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CLINICOPATHOLOGICAL ASSESSMENT OF PIGMENTED SKIN LESIONS IN A SAMPLE OF IRAQI PATIENTS

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ABSTRACT

Background: Pigmented skin lesions (PSLs) refer to lesions that are black, brown or blue in color. A number of pigmented lesions are difficult to classify because of wide spectrum of histological appearances and raise the possibility of a melanoma. **Methods**: A retrospective study including analysis of 100 randomly selected samples of pigmented skin lesions sent to the Teaching Laboratories of Al-Emamain Al-Kadhmain Medical City (AS) and Medical city from January 2019 to July 2023. **Objectives:** This study aims to assess the type of pigmented skin lesions in a sample of Iraqi patients in correlation with clinicopathological parameters (age, gender, site, size, color, histological type). **Results:** regarding age, most of the studied sample were in age group 61-70 years (20.0%). As for gender, male: female ratio were 1:1. Head and neck region were the mostly effected site including cheeks (12.0%), eyelid (12.0%) and nose (11.0%). most lesions were smaller than 1 cm in size (43.0%) and brown in color (68.0%). non melanocytic lesions(80.0%) were more common than melanocytic lesions(20.0%) with most common pigmented lesion were basal cell carcinoma (32.0%). **Conclusion:** Non-melanocytic lesions is more common than melanocytic lesions while benign and malignant lesions were nearly equal in incidence, the most common benign lesion were benign melanocytic nevi which show female predominance in second decade of life distributed over the face, while the most common malignant pigmented lesion were basal cell carcinoma which show male predominance in 5-7th decade of life mostly on the nose.

I. INTRODUCTION

Pigmented skin lesions (PSLs) refer to lesions that are black, brown or blue in color. These lesions include both melanocytic and non-melanocytic lesions which can be subclassified as keratinocytic, vascular, or reactive. A number of pigmented lesions are difficult to classify because of wide spectrum of histological appearances and raise the possibility of a melanoma.[1]

Cutaneous non melanocytic lesions include pigmented seborrheic keratosis, pigmented basal cell carcinoma (PBCC), pigmented squamous cell carcinoma, epidermal nevi, angiokeratoma & hemangioma.[2]

Benign tumors of nevus cells are called melanocytic nevi, while malignant tumors are called malignant melanomas. Melanocytic lesions are important as malignant melanoma which accounts for only 1% of skin cancers, is responsible for over 60% of cancer related deaths. According to World Health Organisation, the number of melanoma cases worldwide is increasing faster than any other cancer. Nevi and other benign pigmented lesions, except for their cosmetic significance, are important as simulants of melanoma and as potential precursors of melanoma.[3]

Melanocytic nevus is a benign tumor that usually presents in childhood and adolescence. An average white individual can expect to develop 15–40 such lesions during life, reaching the maximum number in the third decade before regression to virtual disappearance by the eighth and ninth decades. They are more common in individuals with pale skin and light-colored eyes. Development of melanocytic nevi is related to the extent of sun exposure during the first two decades of life. Intermittent intense sunlight is of greater importance than chronic exposure.[4]

Malignant melanoma is is the third most common skin cancer but is the single most common potentially lethal neoplasm of the skin. The incidence of melanoma has risen dramatically over the last several decades. However, the mortality has risen less dramatically than the incidence, likely due to earlier diagnosis. There is considerable geographic variation in the incidence of

melanoma, related to exposure to sunlight and the susceptibility of the population.[5]

The peak incidence is around the sixth decade of life. The large majority are associated with sunlight exposure. Therefore most are found in the head and neck area and lower extremity, the latter being particularly common in females.[6]

BCC is the most common cancer in white-skinned people with increasing incidence rates worldwide. Patients with BCC place a large burden on healthcare systems, because of the high incidence and the increased risk of synchronous and metachronous BCCs and other ultraviolet radiation (UVR) related skin cancers (i.e. field cancerization). BCC is a complex disease, in which the interplay between UVR, phenotype (UVR-sensitive) and genotype (somatic mutations and germline mutations/polymorphisms) fulfils a key role in the aetiopathogenesis.[7]

SCC is the second most common skin malignancy affecting whites it is a form of nonmelanoma skin cancer that originates from epithelial keratinocytes or their appendages. Most cases of primary cutaneous SCC are induced by UV radiation. Chronic sun exposure is the major risk factor, other risk factors associated with this malignancy, including HPV infection, occupational exposures, various genodermatoses, scarring dermatoses, chronic wounds, and burn scars. The allogenic transplant population is at most risk for developing cutaneous SCC. It is locally aggressive and, without treatment, has the potential to metastasize to other parts of the body.[8]

Seborrheic keratosis (SK) is also known as seborrheic wart, senile wart and basal cell papilloma. It is a benign, noninvasive, hyperplastic epidermal lesion. It is the most common benign skin lesion found predominantly in middle aged or elderly. As they become old they may progress to become dark brown or black, which can be confused with melanoma. In spite of its melanotic appearance it can be differentiated from a melanoma by its elevated position, distinct border and greasy appearance.[9]

Capillary hemangioma is the most common tumor of infancy, with an female:male ratio of 3:1. In children, capillary hemangiomas are typically cellular and are thus referred to as infantile hemangioendothelioma, juvenile hemangioma, strawberry nevus, and cellular capillary hemangioma. Capillary hemangiomas usually involve the skin or subcutis of the head and neck. They typically proliferate in the first few months of life, then regress and, in many instances, completely involute. In half of untreated patients, superficial lesions involute to normal skin by 5 years of life and from 70 to 90 percent of patients are "cured" by 7 years of age.[10]

This study aims to assess the type of pigmented skin lesions in a sample of Iraqi patients in correlation with clinicopathological parameters (age, gender, site, size, color, histological type).

II. MATERIAL AND METHODS

A retrospective study including analysis of 100 randomly selected samples of pigmented skin lesions sent to the Teaching Laboratories of Al-Emamain Al-Kadhmain Medical City (AS) and Medical city from January 2019 to July 2023.

