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Histopathological spectrum of cutaneous neoplasms - A retrospective study

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Abstract:
Cutaneous neoplasms exhibit a wide histopathological spectrum, often posing diagnostic challenges due to overlapping clinical features. This retrospective study analyzed 66 cases diagnosed between January 2022 and December 2024 at a tertiary care center in Gujarat. Benign tumors were most common (69.7%), with keratinocytic tumors being the predominant type (40.9%). The face was the most frequently affected site (34.9%), and nodular lesions were the typical presentation (63.6%). Histopathology remains essential for accurate diagnosis and timely treatment of skin tumors.

Keywords: Skin neoplasms, benign, premalignant, malignant, histopathology, clinical correlation

Background:
Skincancer is technically not very prevalent as a malignancy in the world, but the incidence of these skin tumors has been increasing tremendously over the past decades **[1]**. The lesions that are classified under these neoplasms constitute a very broad category of lesions that is very heterogeneous in its histological and clinical composition and as such pose a significant diagnostic dilemma **[2]**. Cutaneous tumors are broadly divided into neoplasms of the keratinocytic origin, which involve, among others, basal cell carcinoma, squamous cell carcinoma, melanocytic tumors that include their nevi and melanoma, and adnexal tumor which includes the sweat glands, sebaceous glands, and hair follicle. Also, mesenchymal subcutaneous and skin tumors make a large share of the cutaneous neoplasm spectrum, the examples being dermatofibromas, lipomas, and tumors of a vascular aspect **[4]**. A more complicated type under this category consists of primary cutaneous epithelioid soft tissue tumors arising with those tumors have divergent lines of differentiation. These are tumors of melanocytic, peripheral nerve sheath, angiomatous, fibrohistiocytic, myoid, and myoepithelial origin that carry different considerations in terms of diagnostic and treatment settings **[5]**. Their morphology is overlapping and the behavior of the lesions is variable- with some of them showing an indolent benign and in some cases being aggressive malignancies- hence the histopathology should be carefully determined to get the correct diagnosis **[6]**. Due to the wide spectrum of biological behavior of these neoplasms and the possibility of malignant transformation of premalignant conditions it is critical to obtain accurate histological diagnosis that allows effective clinical decision-making and planning individual treatment **[7]**. Therefore, it is of interest to outline the histopathological spectrum of cutaneous neoplasms in a tertiary care center to enhance diagnostic accuracy in this regard and suggest the relevant management plans.

Materials and Methods:
The present retrospective cross-sectional record-based study was conducted in Department of Pathology of a tertiary care center of Gujarat. Patients of any age or sex, who were clinically suspected to have a cutaneous neoplastic pathology and whose biopsy or excision was sent and diagnosed to be a neoplastic lesion, were included. These encompassed all the neoplastic lesions of skin including epidermal, dermal, subcutis or soft tissue lesion comprising of benign, premalignant and malignant entities. Cases who were suspected to have cutaneous neoplastic pathology but who were histopathologically diagnosed to be reactive or non-neoplastic entity were excluded. We compiled the retrospective record-based data of these 66 included patients who visited dermatology outpatient department at our hospital for consultation from January 2022 to December 2024. The histopathology slides including Haematoxylin and Eosin (H&E) as well as other special stains if available were retrieved for all the included cases. All these slides were re-examined for validation and confirmation of the diagnosis in hospital information system. Statistical analysis was done by Statistical Package for Social Sciences (SPSS) version 21.0. Continuous variables were presented as mean ± standard deviation (SD) and median. Categorical variables were presented as number and percentage (%).

Table 1: Demographic findings in various categories of cutaneous neoplasms

Category	No. of cases (%)	Age (years)									Sex	
		0-10	20-Nov	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Male	Female
Keratinocytic	27 (40.9)	0	0	3	4	7	3	6	2	2	20	7
Melanocytic	7 (10.7)	1	1	1	1	0	1	1	1	0	2	5
Adnexal	9 (13.6)	0	0	0	3	2	2	2	0	0	5	4
Vascular	12 (18.2)	0	1	2	3	1	2	1	2	0	6	6
Fibrohistiocytic	6 (9.1)	1	0	1	2	1	1	0	0	0	2	4
Myoid	1 (1.5)	0	0	0	1	0	0	0	0	0	1	0
Neural	3 (4.5)	0	0	0	0	2	1	0	0	0	2	1
Lymphoid	1 (1.5)	0	0	0	0	0	1	0	0	0	0	1
Total	66	2	2	7	14	13	11	10	5	2	38	28
Percentage	100	3	3	10.6	21.2	19.7	16.7	15.2	7.6	3	57.6	42.4

