

A Varied Presentation of Dermal Adnexal Tumours: An Institutional Study

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Abstract

Introduction: Adnexal skin tumours are a heterogeneous group of uncommon tumours usually misdiagnosed clinically due to a huge variety of types and their variants. Histopathology usually helps in establishing the diagnosis. The study was conducted to analyse the morphological, clinical and histological features of adnexal tumours (ATs) of the skin at our centre over a period of 5 years. **Materials and Methods:** A retrospective study was conducted over a period of 5 years (January 2016–January 2021), comprising 85 ATs of skin diagnosed in the Department of Pathology, Sri Devaraj URS Medical College, Kolar, Karnataka, India. All the consecutively reported AT cases were reviewed and reclassified as ATs arising from sebaceous glands, hair follicles or sweat glands. The concordance of clinical and histopathological diagnosis was also assessed. **Results:** Most of the ATs were benign, with the head and neck being the most common location (61.15%), followed by the trunk (22.3%). Nearly 39% of the tumours were of hair follicle differentiation, 30% sweat gland differentiation and sebaceous gland tumours accounted for 31%. The most common varieties of tumours encountered in the present study included sebaceous cysts and pilomatricoma. The concordance between the clinical and histopathological diagnosis was found to be 50% approximately. **Conclusion:** Histopathology is the gold standard for diagnosing ATs as they are often misdiagnosed clinically.

Keywords: Adnexal tumour, apocrine, appendageal unit, eccrine, pilosebaceous unit

INTRODUCTION

Although skin adnexal tumours (SATs) as a distinct clinicopathological entity are not uncommon, they present as a ‘Diagnostic Mirage’ because of multiple reasons. Proper classification, nomenclature and histopathological diagnosis remain a challenge because SATs usually have characteristics that are uncommon, complex and overlap with a difficult nomenclature. Although SATs can involve both adult and paediatric populations, there is a well-documented inter-observer variability in the classification of SATs. SATs involve tumours with apocrine, eccrine, follicular, sebaceous and mixed differentiation resulting in complex histological variations exhibiting apocrine or eccrine differentiation along with predominant glandular/ductal features. Different neoplasms have been described under a single name (e.g. acrospiroma), and various names have been used to describe similar lesions (e.g. trichoepithelioma and a cribriform variant of trichoblastoma) or various components of the morphological spectrum of a single

lesion (e.g. fibrofolliculoma and trichodiscoma). Whereas most of the SATs at benign and complete excision are sufficient, they may be the initial sign of familial syndromes, which represent premalignant lesions and internal malignancies. Hence, current identification diagnosis and classification are of great importance with therapeutic implications. In the present study, we have attempted to identify, analyse and observe the frequency and characteristic features to correctly diagnose benign versus malignant SATs and avoid diagnostic pitfalls.^[1] The aim of this study is to identify the spectrum and microscopic features of SATs.

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MATERIALS AND METHODS

The present study was a retrospective, cross-sectional descriptive study conducted over a period of 5 years, from January 2016 to December 2020. A total of 85 cases diagnosed as SATs on histopathology were included in this study, of which 15 cases also underwent cytological evaluation, and 06 cases were available for cyto-histo correlation. All the Ethical Clearance was obtained from the Ethical Committee Board of the Institute (ETH/GMC/2020.0987).

Fine needle aspiration cytology (FNAC) was performed with a 22-G needle attached to a 10-ml syringe. The material obtained was smeared on glass slides and stained with Giemsa stain. A thorough history was taken, and a detailed clinical examination was performed at the time of the procedure.

Histopathological analysis was carried out on formalin-fixed, paraffin-embedded tissue sections, which were stained with haematoxylin and eosin. Special stains such as periodic acid–Schiff with or without diastase and immunohistochemistry were performed as and when required. The tumours were classified according to the pre-dominant pattern of differentiation into follicular, sebaceous, eccrine and apocrine tumours.^[2]