The clinicopathological data that were collected from patients pathology reports included:

- Age
- Gender
- Site
- Size
- Histological diagnosis

Exclusion criteria

Incomplete clinical or pathological data from referring physicians.

Formalin-fixed paraffin-embedded tissue blocks were collected. Then, sections 4-6 mm stained routinely with hematoxylin & Eosin and the diagnosis was revised by two pathologists.

All statistical analyses were performed utilizing SPSS, version 26 and including mean, standard deviation. frequency and percentage using Yates Chi square with p. value <0.05 regarded as statistically significant.

III. RESULTS

The period of our study was of 5 years duration from January 2019 to July 2023. The total number of cases that were diagnosed as Pigmented skin lesions was 100.

Regarding age, most of the studied sample cases were in the age group 61-70 years (20%) as illustrated in chart (1). As for gender, the male to female ratio was 1:1.

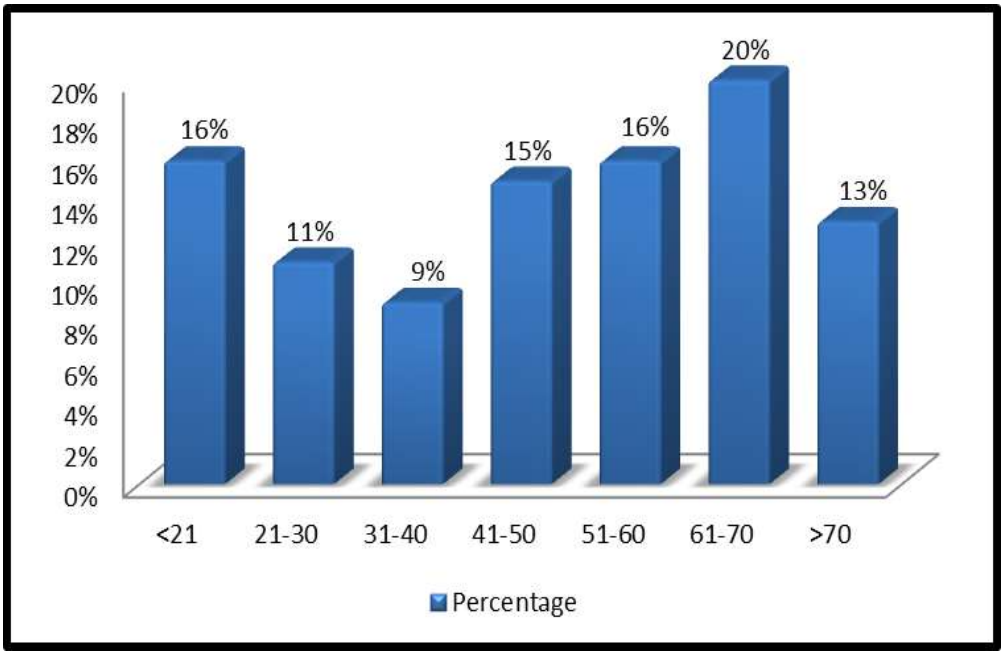

Chart (1): Distribution of pigmented lesions among different age groups.

According to site, Most commonly involved sites were the head and neck region including the cheek (12.0%), eyelid (12.0%) & nose (11.0%), While the benign melanocytic lesions and basal cell carcinoma were distributed predominantly over the head & face, lesions of malignant melanoma showed predilection for extremities, as illustrated in chart (2).

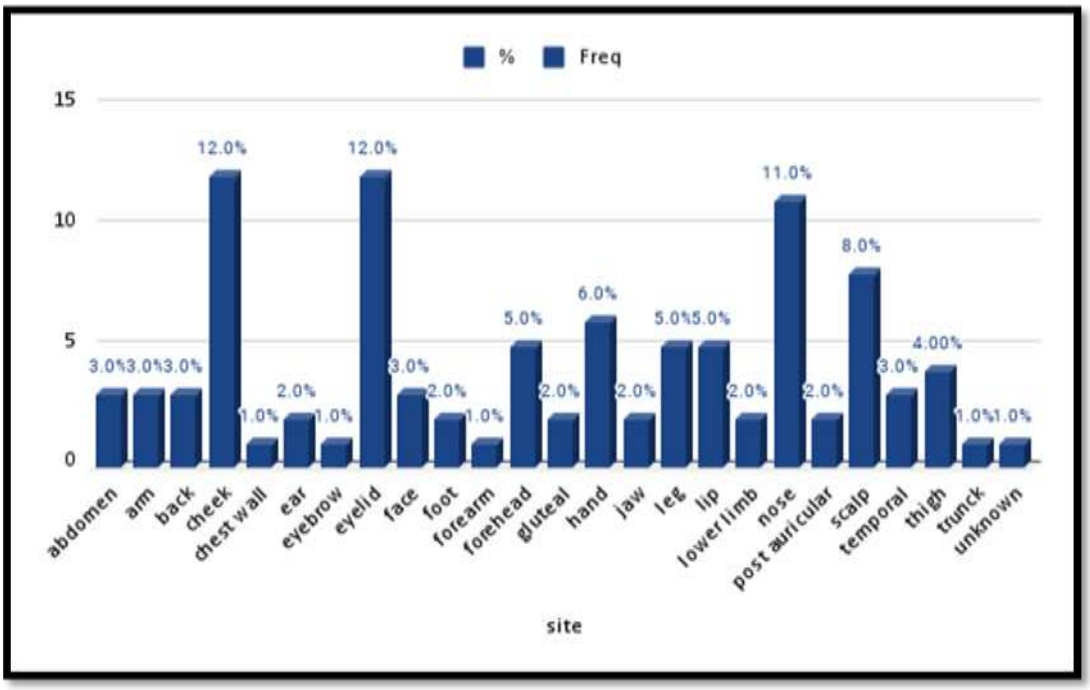

Chart (2): Distribution of pigmented skin lesions on various sites.

