



## Histomorphological study of Premalignant and Malignant Lesions of Skin.

### KEYWORDS

malignant skin lesions, Benign skin lesions, Skin histology

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**ABSTRACT** Background: Histopathology remains the gold standard for the diagnosis of skin tumors. There is limited data on the distribution and occurrence of these skin tumors in literature. In addition, premalignant tumors of skin are commonly seen on sun-exposed areas, especially in tropical countries like India. It is important to recognize these distinctive entities based on that clinical data with histomorphological features and guide the dermatologists for treatment and prognostication. The present study aims to study the premalignant and malignant tumors of skin in a tertiary care teaching hospital and to categorize them according to their histopathological features.

*Aims and Objectives:* 1. To study the various clinico-histopathological features including age, sex, site distribution skin tumors.

2. To find the frequency of benign, malignant and premalignant tumors of the skin.

*Materials and Methods:* Skin biopsies and surgically resected specimens of skin tumors done for diagnostic and therapeutic purposes were studied. They were then categorized based on their clinical and histopathological features.

*Result:* A total of 51 patients were studied with clinic-pathological correlation. Most of the tumors were benign followed by malignant and premalignant condition. Majority of skin tumors were seen in the age-group of 51-60 years followed by 11-20 years with the head and neck area being the most common site. The most common type of skin tumor was found to be keratinocytic (52.9%) with the squamous cell carcinoma as the most common tumor.

*Conclusion:* Squamous cell carcinoma is the most common skin tumor of skin mainly seen on sun exposed areas. Histopathology plays a major role in identifying the varied features of premalignant and adnexal tumors of skin.

### Introduction

The skin is the largest organ of the body and more than hundred different types of tumors are known to be clinically apparent on the skin. This is because of the complexity of the structure of skin being made up of multiple cell types. These different cell types may undergo malignant transformation at various stages of differentiation, leading to tumors with distinct histology and varied clinical behavior such as squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). These cancers are also called as non-melanoma skin cancers (NMSC).<sup>1</sup>

Non-melanoma skin cancers are one of the most common human cancers. In spite of the growing public awareness of the harmful effects of sun exposure, incidence continues to rise. A 3 to 8% yearly increase in incidence of non-melanoma skin cancer has been reported since 1960 worldwide. Incidence of basal-cell carcinoma alone is increasing by 10% per year worldwide, suggesting that prevalence of this tumor will soon be equal to that of all other cancers combined.

Furthermore, an estimated 40–50% of patients with a primary carcinoma develop at least one or more further basal-cell carcinomas within 5 years. The estimated incidence of non-melanoma skin cancer in the USA is more than 1,000,000 cases per year, of which roughly 20–30% are SCC's.<sup>2</sup>

In India, skin cancers constitute about 1-2% of all diagnosed cancers. Basal cell carcinoma is the commonest form of skin cancer worldwide, but various studies from India have consistently reported SCC as the most prevalent skin malignancy. Although complete data of incidence is not available, various cancer registries in India reported cumulative incidence of skin cancer varying from 0.5 to 2 per 100 000 population. Although, the incidence of skin cancers in India is lower as compared to the Western world, because of a large population, absolute number of cases is estimated to be significant.<sup>3</sup>

Comparison of the site distribution and age pattern of different types of skin cancer can be an important source of etiological clues,<sup>4</sup> and thus was included in our study. Also any premalignant conditions were also included.

Thus this study was undertaken to determine the clinicopathological features of benign and malignant tumors of skin including premalignant conditions of skin.

### Aims and Objectives:

- To study and characterize the skin tumors based on histopathological features.
- To study the various clinicohistopathological features including age, sex, site distribution and clinical presentation of skin tumors.
- To find the frequency of benign, malignant and pre-

malignant tumors of the skin.

### Materials and Methods:

Skin biopsies and surgically resected specimens of skin tumors done for diagnostic and therapeutic purposes of indoor and outdoor patients visiting the tertiary care hospital during the study period were included. Clinical history and other findings were obtained as per case proforma.