RESULTS

A total of 85 cases were studied over a period of 5 years, from January 2016 to January 2021, which comprised 45 males and 40 females. Maximum incidence of SATs was found in the age group of 40–59 years (31/85;36.47%) followed by 20–39 years (27/85;31.76%), more than 60 years (23/85; 27.05%) and 0–19 years (4/85; 4.7%), respectively. Nearly 91.77% of cases were benign, with sebaceous cyst being the most common benign tumour (19/85; 22.35%) with an equal incidence in both males and females (1:1). It was more common in the age group of 20–39 years (8/85; 9.41%) followed by equal distribution in 40–59 years (4/85;4.7%) and more than 60 years (4/85;4.7%). The least incidence of the sebaceous cyst was seen in the age group of 0–19 years (2/85; 2.35%). The second most prevalent benign tumour was pilomatricoma, a follicular differentiation tumour (11/85; 12.9%) with the maximum incidence in 40–59 years (5/85; 5.88%). Further, among benign tumours, tumours of follicular differentiation had maximum incidence (37.5%), which comprised trichilemmal cyst (8/85;9.4%), trichoadenoma (6/85;7.05%), trichoepithelioma (4/85; 4.7%) and trichofolliculoma (TF) (3/85; 3.52%). Tumours of sebaceous differentiation (29.4%) were the second most prevalent tumour consisting of the sebaceous cyst (19/85; 22.35%) and sebaceous adenoma (7.05%; 6/85). Tumours of eccrine (13%; 13/85) differentiation comprised eccrine syringoma (4.7%; 4/85), chondroid syringoma (3.52%; 3/85), nodular hidradenoma (3.52%; 3/85), eccrine poroma (2.35%; 2/85) and eccrine acrospiroma (1.17%; 1/85) were the third most prevalent group.

The least common SATs were cylindroma (1/85; 1.17%) seen only in the age group of 20–39 years and are one of the types of

tumours of apocrine differentiation which together constituted 9.39% of all the SATs included in this study. The other apocrine tumours were apocrine hidradenoma (3.52%; 3/85) and syringocystadenoma papilliferum (4.7%, 4/85). 11.4% (7/85) of cases were malignant, with adenoid cystic carcinoma being the most common malignant tumour (3/85; 3.52%) followed by sebaceous carcinoma (2/85; 2.35%) and trichoblastoma (2/85; 2.35%). The malignant SATs were more prevalent in the age group of 60 years and above (5/85; 5.88%). Further, maximum cases were from eccrine differentiation (3/85; 3.52%), followed by the equal distribution of cases in follicular (2/85; 2.35%) and sebaceous differentiation (2/85; 2.35%), respectively [Table 1]. Among anatomical distribution, most of the tumours were located in the head and neck (61/85; 76.76%), trunk (20/85; 23.52%) and extremities (4/85; 4.7%), respectively [Table 2]. In this study, the most common group with SATs was those between 40 and 59 years. The total male: female ratio was 1.17:1, with the head and neck being the most common site of the tumour. The total incidence of benign tumours was 91.77% and malignant 8.23%, with sebaceous tumour as the most prevalent benign tumour and adenoid cystic carcinoma as the most prevalent malignant tumour [Table 3]. Cyto-histo correlation was done for six cases (6/85; 7.05%) of SATs, out of which three cases of pilomatricoma (3/6; 50%) correlated and one case each of chondroid syringoma (1/6; 16.66%), trichoepithelioma (1/6; 16.66%) and trichilemmal cyst (1/6; 16.66%) correlated [Table 4].

DISCUSSION

In routine practice, SAT remains a diagnostic challenge both for the clinician and pathologist because of (a) diverse clinicopathological presentations, (b) multiple tumours with numerous variations and (c) difficult nomenclature. Hence, SATs were aptly described as ‘Troublesome’ by Cotton.^[2] Instead of mature cells, SATs originate from multipotent stem cells, which can differentiate into specific tumours influenced by genetics, local vascularity and the microenvironment of the epidermis and dermis.^[7] Among the SATs, the most common differentiation is sweat gland differentiation (56.0%), followed by hair follicle differentiation (28.0%) and the least frequent being sebaceous gland differentiation (16.0%).^[8] The overall incidence of SAT in India is very low. The head-and-neck region is the most common site of SAT, followed by the axilla, trunk and the legs.^[5] SATs may be superficial manifestations of some syndromes associated with internal malignancies, such as trichilemmomas in Cowden’s disease and sebaceous tumours in Muir–Torre syndrome.^[9] SATs are usually benign, but malignant neoplastic counterparts do exist, which are highly aggressive and have a poor clinical outcome with potential for nodal and distant metastasis.^[1] Therefore, establishing the diagnosis of malignancy in any SAT is of utmost therapeutic and prognostic importance. Distinguishing between a benign SAT and its malignant counterpart is of therapeutic and prognostic importance because malignant SATs are highly aggressive with a poor clinical course due to the

Table 1: Distribution of tumours of epidermal appendages with respect to age and sex

