

**ORIGINAL RESEARCH****A Retrospective study to assess Clinicopathology of Malignant Melanoma**

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**INTRODUCTION-**

Malignant melanoma is a type of skin cancer which arises from the pigment-producing cells - melanocytes. Malignant Melanomas typically occur in the skin but rarely occur in the mouth, intestines or eye (uveal melanoma). Also may occur anywhere on the body. Symptoms of malignant melanoma include a new, unusual growth or a change in an pre-existing mole. Treatment may involve surgical excision, radiation or in some cases, chemotherapy.

**OBJECTIVES:** To document the pattern of clinico-pathological spectrum of malignant melanoma cases at SMS Medical college, Jaipur.

**Methods:** The present study was a retrospective study conducted in SMS Medical college, department of pathology, Jaipur between 2013 to 2019. During this period total 90 cases received and diagnosed on biopsy.

**Results-** We received 100 cases in our department with age range from 10 to 86 years. M: F ratio was 1.4:1 with male predominance. Most common age group is 51-60 year. In our study melanoma are predominantly non cutaneous origin (58) like rectum followed by anal canal, nasal-sinonasal, oral cavity and lymph node, followed by cutaneous melanoma (42). Majority of histologic subtype of melanoma are nodular melanoma 18 followed superficial spreading melanoma 15 then acrolantigeous 9. Half (50%) of the excisional biopsies were at Clark's level III.

**Conclusion-** Malignant melanoma is aggressive tumor, more common in male than female. Nodular melanoma and superficial spreading was commonest histologic type malignant melanoma in our population.

**Key word-** malignant melanoma, nodular, Clark's level

**INTRODUCTION-** Malignant melanoma, which arises from melanocytes, is a significant disease entity since it accounts for the majority (75%) of skin cancer-related fatalities. (1) A tumour of melanocytic origin, malignant melanoma (MM) has the potential to be fatal and aggressive. It accounts for over 75% of all skin cancer-related deaths although making up only 3% of all skin malignancies identified each year. (2) The World Health Organization reports that more malignant cancer cases are being diagnosed globally than any other type of cancer. (3) Geographically speaking, there are "high incidence regions," like Australia, and "moderate incidence regions," like Canada and the United States.(4) It is a rare condition in India.(2) To ascertain the clinical and pathological

characteristics of malignant melanoma diagnosed in patients at SMS Medical College, the current investigation was conducted.

### Material and method-

A retrospective study was conducted on 100 cases diagnosed histopathologically as Malignant melanoma from 1<sup>st</sup> January 2013 and 31<sup>st</sup> December 2019 in the Department of Pathology of the SMS Medical college, jaipur, India. Clinical information was gathered from hospital records, including post therapy and other investigational details. The pathology report included information on the physical appearance and tumour size. All biopsies were performed on grossly recognisable regions. Hematoxylin and eosin (H and E) were frequently used to stain sections taken from specimens that had been fixed in paraffin. The tumor's histopathological characteristics, including cell type, invasion (as measured by Clarke's technique), pigmentation, mitotic activity, and dermal lymphocytic infiltration, were assessed. On tissue sections with questionable morphology, immunohistochemical markers like HMB 45, melan A, and S100 protein were employed.

