

## THE STUDY ON CLINICOPATHOLOGICAL CORRELATION OF EPIDERMAL LESIONS IN A TERTIARY CARE CENTER – A GAMUT OF NON-NEOPLASTIC TO MALIGNANT LESIONS

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### ABSTRACT

**Objectives:** This study aimed to analyze the histopathological spectrum of epidermal lesions and correlate them with age, gender, and site, highlighting histopathology's essential role in accurate cutaneous lesion diagnosis.

**Methods:** This combined prospective and retrospective study was conducted over 2 years in the pathology department of a tertiary care hospital. A total of 182 skin specimens were examined using hematoxylin and eosin staining, with special stains when needed. Clinical data were collected, and cases were histologically classified and statistically analyzed using IBM SPSS Version 24.

**Results:** The most prevalent category was epidermal cysts, comprising 65.39% of all lesions (119/182), with keratinous epidermal type cysts (41.2%) being the most common subtype. These were frequently seen on the back and face. Other cystic variants included pilar cysts, dermoid cysts, steatocystomas, and infected cysts with abscess formation. Cutaneous malignancies represented 11.54% of cases (21/182), including squamous cell carcinoma, verrucous carcinoma, and five histological variants of basal cell carcinoma, predominantly located on sun-exposed areas such as the face. Benign tumor-like lesions included seborrheic keratosis (7.14%), fibroepithelial polyps (5.49%), verrucous lesions (4.39%), melanocytic nevi (3.85%), and Bowen's disease (2.19%). Lesions were most common in the 41–50-year age group (23.63%), and females were slightly more affected (M:F ratio 1:1.09). The head and neck region (35.16%) and back (25.82%) were the most common anatomical sites.

**Conclusion:** This study emphasizes the predominance of benign epidermal cysts among cutaneous lesions, with a noteworthy representation of cutaneous malignancies. The findings highlight the crucial role of histopathology in accurate diagnosis, subclassification, and management planning. Establishing clinicopathological correlations can aid in early detection, particularly of malignant or atypical variants, thus optimizing patient care.

**Keywords:** Basal cell carcinoma, Cutaneous malignancies, Epidermal cysts, Histopathology, Melanocytic nevi, Seborrheic keratosis, Squamous cell carcinoma, Verrucous lesions.

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### INTRODUCTION

The skin is a complex organ with intricately regulated cellular and molecular interactions that govern many vital responses to our environment. Apart from signifying numerous internal illnesses, cutaneous neoplasia can be categorized into several groups, each of which reflects distinct biologic behaviors. These include benign tumors, malignant epidermal tumors, hamartomas, hyperplasia, cysts [1,2], and some may be metastatic deposits of internal cancers [3] (Kligman, 2002 #728), which can result in morbidity and mortality. Certain tumors are linked to syndromes such as Cowden's disease. Clinical diagnosis of these diverse entities is often challenging because of the similar gross findings and morphological overlap of numerous epidermal tumors and cystic lesions [2]. Hence, the histopathological examination is mandatory for diagnosis and its pattern analysis [4-6]. The aim of the present study was to observe and analyze the incidence of common types of cutaneous cystic lesions, tumors, and tumor-like lesions and their histopathological patterns.

Furthermore, cutaneous tumors differ in their histological types, which have a significant role in the determination of prognosis and patient care. The present study aimed to study the histopathological spectrum of cutaneous lesions in correlation with the age, gender, and location of occurrence at a tertiary care hospital. The results of the study may contribute to creating awareness among the public and also aid in future research.

### METHODS

This is a prospective and retrospective study conducted in the Department of Pathology at our institute. The study was done from

September 2022 to August 2024, covering a duration of 2 years, and included a total of 182 cases of skin lesions. The approval from the institutional ethics committee was obtained before the start of the study (Ethical committee approval number: 002/SBMCH/IHEC/2023/2000).

