Epidermal Appendageal Tumours-Histopathological Study at a Tertiary Care Hospital

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Abstract

Background: Skin appendageal tumours are a heterogeneous group of tumours with considerable clinical and histopathological overlap. The overall incidence of Skin adnexal tumours (SATs) is low in Indian population. In some cases, the diagnosis of adnexal neoplasms poses unique difficulties due to complex nomenclature, and expression of one or more lines of appendageal differentiation in the same lesion. The study was aimed to evaluate the histopathological spectrum of skin appendageal tumours and to correlate SATs with various demographic and clinical data. **Material and Methods:** This observational and descriptive cross-sectional study was conducted on a total 55 skin biopsies diagnosed as SATs over a period of 2 years. **Results:** Peak age incidence of SATs was observed in the 5th decade with marginal female preponderance (M: F = 1:1.11). The most commonly affected site was head and neck region (69%); followed by extremities (27%) and trunk (4%). Out of total 55 cases of SATs, 50 cases (90.91%) were benign tumours and 05 cases (9.09%) were malignant tumours. The sweat gland tumours constituted the largest group (43.64%); followed by hair follicle tumours (36.36%) and sebaceous gland tumours (20%). Amongst all SATs, nodular hidradenoma was the commonest benign tumour (16.36%) and sebaceous cell carcinoma (7.27%) was the most common malignant tumour. **Conclusion:** The study confirmed that skin appendageal tumours are rare tumours. Histopathology proves to be the gold standard tool to confirm the diagnosis.

Key words: Skin adnexal tumour, Histopathology, Eccrine, Apocrine , Sebaceous, Hair follicle

Introduction

Skin adnexal tumours (SATs) are a wide and heterogeneous group of neoplasms that differentiate towards one or more of the skin appendages or recapitulate events occurring during embryonic development. These tumours originate from multipotential stem cells present within the epidermis or its appendageal structures[1]. Skin adnexal tumours are classified into four groups that exhibit histologic features analogous to hair follicles, sebaceous glands, apocrine glands and eccrine glands[2]. The classification of these tumours is complex. Although, remarkable histopathological variability is

observed in most of the SATs, some tumours reveal a considerable morphological overlap; which makes the diagnosis challenging in those instances. Some lesions have a distinct clinical presentation, making the clinical diagnosis straight forward. However, in most cases morphological examination is mandatory for correct diagnosis. Adnexal neoplasms may constitute cutaneous markers of a wide range of hereditary syndromes[3]; for example multiple trichoepithelioma in Cowden syndrome and sebaceous adenomas in Muir – Torre syndrome[4]. Therefore, correct diagnosis is important to alert the clinician about the possibility of these conditions. Most of the published series reveal overall rarity of skin adnexal tumours with benign tumours far more common as compared to their malignant counterparts. Malignant skin adnexal tumours are locally aggressive and have the potential for nodal involvement and distant metastasis with a poor clinical outcome. Therefore, establishing the diagnosis of malignancy in skin tumours is important for therapeutic and prognostic purposes[5].

The study was undertaken to classify SATs, to evaluate the histopathological spectrum of skin appendageal tumours and to estimate the frequency of different SATs with respect to their histopathological types, patients' clinical and demographic data.

Material and Method

This Descriptive and observational, cross sectional study was conducted on a single centered hospital based population from a tertiary care institute of a Gujarat state- AMC MET Medical College and Sheth L.G. General Hospital, Ahmedabad during the period from July 2018 to October 2020. The study sample consisted of total 55 biopsies diagnosed as SATs during the study period.

Inclusion criteria:

- All the skin biopsies diagnosed as skin adnexal tumours histopathologically.

Exclusion criteria:

- Poorly preserved and inadequate biopsy material for histopathological examination
- Cases clinically diagnosed as appendageal tumours, but not proven histologically to be adnexal tumours

The patients' demographic and clinical details were obtained from biopsy requisition forms, case sheets of patients or by personal consultation with clinicians. Histopathological examination was done on formalin fixed and paraffin processed tissue after performing Haematoxylin and Eosin (H & E) stain. Special stains like PAS was performed whenever required. The tumours were classified using the recent World Health Organization International Histological Classification of skin Tumours[2,3]. We included hyperplastic , hamartomatous and cystic lesions besides typical benign and malignant tumours in the study. The data were expressed as mean, median and percentage and were analyzed using microsoft Excel software.

This study was approved by the AMC MET Institutional Review Board.