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Table 2: Frequencies of presentation of cases at various sites

Site		No. of cases	Percentage of cases (%)	
Upper limb	Armpit	1	22.70%	Extremities 39.4%
	Arm	4		
	Forearm	2		
	Hand finger	2		
	Index finger	2		
	Middle finger	1		
	Little finger	2		
	Thumb	1		
	Total	15		
Lower limb	2		16.70%	
	Gluteal region / Buttock	3		
	Inguinal skin fold	1		
	Calf	1		
	Ankle	1		
	Sole of foot	1		
	Foot	2		
	Total	11		
Scalp	7		10.60%	Head and neck 48.5%
Face	1		34.90%	
	Forehead	1		
	Temple	1		
	Cheek	7		
	Nose	2		
	Ear pinna	3		
	Chin	2		
	Lower lip	2		
	Upper eyelid	2		
	Lower eyelid	2		
	Total	23		
Neck	2		3%	
Back	4		6%	
Chest	1		1.55%	
Abdomen	1		1.55%	
Genitalia	Glans Penis	1	3%	
	Vulva	1		
	Total	2		
Total	66		100%	

Table 3: Categorization of cases determined by the clinical characteristics of the lesion

Clinical appearance of the lesion	No. of cases	Percentage of cases (%)
Nodular	42	63.6
Ulcer	7	10.6
Plaque	4	10.6
Plaque with papule	2	
Verruccous plaque	1	
Total	7	
Papule	7	10.6
Warty	3	4.6
Total	66	100

Table 4: The distribution of the cases according to site, clinical presentation and histopathological findings

Category	Entity	Benign/ Pre-malignant /Malignant	No. of cases	Site	Type of lesion	Acute / Chronic presentation
Keratinocytic	Pseudoepitheliomatous hyperplasia	Benign	2	1 Neck	1 Plaque	Acute
				1 Left lower limb	1 Ulcer	
	Pseudokeratotic and micaceous balanitis	Benign	1	Glans Penis	Plaque	Chronic
	Acrochordon (Benign fibroepithelial polyp)	Benign	3	2 Left gluteal region	Nodular	Chronic
				1 Back		
	Fibrokeratoma	Benign	1	Right hand little finger	Papule	Acute
	Benign cutaneous horn	Benign	2	1 Left gluteal region	Nodular	Acute
				1 Left hand finger		
	Verruca vulgaris	Benign	1	Left forearm	Plaque with few papules	Chronic
	Verruca plantaris	Benign	1	Sole of foot	Ulcer	Acute
	Myrmecia wart	Benign	1	Right little finger	Nodular	Chronic
	Condyloma	Pre-malignant	2	Right upper arm	Nodular	Acute