We included all the biopsies and resected specimens received from the Department of Dermatology and Venereology and Surgery for histopathological examination. Clinical details, such as age, duration of disease, location, and clinical features, were obtained from the request forms filled by the clinician. Routine grossing and processing were done for all the cases as per the structured protocol. The hematoxylin and eosin-stained slides were examined microscopically to determine the histopathological diagnosis. Special stains were performed whenever necessary.

#### Inclusion criteria

All tumors and tumor-like lesions arising from the epidermis, cystic lesions of the skin are included in the study.

#### Exclusion criteria

Appendageal tumors, dermal-based lesions, soft-tissue tumors.

#### Statistical analysis

The collected data were entered into a Microsoft Excel Worksheet 2010, and the data were taken into IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA) software for the calculation of frequency and percentage.

## RESULTS

The present study is a prospective and retrospective study that included 182 skin specimens. The clinical details, such as age, gender, and location of skin lesions, were tabulated. The histopathological diagnosis was established and correlated with the median age of incidence and common locations.

Demographic results of the study suggest that the cutaneous lesions were common in the age group of 41–50 years (23.63%), followed by 21–30 years (20.32%) (Table 1). Gender-wise distribution showed that 95/182 cases (52.19%) were females and 87/182 (47.80%) were males. The male: female ratio was 1:1.09, suggesting a slight female predominance in our study. The present study included the location specificity among the study participants and found that the majority of the lesions occurred in the head and neck region (35.16%), followed by the back (25.82%) (Table 2).

In the present study, the majority were epidermal cysts (65.39%), which included keratinous cysts of epidermal type (41.20%), pilar type (6.59%), and dermoid cyst (6.25%) (Fig. 1a-e). Keratinous cysts of verrucous type (3.29%) and rare association of keratin granuloma (1.64%) and dystrophic calcification (1.09%) with keratinous cysts were noted (Tables 3 and 4 and Fig. 2a-c). This was followed by

**Table 1: Age incidence among the study participants**

Age (years)	Number of cases	Percentage
<20	08	4.39
21–30	37	20.32
31–40	32	17.58
41–50	43	23.63
51–60	31	17.03
61–70	18	9.89
71–80	11	6.04
>81	2	1.09
Total	182	100

Mean±SD=44.04±16.74 years. Chi-square statistic ( $\chi^2$ )=69.25; p-value=2.09×10<sup>-12</sup>

**Table 2: Location-wise distribution of epidermal lesions among study participants**

Location	Number of cases	Percentage
Head and neck	64	35.16
Chest wall	09	4.95
Breast	03	1.65
Back	47	25.82
Abdomen	08	4.39
Upper limb	11	10.44
Lower limb	21	11.54
Genitals	05	2.75
Gluteal region	11	6.04
Multiple sites	03	1.65
Total	182	100

Mean: 18.20; Standard deviation: 20.72; Chi-square statistic ( $\chi^2$ ): 212.29; p-value: <0.0001

**Table 3: Distribution of epidermal lesions among study participants**

Histopathological type	Number of cases	Percentage
Epidermal cysts	119	65.39
Seborrheic keratosis	13	07.14
Verrucous lesions	08	04.39
Bowen's disease	04	02.19
Cutaneous malignancies	21	11.54
Melanocytic nevus	07	03.85
Fibroepithelial polyp	10	05.49
Total	182	100

Mean=2.21; Standard deviation (SD)=1.94; Standard error of the mean (SEM)=0.14. Chi-square statistic ( $\chi^2$ )=394.92; p-value: <0.0001

cutaneous malignancies 21/182 (11.54%), including squamous cell carcinoma, verrucous carcinoma, and basal cell carcinoma (Table 5). This study also showed tumor such as lesions which included 13/182 cases (07.14 %) of seborrheic keratosis (Fig. 3a) and its variants (Table 6), 10 cases (5.49%) of fibroepithelial polyp (Fig. 3b), 8/182 cases (4.39%) of verrucous lesions (Table 7), 7 cases (3.85%) of nevi, and four cases of Bowen's disease (Fig. 5 and Table 3). The median age and common locations of incidence are tabulated (Tables 4-7). The occurrence of nevus was noted predominantly among females (5/7 cases), and the face was the most common location, followed by the back.