Cases diagnosed as skin neoplasms benign and malignant as well as premalignant lesions of skin were included in the study. The detail gross examination was done and recorded. The histopathological processing and staining were done by standard Hematoxylin and Eosin method and were studied.

Tumors of the deeper subcutaneous tissue, soft tissue tumors of the skin, haematolymphoid tumors of the skin, neural tumors of the skin and metastasis in skin were excluded from the study.

Fifty one cases were selected on the basis of simple random sampling procedure and analyzed. The present study does not include follow up of patients.

### Results

Fifty one patients with skin tumors were studied during the study period, in the department of pathology at a tertiary care hospital. The following data was recorded and analyzed.

#### 1. Type and sex distribution of tumors:

Most of the tumors were benign 31(64.7%). Malignant tumors were 16(31.4%). Two (3.9%) premalignant conditions were also seen. (Table 1)

30(58.8%) cases were in males, whereas 21(41.2%) cases were females.

#### 2. Age distribution of lesions:

The cases were distributed from the age of 6 years to the age of 86 years.

Majority of the cases were in the age group of 51- 60 years (19.6%), followed by 11-20 years (17.6%). The malignant tumors were mainly seen in the age group of 51-60 years (11.7%) and 61- 70 years (9.8%). Majority of benign tumors were in the age group of 11-20 years (17.6%) and 21-30 years (15.6%). (Table 2)

#### 3. Site distribution of lesions:

Head, neck, face was the most common site for tumors (52.9%). Majority of benign tumors (41.2%) and malignant tumors were present on the head, neck, face (11.7%) followed by upper limbs (11.7%).

#### 4. Distribution of tumors according to histopathological classification:

The cases were divided into keratinocytic , adnexal and melanocytic tumors.

Majority of the tumors were keratinocytic (52.9%), which included malignant (29.4%) and benign tumors (23.5%). In the present study, adnexal tumors consisted of only benign tumors (29.4%). Melanocytic tumors (17.6%) comprised of both benign (15.7%) and malignant tumor (1.9%). (Table 3)

#### 5. Histopathological diagnosis:

Squamous cell carcinoma (21.6%) was the most common,

followed by nevus sebaceous of Jadassohn (13.7%) and intradermal nevus (12%). Seborrheic keratosis (9.8%), basal cell carcinoma (7.8%), verrucae vulgaris (5.8%), pilomatricoma (5.8%) and others (23.5%) were seen in the decreasing order of frequency. (Table 4)

#### 6. Clinicopathological correlation:

All clinically diagnosed cases of squamous cell carcinoma (21.6%) and basal cell carcinoma (7.8%) were confirmed on histopathology.

Nevus sebaceous of Jadassohn formed 13.7% of cases on histopathological examination, but only 3.9% cases were suspected clinically. All the 12% cases of intradermal nevus diagnosed on histopathology, were not suspected clinically.

9.8% of cases which were diagnosed as seborrheic keratosis on histopathology were clinically suspected only in 7.8% of cases. (Table 5)

### Discussion

Skin not only forms the largest organ of the body, but its lesion are varied and poses a great challenge to the histopathologist. The tumors of skin can arise either from the epidermis or the dermal appendages which include premalignant, benign and malignant tumors. In the present study the following skin tumors were found. Keratinocytic tumors (52.9%), Adnexal tumors (29.4%) and Melanocytic tumors (17.6%).

#### Keratinocytic tumors (52.9%) consisted of

Malignant tumors (29.4%)	Benign tumors (23.5%)
Squamous cell carcinoma (21.6%)	Seborrheic keratosis (9.8%)
Basal cell carcinoma (7.8%)	Verrucae vulgaris (5.8%)
	Squamous cell papilloma (1.9%)
	Keratoacanthoma (1.9%)
	Actinic keratosis (1.9%)
	Bowen's disease (1.9%)

Adnexal tumors (29.4%) consisted of only benign tumors. Nevus Sebaceous of Jadassohn (13.7%), Pilomatricoma (5.8%), Trichoepithelioma (3.9%), Nodular hidradenoma (1.9%), Eccrine hydrocystoma (1.9%) and Sebaceoma (1.9%).