Results

In this study, out of total 15560 biopsies received, only 55 cases (0.35%) were reported as the skin adnexal tumours. The age of the patients ranged from 6-80 years with mean and median age being 36.93 years and 38 years respectively. The maximum number of cases were observed in the 5th decade (12/55 cases, 21.82%); while the minimum number of cases were found in 1st decade (2 /55 cases, 3.64%). Malignant lesions were noted after 5th decade. A marginal female preponderance was seen with male to female ratio being 1:1.11.

The distribution of cases according to tumour differentiation with specific tumour types and their locations is depicted in Table:1. Major site of involvement was the head and neck region (69%); followed by extremities (27%) and trunk (4%) in descending order of frequency.

Out of total 55 cases of SATs, 50 cases (90.91%) were diagnosed as benign tumours and 05 cases (9.09%) were diagnosed as malignant tumours. Sweat gland differentiation was observed predominantly (24 cases, 43.64%); including 21 cases (38.18%) of eccrine differentiation and 3 cases (5.45%) of

apocrine differentiation. This was followed by hair follicle differentiation (20 cases, 36.36%) and sebaceous differentiation (11 cases, 20%). Amongst the eccrine differentiation and amongst the all benign SATs, nodular hidradenoma (16.36%) was the commonest tumour encountered. Eccrine poroma (9.09%) was another common lesion found in the category of eccrine SATs. Site specific predilection was not observed for nodular hidradenoma. Four fifth of eccrine poroma were located on foot. Apocrine hidrocystoma (2 cases, 3.63%) was the main lesion noted in the category of SATs with apocrine differentiation. Amongst hair follicle differentiation, trichoepithelioma was the most common (10.90%); followed by proliferating trichilemmal cyst/ pilar tumour (9.09%). Four out of six cases of trichoepithelioma were found on face. Three fifth cases of proliferating trichilemmal cyst/pilar tumour were located on the scalp. Amongst the benign SATs with sebaceous differentiation, nevus sebaceous (7.27%) was the commonest lesion; followed by sebaceous hyperplasia (5.45%). All four cases of nevus sebaceous were located on the scalp; while all three cases of sebaceous hyperplasia were on the face.

The majority of malignant tumours showed sebaceous differentiation. Amongst the malignant SATs, sebaceous cell carcinoma was the most common (7.27% of all tumours and 80% of all malignant tumours), and the majority of sebaceous cell carcinomas (3/4 cases, 75%) were found on the eye lid.