Epidermal-type keratinous cysts were the most common subtype (33.52%), predominantly affecting males with a median age of 42 years. Inflamed (6.5%) and pigmented variants (1.09%) localized mainly to the face and back. Pilar cysts (6.04%) were frequently seen in the head and neck region. Rare subtypes included those with granuloma, calcification, or abscess, mostly on the back. The verrucous type (3.29%) occurred in younger patients, with lesions distributed across multiple sites. The cohort had a mean age of 43.11 years (standard deviation [SD]=4.38 years; standard error of the mean [SEM]=0.43 years).

The table shows that classical seborrheic keratosis was the most frequent subtype (46.15%), with a median age of 68.5 years and female predominance. The pigmented variant (30.76%) mainly affected the face and abdomen. Less common types included acanthotic and melanoacanthoma variants. Overall, 69.2% of cases occurred in females. The mean age of occurrence was 68.69 years, with SD=4.49 and SEM=1.24 years.

Table 5 data present the histological subtypes of cutaneous malignancies, with squamous cell carcinoma being the most common malignancy (23.81%), with a median age of 52 years and a slight female predominance. Verrucous carcinoma (19.05%) showed male predominance and was commonly found on the leg and gluteal region. Basal cell carcinoma comprised multiple variants, with the conventional type (19.05%) and pigmented variant (14.29%) being most frequent, predominantly affecting the face. Most malignancies occurred in females (13/21), particularly in sun-exposed regions. The mean age was 58.57 years, with SD=12.38 and SEM=2.70 years.

Table 7 presents eight cases of verrucous lesions, with verruca vulgaris (Fig. 4a) and deep palmoplantar warts (Fig. 4b) being the most common (25% each), primarily affecting males. The median age of presentation ranged from 21 to 61 years, with a mean age of 36 years (SD=13.45; SEM=4.76 years). Lesions were most commonly located on the face, foot, and upper limbs. Cornu cutaneum was exclusively seen in females, whereas verruca plana (Fig. 4c) and vulgaris showed male predominance. Verrucous leukoplakia was the least frequent but notable for its older age of onset (61 years).

In Fig. 5a, parakeratosis and irregular epidermal architecture are evident, while Fig. 5b highlights keratinocytic atypia with nuclear hyperchromasia and architectural disarray. Fig. 5c demonstrates marked pleomorphism with enlarged, irregular nuclei, and Fig. 5d shows increased mitotic activity, collectively supporting the diagnosis of intraepidermal squamous cell carcinoma in situ (Bowen's disease).

## DISCUSSION

Skin is known to be the largest and multifunctional organ in the body, and this multifunctionality is attributed to its intricate architecture. Exposure to environmental toxins, radiation, and chemicals predisposes the skin to various pathologies. Skin has a critical role in setting a barrier from external adversities, along with the regulation of thermal, electrolyte, and fluid balance [3].

Epidermal cysts are the most common cutaneous condition encountered in day-to-day practice. The common locations include the head and neck, trunk, and limbs. Conditions such as a needle prick can lead to an implantation dermoid cyst [4]. Certain adnexal neoplasms arising from

Table 4: Histological subtypes of epidermal cysts:

Histological Subtype	Number of cases	Percentage	Median age (years)	Common location	Male	Female
Keratinous cyst and its subtypes						
Epidermal type (Figure 1a-e)	61	33.52	42	Back, face, gluteal region, scrotum	37	24
Inflamed keratinous cyst	12	6.5	48	Face, back	4	8
Pigmented epidermal type	02	1.09	48	Back	2	0
Pilar type	11	6.04	41	Head and neck	6	5
Inflamed pilar type	01	0.55	57	Chest	0	1
With keratin granuloma (Figure 2c)	03	1.64	49	Back	2	1
With dystrophic calcification (Figure 1f)	02	1.09	49.5	Back	0	2
Infected keratinous cyst with abscess	05	2.74	52	Back, abdomen	4	1
Verrucous type (Figure 2a)	06	3.29	32	Head, neck, back, limbs	2	4
Hybrid epidermal+pilar type	02	1.09	38.5	Neck	2	0
Dermoid cyst	07	6.25	31	Head and neck	5	2
Steatocystoma	05	4.20	30	Neck, chest, trunk, abdomen	3	2
Thyroglossal cyst	02	1.68	27	Neck	1	1
Total	119	100	-	-	59	46