Regarding the size, most cases were less than 1 cm (43.0%) followed by lesions measured 1 to or equal to 2 cm (31.0%) mostly is of basal cell carcinoma, while the largest lesion >5 cm was of benign melanocytic naevi , as illustrated in chart (3).

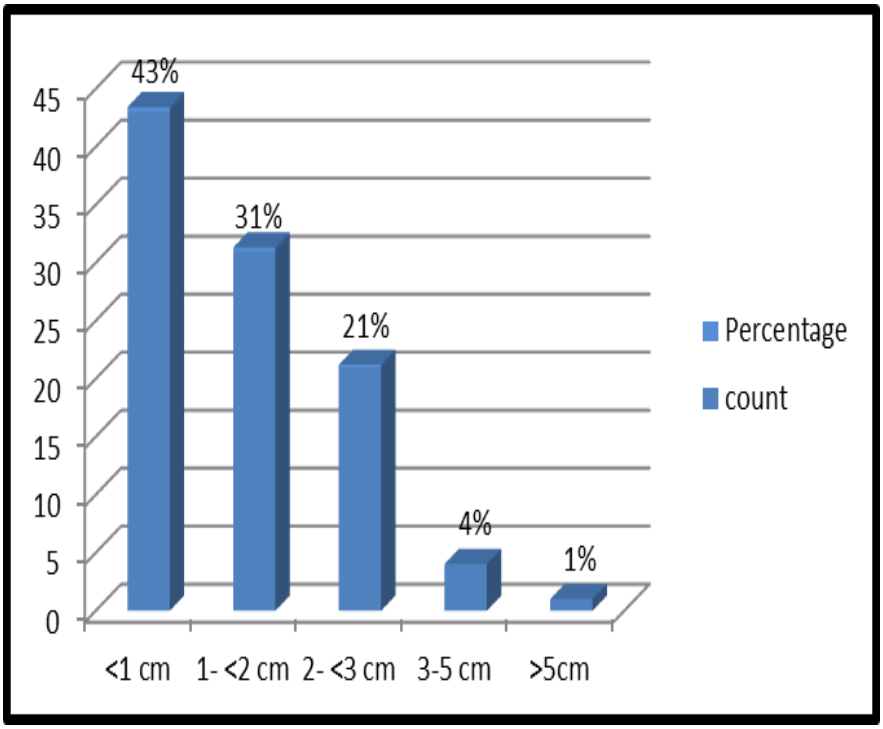

Chart (3): Distribution of pigmented lesions among different size groups.

While according to lesions color, Most cases were of brown color (68.0%) followed by black color (16.0%), as illustrated in chart (4).

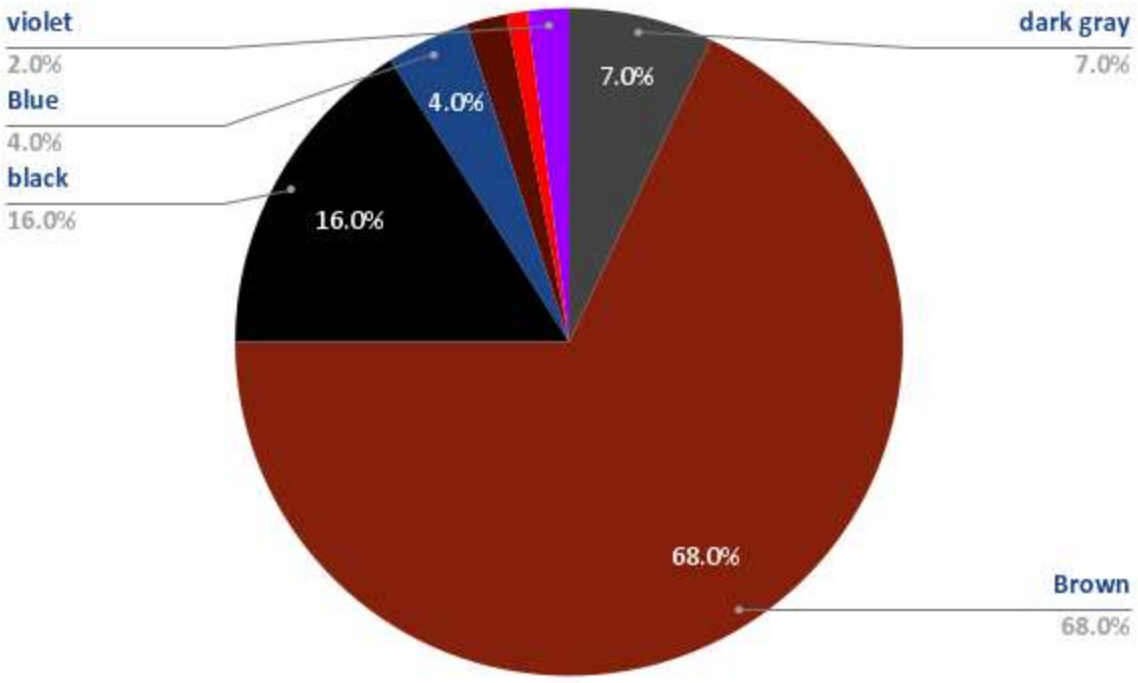

Chart (4): Distribution of pigmented lesions amoung different colors.

These cases after being processed and reported were further categorized as under melanocytic (20.0%) & non-melanocytic lesions (80.0%); as illustrated in table (1)

Table (1): Distribution of pigmented Melanocytic and Non melanocytic lesions.

Lesions		No of cases	Percentage
Melanocytic	Benign naevi	12	12.0%
	Melanoma	5	5.0%
	Dysplastic naevi	3	3.0%
Non Melanocytic	Basal cell carcinoma	32	32.0%
	Squamous cell carcinoma	12	12.0%
	hemangioma	11	11.0%
	Seborrheic keratosis	7	7.0%
	Pyogenic granuloma	4	4.0%
	Angiokeratoma	3	3.0%
	Epidermal naevi	3	3.0%
	Kaposi sarcoma	2	2.0%
	Keratoacanthoma	2	2.0%
	Dermatofibroma	2	2.0%
	dermatofibrosarcoma protubrans	1	1.0%
	squampus cell papilloma	1	1.0%
Total		100	100%

Another classification that classified pigmented skin lesions into melanocytic (20.0%), keratinocytic (57.0%), vascular (20.0%) and reactive lesions (3.0%), as illustrated in table (2).