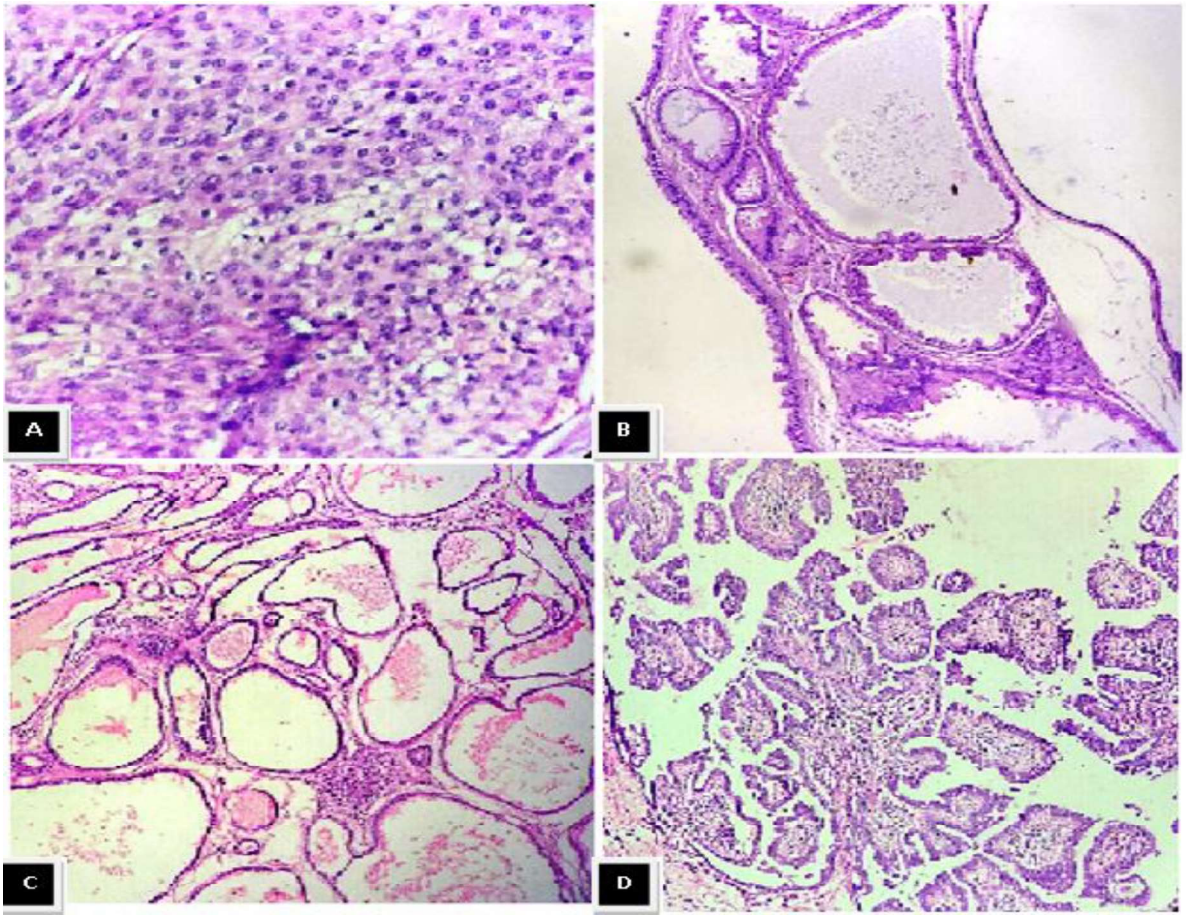


Figure-1: **(A) Nodular hidradenoma:** The tumour comprises clear and polygonal cells (H&E ×400). **(B) Apocrine hidrocystoma:** Multiloculated cystic lesion lined by epithelial cells showing decapitation secretion (H&E ×100). **(C) Papillary eccrine adenoma:** The dilated tubular structures contain amorphous eosinophilic material (H&E ×40). **(D) Syringocystadenoma papilliferum:** The tumour shows a cyst with numerous papillary projections. (H&E ×100).

Table -1 Distribution of SATs with respect to their differentiation and specific tumour types

Nature of lesion	Location	Tumour differentiation and subtypes			
		Hair follicle differentiation N (%)	**Sebaceous differentiation N (%)**	**Apocrine differentiation N (%)**	**Eccrine differentiation N (%)**
Benign 50 (90.91%)	**Head and Neck 34 (62%)**	Trichoepithelioma 5 (9.09%)	Nevus Sebaceous, 4 (7.27%)	Apocrine Hidrocytoma 1 (1.82%)	Nodular hidradenoma 4 (7.27%)
		Proliferating trichilemmal cyst/pilar tumour 4 (7.27%)	Sebaceous hyperplasia 3 (5.45%)		Eccrine Spiradenoma 1 (1.82%)
		Pilomatricoma 2 (3.64%)			Chondroid syringoma 1 (1.82%)
		Trichofolliculoma 2 (3.64%)			Papillary Eccrine adenoma 1(1.82)
		Trichilemmoma 1 (1.82%)			Eccrine Cylindroma 1(1.82%)
		Trichoadenoma 1 (1.82%)			Syringoma 1(1.82%)
		Trichoblastoma 1 (1.82%)			
		Dilated pore 1 (1.82%)			
	Total	17	07	01	09
	Extrimities 14 (25%)	Trichoepithelioma 1 (1.82%)		Apocrine Hidrocytoma 1 (1.82%)	Eccrine poroma 5 (9.09%)
		Proliferating Trichilemmal cyst/ pilar tumour 1 (1.82%)			Nodular hidradenoma 4 (7.27 %)
					Chondroid syringoma 1(1.82%)
					Papillary eccrine adenoma 1(1.82%)
	Total	02	00	01	11
	Trunk 2 (4%)			Syringo cystadenoma papilliferum 1(1.82%)	Nodular hidradenoma 1(1.82%)
	Total	00	00	01	01
Malignant 5 (9.09%)	**Head and Neck 4 (7%)**		Sebaceous carcinoma 4 (7.27%)		
	Total	00	04	00	00
	Extremities 1 (2%)	Pilomatrix carcinoma 1 (1.82%)			
	Total	01	00	00	00
	Trunk 0 (0%)				
Total	**55 (100%)**	**20 (36.36%)**	**11 (20%)**	**3 (5.45%)**	**21 (38.18%)**

