

Histomorphological Spectrum of Adnexal Tumours of the Skin: A Descriptive Study from a Tertiary Care Centre in Karnataka, India

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ABSTRACT

Introduction: Skin Adnexal Tumours (SAT) are a category of rare and most uncommon tumours. They could display multiple lines of differentiation such as follicular, eccrine, apocrine, sebaceous, and sometimes mixed differentiation, generating a mistaken diagnosis that might lead to unwarranted and unnecessary interventions.

Aim: To describe the types and microscopic features of adnexal tumours.

Materials and Methods: The present study was a retrospective study on SAT received for histopathology at the Department of Pathology, Mandya Institute of Medical Sciences, Mandya, Karnataka, India, from January 2018 to June 2022 during the study period of September 2022 to March 2023. The records of patients including age, gender and site were retrieved from the registers maintained at the department and Haematoxylin and Eosin (H&E) stained slides were examined and the data was analysed by descriptive statistics.

Results: A total of 62 cases were included in the study out of which, 59 (95.2%) cases were found to be benign and 3 (4.8%) cases were malignant. The mean age was found to be 43.87 years.

A total of 28 (45.1%) cases were seen in the age group of 21 to 40 years. Females outnumbered the males with 32 cases (51.6%). A maximum number of cases belonged to the group of sweat gland tumours (29/62, 46.8%) followed by hair follicle tumours (21/62, 33.9%) and sebaceous gland tumours (12/62, 19.3%). Nodular hidradenoma was the commonest sweat gland tumour (12/29, 41.4%), pilomatricoma was the commonest hair follicle tumour (10/21, 47.6%) and sebaceous adenoma was the commonest sebaceous gland tumour (10/12, 83.3%). The most common malignancy was sebaceous carcinoma (2/3, 66.67%) in females. The male-to-female ratio was found to be 1:1.06.

Conclusion: The incidence of SAT was low with the majority being benign tumours. Malignant tumours are even rarer and are often mistaken for cutaneous epithelial malignancies. These lesions may prompt the clinician towards unwanted surgery or treatment for the patient. They exhibit a wide variety of morphological patterns which may be confused for primary from other sites. In such cases, histopathological examination becomes necessary. Hence, a combination of good clinical expertise and histopathological confirmation by the Pathologist helps appropriately to manage the patient.

Keywords: Biopsy, Nodular hidradenoma, Pilomatricoma, Sebaceous adenoma, Sebaceous carcinoma

INTRODUCTION

The largest sensory organ of human body is the skin, which accounts for about 15% of total body weight. It is a complex organ having multiple functions. Primarily, it acts as a barrier against various harmful environmental agents [1]. Adnexae are structures present within the skin that aide in its function. They are represented by three histologically distinct structures: (a) the pilosebaceous unit; (b) the eccrine sweat glands; and (c) the apocrine glands [2,3]. These tumours may express one or more lines of appendageal differentiation during neoplastic transformation as they arise from multipotent stem cells present within epidermis or its appendageal structures [4]. Neoplastic lesions of the skin and adnexae are increasing over the past few decades [5]. Diagnosing them as benign or malignant, poses a challenge for clinicians in many ways. Biopsy for histopathological examination is the gold standard method to arrive at a diagnosis. Treatment options often include surgery which cannot be performed unless there is a confirmed diagnosis.

The spectrum of SAT ranges from a benign tumour that can be excised completely to a malignant, aggressive tumour which can metastasise [6]. Many of these tumours are associated with hereditary syndromes such as Birt-Hogg-Dube syndrome, Brooke-Spiegler syndrome, Cowden syndrome and Muir-Torre syndrome [7]. Since non neoplastic skin lesions are much more common than adnexal tumours of skin, clinicians tend to misinterpret and misdiagnose

adnexal tumours as other skin lesions. The present study aimed at histopathological analysis of the SAT in a tertiary care hospital to identify the characteristic features that help in identification of these specific tumours in various age groups, gender, anatomical location, types and microscopic features of adnexal tumours of skin and highlights the importance of the possibility of adnexal tumours among skin lesions.