Melanocytic tumors (17.6%) consisted of Intradermal nevus (12%), Compound nevus (1.9%), Spitz nevus (1.9%), and Malignant melanoma (1.9%).

#### Skin cancer:

Majority of the epidemiological studies report that skin cancers represent about 20-40 percent of all cancers. In United States about 300-400 new cases occur for every 100,000 population per annum and in United Kingdom about 100 new cases for every 100,000 population per annum are known to occur.

Skin cancer is attributed to solar ultraviolet light exposure and is seen in white skinned people working outdoors in sunlight. The frequency of skin cancer is also seen to increase with age. Skin cancers are known to commonly occur in sixth, seventh and later decades.<sup>5</sup> However in a study conducted in Africa by Samaila et al. a peak age distribution in fourth and fifth decades was seen.<sup>6</sup> Skin can-

cers are commonly seen on the face, neck, and other sun exposed areas. The frequency of non-melanoma skin cancer is about 1.6 times higher in men than women.<sup>5</sup> However melanoma is reportedly more common in women.

In a study of cutaneous malignancies in Africa between 1991 and 2000 done by Samaila et al.<sup>6</sup> three hundred and eighty two cutaneous malignancies were analysed. Nonmelanoma skin tumors were the commonest and accounted for 254 (66.8%). They comprised of squamous cell carcinoma 239 (62.9%), basal cell carcinoma 15 (3.9%) and malignant adnexal tumors which were the least common accounting for 2 (0.5%). Malignant melanoma cases were 54 (14.1%). There were two peak age distributions in the fourth and fifth decades (63.6%) for all tumors. The lower limb was the prevalent site for all tumors with 65% cases.<sup>6</sup>

In findings in the present study were in accordance with these studies in terms of distribution of cases, but the head and neck were the commonest site in our study.

#### **Non-melanoma skin cancer (NMSC):**

Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are together often known as non-melanoma skin cancer (NMSC). BCC is more common than SCC in whites, but many studies in dark skinned people and Asians indicate that SCC is more common in them.<sup>7</sup> NMSC occurs mainly in the sun-exposed regions predominantly the face and neck.

Risk factors for the development of SCC in darkly pigmented individuals include chronic scarring and areas of chronic inflammation and are associated with a greater potential for metastasis. The most frequent tumor occurring in scarred skin is SCC, and has an overall poor prognosis.<sup>8</sup>

In the present study a total of 51 skin neoplasms were studied.

Malignancies accounted for 31.4 percent of the cutaneous neoplasms, which is higher than the reported cases of Samaila et al.<sup>6</sup> which reported 10.8% occurrence of cutaneous malignancies in their study.

#### **Type of malignancies:**

In the present study the most common cutaneous malignancy was SCC (68.7%) followed by BCC (25%) and malignant melanoma (6.3%).

When compared with the study of Noorbala et al.<sup>5</sup> it showed BCC (76.9%) to be the most common, followed by SCC (18.1%) and malignant melanoma (2.7%).

However when compared with the Nigerian study of Samaila et al.<sup>6</sup> which showed SCC (62.9%) as the most common tumor, malignant melanoma (14.1%) and BCC (3.9%).

Thus for NMSC the current study is in concordance with the Indian study by Adinarayan et al.<sup>8</sup> and Nigerian study which shows SCC to be the most common malignancy and the reported differences could be attributed to racial and regional variations.

#### **Sex distribution of malignancies:**

In the present study cutaneous malignancies were more common in males than in females which are in concordance with the studies conducted by Noorbala et al.<sup>5</sup>, Samaila et al.<sup>6</sup> and Adinarayan et al.<sup>8</sup>

In the present study 81.8% cases of SCC and 75% of BCC were present in males. The studies done by Noorbala et al.<sup>5</sup> Adinarayan et al.<sup>8</sup> and Samaila et al.<sup>6</sup> also show that SCC and BCC are more common in males.