Mean age=43.11 years; Standard deviation (SD)=4.38 years; Standard error of the mean (SEM)=0.43 years; Chi-square statistic ( $\chi^2$ )=334.03; p-value:<0.0001

Table 5: Histological subtypes of cutaneous malignancies

Histological subtype	Number of cases	Percentage	Median age (years)	Common location	Male	Female
Squamous cell carcinoma	05	23.81	52	Foot, neck	2	3
Keratoacanthoma	01	04.76	14	Genitals	0	1
Basosquamous variant	01	04.76	75	Face	0	1
Verrucous carcinoma	04	19.05	58	Leg, gluteal region, buccal mucosa	3	1
Basal cell carcinoma						
Conventional type	04	19.05	62	Face	1	3
Pigmented variant	03	14.29	60	Face	1	2
Adenoid variant	01	04.76	73	Face	1	0
Keratotic variant	01	04.76	76	Face	0	1
Fibroepithelial type	01	04.76	72	Face	0	1
Total	21	100	-	-	8	13

Mean±SD=58.57±12.38 years; SEM=2.70 years; Chi-square statistic ( $\chi^2$ )=9.43; p-value: <0.0001

Table 6: Histological subtypes of seborrheic keratosis

Histological subtype	Number of cases	Percentage	Median age (years)	Common location	Male	Female
Classical type	06	46.15	68.5	Face, thigh, inframammary	2	4
Pigmented variant	04	30.76	73.5	Face, abdomen	0	4
Acanthotic variant	01	7.69	69	Abdomen	0	1
Melanoacanthoma variant	02	15.38	59.5	Face, leg	2	0
Total	13	100	-	-	4	9

Mean age=68.69 years; Standard deviation (SD)=4.49 years; Standard error of the mean (SEM)=1.24 years; Chi-square statistic ( $\chi^2$ )=4.54; p-value:<0.0001

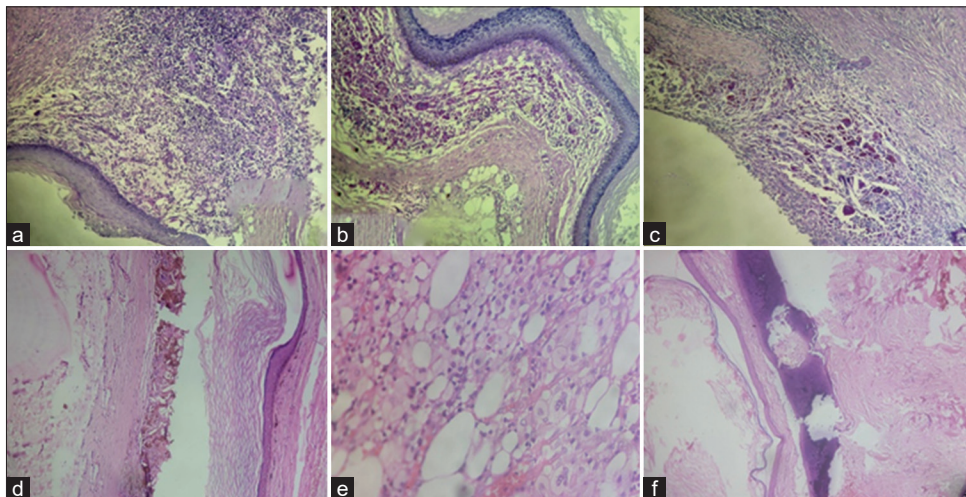


Fig. 1: Histopathological features of keratinous cysts of epidermal type stained with hematoxylin and eosin (H&E) and periodic acid-Schiff (PAS), viewed at ×100 and ×400 magnification. (a-c) Inflamed keratinous cyst, H&E. (b) Same cyst showing cyst wall with keratin lining, PAS stain, ×100 and ×400. (d) Pigmented keratinous cyst, H&E, ×100. (e) Cyst with xanthogranulomatous reaction, H&E, ×100. (f) Cyst with dystrophic calcification, H&E, ×100