MATERIALS AND METHODS

This was a retrospective study conducted at a tertiary care centre in Department of Pathology, Mandya Institute of Medical Sciences, Mandya, Karnataka, India. Data was collected from January 2018 to June 2022 and analysed from September 2022 to March 2023. The study was done after obtaining approval from the Institutional Ethics Committee (IEC), bearing the number MIMS/IEC/2022/678 and dated 27/10/2022.

Inclusion criteria: All cases of biopsy for adnexal tumours of skin received during the study period were included in the study.

Exclusion criteria: All cases who were already under treatment for adnexal tumours of skin were excluded from the study.

Study Procedure

A total of 1,512 skin biopsies were received during the study period out of which 62 cases were diagnosed as adnexal tumours of skin.

Fixation of the excised specimens was done in 10% neutral buffered formalin. After tissue processing, 4 μ to 5 μ thick tissue sections were taken. The sections were stained using H&E stain. The slides were evaluated to arrive at a final diagnosis categorised according to the World Health Organisation (WHO) classification, 4th edition published in 2018 [2]. All cases of biopsy for adnexal tumour were retrieved from histopathology registers and reviewed. The findings were analysed using descriptive statistics. Since the study was a retrospective and descriptive study, the individual parameters were not comparable to obtain a statistical significance.

STATISTICAL ANALYSIS

Data was analysed using Microsoft Excel, version 2014 and the results were expressed in percentage.

RESULTS

A total of 62 patients underwent biopsy for SATs during the study period. Female patients outnumbered the males with 32 (51.6%) females and 30 (48.4%) males. The male to female ratio was 1:1.06. The adnexal tumours were distributed in various anatomical locations of the body with most common being the head and neck region (54.90%) cases followed by lower extremities (14.5%) [Table/Fig-1].

Site	N (%)
Head and neck	34 (54.90)
Lower extremities	9 (14.50)
Upper extremities	8 (12.90)
Chest	5 (8.10)
Back	3 (4.80)
Abdomen and pelvis	3 (4.80)
Total	62 (100)

[Table/Fig-1]: Anatomical distribution of the adnexal tumours.

The mean age was found to be 43.87 years in the present study. The age group of 21-40 years had maximum number of cases (28, 45.1%) followed by 41-60 years (23, 37.1%). Among children and adolescents, sweat gland tumours were more common whereas in the age group of 21-40 years, sweat gland tumours and follicular tumours were seen equally. Among the age group of 41-60 years, sweat gland tumours were more common [Table/Fig-2].

Origin	Diagnosis	Age group (years)				
		0-20	21-40	41-60	61-80	Total
Sweat glands (29)	Nodular hidradenoma	0	6	6	0	12
	Chondroid syringoma	1	2	2	0	5
	Eccrineporoma	0	2	2	0	4
	Hidradenoma papilliferum	1	2	0	0	3
	Cylindroma	0	0	1	1	2
	Spiradenoma	0	0	1	0	1
	Syringocystadenoma papilliferum	0	0	1	0	1
	Spiradenocarcinoma	0	0	0	1	1
	Follicular (21)	Pilomatricoma	0	7	2	1
Trichoepithelioma		0	4	3	2	9
Trichofolliculoma		0	0	0	1	1
Proliferating trichilemmal tumour		0	1	0	0	1
Sebaceous gland (12)		Sebaceous adenoma	0	4	4	2
	Sebaceous carcinoma	0	0	1	1	2
Total (%)		2 (3.3%)	28 (45.1%)	23 (37.1%)	9 (14.5%)	62 (100)

[Table/Fig-2]: Distribution of skin lesions based on the age of the patient.

Among females, nodular hidradenoma was the commonest SAT observed (21.8%) followed by 18.75% of trichoepithelioma and

pilomatricoma. Among males, sebaceous adenoma was the commonest SAT (30%) followed by 16.7% of nodular hidradenoma [Table/Fig-3].