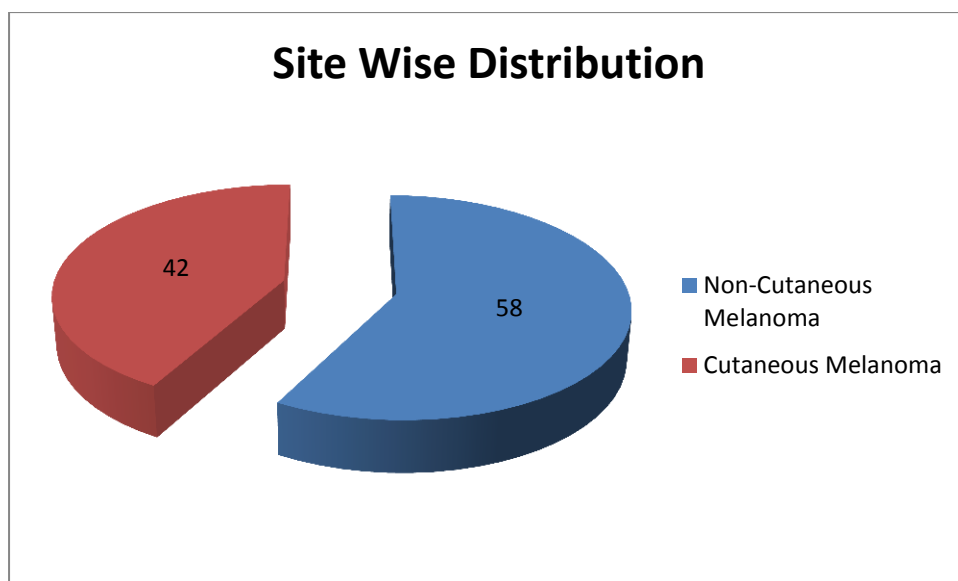
### Results-

Total 100 cases of malignant melanoma analysed with biopsy examined in which 58 are non cutaneous and 42 cutaneous [Table 1]. The most common age group is 51-60 followed by 41-50. 9 cases are seen in very young age group below 30 year of age [Table 2].

Site wise distribution of total cases [Table 1]

Type	Number
Non-Cutaneous Melanoma	58
Cutaneous Melanoma	42
Total	100

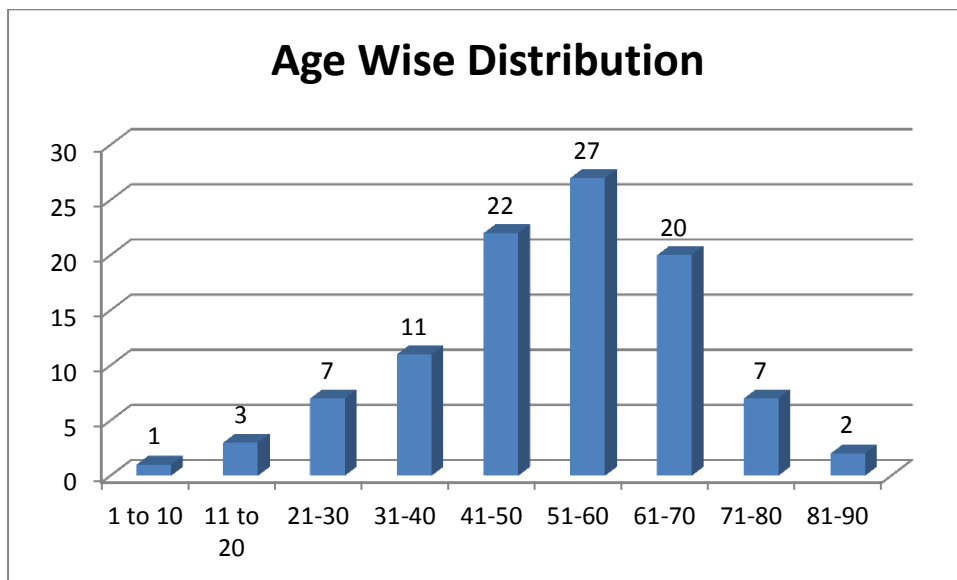
Graph 1-



Age group wise distribution of total cases [Table 2]

Age group	No. Of cases	Percentage (%)
1-10	1	1
11-20	3	3
21-30	7	7
31-40	11	11
41-50	22	22
51-60	27	27
61-70	20	20
71-80	7	7
81-90	2	2
<b>Total</b>	<b>100</b>	<b>100</b>

Graph 2-

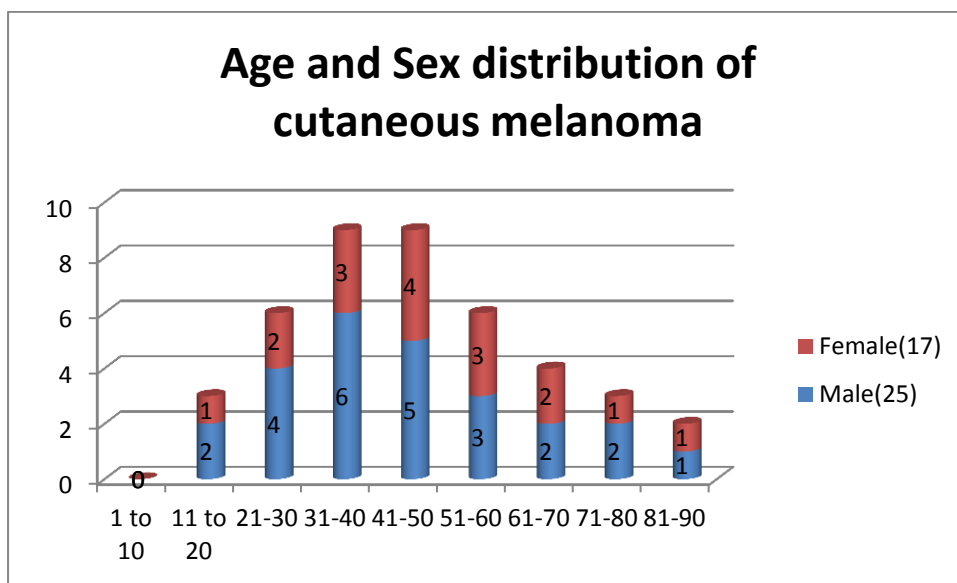


In our study male(n=60)are more common involved then female(n=40).