#### **Age distribution of malignancies:**

In the present study majority of the malignant tumors occurred in the sixth and seventh decades which correlate with the study of Noorbala et al.<sup>5</sup> and Adinarayan et al.<sup>8</sup> however in the study conducted by Samaila et al.<sup>6</sup> the skin malignancies peaked in the fourth and sixth decade.

In the present study majority of cases of SCC were seen in the sixth and seventh decade. In contrast, according to Noorbala et al.<sup>5</sup> majority of cases of SCC were seen in the seventh and eighth decade and while according to Adinarayan et al.<sup>8</sup> it was in fifth and sixth decade. In the study done by Samaila et al.<sup>6</sup> majority of cases of SCC were seen in the fourth and fifth decade.

In the present study cases of BCC were evenly seen distributed in the fourth, fifth, sixth and seventh decades which is in accordance with other studies.

(Table 8)

#### **Site distribution of malignant tumors.**

In the present study the most common site for skin malignancies was the lower limb which was in concordance with the study conducted by Samaila et al.<sup>6</sup> However the other studies conducted by Noorbala et al.<sup>5</sup> and Adinarayan et al.<sup>8</sup> show that head, neck, face region was the most common site for cutaneous malignancies.

In the present study majority of the cases of SCC were seen in the lower limb which is consistent with the study conducted by Samaila et al.<sup>6</sup>

However the other studies conducted by Noorbala et al.<sup>5</sup> and Adinarayan et al.<sup>8</sup> show that head, neck, face region was the most common site for SCC.

In the present study head, neck, face was the most common site for BCC which is consistent with the studies done by Noorbala et al.<sup>5</sup>, Samaila et al.<sup>6</sup> and Adinarayan et al.<sup>8</sup>(Table 7)

In the present study all cases of SCC were of low grade and well differentiated type on histology.

#### **Skin Adnexal tumors:**

Kamyab-Hesari et al.<sup>9</sup> conducted a study on adnexal tumors in Iran and studied a total of 1016 adnexal tumors from 2006 to 2010. Their study showed a 3.3% prevalence of adnexal tumors. Sebaceous carcinoma (36.5%) was the most common malignant adnexal tumor.

In the present study out of 51 cases, 15 adnexal tumors were found and all of them were benign (100%). The adnexal tumors were slightly more common in females (53.3%) with the most common site being head, neck and face (73.4%) which correlates with the studies done by Kamyab-Hesari et al.<sup>9</sup> and Radhika et al.<sup>11</sup>

The tumors of the sebaceous gland (53.3%) were the most common adnexal tumor with Nevus sebaceous of Jadassohn being the most common type in the present study which correlates with the study done by Kamyab-Hesari et al.<sup>9</sup>, but in the study by Radhika et al.<sup>10</sup> they found that

sweat gland tumors as the most common. (Table 8)

The mean age of diagnosis for adnexal tumors in the present study (34.6 years) also correlates well with the study done by Kamayab-Hesari et al.<sup>9</sup>(34.5 years).

Melanocytic tumors:

Melanocytic tumors (17.6%) consisted of Intradermal nevus (12%), Compound nevus (1.9%), Spitz nevus (1.9%), and Malignant melanoma (1.9%).

The number of cases were too less to be statistically compared with other studies.