Table (2): Distribution of pigmented Melanocytic and Non melanocytic lesions.

Lesions		No of cases	Percentage
Melanocytic	Benign naevi	12	12.0%
	Melanoma	5	5.0%
	Dysplastc naevi	3	3.0%
Keratinocytic	Basal cell carcinoma	32	32.0%
	Squamous cell carcinoma	12	12.0%
	Seborrheic keratosis	7	7.0%
	Epidermal naevi	3	3.0%
	Keratoacanthoma	2	2.0%
	squampus cell papilloma	1	1.0%
Vascular	hemangioma	11	11.0%
	Pyogenic granuloma	4	4.0%
	Angiokeratoma	3	3.0%
	Kaposi sarcoma	2	2.0%
Reactive	Dermatofibroma	2	2.0%
	dermatofibrosarcoma protubrans	1	1.0%
Total		100	100%

Pigmented skin lesions were also sub classified into benign and malignant, the most common benign lesion were benign melanocytic nevi (12.0%) while most common malignant tumor were basal cell carcinoma (32.0%), as illustrated in table (3).

Table (3): Distribution of Benign and malignent pigmented lesions.

Lesions		No of cases	Percentage
Benign	Benign naevi	12	12.0%
	Hemangioma	11	11.0%
	Dysplastic naevi	3	3.0%
	Seborrheic keratosis	7	7.0%
	Pyogenic granuloma	4	4.0%
	Angiokeratoma	3	3.0%
	Epidermal naevi	3	3.0%
	Keratoacanthoma	2	2.0%
	Dermatofibroma	2	2.0%
	Squampus cell papilloma	1	1.0%

Malignant	Basal cell carcinoma	32	32.0%
	Squamous cell carcinoma	12	12.0%
	Melanoma	5	5.0%
	Kaposi sarcoma	2	2.0%
	Dermatofibrosarcoma protubrans	1	1.0%
Total		100	100%

In this classification, Pearson correlation showed a statistically significant correlation between the age and type of tumour as revealed by the Chi-square test with a p-value of < 0.001, between the site and the tumour type with a p-value of 0.008 and between the colour and tumour type with a p-value of 0.003.

However, there was no statistically significant correlation between sex and tumour with a p-value of 0.423 and between the size and the type of tumours with a p-value of 0.227, as illustrated in table (4).

Table (4): Distribution of benign and malignant lesions among age , gender, site, color and size.

	Benign	Malignent	P value
Age	More common in age group younger than 21 y (27.1%)	More common in age group 61-70 y (36.5%)	< 0.001
Gender	More common in females (54.2%)	More common in males (53.8%)	0.423
Site	More in the head (54.2%)	More in the head (76.9%)	0.008
Color	Mainly brown (52.1%)	Mainly brown (82.7%)	0.003
Size	Most lesions were smaller than 1 cm (52.1%)	most lesions size were in size group 1-<2 cm (38.5%)	0.227

Among melanocytic lesions, benign melanocytic naevi were the most common (12.0%), of these 12 cases 9 (75.0%) cases were of intradermal naevi and 3 (25.0%) cases were of compound nevi, as illustrated in chart (5), with female: male ratio were 2:1.

There were 5 (5.0%) cases of malignant melanoma with female predominance, female: male ratio were 4:1.

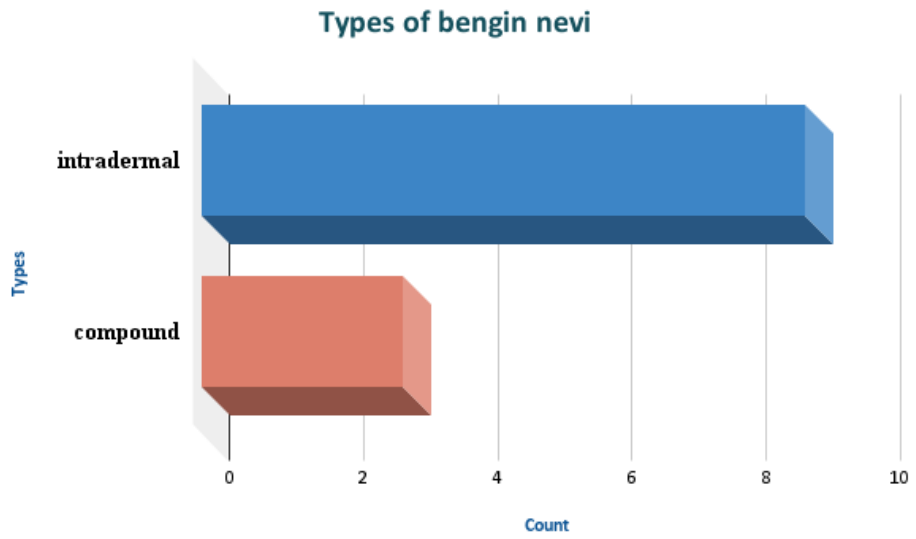

Chart (5): Frequency of benign melanocytic nevi.

Also, among non-melanocytic lesions, basal cell carcinoma were the most common among both sexes (32.0%) followed by squamous cell carcinoma (12.0%).

Of the 32 cases of basal cell carcinoma, there were 16(50.0%) cases of classical nodular type, 7 (21.9%) cases of pigmented variant, 5(15.6%) cases of basosquamous variant, 3 (9.4%) cases of adenoid cystic variant & 1 (3.1%) case of ulcerative variant, as illustrated in chart (6) with male predominance, male: female ratio were 2:1.