Table 7: Histological subtypes of verrucous lesions

Histological subtype	Number of cases	Percentage	Median age	Common location	Male	Female
Verruca vulgaris	02	25	23 years	Face, forearm	2	0
Deep palmoplantar wart	02	25	33 years	Foot	2	0
Verruca plana	01	12.5	21 years	Upper limb	1	0
Cornu cutaneum	02	25	47 years	Foot	0	2
Verrucous leukoplakia	01	12.5	61 years	Lip	0	1
Total	08	100	-	-	5	3

Mean±SD=36.00±13.45 years; SEM=4.76 years; Chi-square statistic ( $\chi^2$ )=0.75; p-value: 0.95

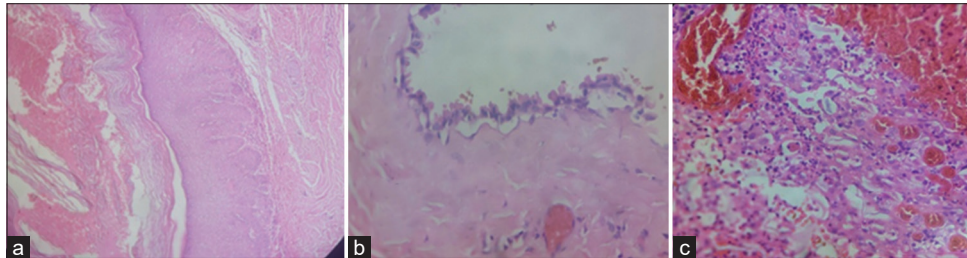


Fig. 2: (a) Verrucous cyst, H&E; ×100. (b) Steatocystoma; ×100. (c) Keratingranuloma, H&E; ×400

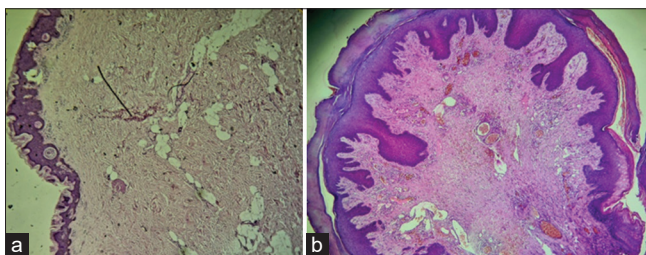


Fig. 3: Histopathological features of benign epidermal lesions stained with hematoxylin and eosin, viewed at ×100 magnification. (a) Seborrheic keratosis showing hyperkeratosis, acanthosis, and horn cyst formation. (b) Fibroepithelial polyp demonstrating fibrovascular cores lined by benign squamous epithelium

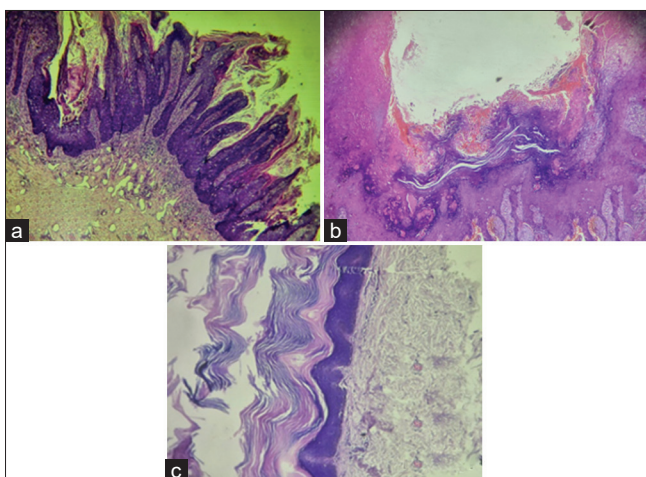


Fig. 4: (a) Histopathological features of verrucous lesions stained with hematoxylin and eosin, viewed under ×100 magnification. (a) Verruca vulgaris showing papillomatosis and hyperkeratosis. (b) Deep palmoplantar wart with compact orthokeratosis and pronounced epidermal hyperplasia. (c) Verruca plana with flat epidermal hyperplasia and minimal keratinization

