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Research Article
Evaluation

Evaluation of Some common clinical factors in extensive vitiligo- a case control study

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Introduction: Vitiligo is a common depigmenting disorder with profound stigma. Prevalence of vitiligo is 0.5% to 1%. Information about association of progressive vitiligo are well known. Prognostic factors of vitiligo also enlisted. However, little information is available on the risk factors for developing extensive vitiligo. **Aims and Objectives:** Aims of the study was to identify – factors which are associated with extensive vitiligo (involving more than 5% of the body surface area). The following risk factors were evaluated, Onset before 20 years of age, Duration of disease greater than 2 years, Presence of Koebner's phenomenon, Family history of vitiligo, Presence of leucotrichia and Mucosal involvement. **Materials and Methods:** A case control study were designed. Patients with Vitiligo > 5% body surface area involvement were classified as cases and <5% body surface area were labeled as controls. The frequency of evaluating associated clinical factors among the cases and controls were used to evaluate the extensive vitiligo's association with risk factors (disease risk associated exposure). **Results:** Two hundred and eleven patients were evaluated. The mean age at onset was 19.07+13.51 (+SD) years. Acrofacial vitiligo was the commonest type of vitiligo. Duration of disease more than 2 years, presence of Koebner's Phenomenon, Family history, Symmetry of lesions, milky white colour of lesion, presence of Leucotrichia, mucosal involvement and Acrofacial type vitiligo had statistically significant (p<.05) association with extensive vitiligo. Ratio of the odds of the outcomes in two groups was noted significant with Duration of disease more than 2 years, Koebner,s Phenomenon, Mucosal involvement and Leucotrichia. **Conclusion:** This case-control study has demonstrated a weak association between extensive vitiligo and duration of disease greater than 2 years. It has also indicated that koebner's phenomenon, mucosal involvement and leucotrichia are additional risk factors.

Keywords: Duration of disease, Extensive vitiligo, Koebner's phenomenon, Leucotrichia, Mucosal involvement, Risk factors

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Introduction

Vitiligo is a common depigmenting disorder with profound stigma. The published prevalence of vitiligo is 0.5% to 1%. Large studies in China, India, and Denmark have found the prevalence to be .093%, 0.005%, and 0.38%, respectively. Gujarat, India is considered to have the highest prevalence in the world, at about 8.8%. Men and women are equally affected [1]. In a meta-analysis , the prevalence of vitiligo were 0.1% (0.1%, 0.2%) in Asia, 0.4% (0.1%, 0.7%) in Africa, 0.2% (0.1%, 0.4%) in America, 0.4% (0.2%, 0.5%) in Europe, 1.2% (0.5%, 1.8%) in Oceania (only one study) and 0.1% (0%, 0.1%) in Atlantic, respectively [2].

Vitiligo may develop at any age, the median age of onset is about 20-23 years, i.e. about half the individuals develop vitiligo before the age of 20 years. About a quarter of those affected by vitiligo were less than 10 years of age at onset [3,4,5]. One fourth to one third of patients with vitiligo have family members with disease and the disease is transmitted in a multifactorial genetic pattern.

This study also demonstrated that close biologic relatives have an increased risk of developing vitiligo compared with controls [5,6]. Hann et al, [7] found that progressive vitiligo was associated with a positive family history, non-segmental clinical type, and longer duration of disease, Koebner's phenomenon and mucous membrane involvement [7].

Other workers have also listed prognostic factors in vitiligo. A good prognosis is expected in lesions on neck and face and in colored races [8]. A poor prognosis may be associated with lesions on the so-called resistant sites such as bony prominences, non-fleshy, non-hairy and mucosal areas, association of greater percentage of white hair, persistent friction and itching on the affected area.

Emotional labiality and psychic turmoil associated systemic ailments, here do familial background, old age and iatrogenic factors injudicious use of topical and systemic medication particularly the photochemotherapeutic agents [9]. Some of those prognostic factors refer to the likely response to therapy while others to the progression of disease. However, little information is available on the risk factors for developing extensive vitiligo.

