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Original Research Article

Clinico-Pathological Profile of Vitiligo Cases in a Tertiary Care Hospital of North India

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ABSTRACT

Context: Vitiligo is a hypopigmentation disorder of skin. It can be suspected clinically but histo-pathological demonstration of absence of melanocytes in skin biopsy is essential for definitive diagnosis of vitiligo.
Methods and Material: Skin biopsies were conducted on 113 patients who were suspected of having vitiligo by dermatologists in Govt. Medical College, Amritsar during one year of duration.
Statistical analysis used: Chi square test, Yate's Correction
Results: Out of total 113 participants, 84 were diagnosed as vitiligo by biopsy. Vitiligo vulgaris was the most common observed form of vitiligo. All vitiligo cases demonstrated the absence of melanocytes and it was an exclusive finding in vitiligo cases i.e. not demonstrated in any non-vitiligo cases. Whereas other common findings like Perivascular/ peri-adnexal mononuclear inflammatory infiltrate, loss of melanocytes were also seen in other non-vitiligo cases.
Conclusions: Diagnosis of vitiligo is most likely when a young female patient presents with hypopigmented macular patches since long duration. Clinical diagnosis of vitiligoshould be supplemented with diagnostic procedures like histopathology.
***Key-words**:* Vitiligo, Histo-pathological diagnosis, Vitiligo vulgaris

INTRODUCTION

Vitiligo is one very important disorder of hypopigmentation of skin. It is an acquired disorder of the skin and mucous membranes that is characterized by well circumscribed, depigmented macules and patches, that occurs secondarily to selective destruction of melanocytes. [1,2]

Vitiligo is relatively frequent. It affects 0.5–2% of the general population, being more prominent in darker complexioned people and after solar exposure. [3,4] Vitiligo is characterized by the destruction and absence of melanocytes in postnatal life. Pigment cells of the skin, follicles, and other extracutaneous sites are commonly involved in the destructive process. Histologic studies and histochemical and immunohistochemical stains have confirmed the absence of melanocytes in the depigmented skin and marked abnormalities in the pigment cells and keratinocytes of the spreading edge and at distant sites from a vitiliginous lesion.

Vitiligo is classified based on the distribution, pattern and extent of depigmentation. Nordlund and Lerner, [5] describes three types of vitiligo namely, localized, generalized and universal vitiligo. Localized vitiligo can further divide into focal (one or a few macules in nondermatomal distribution), segmental (one or more macules in dermatomal distribution), mucosal (depigmentation of lips, oral mucosa and genitals) and generalized vitiligo divides into acrofacial (distal parts of the extremities and face), vulgaris (scattered macules all over the body) and mixed(different types at the same time) types. In universal type nearly complete or complete depigmentation of the skin appears. The clinical phenotype of vitiligocan be changed during the years. Nordlund and Lerner, [6] describes three types of vitiligo namely, localized, generalized and universal vitiligo. Localized vitiligo can further divide into focal (one or a few macules in nondermatomal distribution), segmental (one or more macules in dermatomal distribution), mucosal (depigmentation of lips, oral mucosa and genitals) and generalized vitiligo divides into acrofacial (distal parts of the extremities and face), vulgaris (scattered macules all over the body) and mixed (different types at the same time) types. In universal type nearly complete or complete depigmentation of the skin appears. The clinical phenotype of vitiligocan be changed during the years. However, vitiligo cases can be suspected clinically but definite diagnosis is done by showing absence of melanocytes in biopsy sample. Therefore, this study was done to determine the clinic-pathological profile of suspected vitiligo cases.