**Conclusion**

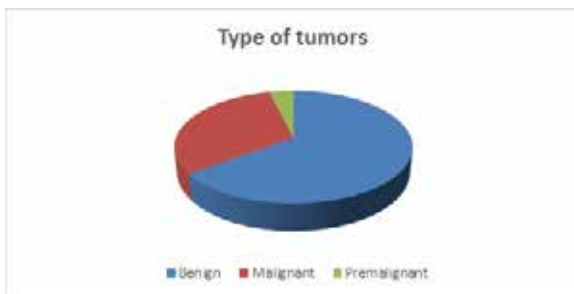
In the present study, most of the cases of squamous cell carcinoma's were found at the site of lower limb indicating that other etiological factors are more important in the causation of skin cancer than exposure to ultraviolet radiation, which was consistent with the various studies of non-melanoma skin cancer done in India and Africa. Age distribution of malignancies was consistent with various studies.

The present study also shows that although the clinical examination and history is important in the diagnosis of skin tumors, histopathological examination is necessary for the exact diagnosis.

**Charts and Tables:**

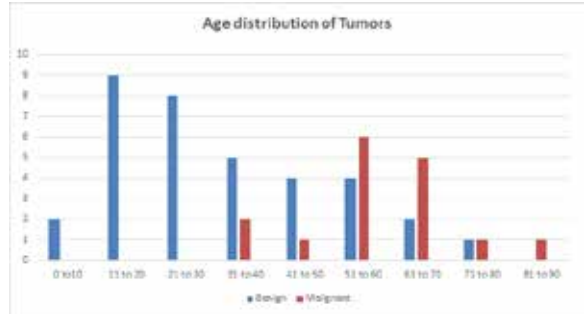
**Table 1. Types of cutaneous tumors.**

Type of tumor	Number	Percentage
Benign	33	64.7%
Malignant	16	31.4%
Premalignant	2	3.9%



**Table 2. Age distribution of Tumors.**

Age group	Benign	Malignant	Total
0-10	2(3.9%)	0(0%)	2(3.9%)
11-20	9(17.6%)	0(0%)	9(17.6%)
21-30	8(15.6%)	0(0%)	8(15.6%)
31-40	5(9.8%)	2(3.9%)	7(13.7%)
41-50	4(7.8%)	1(1.9%)	5(9.8%)
51-60	4(7.8%)	6(11.7%)	10(19.6%)
61-70	2(3.9%)	5(9.8%)	7(13.7%)
71-80	1(1.9%)	1(1.9%)	2(3.9%)
81-90	0(0%)	1(1.9%)	1(1.9%)



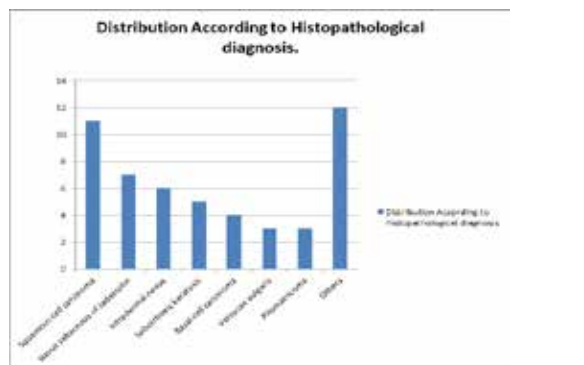
**Table 3. Distribution according to Histopathological Classification.**

Histopathological Classification	Benign	Malignant	Total
Keratinocytic	12(23.5%)	15(29.4%)	27(52.9%)
Adnexal	15(29.4%)	0(0%)	15(29.4%)
Melanocytic	8(15.7%)	1(1.9%)	9(17.6%)



**Table 4. Distribution of tumors according to Histopathological diagnosis.**

Histopathological diagnosis	Number of cases.
Squamous cell carcinoma	11(21.6%)
Nevus sebaceous of Jadassohn	7(13.7%)
Intradermal nevus	6(12%)
Seborrheic keratosis	5(9.8%)
Basal cell carcinoma	4(7.8%)
Verrucae vulgaris	3(5.8%)
Pilomatricoma	3(5.8%)
Others	12(23.5%)