Here, the present study look >5% body surface area involvement as the criteria of extensive vitiligo. Such information may permit early interventions to prevent the spread of vitiligo in the patients at risk. Conversely patients who are not at risk of developing extensive lesions can be reassured.

The aim of the study was to identify – factors which are associated with extensive vitiligo (involving more than 5% of the body surface area) and significance of their relations with extensive vitiligo. The present study can designate them risk factor for extensive vitiligo. The following risk factors were evaluated, Onset before 20 years of age, Duration of disease greater than 2 years, Presence of Koebner's phenomenon, Family history of vitiligo, Presence of leucotrichia and Mucosal involvement.

Materials and methods

Setting: The study was conducted at Dermatology OPD in a Tertiary care Hospital, Eastern part of India.

Duration: It was done between January 2018 and January 2019.

Type of study: A case control study was designed.

Sampling methods: All patients attending the OPD, willing to join the study, after fulfilling the inclusion Criterion and signing the Written Consent Form were included the study.

Sample size calculation Looking for a 0.05 level of significance, estimate a medium effect size of 0.05 and look for a power of 0.08, 64 participants was required in each group for a total of 128 participants. The present study included 113 cases and 98 controls.

Inclusion criteria: Patients having generalized vitiligo with more than 5 percent of the body surface area were classified in the study as cases.

Exclusion criteria: Patients with less than 5 percent body surface area were labeled as controls and included in the study.

Patients who had Segmental vitiligo, Focal vitiligo, Vitiligo confined to the mucous membrane, Chemical Leucoderma, piebaldism, Nevus depigmentatosus, Hypomelanosis of ito, were excluded from study,

Data collection procedure: after fulfilling the inclusion and exclusion criteria, detail history and examination findings were recorded in a printed proforma (Data Record Sheet).

Data analysis: The frequency of evaluating associated clinical factors among the cases and controls were used to evaluate the extensive vitiligo's association with risk factors (disease risk associated exposure).

The analysis was done in two stages. In the first stage, the association of various clinical factors was evaluated which may be potential risk factors with extensive vitiligo.

In the second stage, the odds ratio (OR) was calculated to measure the association between the clinical characteristics (exposure) and extent of affection(outcome), to determine the independent significant clinical factors associated with extensive vitiligo, which can be designated as risk factors for extensive vitiligo. In this study, considered $p<0.05$ was considered as statistically significant.

Ethical consideration: Prior to selection in the study, an informed consent of all the patients was obtained. The patients were given the choice of whether they want to participate in the study or not.

Any scoring system: The surface area of the skin involved by vitiligo was measured using the Lund and Browder [10] chart estimates for adults and infants. Generalized vitiligo was classified with more than 5 percent of the body surface area in the study as cases

Surgical procedure if any: No Surgical intervention was done.

Results

Two hundred and eleven patients were evaluated. There were 113 men and 98 women. The age of the patients varied from 4½ years to 65 years (Mean 28.72+SD 14.89).

There were 113 cases and 98 controls. Out of them, 73 cases and 67 control patients have age of onset less than 20 year ($p>.05$).

Table 1 shows the distribution of age at onset, the mean age at onset was 19.07+13.51 (+SD) years.

Table-1: Distribution of age at onset in vitiligo patients.

Onset age	No of patients	%
0-9	56	26.54
10-19	82	38.87
20-29	25	11.85
30-39	23	10.90
40-49	18	8.53
50-59	7	3.31
Total	211	100

The clinical characteristics of vitiligo patients are as in Table 2.