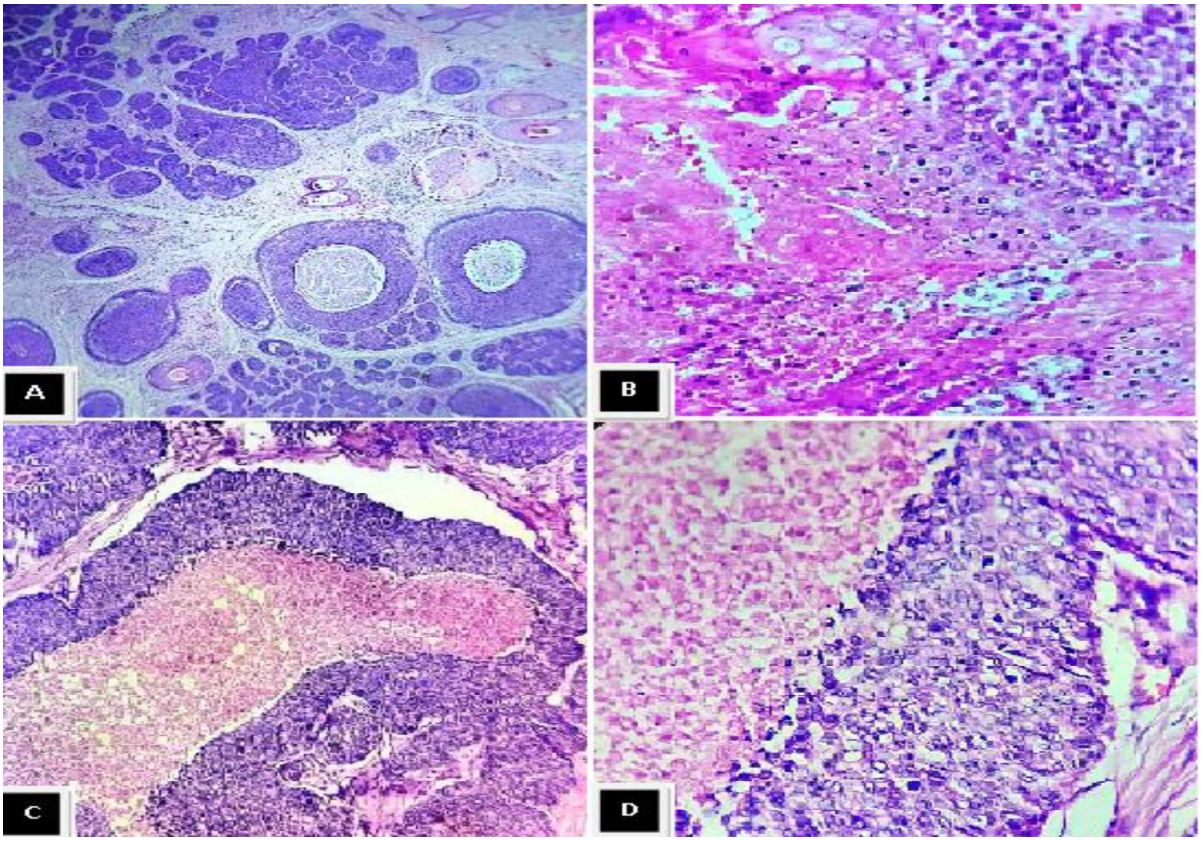


Figure-2: (A) Trichoepithelioma: Tumour islands of basaloid cells and occasional horn cysts. Tumour islands are surrounded by fibroblastic stroma without retraction artifact (H&E × 40).
(B) Pilomatricoma: The epithelial island with transformation of basaloid cells into shadow cells associated with loss of nuclei (H&E ×400). (C) **Sebaceous carcinoma:** Tumour lobule with central necrosis **(**H&E × 40). **(D) Sebaceous carcinoma:** Higher magnification shows tumour cells with marked cytologic atypia and mitotic activity (H&E ×400).