hair follicles and cutaneous appendages, such as trichoepithelioma, trichofolliculoma, trichoblastoma, and adenoid cystic carcinoma,

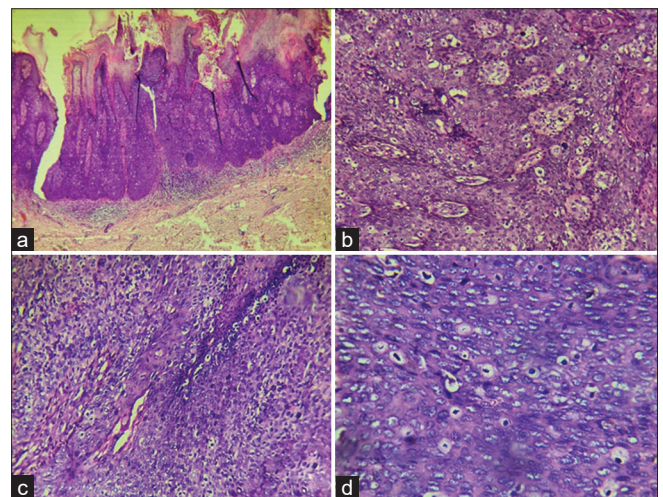


Fig. 5: Histopathological features of Bowen's disease stained with hematoxylin and eosin (H&E). (a) Low-power view (×40) showing parakeratosis and irregular epidermal architecture. (b) High-power view (×400) highlighting keratinocytic atypia. (c and d) High-power views (×400) demonstrating marked pleomorphism and increased mitotic activity

also present as cystic lesions of skin [5]. Warty lesions of epidermis can range from a histopathological spectrum of commonly occurring seborrheic keratosis to a rarer diagnosis of carcinoma [6].

Melanocytes are the pigment-producing cells located in the epidermis. Alterations in the pathways, such as the MAPK and AKT/PI3K pathways, lead to the development of a spectrum of melanocytic lesions. The melanocytic lesions, such as variants of nevus and malignant melanoma, are not uncommon. However, conditions such as congenital melanocytic nevi or neurocutaneous melanocytosis can occur rarely [7,8].

Globally, cutaneous malignancies account for an annual incidence of more than 2 million/year [9]. These neoplasms contribute 1-2% of all cancers. Squamous cell carcinoma is the most common cutaneous malignancy, causing a major health burden. However, basal cell carcinoma, melanoma, lymphoma, and sarcomas are also not uncommon [10]. Sun exposure, along with genetic alterations, contributes to their pathogenesis.

The skin lesions pose a diagnostic challenge due to their wide range of presentation, ubiquitous location of occurrence, broad classification, and complex nomenclature. Thus, histopathology plays a major role in diagnosing the cutaneous lesions. Advanced techniques such as immunohistochemistry can aid in answering the discrepancies or confirming the diagnosis.

The study conducted by Gandhi and Vijayaraghavan (Gandhi, 2018 #726) [11] showed that epidermal cysts contributed to the majority of the cutaneous cysts (62/162), followed by benign epidermal tumors (12.5%) and malignant epidermal tumors (10.5%). The most common epidermal tumor was seborrheic keratosis. This study found that the most common malignant tumor was Basal cell carcinoma. The study conducted by Inbasekaran *et al.* [5] also stated that the common cutaneous cysts were epidermal cysts. The study conducted by Chugtai *et al.* found that epidermal cysts (74.3%), pilar/trichilemmal cysts (15.1%), and dermoid cysts (6.3%) are the common cysts of skin, followed by rarer hidrocystoma (1.9%), steatocystoma (0.3%), verrucous cysts (0.3%), and hybrid cysts (0.2%). They found that the common site of occurrence was the back, and there was a female predominance in their study. These findings are similar to our study findings [12].