Table-2: Clinical Characteristics of Vitiligo

Characteristics		Total (211/100%)
Age of onset	<20 years	140 (66.35%)
	≥20 years	71 (33.64%)
Duration of disease	> 2 years	170 (80.57%)
	< 2 years	41 (19.43%)
Sex distribution	Male	113 (53.55%)
	Female	98 (46.45%)
Family history	Present	67 (31.75%)
	Absent	144 (68.25%)
Koebner's phenomenon	Present	117 (55.45%)
	Absent	94 (44.55%)
Halo Nevi	Present	14 (6.64%)
	Absent	197 (93.36%)
Symmetry of lesions	Symmetry	194 (91.94%)
	Asymmetrical	17 (8.06%)
Leucotrichia	Present	144 (68.24%)
	Absent	67 (31.76%)
Mucosal involvement	Present	152 (72.04%)
	Absent	59 (27.96%)

Acrofacial vitiligo was the commonest type of vitiligo (Table 3).

Table-3: Type of vitiligo

Type	Total (211/%)	p-value
Acrofacial	179(84.83%)	<.05
Vitiligo Vulgaris	19(9.00%)	
Universal Vitiligo	13(6.16%)	
Total	211	

Table 4 showed the variations of clinical characteristics between extensive (>5% BSA) and non-extensive (<5% BSA) vitiligo. Duration of disease more than 2 years, presence of Koebner's Phenomenon, Family history, Symmetry of lesions, milky white colour of lesion, presence of Leucotrichia, mucosal involvement and Acrofacial type vitiligo were statistically significant ($p<.05$). There was no statistical difference between <20 years and ≥20 years of age at onset, gender, presence or absence of Halo Nevus, associate diseases or onset site.

Table-4: Summary of clinical characteristics of extensive and non – extensive vitiligo

Clinical Parameters	Extensive	Non-extensive	chi-square test
	(n=113)	(n=98)	p-value
Age at onset			
- <20 years	73	67	p> 0.05
- ≥20 years	40	31	
Duration of Disease			
- >2years	103	67	p<0.05
- ≤2years	10	31	
Koebner, s phenomenon			
- present	74	43	p<0.05
- Absent	39	55	
Family history of vitiligo			
- present	43	24	p<0.05
- Absent	70	74	
Gender			
- Male	58	55	p> 0.05
- Female	55	43	
Halo nevus			
-Present	6	10	p>0.05
- Absent	107	88	
Symmetry of lesion			
- Symmetrical	103	68	p< 0.05
- Asymmetrical	10	30	
Colour of lesion			
- Milky white	107	87	p<0.05
- Hypopigmented	6	11	
Leucotrichia			
- Present	106	38	p<0.0001
- Absent	7	60	
Mucosal involvement			
- present	104	48	p<0.0001
- Absent	9	50	
Type of vitiligo			
- Acrofacial	98	85	p <0.05
- Vulgaris	4	13	
Onset site			
- legs	45	30	p = 0.0565
- Head	20	29	

Table-5: Odds Ratio of the parameters came as significant in chi-square test.

Characteristics	Odds Ratio (OR)	Confidence Interval 95% CI	Significance level
Duration of disease	4.77	2.19-10.36	p=0.0001
Koebner's phenomenon	2.427 1.89	1.39-4.23 1.04-	p=0.0018
Family History of Vitiligo		3.44	p=0.0359
Symmetry of lesions	0 .79	0.2897-2.1671	p= 0.65
Colour of lesion- milky white	2.2548	0.8016-6.3424	p = 0.1233
Leucotrichia	23.91	10.06-56.85	p<0.0001
Mucosal involvement	12.04	5.47-26.46	p<0.0001
Type of vitiligo	0.9992	0.4501-2.2182	P = 0.9985

In the second stage, the odds ratio of the outcome in two groups was calculated to determine significance of association of risk factors in extensive vitiligo, it was noted with Duration of disease more than 2 years, Koebner's Phenomenon, Mucosal involvement and Leucotrichia (Table 5).

[If P is less than 0.05 it can be concluded that the odds ratio is significant different from 1 and that there is an increased relative risk in one group compared to the other -Medcal C MedCalc version 12 - © 1993-2012 MedCalc Software bvba]. Associated diseases with vitiligo was also observed, a variety of diseases came as association (Table-6).

Table-6: Associated disease in vitiligo patients.