Tumour type and incidence	Incidence (%)	Male: female	0–19 years	20–39 years	40–59 years	> 60 years
Benign						
Follicular						
Trichoepithelioma (4/85)	4.7	4:1	Nil	Nil	3	1
Pilomatricoma (11/85)	12.9	4:7	2	3	5	1
Proliferating trichilemmal cyst (8/85)	9.4	1:3	0	3	2	3
TF (3/85)	3.52	2:1	0	0	3	0
Trichoadenoma (6/85)	7.05	1:1	0	2	4	0
Sebaceous						
Sebaceous adenoma (6/85)	7.05	2:1	0	3	2	1
Sebaceous cyst (19/85)	22.35	1:1.16	2	9	4	4
Apocrine						
Apocrine hidrocystadenoma (3/85)	3.52	2:1	0	1	1	1
Cylindroma (1/85)	1.17	1	0	1	0	0
Syringocystadenoma papilliferum (4/85)	4.7	1:3	0	3	1	0
Eccrine						
Eccrine poroma (2/85)	2.35	1:2	0	0	1	1
Nodular hidradenoma (3/85)	3.52	2:1	0	1	1	1
Eccrine acrospiroma (1/85)	1.17	1	0	1	0	0
Eccrine syringoma (4/85)	4.7	1.5:1	0	1	1	3
Chondroid syringoma (3/85)	3.52	2:1	0	0	1	2
Malignant						
Follicular						
Trichoblastoma (2/85)	2.35	2:1	0	0	2	0
Sebaceous						
Sebaceous carcinoma (2/85)	2.35	1:1	0	0	0	2
Eccrine						
Adenoid cystic carcinoma	3.52, 3/85	3:1	0	0	0	3

TF: Trichofolliculoma

high risk of nodal and distant metastasis and conventional criteria regarding cytological and nuclear atypia alone do not render a tumour malignant. In a study conducted by Tirumalae and Roopa, 16 criteria were suggested to distinguish between benign and malignant SATs, which include.^[10] The criteria used were as follows: (a) symmetry vs asymmetry, (b) well vs ill-circumscribed margins, (c) smooth vs jagged borders, (d) vertical vs horizontal orientation, (e) V-shape of the lesion (f) presence of compressed fibrous tissue around the tumour, (g) clefting between tumour cells and stroma and also clefting between compressed fibrous tissue and surrounding stroma. In addition, complete versus incomplete shelling out of the lesion, ulceration, necrosis *en masse*, irregular vs uniform cells nests, discrete nests and geometric shape of cell nests are important useful criteria. Symmetry, V-shape, stroma-stroma clefting and absence of necrosis proved 100% sensitive in recognising benign tumours. Symmetry means that if one draws a straight line through the centre of the lesion, the two halves appear similar. V-shape implies that the tumour has a broader front towards the top, tapering towards the deeper portions. Clefting is a feature that is generally emphasised in basal cell carcinomas and is situated directly between the cells and the surrounding stroma.^[10] All the benign SATs were characterised by the presence of the following six criteria, namely smooth borders, compressed fibrous tissue, absence

of ulceration, discrete arrangement, preserved adnexa and absence of necrosis.^[10] In addition, the study conducted by Tirumalae and Roopa also highlighted the importance of diagnosis by 'silhouette or scanning magnification', which offers the best impression of a lesion. The same was also endorsed by Ackerman and Boer.^[11] The diagnostic approach depends on the location of the tumour, cell cytoplasm and the color of the tumour, respectively. Some tumours are located superficially and are overlying the epidermis, whereas others are deep-seated within the dermis. Peripheral palisading, keratinous cyst, papillary mesenchymal bodies, trichohyaline granules and ghost cells indicate a hair follicle differentiation. SATs of apocrine origin are associated with apocrine snouts, whereas clear cells indicate lesions of sebaceous origin and tubular features are characterised in sweat gland tumours.^[1] In contrast to the study conducted by Pujani *et al.*,^[12] in our study, the hair follicle tumours constituted the largest group, 38.83% (33/85), followed by sebaceous gland tumours 31.76% (27/85) and sweat gland tumours 29.41% (25/85), respectively. The male-to-female ratio of the patients was found to be approximately equal (1.14:1) in our study group, which is comparable to that Jindal and Patel.^[13] Similar to the study conducted by Jindal and Patel,^[13] 80% of our tumours in the study were <2 mm in size. Tumours were present in age groups ranging from 5 to 80 years. The sixth decade of life showed

the highest incidence of the tumours (21.75%, 18/85) followed by the fourth decade (16.5%, 14/85) and the fifth decade of life (15.29%, 13/85), respectively. Similar to the study conducted by Pujani *et al.*,^[12] around 70% of the SATs in our