The study conducted by Roh *et al.*, on clinical and histopathological investigation of seborrheic keratosis, included 271 clinical cases with female predominance among histologically diagnosed cases (111 females, 95 males; total 206 cases). The median age of occurrence was 60.8±14.6 years. The lesion commonly occurred in the sun-exposed areas compared to the protected areas, with a p-value of 0.028. The commonly encountered variants are acanthotic, mixed, hyperkeratotic, melanoacanthoma, and adenoid types. The study conducted by Kwon *et al.* also showed sun-exposed areas to be the common location of occurrence. In our study, seborrheic keratosis occurred commonly over the face (sun-exposed area), in addition to the abdomen and thighs. This may be attributed to the varying patterns of sun exposure among the present generation [13,14].

Supekar *et al.*, in their study, noted that the most common age group of cutaneous malignancies was 60–70 years, with female predilection. Basal cell carcinoma (41%) is the most common, followed by squamous cell carcinoma (30%), melanoma (9%), and cutaneous lymphoma (1.5%). The common site is the head and neck. The study done by Koyuncuer noted that the mean age was 68.5±13 years. Basal cell carcinoma is seen in 75.6% cases and squamous cell carcinoma in 24.4 % cases. No statistical gender difference was noted (p=0.556). Their study notes 47.6% nodular variant, 28.2% mixed, 12.6% infiltrating, 6.8% adenoid, 2.9% micronodular, and 1 % basosquamous subtypes. They note that basal cell carcinoma commonly occurs over the face, and squamous cell carcinoma over the face and scalp [10,15].

The study conducted by Chauhan *et al.*, on 35 cases of verrucous lesions, showed male predominance (71.4%). Genital (22.8%), cutaneous (68.5%), and oral mucosa (8.5%) are the common locations, and the age ranged from 10 to 73 years, which coincides with our study [16].

Our findings demonstrate that verrucous lesions encompass a wide histological spectrum, with verruca vulgaris, deep palmoplantar warts, and cornu cutaneum being the most prevalent, each constituting 25% of cases. The mean age was 36 years, with a male predominance and common involvement of the foot, face, and lip. These results closely correlate with Chauhan *et al.*, who conducted a retrospective analysis identifying similar histological variants, including verruca vulgaris, deep palmoplantar warts, and cornu cutaneum. Keshvadjian *et al.* (2021) reported a case where verruca vulgaris progressed to cornu cutaneum in an elderly patient, supporting our observation of histological overlap. In addition, their review highlighted that approximately 16.5% of cutaneous horns arise from verruca vulgaris. Cohen presented two cases – one each of verruca vulgaris and inverted follicular keratosis – with cornu cutaneum, attributing 18% of

cutaneous horns to verruca vulgaris, reinforcing our histopathological correlation [16-18].

## CONCLUSION

This study highlights the common occurrence of skin lesions among women and the common age and site predilection for each lesion. Histopathology plays a key role in accurate diagnosis and appropriate classification of skin lesions. This study aids in establishing the clinicopathological correlation of cutaneous lesions, thus enabling the apt diagnosis and timely patient care.

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## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this study. No financial, personal, or professional relationships influenced the research process or outcomes presented in this manuscript.

## AUTHORS' CONTRIBUTIONS

Dr. I R Shinitha was responsible for the study's conceptualization, data collection, slide examination, statistical analysis, and initial drafting of the manuscript. Dr. Shobana B provided academic supervision, confirmed histopathological diagnoses, and contributed to manuscript refinement. Dr. Srismitha S was involved in developing the study methodology, reviewing relevant literature, and assisting with data interpretation. Dr. S Mary Lilly offered overall guidance, performed critical revisions, and approved the final manuscript for submission.

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