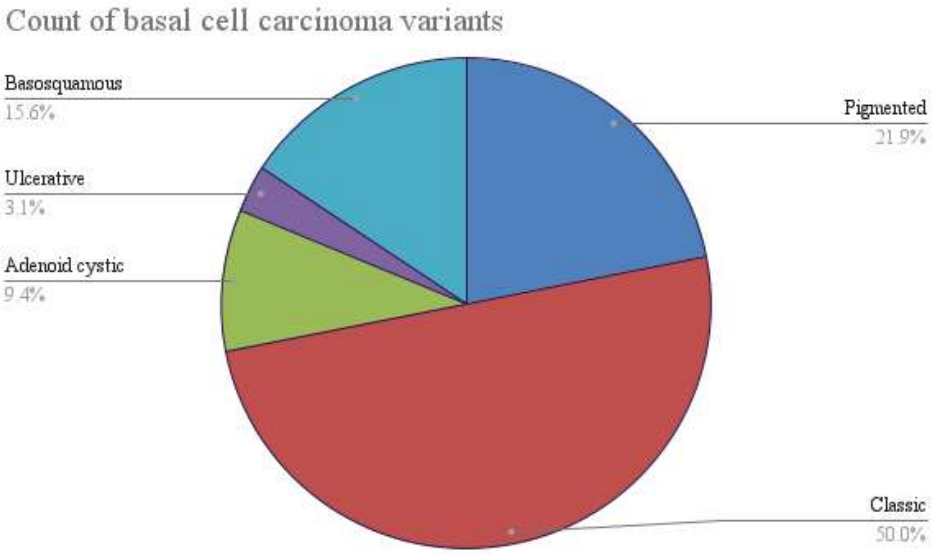

Chart (6): Frequency of basal cell carcinoma variants.

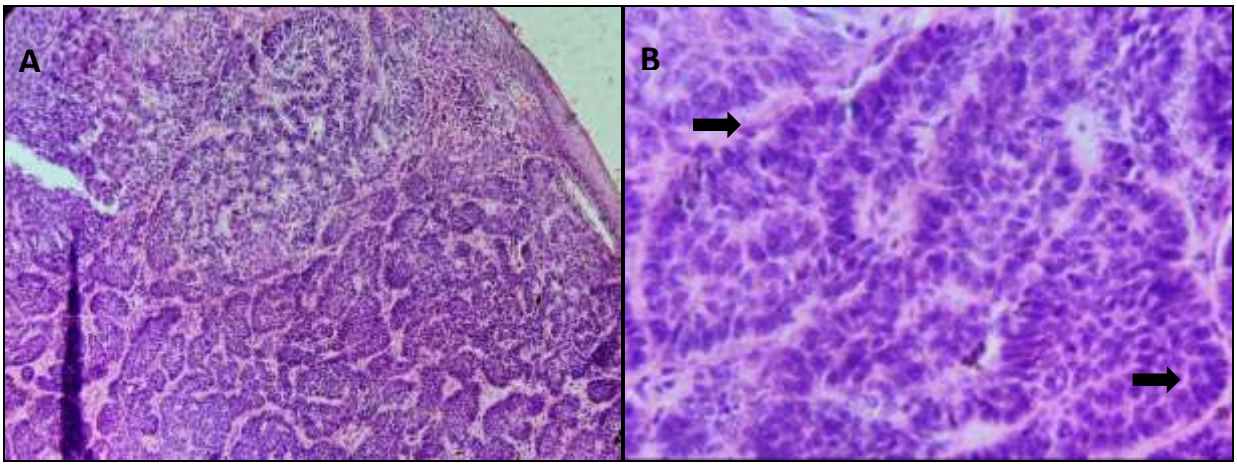

Figure 1: Basal cell carcinoma. a section from skin show nests of basaloid cells with peripheral palisading (black arrow) surrounded by loose stroma and cleft formation (a) , the tumor cells have uniform hyperchromatic nuclei and scant cytoplasm (b). (H&E, A.10x, B.40x)

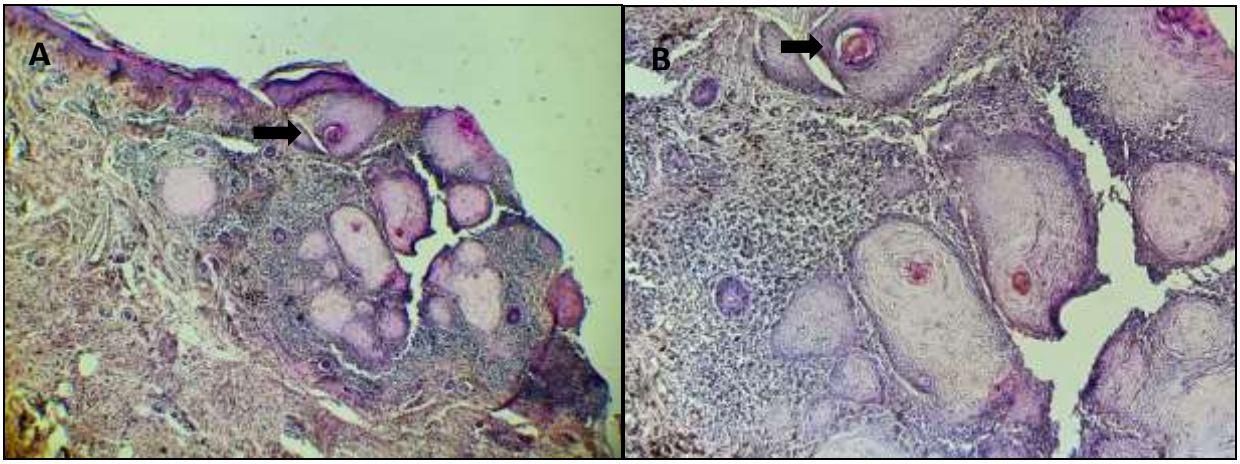

Figure 2: squamous cell carcinoma (well differentiated). a section of skin show a keratinizing squamous nests infiltrating into the dermis with keratin pearls formation (black arrow) (a), tumor cells show marked keratinization, minimal atypia and intercellular bridges (b). (H&E, A.4x, B.10x).