Table 2: Distribution of tumours of epidermal appendages with respect to anatomical site

Tumour type and incidence	Head and neck	Extremities	Trunk
Benign			
Follicular			
Trichoepithelioma	2	Nil	2
Pilomatricoma	11	Nil	Nil
Proliferating trichilemmal cyst	6	Nil	2
TF	2	Nil	1
Trichoadenoma	4	Nil	2
Sebaceous			
Sebaceous adenoma	4	Nil	2
Sebaceous cyst	12	1	6
Apocrine			
Apocrine hidrocystadenoma	2	Nil	1
Cylindroma	1	Nil	Nil
Syringocystadenoma papilliferum	4	Nil	Nil
Eccrine			
Eccrine poroma	Nil	2	Nil
Nodular hidradenoma	3	Nil	Nil
Eccrine acrospiroma	1	Nil	Nil
Eccrine syringoma	2	2	1
Chondroid syringoma	1	Nil	2
Malignant			
Follicular			
Trichoblastoma	2	Nil	Nil
Sebaceous			
Sebaceous carcinoma	1	Nil	1
Eccrine			
Adenoid cystic carcinoma	3	Nil	Nil

TF: Trichofolliculoma

study were located in the head-and-neck region. This is because this anatomical site has a rich collection of eccrine and apocrine glands along with a good number of pilosebaceous units, which provide a conducive environment for the development of SATs.^[1] This was followed by the trunk, which constituted almost 22%, and the least was from the limbs, which together constituted only 4.7% of the entire SATs of this study. Trichiepithelioma^[1] [Figure 1 and Table 1] can occur singly and in multiples. It appears in children and gradually increases with age. The most commonly involved site is facing but can occur anywhere. On microscopy, it consists of multiple horn cysts and lining basal cell epithelium [Figure 1b]. Trichilemmoma^[1] can occur as small tumours measuring 3–8 mm in diameter. On microscopy, it consists of lobular features extending into the dermis. Trichelemmal cysts can occur as subcutaneous nodules, and when they undergo ulceration, it mimics squamous cell carcinoma. Under microscopy, it consists of irregularly shaped lobules of squamous epithelium undergoing abrupt transformation into amorphous keratin. Trichoblastoma ultimately develops into a trichoblast. Under microscopy, it consists of basaloid tumour cells along with Merkel cells.^[1] TF^[1] occurs in adults as a solitary lesion, usually on the face but occasionally on the scalp or neck low-power microscopic examination shows keratin-filled cyst lined by squamous epithelium associated with secondary hair follicles. Pilomatricoma^[1] [Figure 2a and 2b, Table 3] is also called pilomatricoma or calcifying epithelioma of Malherbe. Under microscopy, it consists of a dual population of cells consisting of basophilic cells and eosinophilic shadow cells.^[1] Syringocystadenoma papilliferum^[1] [Table 4] is commonly seen on the scalp and is often associated with the nevus sebaceous. Under microscopy, it consists of several cystic invaginations extend downward from the epidermis forming small cystic areas lined by a double layer of epithelial and myoepithelial cells with evidence of decapitation (apical snout) secretion. Syringomas are small

Table 3: Comparison of prevalence of skin adnexal tumours in various published studies and present study

Studies	Radhika <i>et al.</i> ^[3]	Saha <i>et al.</i> ^[4]	Rajalakshmi <i>et al.</i>	Nair ^[5]	Kaur <i>et al.</i> ^[6]	Present study
Study period	January 1993–December 2003	June 2007–May 2008	2009–2013	3 years	January 2013–December 2015	January 2016–January 2021
Total cases	35	23	21	33	110	85
Most common age group	20–30		30–40	11–20	20–39	40–59
Male: female	0.7:1	1:1.9	1:1.1	1:2.3	1.03:1	1.17:1
Most common site	Head and neck		Head and neck	Head and neck	Head and neck	Head and neck
Benign tumours (%)	77.4	100	90.48	100	82.72	91.77
Malignant tumors (%)	29.63		9.52	-	17.28	8.23
Most common benign tumor	Nodular hidradenoma; nevus sebaceous (14.2% each)	Syrinoma (39.13%)	Pilomatricoma (19.04%)	Syringoma	Pilomatricoma (28.2%)	Sebaceous cyst
Most common malignant tumor	Sweat gland carcinoma (11.4%)		Aggressive digital papillary adenocarcinoma; malignant dermal eccrine syringoma		Sebaceous carcinoma (11.8%)	Adenoid cystic carcinoma