MATERIALS AND METHODS

The present study was performed from September 2010 to August 2012 in Govt. Medical College, Amritsar. All clinically suspected vitiligo cases by dermatologists were biopsied. From each patient, skin biopsy, which included the lesion and an adjacent normal looking perilesional area, was taken after taking informed consent. The relevant clinical history and gross examination was recorded. The tissue was formalin fixed, paraffin embedded, stained for routine hematoxylin and eosin and diagnosis was made. Histo-pathological diagnosis was made by two pathologists independently. Any disagreement was resolved by consulting third pathologist. Blinding was maintained regarding the diagnosis by other pathologist and the Total 119 patients were suspected for vitiligo by dermatologists during the period. Out of these, 6 patients refused for biopsy and were excluded from study. Therefore, total 113 patients were included in the study.

Prior approval from the institutional ethical committee was obtained.

OBSERVATIONS

Table no 1 shows distribution of participants according to final diagnosis based on histopathology of lesions. Out of 113 patients of hypopigmented skin patches included in the study, 84 were diagnosed as Vitiligo by biopsy. Rest 29 cases were classified as non-vitiligo cases.

Table no 1: Distribution of participants according to final diagnosis

Final diagnosis	No. of patients	%
Vitiligo	84	74.34%
Non Vitiligo	29	25.66%
Total	**113**	**100%**

Positive predictive value i.e. ratio of true positive with total positive case, for clinical examination came out as app. 74%.

Table no. 2 shows distribution of Non-Vitiligo cases according to final diagnosis by histopathology. Out of the

Non-Vitiligo cases, histopathologically majority (27.59%) cases were consistent with diagnosis of indeterminate leprosy. 20.69% cases were each of Lichen sclerosusetatrophicus, post inflammatory dermatoses and morphea. 6.89% cases were histopathologically diagnosed as TineaVersicolor and remaining 3.45% case were of Nevus depigmentosus.

Table 2: Distribution of Non-Vitiligo cases according to histopathological diagnosis

Clinical diagnosis	Cases	%
Indeterminate leprosy	8	27.59
Morphea	6	20.69
LSA	6	20.69
Tineaversicolor	2	6.89
Post inflammatory dermatosis	6	20.69
Nevus depigmentosus	1	3.45
Total	**29**	**100**

Table no. 3 shows Distribution of participants according to age groups. The youngest patient in the present study was 6 years old while the eldest being 60 years old. Among all participants, maximum belonged to 11-20 years age group (38.05%) followed by age group of 21 – 30 years(23.89%) The vitiligo cases showed maximum incidence in the age group of 11-20 years comprising 38.10% of cases followed by age groups 21-30 years comprising 30.95% of the cases whereas maximum number of non-vitiligo were in the age group were between 41-50 years (41.37%) followed by 11-20 years (37.93%).

Table no 3: Distribution of participants according to age groups in relation to histopathological diagnosis

Age groups	Vitiligo		Non-vitiligo		Total	
	Cases	%	Cases	%	Cases	%
0-10 yrs	3	3.57	2	6.90	5	4.43
11-20 yrs	32	38.10	11	37.93	43	38.05
21-30 yrs	26	30.95	1	3.45	27	23.89
31-40 yrs	11	13.10	2	6.90	13	11.50
41-50 yrs	2	2.38	12	41.37	14	12.39
>50 yrs	10	11.90	1	3.45	11	9.74
Total	**84**	**100**	**29**	**100**	**113**	**100**

Yate's $X^2 = 30.323$, degree of freedom = 5, $p < 0.05$

Distribution of vitiligo cases according to age was statistically different from non-vitiligo cases.

Table no. 4 summarizes distribution of participants according to sex. Out of total 113 participants, 65.49% were females. Among vitiligo cases, majority (69.05%) patients were females and 30.95% were males. Among Non-vitiligo cases, there was almost equal preponderance among males (44.83%) and females (55.17%).

This difference in the distribution according to sex was statistically insignificant.