	Seborrheic keratosis	Benign	2	1 Right armpit	Nodular	1 Acute
				1 Left ear pinna		1 Chronic
	Acrokeratosis verruciformis of Hopf	Benign	1	Right foot	Plaque with few papules	Chronic
	Actinic keratosis	Pre-malignant	1	Face	Warty	Acute
	BCC (3 pigmented, 1 pigmented nodular, 2 classic)	Malignant	6	2 Left cheek,	3 Ulcer	4 Acute
				2 Nose	2 Nodule	2 Chronic
				1 Left upper lid	1 Plaque	
				1 Left temple		
	SCC	Malignant	3	2 Left ear pinna	1 Ulcer	Acute
				1 Left leg	2 Nodule	
Melanocytic	Epidermal nevus	Benign	2	1 Right inguinal fold of skin	Hyperpigmented Papule	1 Acute
				1 Forehead		1 Chronic
	Congenital melanocytic nevus	Benign	1	Right cheek	Hyperpigmented Papule	Chronic
	Nevus sebaceous / Nevus sebaceous of Jadassohn	Pre-malignant	2	1 Chin	1 Verrucous plaque	1 Acute 1 Chronic
				1 Scalp	1 Plaque	
	Malignant Melanoma	Malignant	2	1 Left index finger	Progressively increasing Nodular swelling	1 Acute
				1 Vulva		1 Chronic
Adnexal	Chondroid Syringoma	Benign	1	Chin	Nodular	Chronic
	Trichoepithelioma	Benign	2	Right cheek	Multiple hypopigmented papules	Chronic
	Pilomatricoma	Benign	1	Neck	Nodular	Chronic
	Eccrine spiradenoma	Benign	1	Back	Nodular	Chronic
	Eccrine hidrocystoma	Benign	1	Right lower eyelid	Nodular	Chronic
	Proliferating Pilar tumor low grade	Pre-malignant	1	Scalp	Nodular	Chronic
	Poorly differentiated sebaceous carcinoma	Malignant	2	1 Left upper eyelid,	Nodular	Chronic
				1 Left lower eyelid		
Vascular	Lobular capillary hemangioma	Benign	4	3 Scalp	Nodular	Acute
				1 Right foot		
	Hemangioma	Benign	1	Lower lip	Nodular	Acute
	Cavernous hemangioma	Benign	1	Left calf	Nodular	Acute
	Capillary hemangioma	Benign	3	1 Scalp	Nodular	2 Acute
				1 Chest		1 Chronic
				1 Left arm		
	Angiofibroma	Benign	2	1 Right ankle	1 Nodular	Chronic
				1 Lower lip	1 Papule	
	Glomus tumor	Benign	1	Right thumb	Nodular	Chronic
Fibrohistiocytic	Dermatofibroma	Benign	2	1 Left arm	Nodular	Chronic
				1 Right forearm		
	Benign fibrous histiocytoma	Benign	2	1 Scalp	Nodular	Chronic
				1 Left middle finger		
	Juvenile Xanthogranuloma	Benign	1	Right cheek	Nodular	Acute
	Fibroblastic rheumatism	Benign	1	Left index finger	Nodular	Acute
Myoid	Cutaneus Leiomyoma	Benign	1	Left cheek	Nodular	Chronic
Neural	Neuroma	Benign	1	Back	Nodular	Chronic
	Neurofibroma	Benign	1	Abdomen	Nodular	Chronic
	Schwannoma	Benign	1	Left hand finger	Nodular	Chronic
Lymphoid	Mycosis Fungoides	Malignant	1	Back	Ulceration with plaque	Acute
Total	-		66	-		

Results:

The spectrum of cutaneous neoplasms was categorized into eight distinct groups based on their cellular origin. These categories encompass keratinocytic, melanocytic, adnexal, vascular, fibrohistiocytic and myoid, neural and lymphoid lesions. The age of the patients were from ten to ninety years, with the highest frequency observed in the 31-40 years age group, which accounted for 14 cases (21.2%) followed by 41-50 years comprising of 13 cases (19.7%). The mean age of the patients was 47.60 ± 18.04 years. Amongst all the included cases, 57.6% were males and 42.4% were females. The most common age group for keratinocytic lesions was 41-50 years predominantly benign in nature, followed by 61-70 years with higher frequency of pre malignant and malignant lesions. Benign lesions were commoner in younger age groups compared to malignant lesions in older age groups. Adnexal, vascular, fibrohistiocytic and myoid lesions were common in 31-40 years age group, neural in 41- 50 years, lymphoid 51-60 years while cases showing melanocytic lesions had a variable age presentation. Males were more commonly affected in keratinocytic, adnexal, neural and myoid cutaneous lesions while females in melanocytic, fibrohistiocytic and lymphoid (**Figure 1**). However, there was 1:1 male: female ratio in vascular cutaneous tumors (**Table 1**). The most common site of

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presentation was face (34.9%) followed by upper limb (22.7%), lower limb (16.7%), scalp (10.6%), back (6%), neck (3%), genitals (3%), chest (1.55%) and abdomen (1.55%) (**Table 2**).

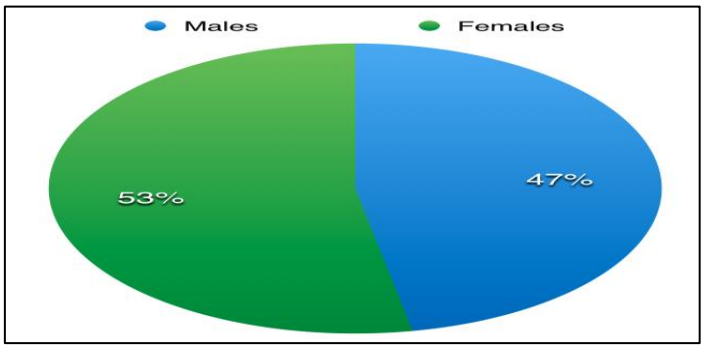

Figure 1: Classification of cases based on the duration of lesion persistence.