Category	Diagnosis	Female	Male	Total (N)
Sweat glands (29)	Nodular hidradenoma	7	5	12
	Chondroid syringoma	1	4	5
	Eccrineporoma	3	1	4
	Hidradenoma papilliferum	2	1	3
	Cylindroma	1	1	2
	Spiradenoma	0	1	1
	Syringocystadenoma papilliferum	0	1	1
	Spiradenocarcinoma	1	0	1
Follicular (21)	Pilomatricoma	6	4	10
	Trichoepithelioma	6	3	9
	Trichofolliculoma	1	0	1
	Proliferating trichilemmal tumour	1	0	1
Sebaceous gland (12)	Sebaceous adenoma	1	9	10
	Sebaceous carcinoma	2	0	2
Total (%)		32 (51.6%)	30 (48.4%)	62 (100%)

[Table/Fig-3]: Distribution of skin lesions based on the gender of the patient.

Among the adnexal tumours, 59 (95.2%) cases were found to be benign and 3 (4.8%) cases were malignant. Among the benign tumours, sweat gland tumours constituted the largest group with a total of 29 cases (46.8%) followed by hair follicle tumours (21/62; 33.9%) and sebaceous gland tumours (12/62; 19.3%). Out of 29 sweat gland tumours, nodular hidradenoma was the commonest with 12 cases (41.4%) followed by five cases (17.3%) of chondroidsyringoma. Out of 21 hair follicular tumours, pilomatricoma was the commonest with 10 cases (47.6%) followed by nine cases (42.8%) of trichoepithelioma. Out of 12 sebaceous gland tumours, majority (83.5%) were sebaceous adenoma and two cases (16.7%) were sebaceous carcinoma [Table/Fig-4].

Origin	Nature	Diagnosis	Frequency	Percentage among the category	Percentage among all adnexal tumours
Sweat glands (29)	Benign	Nodular hidradenoma	12	41.4%	19.4%
		Chondroidsyringoma	5	17.3%	8.1%
		Eccrineporoma	4	13.7%	6.5%
		Hidradenoma papilliferum	3	10.3%	4.8%
		Cylindroma	2	6.8%	3.2%
		Spiradenoma	1	3.5%	1.6%
		Syringocystadenoma papilliferum	1	3.5%	1.6%
		Malignant	Spiradenocarcinoma	1	3.5%
	Follicular (21)	Benign	Pilomatricoma	10	47.6%
Trichoepithelioma			9	42.8%	14.5%
Trichofolliculoma			1	4.8%	1.6%
Proliferating trichilemmal tumour			1	4.8%	1.6%
Sebaceous gland (12)		Benign	Sebaceous adenoma	10	83.3%
	Malignant	Sebaceous carcinoma	2	16.7%	3.2%

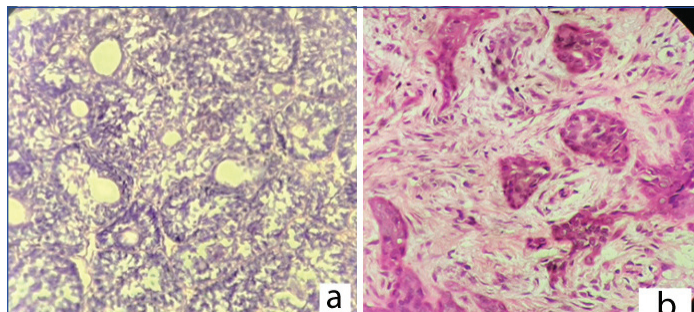
[Table/Fig-4]: Spectrum of adnexal tumours on Histopathological Examination (HPE) according to WHO classification.

Histopathological Features

I. Tumours along sweat gland distribution: The total number of sweat gland tumours in the present study were 29.

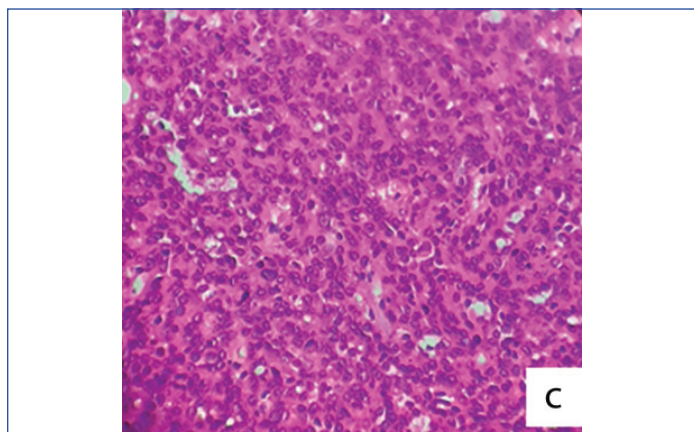
a. Nodular hidradenoma: This particular lesion is characterised by multiple lobules within the dermis comprising of epithelial cells arranged as tubules of varying sizes separated by fibrovascular septa lined by cuboidal to columnar secretory cells. The cells were round to polyhedral with a central round nucleus and eosinophilic to clear cytoplasm. The present study had 12 cases (41.4%) [Table/Fig-5a].