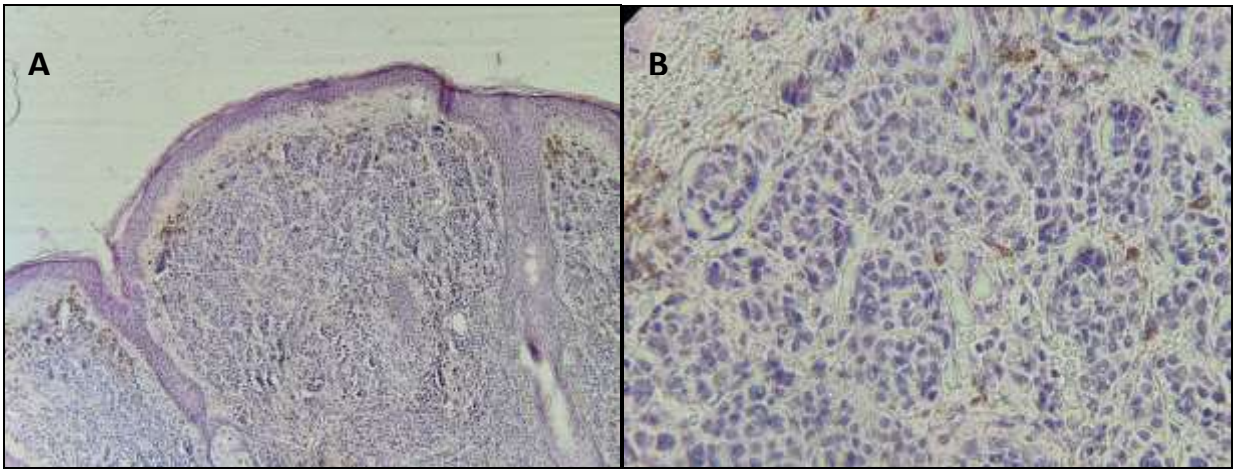

Figure 3: Intradermal nevus. a section of skin show upper dermis containing nests and cords of nevus cells (a), nests contain epitheloid cells with abundant eosinophilic to amphophilic cytoplasm with uniform round nuclei (b). (H&E, A.10x, B.40x).

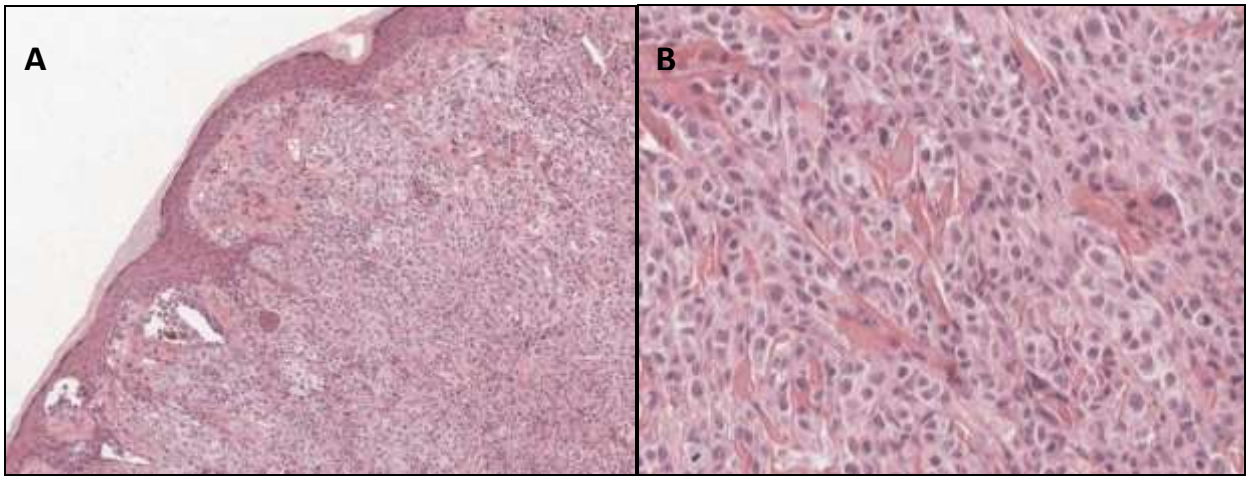

Figure 4: Invasive melanoma. a section from skin show asymmetrical dermal involvement of atypical melanocytes (a), tumor cells show cytological atypia and no maturation (b). (H&E, A.10x, B.40x).

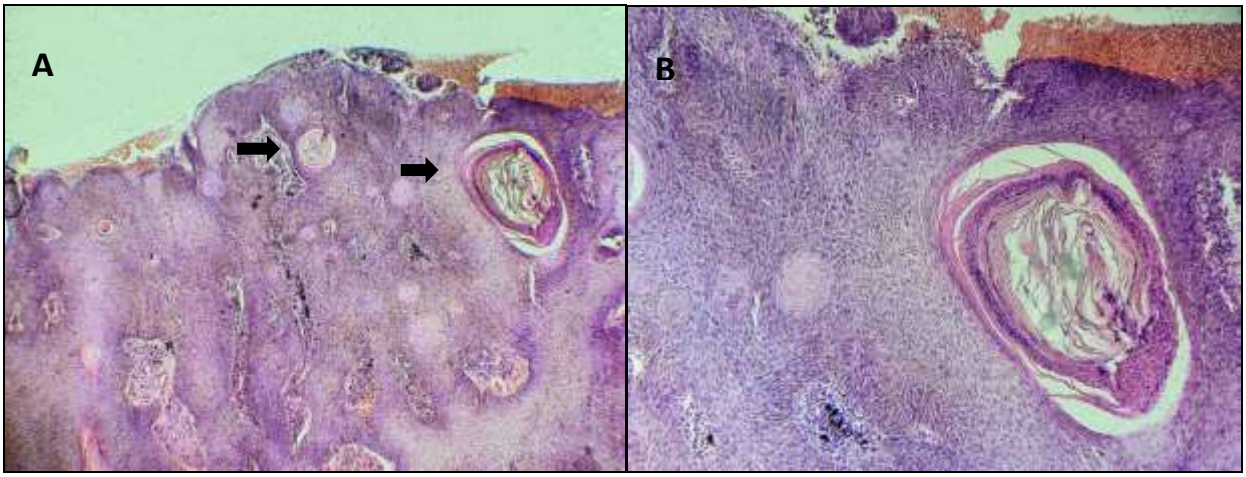

Figure 5: Seborrheic keratosis. a section from skin show acanthosis and expansion of epidermis by basaloid keratinocytes without atypia with horn pseudocysts (black arrow). (H&E, A.4x, B.40x).