The age and sex distribution of cutaneous melanoma are listed [Table 3]

Age group	Male(25)	Female(17)	Total (42)
1-10	0	0	0
11-20	2	1	3
21-30	4	2	6
31-40	6	3	9
41-50	5	4	9
51-60	3	3	6
61-70	2	2	4
71-80	2	1	3
81-90	1	1	2
<b>Total</b>	<b>25</b>	<b>17</b>	<b>42</b>

Graph 3-

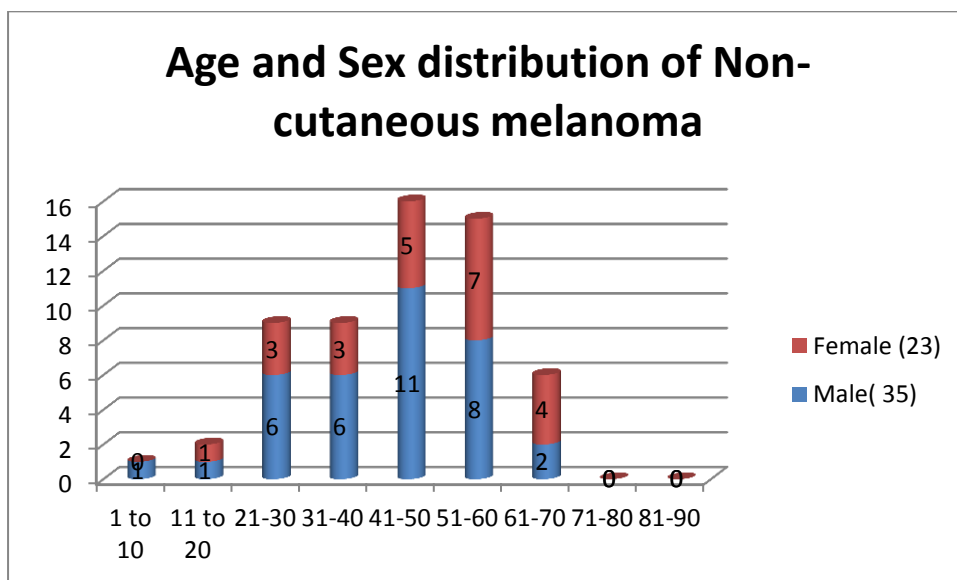


The age and sex wise distribution of non cutaneous melanoma are listed [table 4]

Age group	Male( 35)	Female (23)	Total (58)
1-10	1	0	1
11-20	1	1	2

21-30	6	3	9
31-40	6	3	9
41-50	11	5	16
51-60	8	7	15
61-70	2	4	6
71-80	0	0	0
81-90	0	0	0
<b>Total</b>	<b>35</b>	<b>23</b>	<b>58</b>

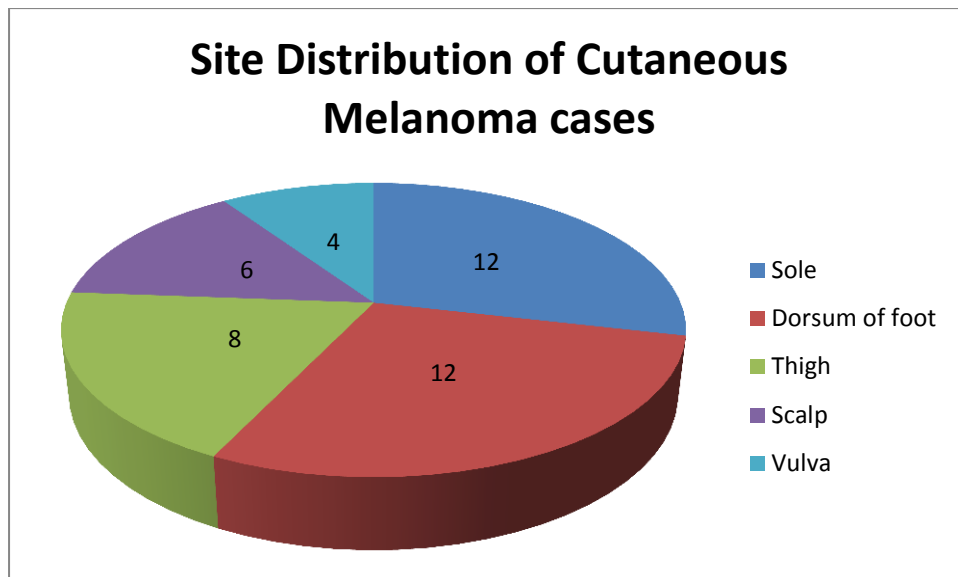
Graph 4-



Site distribution of cutaneous melanoma listed [table 5]