Associated disorders	
Diabetes Mellitus	09 (4.26%)
Hypothyroidism	11 (5.21%)
Alopecia	16 (7.58%)
Allergic disorders	14 (6.63%)
Gynaecological disorders	16 (7.58%)
Tuberculosis	07 (3.32%)
Neuropsychiatric disorders	18 (8.53%)
Gastrointestinal disorders	23 (10.90%)
Orthopedic disorders	08 (3.79%)
Cardiac disorders	09 (4.26%)
Ophthalmic disorders	07 (3.32%)
Hypersensitivity	07 (3.32%)
Lichen planus and lichenoid eruption	05 (2.37%)
Fungal and bacterial infections	24 (11.37%)
Canitis	03 (1.42%)

Discussion

The characteristics of the patient group of the present study appear similar to community surveys and other hospital-based studies. In the present study, the mean age at onset was 19.07+13.51 (+SD) years. Both male and female patients were affected equally and the disease severity was similar in both sexes. These characteristics are similar to those described in previous studies [8,9].

In a study of nonsegmental vitiligo, disease duration and disease extent, a trend could be seen regarding increasing decades of having vitiligo and an association with higher odds for extensive vitiligo at a later age, adjusting for age and sex [11]. The association of extensive vitiligo with a duration of disease greater than 2 years came as attributable to progression of disease with time in the present study also [OR-.4.77, 95% CI- .2.19-10.36,

Significance level p=.0001]. Hann et al [7] found that patients who developed new lesions in the preceding 3 months had disease for a longer than those who did not have new lesions.

The mean duration of patients with and without progression of vitiligo was 8.1 and 4.2 years, respectively these difference were significant (Students t-tests, P<0.05).

Once again, there is a possibility that patient with long standing disease would report only their disease became active while patients with relatively early disease may seek care more often. So, duration of disease can be considered as one risk factor for extensive vitiligo. A community based study may help to clarify these issues.

Koebner's phenomenon was found to be significant associated with extensive disease on bivariate analysis, when the odds ratio was calculated, it was OR-.2.427, 95% CI-.1.39-4.23, Significance level p=.0018 in the present study. Different subtypes of KP, as per the study are [KP1, by history; KP2A and KP2B, by clinical examination (A, lesions on friction areas; B, linear, artefactual lesions).

Koebner"s Phenomenon was significantly associated with larger body surface area involvement in vitiligo in the presence of any KP subtype (p=0.038). The body surface area (BSA) was significantly (P < 0·001) higher in the presence of any KP subtype [12]. An association had found between Koebner's phenomenon and the development or extension of lesions in the previous 3 months. In that study [7], Koebner's isomorphic phenomenon was present in 84 patients (21%) of whom 80 showed progression. Koebner's phenomenon was not present in 316 patients (79%) and 275 of these patients showed progression.

These differences were significant (Fisher's exact test p<0.05). The absence of an association with extensive disease may indicate that Koebner's phenomenon is associated with the developed of new lesions but not with the number and size of new lesions and the eventual extent of disease. In another recent study, koebners phenomenon is significantly associated with involvement of more BSA in comparison to patients with no Koebners Phenomenon [13]. Active progressive disease was positively associated with positive KP (OR, 1.8; p=0.02). Moreover, disease duration longer than 5 years was significantly more associated with positive KP (OR, 2.3; p < 0.0001).

These findings again are in accordance with the fact that KP is an indicator of active disease, which can be accepted as a risk factor for developing extensive lesion.

Similarly, a previous study [7] had found an association between a family history and progressive vitiligo, this factor was also associated with extensive disease in the present study. A family history was present in 67 (31.75%) patients of the present study group. 43 cases and 24 controls had a positive family history of vitiligo.

This difference was statistically significant (chi-square test, p<0.05), but the Odds Ratio came as nonsignificant. So, there is not more relative risk of developing extensive vitiligo in family members of vitiligo patients. Familial occurrence has been reported to vary from 6.25-30% [14].