b. Chondroidsyringoma: This tumour shows tadpole shaped ducts lined by bilayered cuboidal epithelium embedded within a myxoidstroma. The present study had 5 (17.3%) cases [Table/Fig-5b].



[Table/Fig-5]: a) Nodular Hidradenoma displaying tubules of varying sizes lined by bilayered cuboidal epithelium located within the dermis (H&E; 10X). b) Chondroidsyringoma displaying small ductules lined by inner columnar and outer cuboidal epithelium embedded within a chondromyxoidstroma (H&E; 40X).

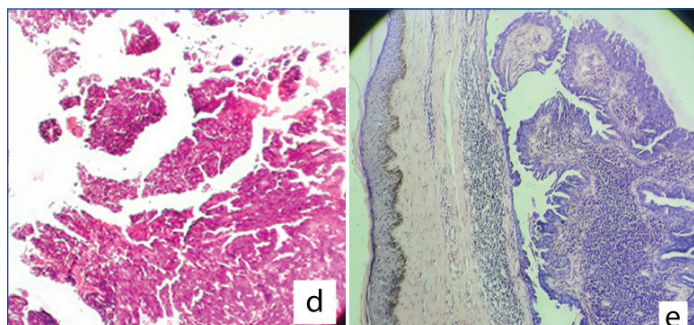
c. Eccrineporoma: It shows islands of basaloid epithelial cells with cytoplasmic clearing within a hyalinised stroma [Table/Fig-5c]. The current study had 4 (13.7%) cases.



[Table/Fig-5c]: Eccrineporoma showing ductules lined by small monomorphic basaloid cells separated by delicate septa (H&E; 40X).

d. Hidradenoma papilliferum: A well circumscribed lesion characterised by tubular and cystic spaces lined by outer myoepithelial cells and inner cuboidal to columnar cells with decapitation secretion thrown into papillary folds [Table/Fig-5d]. The current study had 3 (10.3%) cases.

e. Syringocystadenoma papilliferum: This tumour shows cystic invaginations with papillary projections lined by columnar and cuboidal epithelium in two layers [Table/Fig-5e]. This study had 1 (3.5%) case.

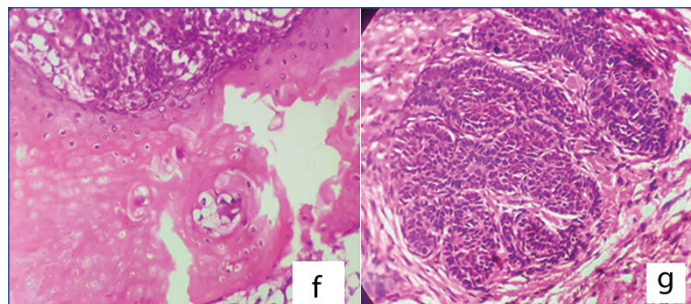


[Table/Fig-5]: d) Hidradenoma papilliferum displaying small papillae lined by inner cuboidal and outer myoepithelial cells with apical secretions (H&E; 10X). e) Chondroidsyringoma displaying small ductules lined by inner columnar and outer cuboidal epithelium embedded within a chondromyxoidstroma (H&E; 10X).

