	00
	Fibroepithelial polyp	1	3	5	2	00
	Dermoid cyst	8	5	1	1	00
	Corn	5	6	1	00	00
	Squamous papilloma	00	1	00	00	00
	Keratoacanthoma	00	00	3	2	00
	Seborrheic Keratosis	00	1	00	1	00
	Warts	7	8	2	1	00
	Linear epidermal nevus	2	00	00	00	00
	Malignant					
	Squamous cell carcinoma	00	1	5	8	00
	Verrucous carcinoma	00	00	1	1	00
	Basal cell carcinoma	1	1	4	4	2

Table: 5 Age-wise distribution of benign Melanocytic Lesion -

Melanocytic Lesion		**0-20**	**21-40**	**41-60**	**61-80**	**81-100**
	Intradermal Nevus	2	8	1	1	00
	Common blue Nevus	00	00	1	00	00
	Compound Nevus	1	00	00	00	00
	Dysplastic Nevus	00	00	1	00	00
	Malignant melanoma	00	1	4	4	00
	Total	**3**	**9**	**7**	**5**	**00**

Table: 5 Age-wise distribution of benign Various Lesions -

Eccrine and Apocrine differentiation-	**Benign**	**0-20**	**21-40**	**41-60**	**61-80**	**81-100**
	Eccrine poroma	2	00	3	4	00
	Eccrine Hidracytoma	00	00	00	1	00
	Hidradenoma	00	1	1	1	00
	Syringocystadenomapapiliferum	2	00	00	1	00
	Cylindroma	00	00	1	00	00
	Spiradenoma	00	1	00	00	00
	Syringoma	00	1	00	00	00
	Sebaceous nevus	1	3	00	00	00
	Low grade adnexal tumor	00	00	1	00	00
Follicular differentiation	**Benign**					
	Trchilemmal cyst	6	19	21	4	1
	Pilomatricoma	3	7	2	1	00
	Trichoadenoma	00	1	00	00	00
	Immature Trichoepithelioma	00	00	2	00	00
	Trichofolliculoma	1	1	00	00	00
	Proliferating Trchilemmaltumor	00	1	00	00	00
	Total	**15**	**35**	**31**	**12**	**1**
Malignant adnexal Neoplasm	Malignant Acrospiroma	00	00	00	1	00
	Malignant adnexal neoplasm	00	1	00	00	00
	Trichilemmal carcinoma	00	00	1	00	00
	Total	**00**	**1**	**1**	**1**	**00**

In the present study the benign Epidermal tumors 335(69.2%) are more common in the age group of 21-40 years, 150(44.7%) cases followed by 41-60 years 86(25.6%) cases, 0-20 yrs 59(17.6%) cases, 61-80 yrs 40(12%) cases. Melanocytic tumors are more common in the age of 21-40years 9 (37.5%), followed by 7 (29.1%) cases in 41-60 years of age, 5 (20.8%) cases in 61-80 years, 3 (12.5%)cases in 0-20 years of

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age.The incidenceof benign adenexalneoplasm are more common in the age of 21-40 years followed by 41-60years , 0-20 years ,61-80 years and than80-100 years. About 68% cases occurs in 21-60 years of age.(Table 5,6,7)

In the present study the incidence of malignant adnexal neoplasm are equal in the age group of 21-40 years, 41-60 and 61-80 years.

DISCUSSION

In thishistopathological study of 484 cases of epidermal & adnexal tumors & tumor like lesions,the benign skin tumours and cysts are more common as compared to malignant. The ratio of benign (444/91.7%) to malignant tumours (40/8.3) was 11.1 : 1. Most studies reviewed showed a varying proportion of Benign & Malignant lesions, but all had preponderance of Benign Lesions.Karki D et al observed benign neoplasm (60%),followed by tumor like lesions (22%) and malignant neoplasm (18%) with abenign to malignant ratio is 3.3:1.[10]Azad S et al study also shows Benign skin neoplasms (72.8%) out-number malignant neoplasm (27.2%) with a benign to malignant ratio of 2.7:1.[11]

In the present study, the benign tumors and cysts of epidermis were most common (69.2%) followed by benign adnexal tumor (19.4%), Malignant epidermal tumors(5.78%), benign melanocytic tumor (3.09%), malignant melanocytic tumor (1.85%) and malignant adnexal were (0.61%). Samanta M et al from Puducherry, studied 52 cases of true tumors (excluding tumor like lesions and cysts) whichshows Malignant Epidermal Tumours being the most common (40.38%), followed by Benign Melanocytic Tumours (17.31%), Benign Tumours of Adnexa (15.38%), Benign Epidermal tumors (11.54%), Malignant Melanocytic Tumours (11.54%) and Malignant Adnexal Tumours (3.85%).[12]