**Table 5. Clinicopathological correlation**

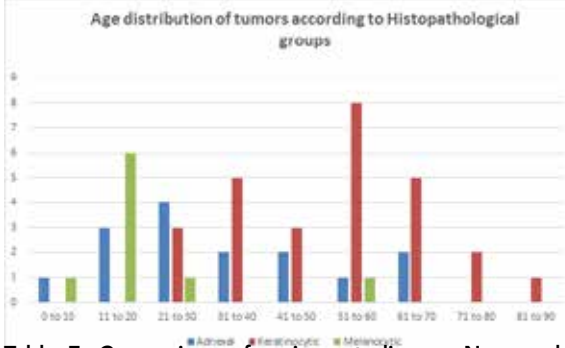
Lesion	Clinical diagnosis		Pathological diagnosis	
	No. of cases	Percentage	No. of cases	Percentage
Squamous cell carcinoma	11	21.6	11	21.6
Nevus sebaceous of Jadassohn	2	3.9	7	13.7



Intradermal nevus	0	0	6	12
Seborrhoeic keratosis	4	7.8	5	9.8
Basal cell carcinoma	4	7.8	4	7.8
Verrucae Vulgaris	4	7.8	3	5.8
Pilomatricoma	0	0	3	5.8
Others	26	51.1	12	23.5

**Table 6. Age distribution of tumors according to Histopathological groups.**

Age groups	Ad-nexal	Keratinocytic	Melanocytic	Total
	1(1.9%)	0(0%)	1(1.9%)	2(3.9%)
11-20	3(5.8%)	0(0%)	6(11.7%)	9(17.6%)
21-30	4(7.8%)	3(5.8%)	1(1.9%)	8(15.6%)
31-40	2(3.9%)	5(9.8%)	0(0%)	7(13.7%)
41-50	2(3.9%)	3(5.8%)	0(0%)	5(9.8%)
51-60	1(1.9%)	8(15.6%)	1(1.9%)	10(19.6%)
61-70	2(3.9%)	5(9.8%)	0(0%)	7(13.7%)
71-80	0(0%)	2(3.9%)	0(0%)	2(3.9%)
81-90	0(0%)	1(1.9%)	0(0%)	1(1.9%)



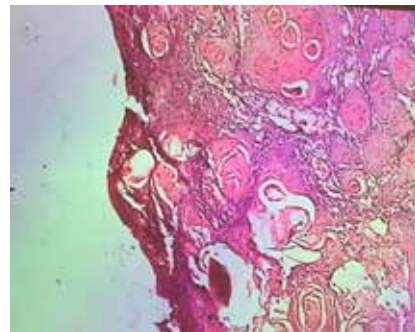
**Table 7. Comparison of various studies on Non-melanoma skin cancer(NMSC) [Squamous cell carcinoma(SCC) and Basal cell carcinoma(BCC)]**

		Adinarayan et al.	Noorbala et al.	Present study	
NMSC	SCC	83.9%	19.1%	73.3%	
	BCC	13.1%	80.9%	26.7%	
Sex	SCC	Male	76.9%	68.7%	81.8%
		Female	23.1%	32.3%	18.2%
	BCC	Male	60%	60.5%	75%
		Female	40%	39.5%	25%
Site	Head, neck, face	SCC	50%	85.3%	18.2%
		BCC	80%	96.8%	100%
	Limbs	SCC	46.1%	6.3%	45%
		BCC	20%	1%	0%

**Table 8. Comparison of various studies on Adnexal tumors.**

		Kamyab-Hesari et al.	Radhika et al.	Present study.
Age	Mean	34.5 years	-	34.6 years
Sex	Female	51%	54.3%	53.3%
Behavior	Benign	93.8%	77.1%	100%
	Malignant	6.2%	22.9%	0%