Site	No of cases
Sole	12
Dorsum of foot	12
Thigh	8
Scalp	6
Vulva	4
<b>Total</b>	<b>42</b>

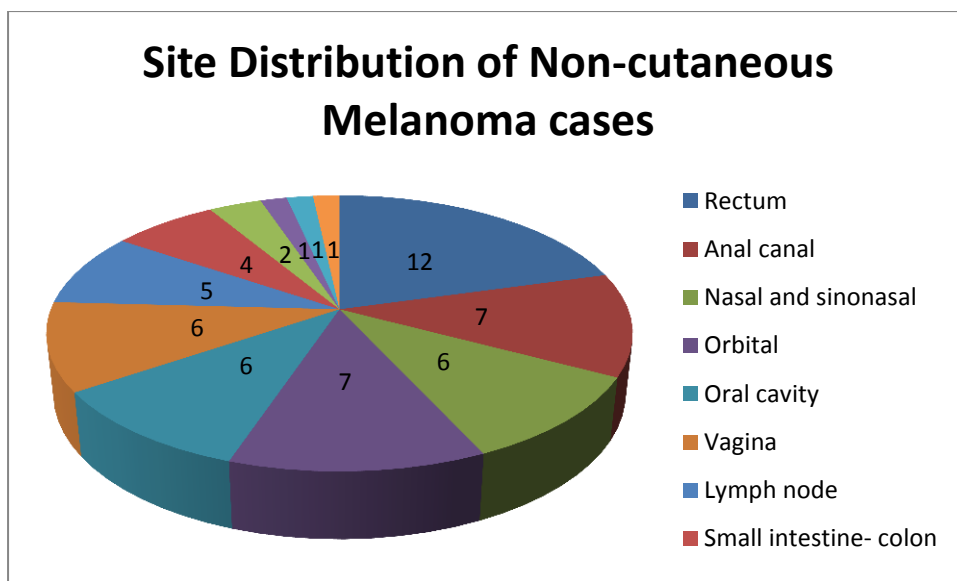
Graph 5-



Site distribution of non- cutaneous melanoma [Table 6]

Site	No of cases
Rectum	12
Anal canal	7
Nasal and sinonasal	6
Orbital	7
Oral cavity	6
Vagina	6
Lymph node	5
Small intestine- colon	4
Right temporal region	2
Paraspinal soft tissue	1
Spinal mass	1
Frontal sol	1
<b>TOTAL</b>	<b>58</b>

Graph 6-



Clark's level in relation to site [Table 6]

Site	Clark I	Clark II	Clark III	Clark IV	Clark V	TOTAL
Sole	2	1	5	2	2	12
Dorsum of foot	1	1	6	3	1	12
thigh	0	1	4	2	1	8
Scalp	0	0	3	2	1	6
Vulva	0	0	2	2	0	4

Histomorphological type wise distribution of cutaneous melanoma [table 7]

Acral lentigious	Superficial spreading	Nodular	Total
9	15	18	42

**Discussion -**

Melanoma is a cancer of pigment laden cells- melanocytes which derive from pluripotent neural crest stem cells. It migrates to and differentiates within the epidermis as well as to other extracutaneous pigment-containing sites. <sup>(5)</sup>

According to the literature the incidence and mortality are decreasing in younger populations, but incidence rates are still increasing in the older age groups. <sup>(2)</sup>

In our study, the highest incidence was observed in the fifth-sixth decade of life, was similar to the previous studies.<sup>(6)</sup>

In our study only 4.4% melanomas occurring in persons younger than 20 years of age and 1.1% in children. Pappo et al study also show almost similar result.<sup>(7)</sup>

The reported male predilection of malignant melanoma in the literature was concordance in this study.<sup>(2, 6, 8)</sup> Wanebo *et al.* and Castel *et al.* reported a female preponderance in their series.<sup>(9, 10)</sup>

In our study non-cutaneous melanoma are common type of melanoma 58cases (58%) then cutaneous melanoma 42 cases (42%) which is dis-concordance with other studies by Chang and Mukhopadhyay *et al.* who reported 82% and 78.57% of the cases, respectively, to be of cutaneous origin.<sup>(6,11)</sup>