Discussion:

Skin adnexal neoplasms comprise a wide spectrum of benign and malignant tumours that exhibit morphological differentiation towards one or more types of adnexal structures found in normal skin. Appendageal tumours are relatively rare, and their clinical appearance is commonly non-specific.
SATs were rarely found lesions at our set up; which comprised only 0.35% of all surgical pathology specimens received during the study period. This rarity of SATs is reflected in most of the published literature worldwide. In the present study, wide age range was noted with peak age group being the 5th decade. All malignant tumours were observed after 5th decade. Only a minimal female preponderance was noted, and head and neck was the most commonly affected site (69%). Comparison of SATs with respect to age, gender and location in different studies is depicted in Table: 2. Wide age distribution was observed in other studies with no major sex preponderance. In all these studies, head and neck was the dominant site affected. The pilosebaceous apparatus is concentrated in the head and neck area, with the pilar element predominant on the scalp and the sebaceous element on the face, chest and upper back. Thus, tumours arising from these structures are found predominantly at these anatomical sites[6]. In this study, majority of tumours with pilosebaceous differentiation were in the head and neck region. Eccrine tumours were distributed roughly equally in the head and neck region and in the extremities.

Table: 2 Comparison of SATs with respect to age, gender and location in different studies:

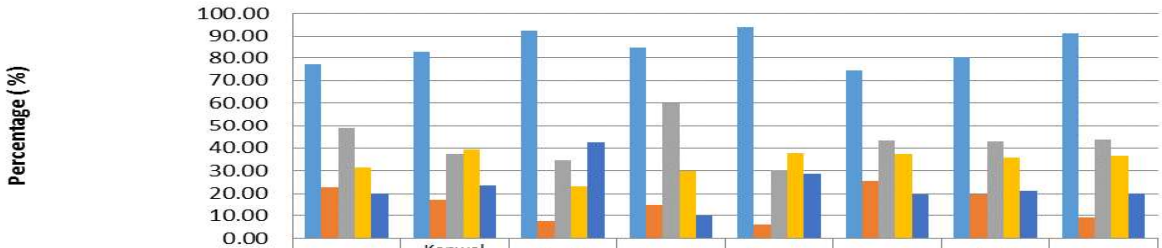
Study	Age	Sex	Location
K. Radhika, B.V. Phaneendra[7]	20-30	0.7:1	Head and neck
Kanwalpreet Kaur, Karuna Gupta[8]	20-39	1.03:1	Head and neck
Sadaf Alam, Misbah Lateefa, Raghumani Mohanty [9]	40–49	1.16:1	Head and neck
Ramya Gandhi, Sowmya Srinivasan[10]	Not described	Not described	Head, neck, and extremities
Jyotsna Suri,Deepti Gupta[11]	31-40	1.44	Head and neck
Dr.Vani.D, Dr.Ashwini.N.S[12]	40 to 49	1:1.68	Head and neck
Ankit Sharma, Deepak G. Paricharak [13]	51–60		Head and neck
Present study	41-50	1:1.11	Head and neck

We didn't find any tumour with multiplicity. Syndromic cases of cutaneous adnexal tumours are usually multiple. Not much is known about etiopathogenesis of SATs except in syndromic cases; in which genetic aberrations are possible etiologic factors. Ultraviolet radiation exposure and immunosupression have been proposed as possible triggering factors[3].

In the present study, the benign SATs outnumbered the malignant ones. The same observation was found in different studies (Figure: 3). Though rare, a malignant counterpart of almost every SAT has been described. Malignant features in SAT include asymmetrical growth, ulceration, jagged/infiltrative borders, irregular arrangement of neoplastic cells, cytonuclear atypia and increased mitotic activity. Sometimes traditional criteria of cellular atypia do not render a tumour malignant. So, enough emphasis must be given to architecture of tumour to rule out malignancy.

Sweat gland tumours were predominant tumours in our study; which was followed by tumours of hair follicle and sebaceous differentiation. In most of the other studies[7,8,10,11,12,13] sweat gland and hair follicle tumours were more common as compared to sebaceous gland tumours. However, in the study of Sadaf Alam et al[9], the sebaceous gland tumours constituted the largest group.