II. Tumours along follicular distribution: The total number of hair follicular tumours in the present study were 21.

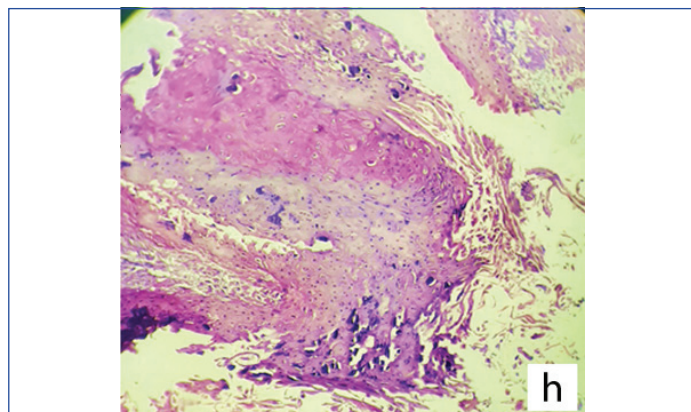
f. Pilomatricoma: This tumour shows islands of peripheral basaloid epithelial cells in sheets and abrupt keratinisation leading to formation of shadow cells towards the centre along with areas of calcification. The current study had 10 cases (47.6%) [Table/Fig-5f].

g. Trichoepithelioma: This tumour showed islands of basaloid epithelial cells with cytoplasmic clearing arranged within hyalinised stroma as small islands with peripheral palisading of nuclei along with horn cysts [Table/Fig-5g]. The current study had 9 (42.8%) cases.



[Table/Fig-5f,g]: f) Pilomatricoma showing islands of basaloid cells with abrupt keratinisation leading to formation of shadow cells (H&E; 10X). g) Trichoepithelioma comprising of convoluted islands of epithelial cells with peripheral palisading surrounded by fibrocollagenous septa within the dermis (H&E; 10X).

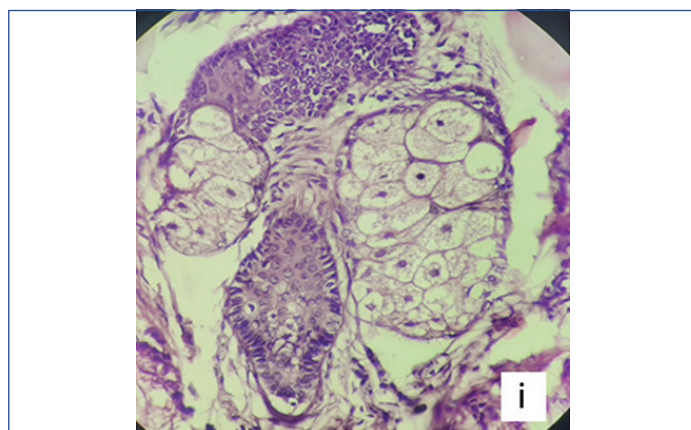
h. Proliferating trichilemmal tumour: This tumour shows proliferating stratified squamous epithelium that changes abruptly into eosinophilic amorphous keratin (trichilemmal keratinisation) and areas of calcification [Table/Fig-5h]. The current study had 1 (4.8%) case.



[Table/Fig-5h]: Proliferating trichilemmal tumour comprising of proliferating squamous epithelium with abrupt keratinisation and areas of calcification (H&E; 10X).

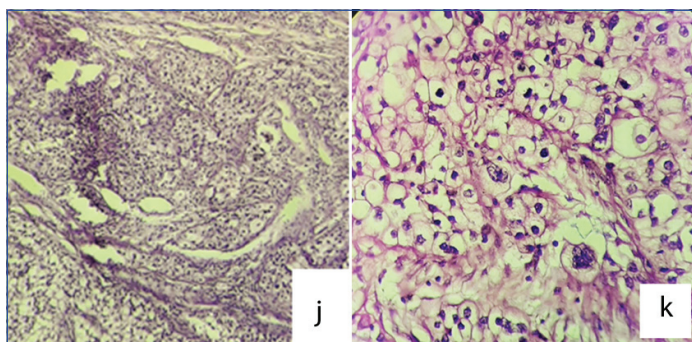
III. Tumours along sebaceous gland differentiation: The total number of sebaceous gland tumours in the present study were 12.

i. Sebaceous adenoma: This tumour is characterised by mature and immature sebaceous epithelial cells arranged in lobules within the dermis [Table/Fig-5i]. The current study had 10 cases (83.3%).