Table 4: Distribution of participants according to sex in relation to histopathological diagnosis

Sex	Vitiligo		Non-vitiligo		Total	
	Cases	%	Cases	%	Cases	%
Male	26	30.95	13	44.83	39	34.51
Female	58	69.05	16	55.17	74	65.49
Total	**84**	**100**	**29**	**100**	**113**	**100**

$X^2 = 1.836$, degree of freedom = 1, $p > 0.05$

Table no. 5 shows that the most common site of onset of disease in vitiligo patients was lower limb constituting 33.33% of cases followed by upper limb(19.05%), face(13.1%) & back (13.%). In the limbs, the site was mostly from the acral regions. On the other hand, abdomen and lower limb was the most common site in non- vitiligo cases (27.59%) from where the biopsy was

taken. This was followed by back (17.24%) and face (13.79%).

Distribution of vitiligo cases according to site of onset was found to be statistically similar to non-vitiligo cases.

Table 5: Distribution of participants according to site of onset of lesion

Site of onset	Vitiligo		Non-Vitiligo	
	Cases	%	Cases	%
Face	11	13.10	4	13.79
Neck	1	1.19	1	3.45
Chest	6	7.14	1	3.45
Abdomen	6	7.14	8	27.59
Back	11	13.10	5	17.24
Upper limb	16	19.05	2	6.89
Lower limb	28	33.33	8	27.59
Mucosa and genitalia	5	5.95	0	0
Total	**84**	**100**	**29**	**100**

Yate's $X^2 = 9.463$, degree of freedom = 7, $p > 0.05$

Table no 6: Distribution of participants according to duration of disease

Duration of disease	Vitiligo		Non-vitiligo	
	Cases	%	Cases	%
0-1mth	5	5.95	0	0
1-6mth	23	27.38	12	41.38
6mth-1yr	2	2.38	4	13.79
1-2yr	16	19.05	4	13.79
2-5yr	1	1.19	2	6.90
5-10yr	15	17.86	6	20.69
>10yr	22	26.19	1	3.45
Total	**84**	**100**	**29**	**100**

Yate's $X^2 = 10.406$, degree of freedom = 6, $p > 0.05$

Table no 6 categorized participants according to duration of disease in relation to histopathological diagnosis of hypo-pigmented patch. The shortest duration of disease in Vitiligo patients was 1 month while the longest presentation was of 18 years period. Majority i.e. 27.38% patients presented with duration of 1-6 months followed by > 10 years (26.19%), 1-2years (19.05%) and 5 – 10 years (17.86%). On the other hand, patients in non-vitiligo group had a shorter duration of disease with majority of them (41.38%) presenting with 1-6 months of complaints followed by 5 – 10 years (20.69%).

It was observed that non-vitiligo cases presented with short duration of history in comparison to Vitiligo cases and this difference in distribution was found to be statistically insignificant.

Table no 7 shows distribution of Vitiligo cases according to clinical presentation. Majority (69.05%) of cases in the Vitiligo category presented with vitiligo vulgaris, followed by localized vitiligo in 28.57% of the cases.

Table 7: Distribution of Vitiligo cases according to clinical type of vitiligo.

Clinical type of vitiligo	Vitiligo	
	Cases	%
Localized	24	28.57
Acrofacial	1	1.19
Vitiligo vulgaris	58	69.05
Universal	1	1.19
Total	**84**	**100**

Table no 8: Distribution of participants according to histopathological findings in skin biopsies

Histopathological Findings	Vitiligo N=84		Post Inflammatory Dermatoses N=6		Indeterminate Leprosy No=8		Morphea No=6		Lsa No=6		T. Versicolor No=2		Nevus Depigmentosus No=1	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Absence of melanocytes	84	100	0	0	0	0	0	0	0	0	0	0	0	0
Loss of Melanin	78	92.86	4	66.67	0	0	1	16.67	2	33.3	0	0	1	100
Pigment incontinence	0	0	6	100	0	0	0	0	0	0	0	0	0	0
Perivascular/ peri-adnexal mononuclear inflammatory infiltrate	78	92.86	2	33.33	8	100	2	33.3	2	33.3	2	100	1	100
Interstitial mononuclear inflammatory infiltrate	78	92.86	2	33.3	8	100	2	33.3	5	83.33	2	100	1	100
Granuloma	0	0	0	0	4	50	0	0	0	0	0	0	0	0
Homogenized papillary dermis	0	0	0	0	0	0	0	0	6	100	0	0	0	0
Ectatic blood vessels	0	0	0	0	0	0	6	100	2	33.3	0	0	0	0
Fungal spores	0	0	0	0	0	0	0	0	0	0	2	100	0	0
Collagen bundles in dermis	0	0	0	0	0	0	3	100	0	0	0	0	0	0