Figure-3: Frequency distribution of SATs in diffent studies



	K. Radhika et al 7	Kanwal preet Kaur et al 8	Sadaf Alam et al 9	Ramaya Gandhi et al 10	Jyotsna Suri et al 11	Dr.Vani et al 12	Ankit Sharma et al 13	Present study
Benign tumours (%)	77.14	82.73	92.31	85.00	93.94	74.50	80.36	91.00
Malignant tumours (%)	22.86	17.27	7.69	15.00	6.06	25.49	19.64	9.00
Sweat gland tumours (%)	48.50	37.37	34.62	60.00	30.30	43.13	42.86	43.63
Hair follicle tumours(%)	31.40	39.09	23.10	30.00	37.87	37.25	35.71	36.36
Sebaceous gland tumours (%)	20.00	23.63	42.31	10.00	28.78	19.60	21.43	20.00

Nodular hidradenoma (16.36%) was the most common benign tumour observed in this study. Some other commonly encountered benign tumours included: eccrine poroma, trichoepithelioma, proliferating trichilemmal cyst/ pilar tumour, pilomatricoma. trichofolliculoma, nevus sebaceous, sebaceous

hyperplasia etc. Amongst the malignant SATs, the sebaceous carcinoma was the most common lesion found in this study. Table:3 depicts the most common SATs observed in different studies among both benign and malignant categories. Nodular hidradenoma and pilomatricoma were commonly observed benign tumours in most of the studies; while sebaceous cell carcinoma and sweat gland carcinoma were common malignant tumours.

Table-3: Most common SATs observed in different studies

Study	Most Common benign tumour	Most Common malignant tumour
K. Radhika et al[7]	Nodular hidradenoma; Nevus sebaceous	Sweat gland carcinoma
Kanwalpreet Kaur et al[8]	Pilomatricoma	Sebaceous carcinoma
Sadaf Alam et al[9]	Sebaceous hyperplasia	Sebaceous carcinoma
Ramaya Gandhi et al[10]	Eccrine acrospiroma	Sweat gland carcinoma
Jyotsna Suri et al[11]	Pilomatricoma	sebaceous carcinoma, Malignant mixed adnexal carcinoma
Dr.Vani D et al[12]	Nodular hidradenoma	Sebaceous carcinoma; Trichoblastic carcinoma
Ankit Sharma et al[13]	Clear cell hidradenoma; Pilomatricoma	sebaceous carcinoma
Samaila et al[14]	Eccrine acrospiroma	Sweat gland carcinoma
Saha et al[15]	Syringoma	-
Rajlakshmi et al[16]	Pilomatricoma	Aggressive papillary digital adenocarcinoma; Malignant dermal eccrine cylindroma
El. Ochi et al[17]	Pilomatricoma	Porocarcinoma; Eccrine Sweat gland carcinoma
Nair et al[18]	Syringoma	-
Present study	Nodular hidradenoma	Sebaceous carcinoma

The great majority of SATs are not diagnosed as such until after excision and pathological study. Skin appendageal tumours are histopathologically challenging to diagnose. Classification systems for these lesions tend to be controversial, but in general, the system groups lesions according to their morphological similarity to normal appendage structures. However, in some instances the tumour may show multilineage appendageal differentiation (hybrid/composite tumour); which makes the exact typing difficult. Some hair follicle tumours may show basaloid features; which may further add the diagnostic problem due to close morphological proximity to the basal cell carcinoma. Trichoepitelioma mimics basal cell carcinoma (BCC); but presence of peripheral clefts, absence of horn cysts and frequent mitoses favors BCC. Similarly, some tumours need to be differentiated from the squamous cell carcinoma (SCC); like proliferating trichilemmal cyst /pilar tumour (PTC). Good circumscription of leiosn with trichilemmal keratinization, presence of pre-existing simple pilar cyst, absent or inconspicuous cytonuclear atypia and minimal mitotic activity are in favor of PTC over SCC.

Conclusion:

Tumours of skin appendages are uncommon, with a wide histological spectrum and complex classification. Benign tumours show a wide age distribution; while malignant tumours are common after 5th decade. Head and neck region constitute the most common site. In this study, tumours with eccrine differentiation are the most common with nodular hidradenoma is the predominant type. Amongst the malignant tumours, sebaceous cell carcinoma is the most common. Though, in some instances, it is difficult to properly categorize the tumour, histopathological examination is the gold standard tool to diagnose the skin adnexal tumours.

Limitations of the study: As this is a single hospital based study, it cannot reliably detect the prevalence of the skin adnexal tumours because of selection bias. We could not apply special histochemistry and immunohistochemistry.