[Table/Fig-5i]: Sebaceous adenoma showing nests of proliferative immature (basaloid) and mature sebaceous epithelial cells (H&E; 40X).

j. Sebaceous carcinoma: This malignant tumour is characterised by irregular lobules of variably atypical cells with multivacuolated cytoplasm and pleomorphic nucleus separated by fibrovascularstroma. Mitotic activity is variable [Table/Fig-5j,k]. The current study had 2 (6.7%) cases.



[Table/Fig-5j,k]: Sebaceous carcinoma showing malignant epithelial cells growing in sheets. On higher power, they show single, round to polygonal, pleomorphic nuclei and moderate to abundant foamy to vacuolated cytoplasm. Tumour giant cells and few abnormal mitotic figures were seen (H&E; 10X and 40X).

DISCUSSION

Adnexal tumours are a category of rare tumours. Some adnexal tumours have extracutaneous counterparts [2]. Most of the tumours can be identified only on microscopic examination. The incidence of SATs among all biopsies in the present study was found to be 4.1%. Sejekan SV and Biligi DS found the incidence to be 2.6% [8]. The present study found 21-40 years to be commonest age group affected similar to the studies done by Pal S et al., and Gopidesi DT et al., who each found 31-40 years to be the commonest age group whereas Sudhakar G et al., found 51-60 years to be the commonest

age group [9-11]. The head and neck region was the most affected site in present study with (54.9%) which was similar to the studies done by Sejekan SV and Biligi DS, Pal S et al., Gopidesi DT et al., Sudhakar G et al., and Saleem R et al., who found 95%, 69%, 73.33%, 64% and 59.4%, respectively [8-12]. Females outnumbered the males in the present study which was similar to Saleem R et al., who found 1:1.08 ratio [12]. Studies done by Sejekan SV and Biligi DS, Pal S et al., Gopidesi DT et al., Sudhakar G et al., and Thakuria SK et al., found male preponderance with 1.14:1, 1.2:1, 1.2:1, 1:1.5 and 1.57:1 ratio, respectively [Table/Fig-6] [8-15].

In the present study, majority of the cases 59 (95.2%) cases were found to be benign and 3 (4.8%) cases were malignant. This was in concordance with the studies done by, Sejekan SV and Biligi DS, Pal S et al., and Sudhakar G et al., who found 94.22%, 94.3% and 95.5% of the tumours to be benign in nature whereas malignant tumours were seen in 5.78%, 5.7% and 4.5%, respectively [8,9,11]. Present study observed that the tumours of sweat gland origin were the most common (46.7%). Nodular hidradenoma was the commonest neoplasm in this group with 12 cases (41.4%) in the current study. This was in concordance with the studies done by Sejekan SV and Biligi DS, Pal S et al., Gopidesi DT et al., Saleem R et al., Thakuria SK et al., and Nayak GD et al., who found 36.43%, 45%, 25.14%, 23.07% and 56.25% of nodular hidradenoma among sweat gland tumours, respectively [Table/Fig-7] [8-10,12,14,16].

Among hair follicle tumours, the present study had 10 cases of pilomatricoma (47.6%) followed by nine cases of trichoepithelioma. Similar observations were made by Sejekan SV and Biligi DS, Pal S et al., Gopidesi DT et al., Saleem R et al., and Thakuria SK et al., who found 32.47%, 59.7%, 50%, 51.55%, and 50% of pilomatricoma among hair follicle tumours whereas Nayak GD et

	Present study, 2023	Saleem R et al., 2023, Lahore [12]	Sudhakar G et al., 2022, Ongole [11]	Sejekan SV and Biligi DS 2022, Bengaluru [8]	Pal S et al., 2021, West Bengal [9]	Saman F et al., 2020, Lahore [13]	Thakuria SK et al., 2020, Assam [14]	Gopidesi DT et al., 2020, Nellore [10]	Omar AM and Natag O 2020, Egypt [15]
Total cases	62	565	68	105	242	45	25	30	18
Study period	2018-22	2018-2022	2017-22	12 months	2011-15	6 months	2017-19	2017-19	2015-19
Age (years)	21-40 years (45.1%) Mean 43.87 years	Mean 42.33 years	51-60 years	Mean 38.5 years	31-40 years (35.12%)	26-50 years (37.78%)	41-50 years (28%)	31-40 years (23.33%)	30-51 years (72.2%)
Male: Female	1:1.06	1:1.08	1.14:1	1.2:1	1.2:1	1.04:1	1:1.5	1.14:1	1.57:1
Site	Head and neck region (54.9%)	Head and neck region (59.4%)	Head and neck region (64%)	Head and neck region (95%)	Head and neck region (69%)	Head and neck region (63%)	Head and neck region (68%)	Head and neck region (73.33%)	Head and neck region (44.4%)