Table no 8 showing histopathological findings in various cases, it was evident that absence of melanocytes was the common finding in all the diagnosed cases of vitiligo i.e. all the cases (Figure 1 & 2). This formed the basis of their diagnosis. In 92.86% of the cases diagnosed as Vitiligo, there was seen loss of melanin (Figure 3). Among the cases of post inflammatory dermatoses, pigment incontinence was a common finding i.e. 100%. Perivascular, periadenexal and interstitial mononuclear inflammatory infiltrate was a finding in 92.86% vitiligo (Figure 4), 100% leprosy, 100% pityriasisversicolor and nevus depigmentosus cases. Ill formed granuloma was seen in 50% cases of leprosy.

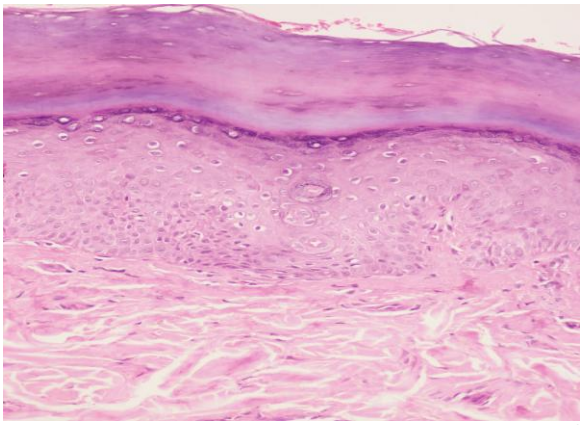

Figure 1: H & E stained section showing absence of melanocytes and melanin in a case of vitiligo (400X)

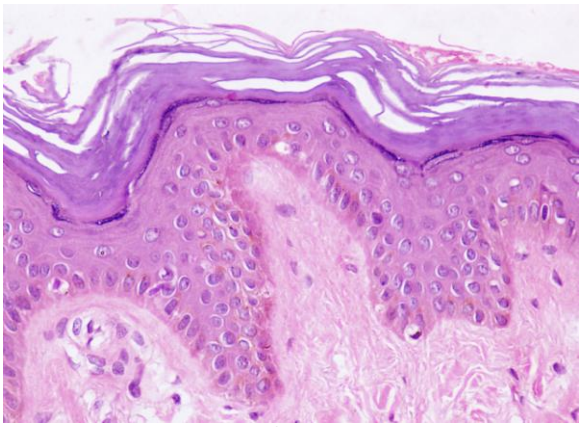

Figure 2: High power view of H & E section showing absence of melanocytes, the case was diagnosed as vitiligo

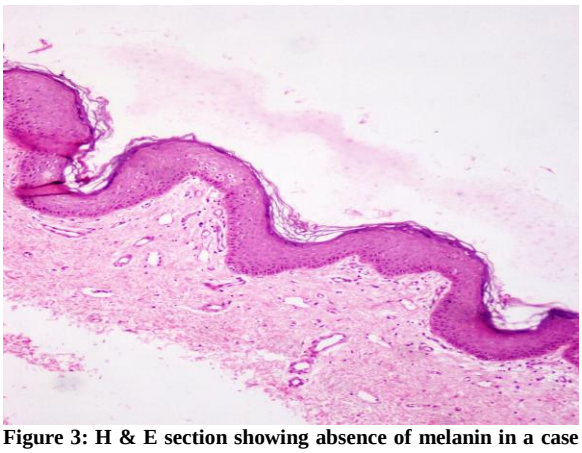

Figure 3: H & E section showing absence of melanin in a case of vitiligo(100X)