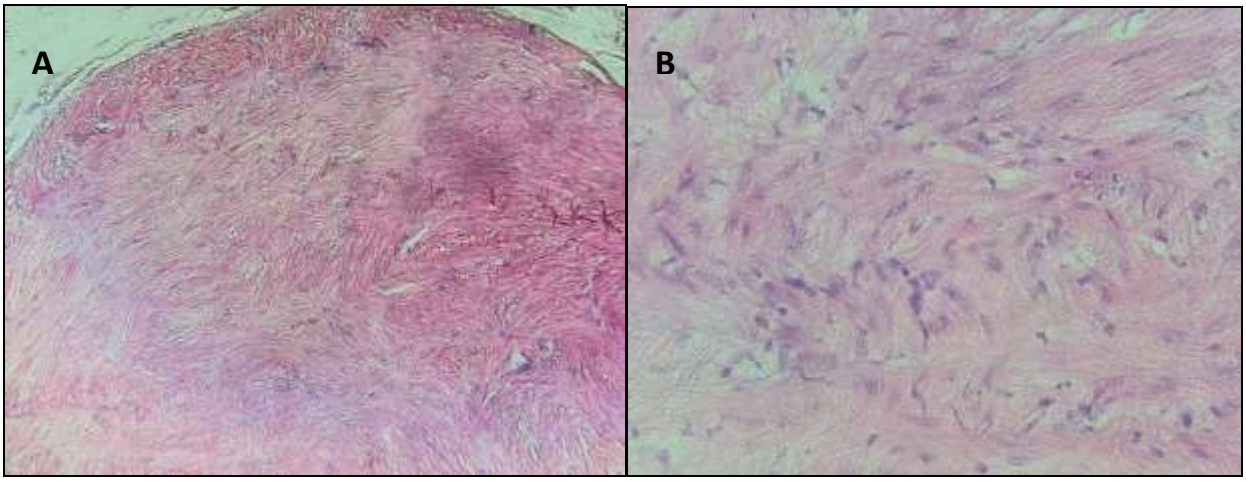

Figure 6: Dermatofibroma. a section from skin show well circumscribed lesion made up of spindle cells in storiform or pinwheel pattern (a), tumor cells are made up of spindled fibroblasts that have thin elongated nuclei and eosiophilic cytoplasm and histiocytes (b). (H&E, A.4x, B.40x).

DISCUSSION

In our study, a total number of 100 pigmented cutaneous lesions were evaluated, Majority of them were non-melanocytic pigmented lesions (80.0%) as compared to melanocytic lesions which were (20.0%) (Table-1). Similar findings were reported in study in India by Singh A. et al. (2020)[1] and Ahmed et al. (2021)[13] in which both show non melanocytic lesions predominance (>60.0%), while Melanocytic lesion were more (54.5%) and (69.6%) of cases in a study conducted by Parvathi M. et al. (2017)[2] and a study in Nepal by Bohra I. et al. (2019)[14] respectively. These differences could be due to sample collection bias.

Benign and malignant pigmented lesions in the current study were nearly equal (48.0%) and (52.0%) respectively, while benign lesions predominate with more than 70% of cases in studies conducted by Singh A. et al. (2020)[1] Khan et al. (2018),[12] Kauser Z. et al. (2018)[9] and Bohra I. et al. in Nepal (2019)[14] these differences could be due different demographic area.

As for gender, The male to female ratio in this study was 1:1, this result closely similar to a study conducted by Bohra I. et al. in Nepal (2019),[14] while female patients were predominant in studies in india conducted by Singh A. et al. (2020)[1] Parvathi M. et al. (2017)[2] Rajendra et al. (2020)[11] Ahmed et al. (2021)[13] and a study in Pakistan by Khan et al. (2018),[12] These differences may be caused by the difference in sample sizes.

Overall, Basal cell carcinoma were the most common lesion (32.0%) which showed increased preponderance among male patients with male :female ratio were 2:1.

Most PSLs in this study presented in 61-70 years of age(as illustrated in Chart-1). While most patients were younger than 60 years of age in studies conducted in Singh A. et al. (2020),[1] Parvathi M. et al. (2017)[2] Rajendra et al. (2020)[11] and Ahmed et al. (2021).[13] this regard to differences in culture and place of researches.

In the current study, most commonly involved site was the head region (as illustrated in Chart-2) including the cheek (12.0%), Eyelid (12.0%) and nose (11.0%), similar finding were found in studies conducted by Singh A. et al. (2020)[1] Parvathi M. et al. (2017)[2] Rajendra et al. (2020),[11] Khan et al. in Pakistan (2018),[12] Kauser Z. et al. (2018),[9] Ahmed et al. (2021),[13] and Bohra I. et al. in Nepal (2019).[14]

Melanocytic nevi are benign neoplastic proliferation or hamartomas of melanocytes.[15] In the present study among the melanocytic pigmented lesions, melanocytic nevi were the most common (12.0%) peak incidence of nevi were in the 2nd decade of life with female:male ratio 2:1 and were distributed over facial region especially the cheek with size mostly smaller than 1 cm presenting with tan to light brown pigmentation. A similar finding were seen in studies conducted by Singh A. et al. in india (2020)[1] and Khan et al. (2018) in Pakistan,[12] in which both showed peak incidence in 2nd - 5th decade of life and facial distribution, with latter study are more common on female. among benign melanocytic lesions, maximum number was of intradermal naevi (75.0%) followed by compound nevi (25.0%) (chart5) that was similar to studies in india conducted by Singh A. et al. (2020)[1] and Parvathi M. et al. (2017)[2], both showed predominance of intradermal nevi.