The present study stated that 27.3% patients had positive family history of vitiligo, first degree relatives were affected in 10.29% of patients. In the present study, first degree, second degree and third-degree relatives were affected in 55.10%, 42.86%, and 26.58% of patients respectively. The group of patients with a positive family history did not appear to differ from patients in the extent of disease. Family history does not have any effect on onset [15] of vitiligo.

Surprisingly, the strongest association of extensive disease was noted with mucosal involvement [p value < 0.0001, OR-.12.04, 95% CI- 5.47-26.46, Significance level p<.0001)] and leucotrichia [p value < 0.0001, OR-. 23.91, 95% CI-10/06-56.85, Significance level p<.0001]. Mucosal involvement occurs rather frequently around body orifices such as the lips, genitals, gingiva, and nipples. In a study of Hann et al [7], mucosal involvement was present in 296 patients (74%), of who 255 showed progression.

They had opinioned that Significant progression of vitiligo in patients with mucosal involvement indicates that it is a poor prognostic factor. Opinion can be drawn in the same line, mucosal involvement might be assumed to be a risk factor of developing extensive vitiligo They didn't put leucotrichia a prognostic sign, though the present study differed. Leucotrichia has been reported in 9-48.4% of the patients with vitiligo [16].

Significance is attached to this finding as these cases also showed resistance to therapy.

Leukotrichia (vellus and terminal) was significantly higher in the 32/51 (62.7%) patients with generalized bilaterally symmetrical vitiligo in comparison to the 10/31 (32.3%) patients with acrofacial vitiligo and the 4/16 (25.0%) patients with unclassified vitiligo (*P*= 0.004). Neither of the two patients with focal vitiligo had leukotrichia but the only patient of universal vitiligo had. Vellus hair involvement was significantly higher in generalized bilaterally symmetrical vitiligo than in acrofacial or unclassified vitiligo. The incidence of scalp leukotrichia also was higher in generalized symmetrical vitiligo than in acrofacial vitiligo. The Vellus Score showed significant associations with Vitiligo Area and Severity Index [16].

It has long been recognized that depigmentation of the mucosa and hair within lesions are poor prognostic indicators for regimentation [9,17,18]. The usual explanation for this has been lack of follicular melanocyes to repopulate depigmented macules. The association with extensive disease cannot be explained on the same grounds. Damage to follicular melanocytes may represent a greater degree of disease activity than depigmentation confined to epidermal melanocytes and thus extensive disease may be more likely in such patients. The current study noted the presence of leucotrichia but did not recorded its extent. The evidence for an association would be stronger if it was demonstrated that patients who had widespread leucotrichia involving many lesions had more extensive disease. This may be worthy of further study.

Interestingly, a previous study [7] had found an association of progressive vitiligo with mucosal involvement. In that study 74% (298/400) with mucosal involvement of whom 255 showed progression: 104 had no mucosal involvement and 100 showed progression. This difference was significant (Fisher's exact test, p> 0.05) and appears to indicate a protective effect of mucosal involvement. The pure mucosal type of vitiligo was not observed in our patients, but mucosal involvement in association with other clinical variants was seen in our patients with late-onset vitiligo and was significantly more common than in the early-onset group.

The development of symmetrical lesions is generally considered to indicate a more widespread or active process in several diseases including vitiligo. So, symmetrical lesions developed early in extensive vitiligo patients may be valued as risk factor.

However, the present did not question patients about this. It was observed that symmetrical lesions were significantly associated with extensive disease but are unable to comment on the value of this finding. Patients with extensive disease would obviously be expected to have more symmetrical lesions at the time of examination than patients with limited disease and this might introduce a bias in the analysis. But literature supports our findings [19].

The classical presentation of the depigmentation is a remarkably symmetrical distribution of depigmentation beginning on the fingers, feet, wrists, elbows, axillae and around the mouth and eyes. There is no explanation for this symmetry. Yet, it is so typical and common that symmetrical depigmentation is one criterion for the diagnosis of vitiligo. (Depigmented patches can be randomly scattered.