In the present study majority of cases are Epidermal tumors and tumor like lesions (363/75%), Epidermal cyst being the most common keratinous lesion-269(55.5%), warty dyskeratosis are 18(3.71%), dermoid cyst 15(3%), cases of fibro-epithelial polyp 11(2.2%), Which is similar to findings of Karki D et al where the Epidermal cyst is most common lesion followed by dermoid and trichilemmal cyst. Similar study also shows that the most common benign neoplasm was epidermal cyst.[10,13]

In the present study out of 28 malignant epidermal tumors squamous cell carcinoma(14/50%) was the most common tumor, followed by Basal cell carcinoma (12-42.8%) and verrucous carcinoma are (2/7.14%). These findings are similar to study of Sheikh S et al which showssquamous cell carcinoma formed the majority (55%) of all malignant tumors.[14] Remainder comprised 22.5% of BCC, 9% of verrucous carcinoma, 6 (6.7%)cases of malignant adnexal tumor. Similarly other studies also shows that incidence of squamous cell carcinoma was highest (55.55%) followed by basal cell carcinoma(30.55%).[10,15,16]

Keratinous tumors (363/484) were more common in males (253/69.7%) as compared to females (110/30.3%) with a Male to female ratio of 2.3:1; which is similar to Bari V et al andSharma A et al.[17,18]

We observed that the benign tumors are more common in the age group of 21-40 years, and malignant keratinous tumors are more common in the age of 61-80years which is similar to the study conducted by Karki D et al.[10] Benign tumours were common in 11-30 years of age, malignant tumours in 61-80 years of age while tumour like lesions were common in 21-30 years of age.

Melanocytic tumors-In this study 24 casesof melanocytic tumors were reported out of which 15 (62.5%) are benign melanocytic nevi and 9 (37.5%) cases of malignant melanoma. The ratio of benign to malignant melanocytic lesion is 1.6:1 which is similar to Samanta et al study 1.5:1.[12] Most common benign Melanocytic nevus was Intradermal nevus 12(80%) out of 15 benign nevi, followed by 1 (6.6%) case each of common blue nevus, dysplastic nevus and compound nevus, which is similar studies showedmalignant melanoma constituted 3 out of 50 melanocytic tumors& 47 intradermal nevus, 13 cases of benign melanocytic naevi, out of these 11 were intradermal and 2 were compound naevi,19 melanocytic tumors i.e. 12 benign nevi, 2 dysplastic nevi, 5 cases of cutaneous malignant melanoma.[13,15,17]

Tumors of skin appendages - there were 97 cases of appendagial tumours out of which 94 (96.9%) were benign (of which Trichilemmal Cysts constituted 54.2% cases) and 3(3.1%) weremalignant, benign to malignant ratio is 31.3:1. Other studie observed 95% of the tumors were benign with only 5% being malignant, benign to malignant ratio is 19:1.[13,19,20]

In the present study out of 94 cases of benign adnexal tumors, the most common were Trichilemmal cyst 51(54.2%) followed by Pilomatricoma 13(13.8%) cases,Eccrine Poroma 9(9.6%) cases, sebaceous nevus 4(4.3%),3(3.19%) cases each of Hidradenoma and syringocystadenoma papilliferum, 2(2.12%) cases each of Trchiepithelioma and Trichofolliculoma, 1(1.06%) cases each of eccrine hydracytoma, Cylindroma, Spiradenoma, Syringoma, Low grade adnexal tumor, Trichoadenoma and Proliferating Trichilemmal tumor. Similar to ours Riyaz et al observedmost common Pilomatrixoma (38.33%), followed by Trichoadenoma, Trichoepithelioma, Trichilemmoma, Sebaceous Trichofolliculoma. Eccrine tumors found were Chondroid syringoma, Syringoma, Eruptive Syringoma, Eccrine spiradenoma, Eccrine Hidrocystoma, Nodular Hidradenoma, Eccrine Poroma and Cylindroma.[21]

In the present study the malignant adnexal tumors constitutes 3.01% of cases with male to female ratio

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of 1:2 and mean age is 60 years, which is similar to other studies[12,21] which reported, 3 cases (5%) and 3.85% of malignant adnexal tumors repectively.

CONCLUSION

The overall incidence of skin adnexal tumors is extremely low in the Indian population. Compared to malignant skin adnexal tumors, benign ones occur more frequently. The majority of malignant tumors develop in older adults, typically those over 50. Benign tumors, however, vary greatly in age. Although skin adnexal tumors can develop anywhere on the body, they most frequently occur in the head and neck area. Based solely on light microscopy, the majority of tumors can be divided into various subgroups. Sweat gland differentiation is more common in skin adnexal tumors.

Pilomatricoma is the most prevalent type of hair follicle tumor in our institutional study, whereas clear cell hidradenoma is the most common tumor with sweat gland differentiation. Amongst the tumors with sebaceous differentiation, sebaceous carcinoma (meibomian carcinoma) is commonest.

Histopathological examination is essential for the accurate diagnosis and management of epidermal and adnexal tumors and tumor-like lesions. Clinicians should always consider histopathological evaluation for any suspicious skin lesion, especially those with non-specific clinical features.

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