References:

1. Perez-Losada J, Balmain A. Stem-cell hierarchy in skin cancer. *Nat Rev Cancer* 2003;3(6):434–443.
2. Tamer S.S. Ahmed , Joseph Del Priore , John T. Seykora. "Tumours of epidermal appendages" In. Lever's Histopathology of the skin: Elder D.E., Elenitsas R, Johnson B.L., Murphy G.F., Xiaowei. Xu; Lippincott Williams and Wilkins, Philadelphia USA 2009,10th edition.pp. 851-853
3. Masi D, Cree I.A., Elder D.E., Kazakov D.V., ,Scolyer R.A., "Appendageal tuimours: introducation" In. WHO classification of skin tumours: Ed. Elder D.E, Masi D, Scolyer R.A, Willemze R: Lyon,IARC 2018, 4th edition, - pp.154
4. Lazar AJ, Murphy GF. The skin. In: Aster KA, editor. Robbins and Cotran Pathologic Basis of Disease. 9th ed. Phildelphia: Elsevier; 2014. pp. 1141–78
5. Alsad KO, Aobaidat N, Ghazarain D. Skin adnexal neoplasms- part I: An approach to tumours of pilosebaceousunit. *J Clinpathol* 2007; 60(2): 129- 44.
6. E. Calonje:Tumours of the Skin Appendages: CHAPTER 53: Rook's Textbook of Dermatology, 8th edition. Edited by DA Burns, SM Breathnach, NH Cox and CEM Griffi ths. © 2010 Blackwell Publishing Ltd.
7. Radhika K, Phaneendra BV, Rukmangadha N, Reddy MK. A study of biopsy confirmed skin adnexal tumours: experience at a tertiary care teaching hospital. J Clin Sci Res 2013;2:132-8.
8. Kanwalpreet Kaur, Karuna Gupta, Deepika Hemrajani, Ajay Yadav, Kalpana Mangal. Histopathological analysis of skin adnexal tumours. Indian Journal of Dermatology, 2017, July-Aug; 62(4):p400-406.
9. Sadaf Alam, Misbah Lateefa, Raghumani Mohanty. Histopathological study of 26 rare skin adnexal tumours over 5 years – a diagnostic dilemma! International Journal of Medical Science and Public Health. 2016, Vol 5 ,Issue 10:1995-98
10. Ramya Gandhi, Sowmya Srinivasan. A Morphologic Study of Cutaneous Adnexal Tumours. National Journal of Laboratory Medicine. 2016 Oct, Vol-5(4): PO08-PO11
11. Jyotsna Suri,Deepti Gupta, K K Koul, Rita Kumari. A Clinicopathological Analysis of Skin Adnexal Tumours: Four Year Retrospective Study. www.jkscience.org. Vol. 18 No. 4, Oct.-Dec 2016: P248-51.
12. Dr.Vani.D, Dr.Ashwini.N.S, Dr.Sandhya.M, Dr.T.R.Dayananda, Dr.Bharathi.M. 5 Year Histopathological Study of Skin Adnexal Tumours at a Tertiary Care Hospital. IOSR Journal of Dental and Medical Sciences. Volume 14, Issue 4 Ver. VII (Apr. 2015), PP 01-05. www.iosrjournals.org
13. Ankit Sharma, Deepak G. Paricharak, Jitendra Singh Nigam, Shivani Rewri, Priyanka Bhatia Soni, Anita Omhare, and Preethi Sekar. Histopathological Study of Skin Adnexal Tumours—Institutional Study in South India. Journal of Skin Cancer Volume 2014, Article ID 543756: P 01 -04
14. Samaila MO. Adnexal skin tumours in Zaria, Nigeria. *Ann Afr Med.* 2008;7:6–10. [PubMed] [Google Scholar]
15. Saha A, Das NK, Gharami RC, Chowdhury SN, Datta PK. A clinico-histopathological study of appendageal skin tumours, affecting head and neck region in patients attending the dermatology opd of a tertiary care centre in eastern India. *Indian J Dermatol.* 2011;56:33–6. [PMC free article] [PubMed] [Google Scholar]
16. Rajalakshmi V, Selvakumar S, Rajeswari K, Meenakshisundaram K, Veena G, Ramachandran P. Case series of skin adnexal tumours. *J Clin Diagn Res.* 2014;8:FC07–10. [PMC free article] [PubMed] [Google Scholar
17. El Ochi MR, Boudhas A, Allaoui M, Rharrassi I, Chahdi H, Al Bouzidi A, et al. Skin adnexal tumours: Histological study about 96 cases. *Pan Afr Med J.* 2015;20:389. [PMC free article] [PubMed] [Google Scholar]
18. Nair PS. A clinicopathologic study of skin appendageal tumours. *Indian J Dermatol Venereol Leprol.* 2008;74:550. [PubMed] [Google Scholar]