benign adnexal neoplasms that are almost always multiple. By far, the most common sites of involvement are the lower eyelids. A mixed tumour (chondroid syringoma) is a biphasic tumour with both epithelial and stromal components.^[1] Epithelial components consist of branching tubular structures with occasional follicular differentiation. The stroma may be of chondroid and mucoid background. Hidradenoma papilliferum is a SAT that is found in the vulval and female perianal regions [Figure 3 and Table -1].^[1] Under microscopy, it consists of frond-like papillae or tubulopapillary structures that are lined by two cell layers, inner epithelial and outer myoepithelial cell layers. Cylindroma [Figure 1] differs in its low-power appearance from jigsaw puzzles [Figure 2]. The nests of cylindroma are commonly surrounded by a rim of densely eosinophilic PAS-positive basement membrane. Cylindroma is also called 'Turban tumours', and it appears as a 'Solitary lesion' and also occasionally may be multiple and covers the entire scalp. Cylindroma under microscopy, it consists of irregularly shaped cell islands with a jigsaw puzzle appearance lined by densely eosinophilic PAS-positive basement membrane material.^[1] Sebaceous adenoma is present as a yellow, circumscribed nodule located on either the face or scalp. Under microscopy, it consists of incompletely differentiated sebaceous lobules. The lobules contain undifferentiated basaloid cells (seboblots). Mature sebaceous cells with vacuolated cytoplasm (sebocytes).^[1] Proper identification of SATs along with correct HPE helps in identifying familial tumour syndromes, which have a high risk of association with internal malignancies and clinical syndrome. In such cases, detailed history elicitation with proper emphasis on family history and along with complete clinical examination is essential as most of these familial cases are usually located in multiple sites and show autosomal dominant inheritance. Hence, sharing complete clinical details along with the pathologist is of vital importance to obtain an accurate diagnosis. None of our cases was multiple or associated with a known hereditary syndrome, which is compatible with a predominantly sporadic occurrence of SATs.^[2] In the present study, majority of SATs were benign and occasional diagnostic discrepancies within the benign SATs are inconsequential as most of them require the same treatment and carry a relatively better prognosis.^[4] However, correct identification of the degree of differentiation is important in applying the diagnostic criteria for malignancy. For example, necrosis *en masse* is a typical feature of benign neoplasms in the period spectrum but is suggestive of malignancy in most other types of SATs.^[1] In

this study, 9 malignant SATs were identified using the criteria as suggested by Rajalakshmi *et al.* In this study, 15 cases underwent cytological evaluation and 6 cases showed positive cyto-histo correlation. The remaining 9 cases were discordant and showed no cyto-histo correlation [Figure 3a and 3b]. This discordance could be due to (a) inadequate sample, (b) poor technique, (c) small size lesions and (d) haemorrhagic background. Cytochemical stains such as PAS, mucicarmine, alcian blue, and reticulin may aid in establishing the

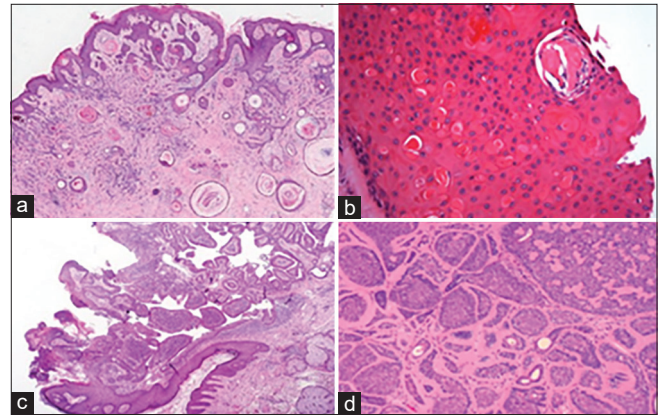


Figure 1: (a) Trichoepithelioma (4/85; 4.7%) with cords of basaloid tumour cells arranged in a pseudoinfiltrative pattern (H and E, $\times 4$), (b) Trichilemmal cyst showing keratinization (H and E, $\times 40$), (c) Syringocystadenoma papilliferum showing epidermis with papillary projections (H and E, $\times 10$), (d) Cylindroma showing basaloid cells (H and E, $\times 40$)