In the present study, there was 5 cases of malignant melanoma(5.0%). most cases presented in late adulthood in 6th decade of life and were distributed in both sun exposed mostly in the hand and foot, Also, there was an overall female predilection similar to studies in india conducted by Singh A. et al. (2020)[1] and Parvathi M. et al. (2017)[2] in this study out of 5 cases, 4 cases were 2 - 3cm in size, similar finding were in study conducted by of Singh A. et al. (2020)[1]

Dysplastic nevi were reported in 3 cases in the current study, two of them were in their 4th decade of life that have brown-black nodules distributed over face and back with female: male ratio were 2:1.

Basal cell carcinoma is most frequent form of skin cancer primarily occurring on sun exposed skin due to UV exposure.[16] In this study 32 cases were reported of basal cell carcinoma out of which 23 cases were distributed over face mostly on the nose (25.0%). Most cases, in our study affected individuals between 5th -7th decade with male preponderance (65.0%) The lesions presented as mostly brown(82.0%) or black nodules or papules measuring less than 2 cm in size. similar finding were seen in studies conducted by Khan et al. Pakistan (2018)[12] Rajendra et al. in india(2020)[11] and Singh A. et al. in india (2020)[1] in which all show most patients were in 6th -8th decade of life and predilection for face but the latter show female predominance.

Of the 32 cases of basal cell carcinoma, there were 16(50.0%) cases of classical nodular type, 7 (21.9%) cases of pigmented variant, 5(15.6%) cases of basosquamous variant, 3 (9.4%) cases of adenoid cystic variant & 1 (3.1%) case of ulcerative variant (chart 6), similar finding were seen in study in india conducted by Rajendra et al. (2020)[11] in which nodular type were the most common.

Squamous cell carcinoma is the second most common skin malignancy, It arises in the sunlight (UVB) damaged skin of fair-colored people,[16] In this study, 12 cases of squamous cell carcinoma were reported out of which 9 were distributed over face mainly on lips and cheeks. most cases, in our study affected individuals between 5th -8 th decade with female preponderance (58.3%). Most lesions were brown in color measuring 1–3cm in size. Similar finding was seen in study in Pakistan conducted by Khan et al. (2018)[12] which show one case of squamous cell carcinoma in the face 80 years old patient.

Seborrheic keratosis is a benign skin lesion, it has been reported to be one of the most common skin tumors seen by dermatologists in their daily clinical practice.[17] In the current study, most lesions were brown in color with slight female predominance (57.1%) and were more common in the 5th, affecting the lower limb mainly in the leg (28.6%) and thigh (28.6%) with size less than 2 cm. similar finding were seen in study in india conducted by Singh A. et al. (2020)[1]

In the present study, 3 cases of epidermal nevi were reported all were brown in color, two of them were females younger than 21 year of age, distributed over abdomen, forehead and scalp with size smaller than 1 cm. these finding were very close to finding seen in study in Pakistan conducted by Khan et al. (2018).[12]

Two case of keratoacanthoma were reported in this study, both younger than 40 years of age with equal male: female ratio, one lesion were in the cheek and the other were in the forearm with size smaller than 1 cm.

Vascular lesions can also present as pigmented lesions due to presence of underlying blood. They may appear black with the naked eye, but under dermatoscopy appear red, purple or blue.[1] In present study, 20% of cases were of vascular etiology. Hemangioma were the most common (11.0%) with most patients were younger than 21 years of age (54.5%) with male predominance (63.6%), most lesions were brown, black or red in color distributed over the abdomen, arm, hand, cheek and forehead, with size range 1-4 cm. hemangioma also reported in study in india conducted by Singh A. et al. (2020)[1] also were red in color but with female predominance and distributed among scalp, hand and foot.

Four cases of pyogenic granuloma were reported in the current study, 3 of them were brown in color and the other lesion were blue in color, most patients were in 2nd-4th decade of life with equal male: female ratio, all lesions were smaller than 3 cm.

Another vascular lesion that was reported to be pigmented in this study is Kaposi sarcoma 2 cases (2.0%) both cases were in the lower limb with equal male:female ratio, both were older than 60 years of age with size less than 2 cm, one lesion were brown and the other were violet. Kaposi sarcoma (KS) is a locally aggressive endothelial proliferation that usually presents with cutaneous lesions in the form of multiple patches, plaques, or nodules.[18]

Angiokeratoma also were reported in this study with 3 cases (3.0%) with black, blue and dark gray colors, all were younger than 50 years of age with male:female ratio were 2:1, distributed over the extremities and forehead with size smaller than 1 cm.

2 cases of dermatofibroma were reported in the current study both were females one were younger than 21 years of age and the other presenting in the 4th decade of life. distributed over the leg and trunk. The lesions were measuring 0.5cm-1.5cm with a brown color. Similar finding were seen in study in india and Pakistan conducted by Singh A. et al. (2020)[1] and Khan et al. (2018),[12] respectively.

There was one case of dermatofibrosarcoma protuberans (DFSP) in a female in her second decade of life as brown raised lesions measuring 1-1.5cm in the thigh. DFSP also were reported in studies conducted by Khan et al. in Pakistan (2018),[12] Singh A. et al. in india (2020)[1], Ahmed et al. in india (2021)[13] and Bohra I. et al. in Nepal (2019).[14]

CONCLUSION

Non-melanocytic lesions is more common than melanocytic lesions while benign and malignant lesions were nearly equal in incidence, the most common benign lesion were benign melanocytic nevi which show female predominance in second decade of life distributed over the face, while the most common malignant pigmented lesion were basal cell carcinoma which show male predominance in 5-7th decade of life mostly on the nose. there was a significant correlation between type of tumor and (age of patient, site and color of tumor).

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