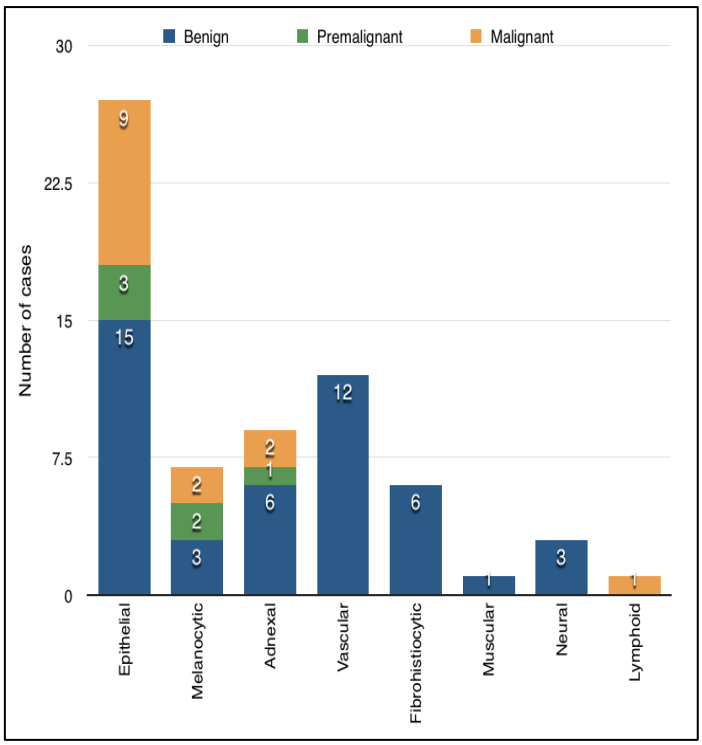

Figure 2: Classification of cases based on the histopathological type of lesion.

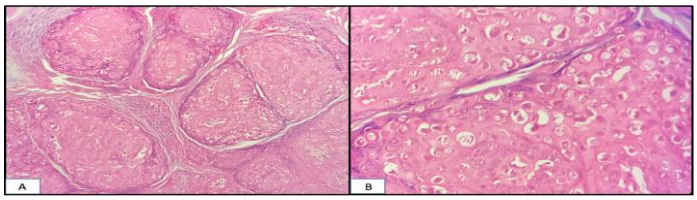

Figure 4: Hematoxylin and Eosin-stained smears showing features of Myrmecia wart A. 100X magnification B. 400X magnification.

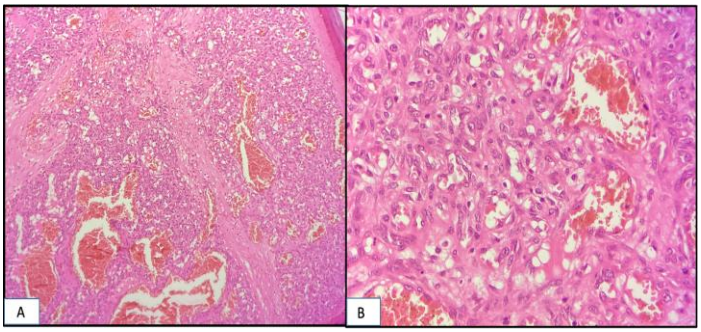

Figure 3: Hematoxylin and Eosin-stained smears showing features of Lobular Capillary Hemangioma A. 100X magnification B. 400X magnification.