This has been labeled atypical vitiligo.) looking the similarity of symmetry of vitiligo lesions with the distribution of some autoimmune endocrine disorders such as thyrotoxicosis, symmetrical involvement of both sides by tumors of malignant lymphoma it was hypothesized that benign lymphocytes honed to specific sites in the skin where they might be responsible for the symmetry of vitiligo [20]. Although his ideas are no longer popular, they are based on the known propensity of cutaneous lymphocytes to migrate to specific sites in the skin and the role of lymphocytes in causing depigmentation. His ideas are worthy of reconsideration [19].

Acrofacial vitiligo is often associated with mucosal involvement and it is tempting to conjecture that the strong association between mucosal involvement and extensive disease in the present study was due to disease being more widespread in the acrofacial type of vitiligo. However, there was no significant different in the proportion of patients who had acrofacial vitiligo in cases and controls. The present study was unable to explain this association.

A weaker but significant association was noted with the age at presentation greater than 20 years [p values = 0.005, adjusted OR with 95% CI 2.3 (0.9 – 5.3)].The age at presentation over 20 years was significant with the age at onset of disease, it is difficult to explain this association which may reflect a difference in health-seeking behavior at different ages.

A study on effect of ageat onset on disease characteristics in vitiligo, Patients with disease onset after 30 years had a significantly higher association with precipitating factors such as trauma, stress, and drugs in comparison with early-onset vitiligo (p< .004). However, the difference did not reach statistical significance when these factors were analyzed individually.

There was a significantly higher association with other nonautoimmune diseases (p= .05), a higher incidence of positive family history (p< .0001), and a higher association with leukotrichia (p< .002) in late-onset disease. Early-onset nonsegmental vitiligo was associated with a higher incidence of photosensitivity and pruritus compared to early-onset segmental vitiligo [21]. Theydidn't mention whether vitiligo in late onset are more extensive, but presence of multiple factors may explain the association of extensive vitiligo. In one of the largest series of childhood vitiligo, Analysis of this group of patients revealed that early-onset childhood vitiligo was more likely to progress and involve a greater percentage of BSA [22].

Previous studies have indicated a correlation between the site of a lesion and its propensity to spread to other areas [23]. They also indicated that the response to treatment varies according to the site of the lesion when initial sites were the posterior trunk and hands, there was more widespread progression to other body areas, whereas there was less progression when the initial sites were the face, and upper or lower extremities[9,18,24,]. Site of lesion also important for therapeutic purpose, as few areas are more treatment responsive(face) than others [25].

They also inferred that the prognosis of vitiligo may be predicted by the location of the initial lesions; however, certain factors like Male sex, patient age of 15 years or under, and duration of disease of 2 years or less showed increased repigmentation with statistical significance. Therefore, these factors may be good prognostic indicators [25]. In the present study, no association was observed between the site of onset and extensive vitiligo (p = 0.0565).

Limitations

The present study have taken some common clinical factors associated with extensive vitiligo, drawn the relation and significance in these association, so that the present study can designate them as risk factors.

Truly speaking, at present there is information of prognostic factors of vitiligo but nothing about risk factors. The present study retrospectively looked in the past for the possible exposures, patients might have had to a risk factor. But a prospective study with the same associated factors in vitiligo and their progression to extensive vitiligo will be more appropriate to designate them as truly risk factors.

That needs large prospective study. Due to the retrospective nature of the study design, case-control studies are subject to recall bias. So, Selecting the patients for the control group is a very critical component of research based on case-control studies. large population-based Cohort studies, initially classifying patients into two groups based on their presence of clinical factors and over time to see who develops the extensive disease and others may not be the most appropriate study design to assort risk factors.

Conclusion

This case-control study has demonstrated that Duration of disease more than 2 years, presence of Koebner's Phenomenon, Family history, Symmetry of lesions, milky white colour of lesion, presence of Leucotrichia, mucosal involvement and Acrofacial type vitiligo were statistically significant (p<0.05). It has also indicated that significant association between extensive vitiligo and duration of disease greater than 2 years. koebner's phenomenon, mucosal involvement and leucotrichia were noted.

What the study adds to the existing knowledge?