[Table/Fig-6]: Comparison of present study with various other similar studies [8-15].

Origin	Diagnosis	Present study (n=62)	Saleem R et al., (n=565) 2023 [12]	Sejekan SV and Biligi DS (n=105) 2022 [8]	Pal S et al., (n=242) 2021 [9]	Gopidesi DT et al., (n=30) 2020 [10]	Thakuria SK et al., (n=25) 2020 [14]	Nayak GD et al., (n=43) 2020 Odisha [16]
Sweat glands (29)	Nodular hidradenoma	12	88	-	47	9	3	9
	Chondroidsyringoma	5	48	2	7	-	-	1
	Eccrineporoma	4	75	5	12	3	1	-
	Hidradenoma papilliferum	3	21	-	-	3	-	-
	Cylindroma	2	8	1	5	1	1	3
	Spiradenoma	1	46	3	9	2	3	-
	Syringocystadenoma papilliferum	1	29	-	11	2	2	1
Follicular (21)	Spiradenocarcinoma	1	-	-	-	-	-	-
	Pilomatricoma	10	83	25	49	4	4	8
	Trichoepithelioma	9	12	3	17	-	2	1
	Trichofolliculoma	1	9	2	2	-	2	-
Sebaceous glands (12)	Proliferating trichilemmal tumour	1	28	4	3	-	-	13
	Sebaceous adenoma	10	10	11	4	1	-	1
	Sebaceous carcinoma	2	-	5	2	1	3	1

[Table/Fig-7]: Comparison of histopathological diagnoses among various studies [8-10,12,14,16].

al., found proliferating trichilemmal tumour to be the commonest tumour (59%) [9,10,12,14,16]. Among sebaceous neoplasms, the current study had 10 cases of sebaceous adenoma (83.34%). Similar observations were made by Gopidesi DT et al., and Saman F et al., with 50% of adenomas each [10,13].

Among the malignant tumours, sebaceous carcinoma was most common (66.67%). This was similar to the study done by Gopidesi DT et al., Saman F et al., and Nayak GD et al., who found the sole malignancy to be sebaceous carcinoma (100%) [10,13,16]. Sejekan SV and Biligi DS and Thakuria SK et al., found that sebaceous carcinoma was the commonest malignancy encountered with 83.34% and 75% [8,14]. Among 62 cases, clinical suspicion of SAT was found in 12 cases only (19.35%). Rest of the cases were thought to be non neoplastic skin disorders clinically. Both the cases of sebaceous carcinoma were thought to be epidermal malignancies on clinical examination and were diagnosed as malignant SAT only after histopathological examination. Moreover, they are rare tumours and their exact incidence is still unclear [15]. The diagnosis of SATs is based mainly on histopathology and a strong clinical suspicion based on the site of the lesion. Ancillary techniques such as immunohistochemistry were of less importance in their diagnosis.

Limitation(s)

The number of malignancies in the present study were three cases. A higher number of cases with more varied diagnoses would have been beneficial. The data on clinical presentation of the tumours is not sufficient in the study owing to limited availability of the same.

CONCLUSION(S)

Although skin lesions are frequently encountered but due to an overlap between the presentations of some adnexal tumours with other skin lesions, they are often misdiagnosed as non neoplastic. They are often encountered on sun exposed areas where they can be mistaken for cutaneous malignancies. The location of these lesions, a good thorough clinical examination, probability of the occurrence of these lesions and adequate knowledge of histopathological examination are helpful in diagnosing them accurately. The present study will help in improving the knowledge and awareness regarding the rare adnexal tumours of skin occurring in this region.

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