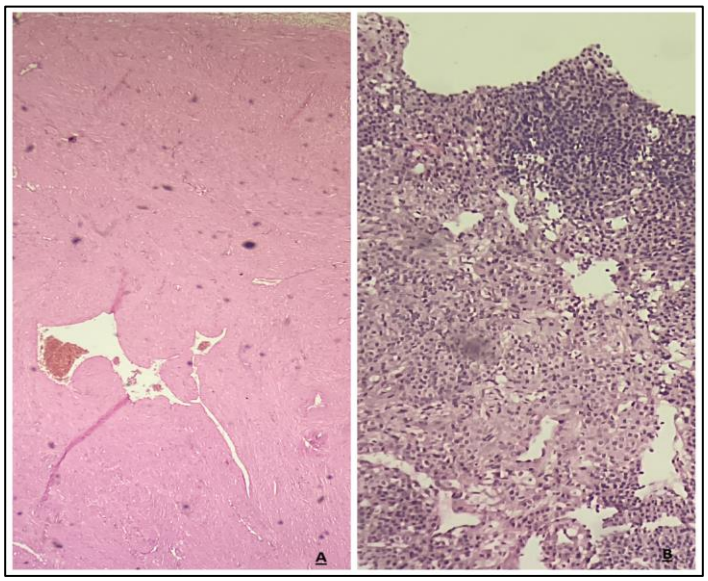

Figure 5: (A) Photomicrograph of Benign fibrous histiocytoma showing nodular proliferation of Spindle cells with plump vesicular nucleus and pale eosinophilic cytoplasm and perivascular hyalinization - Hematoxylin and Eosin 10X view (B) Photomicrograph of Glomus tumour with round monomorphic cells and round nucleus of glomus cells - Hematoxylin and Eosin 20X view

Keratinocytic tumors had a varied site of presentation of which face, upper limbs and lower limbs were most commonly affected. Adnexal tumors were common on face and scalp; melanocytic and myoid tumors on face; vascular tumors on scalp and lower limbs; fibrohistiocytic tumors in upper limbs; while lymphoid and neural tumors presented on back. Basal cell carcinoma (BCC) was commonly observed on the cheek and nose, whereas squamous cell carcinoma (SCC) was frequently found on the ear pinna and sebaceous carcinoma on the eyelids. Based on the duration of persistence of lesion, the cases were categorized as acute if the duration was ≤ 6 months and chronic if > 6 months. Chronic presentation was more common than the acute presentation in our cases of cutaneous neoplasms. Acute clinical presentation was usually seen in seborrheic keratosis,

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Pseudoepitheliomatous hyperplasia (PEH), BCC, SCC, hemangioma, cutaneous horn and mycosis fungoides (MF). Most common presentation was nodular swelling or growth (63.6%) (**Table 3**). Three cases with nodular presentation had hyperpigmented nodule, of which two turned out to be seborrhoeic keratosis and one benign cutaneous horn. One case of Wilson's disease acutely presented with plaque and turned out to be PEH. Two cases with presentation as a plaque had papules also along with plaque. One was Acrokeratosis Verruciformis of Hopf (AKV) and another was a clinically suspected case of lichen planus which turned out to be verruca vulgaris on histopathology. One case had a verrucous plaque which turned out to be nevus sebaceous of Jadassohn. Other three cases of plaque turned out to be pigmented BCC, nevus sebaceous and Pseudoepitheliomatous Keratotic and Micaceous Balanitis (PKMB). Out of seven cases with ulcer, three were pigmented BCC, one SCC, one verruca plantaris, one PEH and one MF. Two cases had a history of plaque before which converted to ulcer formation. One was a case of BCC and another MF. Out of seven cases of papules, three were hyperpigmented and two were hypopigmented. Hyperpigmented papules were seen in two cases of epidermal nevi and one congenital melanocytic nevus. Hypopigmented papules were seen in two cases of trichoepithelioma. One case of fibrokeratoma and one case of angiofibroma also presented with papules. There were three cases with warty growth of which two were condyloma and one actinic keratosis. Histopathological examination classified these cases into eight unique groups according to their cellular origin. Within each group, they were further divided based on the presence or absence of malignancy, specifically categorized as benign, premalignant, or malignant. A total of 69.7% of the cases were classified as benign, 9.1% as pre-malignant and 21.2% as malignant (**Figure 2**). Benign tumors like chondroid syringoma, trichoepithelioma, pilomatricoma, eccrine spiradenoma, eccrine hidrocystoma, lobular capillary hemangioma (LCH) (**Figure 3**), hemangiomas including capillary and cavernous types, angiofibroma, glomus tumor, acrochordon (benign fibroepithelial polyp), benign cutaneous horn, verruca vulgaris, verruca plantaris, myrmecia wart (**Figure 4**), seborrheic keratosis, AKV, PEH, PKMB, epidermal nevus, congenital melanocytic nevus, dermatofibroma, benign fibrous histiocytoma (BFH), juvenile xanthogranuloma (JXG), fibroblastic rheumatism, cutaneus leiomyoma, neuroma, neurofibroma (NF) and schwannoma were identified. Premalignant lesions comprised of condyloma, actinic keratosis, nevus sebaceous / nevus sebaceous of Jadassohn and proliferating pilar tumor. Malignant lesions included BCC, SCC, malignant melanoma, sebaceous carcinoma and MF. LCH represented the most frequently occurring benign tumor, while nevus sebaceous and condyloma were identified as the predominant premalignant lesions **[3, 4]**. BCC emerged as the most prevalent malignant lesion among the cases examined. Based on the cell of origin, keratinocytic tumors were most common (40.9%), followed by vascular tumors (18.2%) and adnexal (13.6%). The distribution of all the cases according to the site, clinical presentation and histopathology is depicted in **Table 4**.