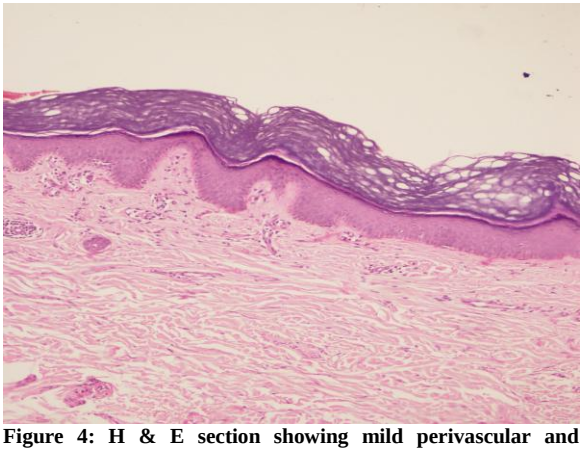

Figure 4: H & E section showing mild perivascular and interstitial inflammatory infiltrate in vitiligo (40X)

DISCUSSION

Vitiligo is a progressive, common acquired pigmentary disorder of the skin and hair characterized by well-circumscribed milky white macules, resulting from loss of melanocytes. The natural course of the disease remains largely unknown. For diagnosis of Vitiligo, absence of melanocytes is considered confirmatory.

In the present study, positive predictive value of clinical examination for diagnosing Vitiligo came approximately 74% that is not high enough to diagnose Vitiligo by clinical examination alone.

In present study, majority of Vitiligo patients were distributed in the second and third decade i.e. age group of 11-20 years (38.10%) and 21-30 years (30.95%). While,

a study conducted by Kumar et al showed that a sizeable number of patients (86 out of 224 new patients) have their onset of Vitiligo between 21 to 30 yrs of age, [7] the age group which showed second most common incidence in present study. Almost similar results were seen in an observational study conducted by Suman Singh et al on 275 patients in Banaras Hindu University, Varanasi where majority of patients (40%) were found in the 11-20 years age group. [8] Contrary to this Howtiz et al [9] (1977) showed age of onset of Vitiligo to be in between 40-60 years.

In the present study, majority of Vitiligo patients were females (69.05%), showing female preponderance with a male-to-female ratio (M:F) of 1/ 2.2. Similarly, in a study done by Kumar et al, [7] there were 55% females and 45% males in the study group, with a M:F ratio of 1:1.2. The study done by Suman et al [8] also showed female predominance with 59% females and 41% males incidence and an M:F ratio estimated to be 1:1.4. In a study conducted by Chiriac et al [10] 57 cases of Vitiligo were enrolled for a period of 12 months out of which 68.4% cases were females while 31.6% cases were that of males with a M:F ratio of 1:2.2. Sex distribution in this study is also in accordance with the various other studies viz. study of Kovacs, 1998; Al-Mutairi& Sharma, 2006; Shajil et al, 2006; Martis et al., 2002 and Nunes&Esser, 2011. However, the female preponderance was also observed in non-Vitiligo cases i.e. 1 / 1.2 but it was less than Vitiligo cases.

In the present study, maximum numbers of biopsies i.e. in 33.33% cases were taken from the lower limb, followed by 19% cases from upper limb. Similar result was observed in the study undertaken by Kumar et al, [7] where most common site of onset of Vitiligo was lower limb (34.37%) followed by upper limbs (24.55%). In study done by Suman et al [11] in which the most common site of onset was lower limb (44%) followed by face/trunk (18.5%). In contrast to the present study, in a study by Karelson et al, the most common site of onset Vitiligo was the upper limb in 55 patients (35.5%), followed by trunk in 37(23.9%), lower limb in 27 (17.4%), head and neck in 23 (14.8%), body folds in 13 (8.4%) patients. [12]

In non-Vitiligo cases, most common sites were lower limbs and abdomen.