In our study nodular cutaneous melanoma( 45.9%) was the most common type of melanoma, which is expected because in India, superficial spreading melanoma and nodular melanoma are commonly found.<sup>(12)</sup>

In our study, among cutaneous melanoma, the lower extremities were the most common site, which is accordance with the previous studies by Radhika *et al.* And Tjarta *et al.*<sup>(13, 14)</sup>

According to the literature, lower extremities are the most common site of involvement in males, while the trunk is the most common site in females. However, in western studies, the opposite has been observed. In our study, maximum number of cutaneous cases were observed in lower extremities such as the sole and dorsum of foot in both sexes. A similar result was found by Kumar *et al* and other studies.<sup>(8, 15, 16)</sup>

In our study, lymph node was the most common site of metastasis. These results were similar with the Radhika et al and other studies studies.<sup>(6, 13)</sup>

The prognosis of non- cutaneous melanoma is poor than primary cutaneous melanomas because of the higher stage at the time of diagnosis, the rich vascular and lymphatic supply of mucosal sites, and the lack of clinical suspicion of the tumor because of its rarity. The initial treatment is surgical resection, but the location may make it technically difficult to obtain complete tumor removal. Unlike cutaneous melanoma, sun exposure is not a risk factor for noncutaneous melanomas. Dark-skinned individuals may have a higher incidence of some noncutaneous melanomas such as ano-rectal melanomas. It is important for clinicians and pathologists to recognize primary noncutaneous melanomas to provide early detection and optimum management.<sup>(4)</sup>

Prasad *et al* found 15 cases in upper alveolus and 9 in hard palate, whereas in our study, we found five cases (5.5 %) in oral cavity malignant melanoma.<sup>(17)</sup>

Oral melanosis has suggested as a predisposing factor for the development of oral melanoma in 30–73% of the patients. Although the incidence of melanosis in India is low, there is a higher occurrence of primary oral melanoma, thereby contraindicating this hypothesis.<sup>(18)</sup>



Ano-rectal melanoma is an extremely rare malignancy with worse prognosis that is thought to arise from melanocytes of mucosa around the anorectal junction. It constitutes about 0.05% of all anorectal malignancies. The largest series from a single center included 85 cases from the Memorial Sloan-Kettering Cancer Center, reported by Brady *et al.* in 1995. It is mostly seen in the sixth decade, with a female predominance. In our study, we found only 7 cases of ano-rectal melanoma.<sup>(19)</sup>

Tariq *et al.* conducted a clinicopathological study on 61 cases of anorectal melanoma for a period 10 years. In their study, 8% of the cases had distant metastasis to liver and vertebral column. In our study, 4 cases initially presented with lymph node metastasis and 1 case had frontal SOL.<sup>(20)</sup>

Melanoma of female genitalia comprises 3–7% of all melanocytic tumors, vulval skin being a common site (1–2%). Of all the vulval malignant neoplasms, melanoma comprises 3.6%–10%, in our study 3 cases (3.3%) of vulvar melanoma found.<sup>(21)</sup>

Research about vulvar melanoma is limited due to the low incidence of cases per center and low numbers of international collaborative studies or meta-analyses.<sup>(22)</sup>

It is known that melanoma has a wide spectrum of histologic differentiation- epithelial, hematologic, mesenchymal, and neural tumors, so when necessary, immunohistochemistry is the primary tool to establish the correct diagnosis. HMB-45, S-100 protein and Melan-A are the three most useful immunomarkers to identify melanocytes and to diagnose melanomas.<sup>(23)</sup>

S-100 protein is the most sensitive marker of melanocytic differentiation. Probably 95% of primary cutaneous melanomas express this marker.<sup>(24)</sup>

HMB-45 has an additional utility to differentiating benign melanocytic lesions from MM as benign lesions (e.g., dermal nevi) tend to show decreased expression with lesion depth/maturation, whereas melanoma often shows more consistent staining in the deeper component. However, many exceptions present, particularly in the setting of certain nevic variants of melanoma. So we used S100, HMB-45 and melan A for confirming melanocytic origin and differentiating benign from malignant lesions.<sup>(25)</sup>

The prognostic factors in primary skin melanoma were studied by Clark (1969) and Breslow (1970) who observed that tumor thickness was an important indicator of behavior.

In our study, the majority of cases presented in Clark's level III and IV, which is consistent with earlier studies reported by Mukhopadhyay *et al.* and Kuno *et al.*<sup>(6,26)</sup>

**Conclusion-** Malignant melanoma is aggressive tumor, more common in male than female. Nodular melanoma and superficial spreading was commonest histologic type of malignant melanoma in our population.

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