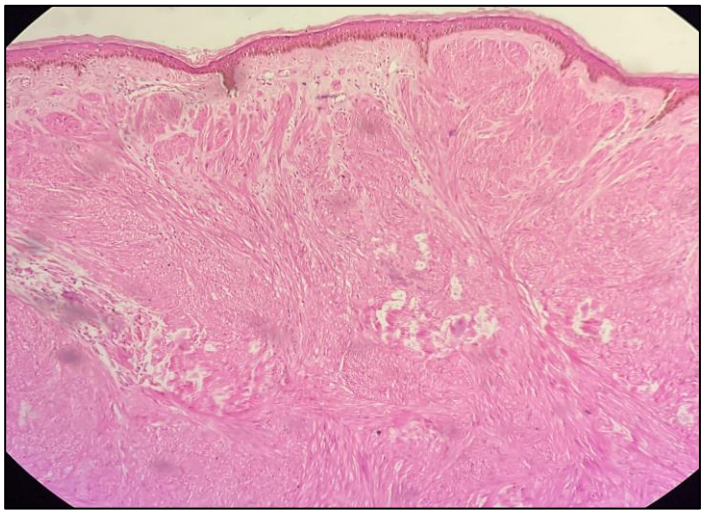

Figure 8: Photomicrograph of Cutaneous leiomyoma showing circumscribed tumour with interlacing smooth muscle cells - Hematoxylin and Eosin 20X view

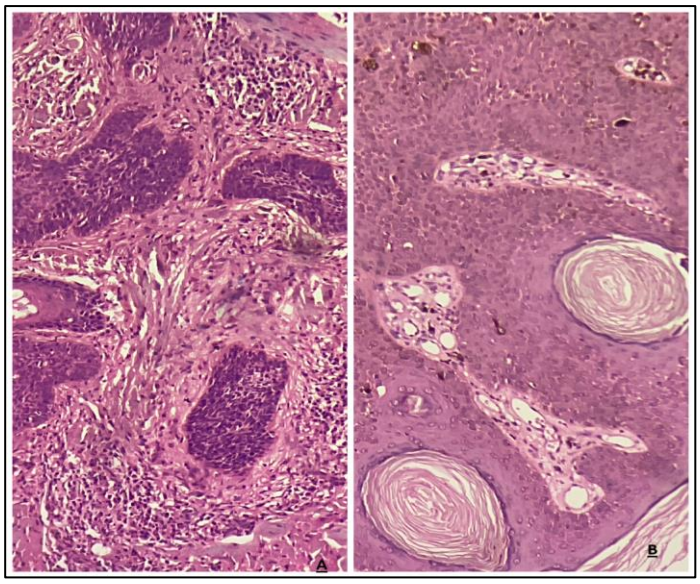

Figure 6: (A) Photomicrograph of Basal cell carcinoma showing basaloid nest invading stroma with peripheral palisading and Cleft formation between nest and stroma - Hematoxylin and Eosin 10X view (B) Photomicrograph of seborrheic keratosis showing pseudocyst formation and keratinocyte proliferation - Hematoxylin and Eosin 10X view