The shortest duration of disease in Vitiligo patients was 1 month while the longest presentation was of 18 years period. Maximum patients (27.38%) presented with a duration of 1-6 months followed by 26.19% with > 10 yrs duration. In a study conducted by Karelson et al [12] the mean duration of Vitiligo was 16.9 years (0.5 - 58 years) for all patients, 16.2 years for males and 17.2 years for females. In study conducted by Suman et al, [8] the duration of disease varied from six months to 20 years and maximum percentage(58%) of cases were of less than 5 years duration. In non-Vitiligo cases, more than half cases presented with < 1 year history.

In the present study, out of all histologically diagnosed Vitiligo cases, 69.05% were affected with Vitiligo vulgaris, which is characterized by multiple, bilateral, symmetrical lesions involving upper and lower limbs and trunk followed by localized Vitiligo in 28.57% of the cases. Karelson et al also drew similar results in a study done on 155 Vitiligo patients, Vitiligo vulgaris was the most common clinical type, observed in 126 cases (81.3%), followed by acrofacial, focal, segmental and universal vitiligo in the descending order of frequency. [12] In another study carried out by Kumar et al, [7] similar results were obtained and generalized vitiligo (Vitiligo vulgaris), was the most commonly seen clinical type. This was followed by localized Vitiligo, acrofacial vitiligo anduniversal

vitiligo types. Suman et al studied 200 cases of Vitiligo where vitligo vulgaris (45.5% cases) was the most prevalent subtype followed by acrofacial (21.5%), focal (18.5%) and segmental Vitiligo (11%). [8]

In the present study, various histopathological features of all the skin biopsies were compared which consisted of absence of melanocytes, which forms the most important feature forming the basis of diagnosis of Vitiligo along with other features such as melanin content, nature of inflammatory infiltrate and its distribution along vessels and adnexal structures. Absence of melanocytes was the common finding in all the diagnosed cases of Vitiligo (100%). Perivascular, periadenexal and interstitial mononuclear inflammatory infiltrate was also a common finding seen in 92.86% of Vitiligo cases.

Similar results were seen in a study by You Chan Kim et al, [13] where they examined 100 patients with Vitiligo who presented to the Department of Dermatology, Ajou University Hospital, Suwon, Korea, between January 2003 and December 2004. They also studied 30 cases of nevus depigmentosus for comparison. In their results, histologically, lesions of Vitiligo showed more basal hypopigmentation than perilesional normal skin in 78% of the cases. The Vitiligo skin showing mild dermal inflammation accounted for 41% of the cases. With Fontana Masson staining, 16% of cases of Vitiligo showed the presence of melanin. Other features such as hyperkeratosis, acanthosis, exocytosis, spongiosis, melanophages, rete ridge elongation, and telangiectasia were observed in the Vitiligo skin.

Therefore, the most important change of Vitiligo described by light microscopy is the partial or complete loss of melanin because of the loss of melanocytes. Other changes can also be observed, such as interface dermatitis with lymphocytic infiltrate in the superficial dermis. These changes are more prominent in active Vitiligo than in the stable.

CONCLUSION

Clinical diagnosis has positive predictive value of approximately 74% for diagnosing vitiligo. Therefore, clinical diagnosis of Vitiligo should be supplemented with diagnostic procedures like histopathology. Diagnosis of Vitiligo is most likely when a young female patient presents with hypopigmented macular patches since long duration. In the other cases, differential diagnosis of other diseases like indeterminate Leprosy, Morphea, LSA and Post inflammatory dermatosesshould be considered. Diagnostic procedures should be considered especially in these cases.

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