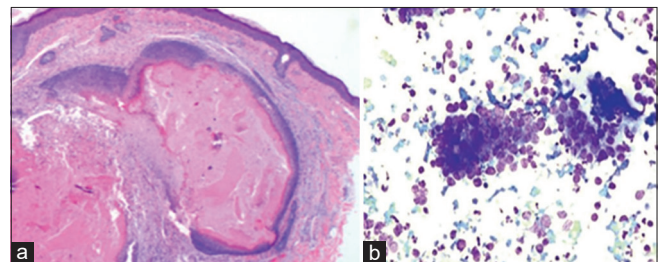


Figure 2: (a) Pilomatrixoma^[1] is also called pilomatricoma or calcifying epithelioma of Malherbe (H and E, $\times 4$), (b) Fine needle aspiration smear of pilomatrixoma showing clusters of basaloid cells with scant cytoplasm and indistinct cell borders (Giemsa stain, $\times 4$)

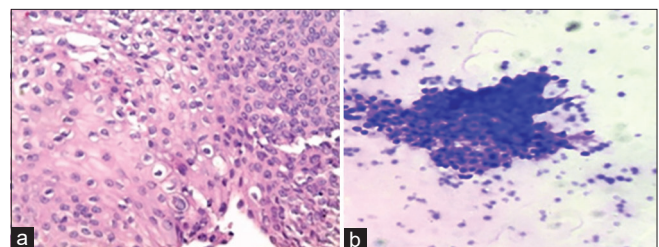


Figure 3: (a) Histopathological image of nodular hidradenoma showing focal point of squamous differentiation (H and E, $\times 40$), (b) Fine needle aspiration smear of nodular hidradenoma showing dual population of cells consisting of basaloid and polyhedral cells with clear cytoplasm (Giemsa stain, $\times 10$)

Table 4: Cyto-histo correlation in various skin adnexal tumour

Number of cases	Cytological diagnosis	Histological diagnosis
3	Pilar tumour (pilomatrixoma)	Pilar tumour (pilomatrixoma)
1	Chondroid syringoma	Chondroid syringoma
1	Adnexal tumour with atypia	Trichoepithelioma
1	Benign adnexal tumour	Trichilemmal cyst

diagnosis.^[12] PAS stain highlights the characteristic eosinophilic globules in a spiradenoma as well as the basement membrane material surrounding the nests of tumour cells and small round droplets in a case of cylindroma. Alcian blue stain helps in demonstrating the intense staining of the stroma in a case of chondroid syringoma. Other stains such as Hale's colloidal iron stain for acid mucin and Prussian blue for iron deposits within apocrine lesions are also reported.

Most SATs express different types of cytokeratins. Monoclonal CEA and EMA can be seen in tumours with ductal differentiation. EMA is noted in tumours with sebaceous differentiation. GCDPF-15 and androgen receptors are expressed in apocrine lesions, but estrogen and progesterone receptors are noted in different sweat glands lesions and are non-specific. Hence, morphological evaluation is very important in evaluating SATs, and special stains along with immunohistochemical stains may serve as additional tools. However, we have successfully diagnosed malignant SATs purely on characteristic histomorphological features as no additional investigations were necessary.^[1] Although cytology remains a useful diagnostic tool for the diagnosis of SAT, its full potential is not yet realised.^[13] After clinicopathological correlation, the possibility of SATs should always consider in the differential diagnosis during the cytological evaluation of cutaneous nodules.^[4]

Cytological diagnosis of SATs is relatively rare due to multiple reasons, which include (a) routine use of excisional biopsies for the diagnosis of SATs and (b) scarcity of reports in the medical literature on the cytological aspects of SATs.^[3] However, cytological diagnosis is extremely useful in the management of SATs as a malignant change in an SAT is usually missed clinically but can be seen when subjected to FNAC and subsequently confirmed by histopathology.^[14] Our study was compared with similar studies done by several other authors, including the one done by Kaur *et al.*^[6] Refer [Table 4].

CONCLUSION

SATs are characterised by heterogeneity as they have variable subtypes with similar presentation and variable nomenclature. This is because they include a diverse group of benign and malignant lesions that can present as single or multiple entities with sporadic or familial inheritance either

located superficially in the epidermis or in the deep dermis. SATs are a heterogeneous group of lesions that are usually misdiagnosed due to variable clinic-pathological presentations. Hence, concordance between clinical and histopathological diagnosis remains the gold standard for deriving the accurate identification of SATs.

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Conflicts of interest

There are no conflicts of interest.

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