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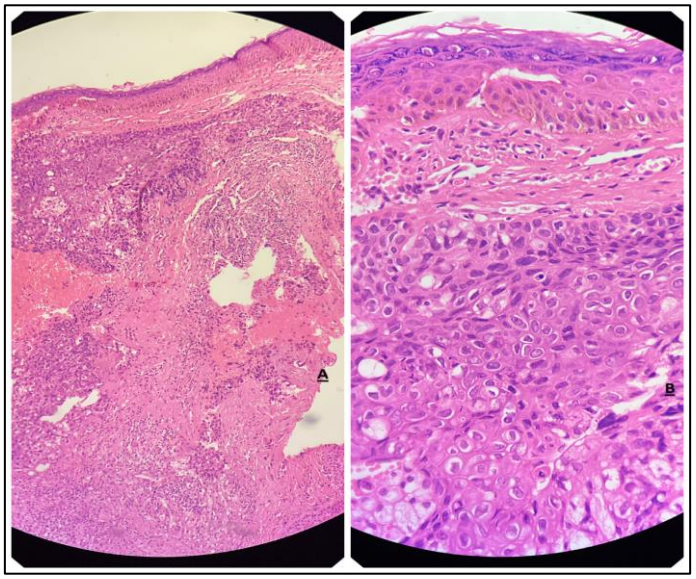

Figure 7: Photomicrograph of Poorly differentiated Sebaceous carcinoma showing nodular aggregates of tumour cells with sebaceous differentiation and anaplastic features - Hematoxylin and Eosin 20X view

Discussion:

The skin consists of various cell types that operate in a mutually dependent and collaborative manner **[5]**. The epidermis primarily consists of keratinocytes, melanocytes, Langerhans cells and Merkel cells. Epidermal appendages, which extend from the epidermis into the dermis, include specialized cells such as follicular epithelial cells, sebaceous cells and the cells of eccrine and apocrine glands. Additionally, lesions in the dermis and the underlying subcutaneous and soft tissues may manifest clinically as skin tumors. Different skin tumour consists of different cells **[6]**. In routine clinic patient can have variety of benign, pre malignant or malignant tumours. Due to the heightened ultraviolet radiation caused by the depletion of the ozone layer, it is anticipated that the incidence rates of skin malignancies will rise in the future, unless changes in human behavior aimed at reducing sun exposure can mitigate these expected increases **[7]**. The precise identification of skin lesions is essential to prevent the oversight of malignancies and to ensure that they are addressed promptly, thereby reducing the risks of morbidity and mortality **[8]**. Skin biopsy serves as a crucial technique that aids clinicians in establishing a definitive diagnosis and directing patient management. In this research, benign tumors were found to be more prevalent than malignant tumors, accounting for 69.7%. This finding is consistent with previous studies conducted by Thapa *et al.* (57.34%), Shrivastava *et al.* (63.8%), Narhire *et al.* (69.4%) and Kaur *et al.* (67.27%) **[1, 9-11]**. In contrast to the findings of this study, several researches conducted by Gundalli, Nandyal and Samanta have reported a higher prevalence of malignant tumors. This discrepancy may be attributed to an increased number of referrals to higher-level medical centers, as well as variations in geographical factors **[12-14]**. Keratinocytic tumors were the most prevalent, accounting for 40.9% of cases, followed by vascular tumors at 18.2% and adnexal tumors at 13.6%. In contrast, the study conducted by Thapa *et al.* reported that keratinocytic tumors comprised the majority at 66.9%, with adnexal tumors at 19.0% and melanocytic tumors at 14.0%. This finding aligns with the results from Uplaonkar *et al.* where keratinocytic tumors represented 41.7%, appendageal tumors 38.9% and melanocytic tumors 19.4% **[1, 15]**. In the research conducted by Pappala *et al.* keratinocytic tumors accounted for 60.52%, melanocytic tumors represented 23.3% and appendageal tumors comprised 16.3% **[16]**. Similar to our study Goel *et al.* also found keratinocytic tumor as the most prevalent type of tumor **[17]**.