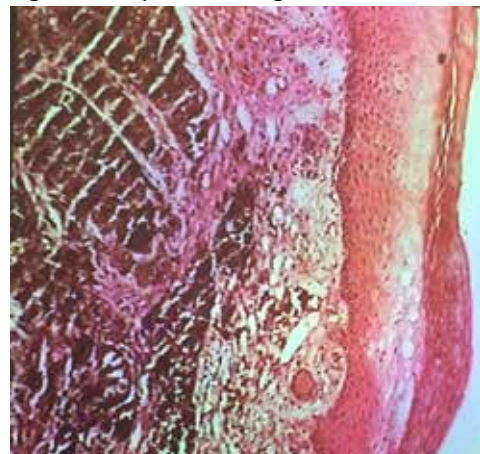
Location	Head, neck, face	83.5%	45.7%	73.4%
	Extremities	12%	11.4%	6.6%
	Trunk	4.5%	8.5%	20%
Histo-pathological origin	Sebaceous gland	52.7%	20%	53.3%
	Nevus sebaceous of Jadassohn	77%	14.2%	46.6%
	Sebaceoma	0.9%	-	6.6%
	Hair follicle	26.1%	31.5%	33.4%
	Pilomatricoma	36.2%	5.7%	20%
	Trichoepithelioma	15.9%	5.7%	13.3%
	Sweat gland	21.2%	48.5%	13.3%
	Nodular hidradenoma	24.6%	14.2%	6.6%
Hydrocystoma	12%	-	6.6%	



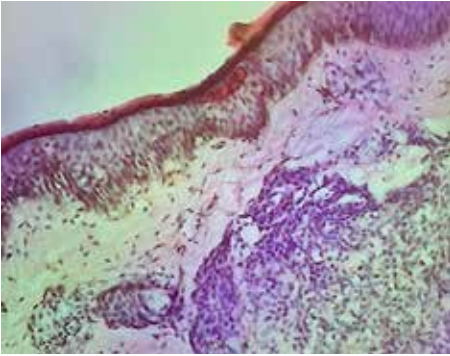
**Fig.1 Well differentiated squamous cell carcinoma showing malignant squamous cells and keratin pearls. (H & E 10x).**



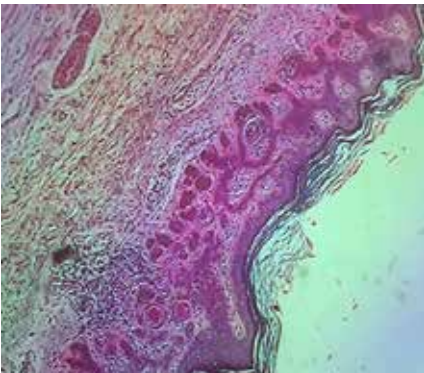
**Fig. 2 Clinical photo of squamous cell carcinoma showing an ulceroproliferative growth on the left foot.**



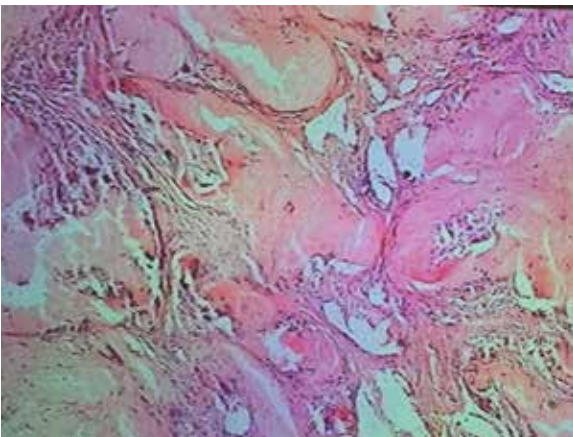
**Fig. 3 Malignant melanoma: skin with heavily pigmented malignant melanoma cells in the dermis. (H & E 10x).**



**Fig 4. Intradermal nevus: Nests of nevus cells confined to the dermis. (H & E 10 x).**



**Fig. 5 Seborrheic keratosis: Hyperkeratosis, pseudo-horn cysts, and reticulated pattern of the epidermis. (H & E 10x).**



**Fig. 6. Pilomatricoma: Basaloid cells surrounding ghost cells and few squamous cells.**

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