Whereas in the research conducted by Gundalli *et al.* and Narhire *et al.* the most frequently observed tumor was the benign skin adnexal tumor, accounting for 54.7% **[10, 12]**. Several other studies identified benign melanocytic tumors as the most prevalent type of skin tumors **[9, 14].** Research conducted by Kaur *et al.* indicated that cutaneous neoplasms are more prevalent in males compared to females, aligning with the findings of the current study **[11, 17]**. In contrast, few other studies indicated a predominance of females **[1, 9 and 18]**. In the current research, cutaneous neoplasms were identified in individuals aged between 10 and 90 years, with the highest prevalence noted during the fourth and fifth decades of life. Keratinocytic lesions were predominantly observed in the fifth decade, primarily exhibiting benign characteristics, while the seventh decade showed an increased occurrence of pre-malignant and malignant lesions. Adnexal, vascular, fibrohistiocytic and myoid lesions were frequently found in the fourth decade, neural lesions in the fifth decade and lymphoid lesions in the sixth decade. Cases involving melanocytic lesions displayed a diverse age distribution. Whereas in other studies, the majority of cutaneous tumors were reported in the third and sixth decades of life, with benign neoplasms being more prevalent among the younger population **[11, 13, 18 and 19]**. In the study done by Thapa *et al.* it was observed that most cutaneous tumors occurred in individuals during their sixth decade of life, in contrast to the study done by Sherpa and KC which identified the third decade as the most prevalent age group for these tumors **[1, 19].** In the current study, the head and neck region was identified as the most frequently affected area, accounting for 48.5% of cases, with the face being the most commonly involved subregion. This was followed by the extremities, which represented 39.4% of the cases, consistent with findings from several other studies **[1, 9, 10, 17 and 20]**. It can conclude that sun exposed area have high chance of development of skin tumours. In our research, LCH emerged as the most prevalent benign cutaneous neoplasm, while acrochordon was identified by Thapa *et al.* squamous papilloma by Pappala *et al.* and verrucas by Shrivastava *et al.* Kaur *et al.* **[1, 9, 11, 16 and 17]**. Trichoepithelioma emerged as the predominant skin adnexal tumor in our research, differing from the findings of Gundalli *et al.* Thapa *et al.* Shrivastava *et al.* and Sherpa and KC, where pilomatricoma was more prevalent **[1, 9, 12 and 19]**. However in the study done by Gowda *et al.* syringoma

represented the most prevalent type of cutaneous appendageal tumor **[21]**. BCC emerged as the predominant cutaneous malignant neoplasm in this study, aligning with the findings of Nair *et al.* while contrasting with the highest prevalence of SCC reported by Deprez *et al.* LeBoit *et al.* and Thapa *et al.* **[1, 22-24]**. Clinically, there exists a significant dilemma, as provisional diagnoses may differ markedly from the definitive histopathological findings, particularly due to the multitude of entities that can present similarly, especially among benign lesions. The current study illustrates this point, where a case initially suspected to be an epidermal cyst or mucocele was ultimately identified as a chondroid syringoma. Additionally, a lesion that raised suspicion for papilloma or a mucous retention cyst was confirmed to be a hemangioma. One case initially thought to be acrochordon was diagnosed to be a neuroma, while a lesion suspected to be either a cylindroma or dermatofibrosarcoma protuberans (DFSP) was found to be a neurofibroma. A patient presenting with a differential diagnosis of trichofolliculoma, trichoblastoma and sebaceoma was ultimately diagnosed with a benign fibrous histiocytoma (BFH). Furthermore, a case clinically suspected to be a lipoma or hematoma was confirmed as an eccrine spiradenoma and another case initially thought to be a sebaceous cyst was diagnosed as an eccrine hidrocystoma. Lastly, a case of verrucous vulgaris was clinically misidentified as lichen planus. (**Figures 5 to 8**) present photomicrographs of several cutaneous skin tumors, with details provided in the legends.

Conclusion:

Diagnosing skin tumors poses distinct challenges, partly due to the variety of tumors. Correctly identifying skin lesions is crucial in order to avoid missing potential malignancies and to facilitate early treatment, required to minimize morbidity and mortality. Histopathological examination serves as a crucial tool in the diagnosis of skin tumors. Thus, it is essential to correlate clinical characteristics with both gross and microscopic findings.

Author contributions:

Garima Anandani conceptualized the idea and Payal Bhatt collected the data. Garima Anandani drafted the manuscript and performed the data analysis. Parth Goswami and Yashdeep Singh Pathania contributed in reviewing and supervising the manuscript. All authors contributed to the article and approved the submitted version.

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The authors confirm that the ethical policies of the journal have been adhered to. Ethical approval was taken by the Institutional Ethics Committee (IEC Approval number: AIIMS/RAJKOT/5th/ER/12). No identification details of the patient have been shared in the article.

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