Duration of disease more than 2 years, Koebner's Phenomenon, Mucosal involvement and Leucotrichia may consider as risk factors in extensive vitiligo

Author's contributions

Dr. Suchibrata Das: Concept, study design, manuscript preparation, data analysis.

Dr. Nirmalya Kumar Das: Data analysis, manuscript correction

Reference

01. Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo- A comprehensive overview Part II. J Am Acad Dermatol. 2011;65(3)473-491.
doi: 10.1016/j.jaad.2010.11.061 [Crossref]

02. Zhang Y,CaiY,Shi M, Jiang S, Cui S, Wu Y, et al. The Prevalence Of Vitiligo- A metaanalysis. PLoS One. 2016 Sep 27;11(9)e0163806. doi: 10.1371/journal.pone.0163806 [Crossref]

03. Das SK, Majumder PP, Chakraborty R, Majumdar TK, Haldar B. Studies on vitiligo I- Epidemiological profile in Calcutta, India. Genet Epidemiol. 1985;2(1)71-78. doi: 10.1002/gepi.1370020107 [Crossref]

04. Das SK, Majumder PP, Majumder TK, Haldar B. Studies on vitiligo II. Familial aggregation and genetics. Genet Epidemiol. 1985b;2(2)255-262. doi: 10.1002/gepi.1370020303 [Crossref]

05. Majumder PP, Das DK, Li CC. A genetic model for vitiligo. Am J Human Genet. 1988;43(2)119-125. [Crossref]

06. Majumder PP, Nordlund JJ, Nath SK. Pattern of familial aggregation of vitiligo. Arch Dermatol. 1993;129(8)994-998. doi: 10. 1001/archderm.1993.01680290066010 [Crossref]

07. Hann SK, Chun WH, Park YK. Clinical characteristics of progressive vitiligo. Int J Dermatol. 1997;36(5)353-355. doi: 10.1046/j.1365-4362.1997.00162.x [Crossref]

08. Du Vivier A, Disorder of pigmentation, In Du Vivier A, Mckee PH, Editors, Atlas of clinical dermatology, 2nd Edition. London- Gower Medical Publication. 1992;25;8. [Crossref]

09. Dutta AK, Dutta PK. Pigmentary disorders, In Valia RG, Valia AR, editors, IADVL Textbook and Atlas of Dermatology, 1st edition. Bombay- Bhalani Publishing House. 1994;500-586. [Crossref]

10. Lund CC, Browder NC. The estimation of area of burns. Surg Gynecol Obstet. 1944;7(1)352-358. [Crossref]

11. Teulings HE, Ceylan E, Overkamp M, Vrijman C, Bos JD, Nijsten TE, et al. Nonsegmental vitiligo disease duration and female sex are associated with comorbidity and disease extent- a retrospective analysis in 1307 patients aged ≥ 50 years. Br J Dermatol. 2016;175(4)821-824. doi: 10.1111/bjd.14640 [Crossref]

12. Van GeelN, SpeeckaertR, DeWolf J, BrackeS, Chevolet I, Brochez L, et al. Clinical significance of Koebner phenomenon in vitiligo. Br J Dermatol. 2012;167(5)1017-1024. doi: 10.1111/j.1365-2133.2012.11158.x [Crossref]

13. Khurrum H, AlGhamdi KM, Bedaiwi KM, AlBalahi NM. Multivariate Analysis of Factors Associated with the Koebner Phenomenon in Vitiligo- An Observational Study of 381 Patients. Ann Dermatol. 2017;29(3)302-306. doi: 10.5021/ad.2017.29.3.302 [Crossref]

14. Shagil EM, Agarawal D, Vagadia K, Marfatia YS, Begum R. Vitiligo- clinical profiles in Vadodara, Gujrat. Indian J Dermatol. 2006;51(2)100-104. doi: 10.4103/0019-5154. 26928 [Crossref]

15. Mahajan VK, Vashist S, Chauhan PS, Mehta KI, Sharma V, Sharma A. clinico-epidemiological profile of patients with vitiligo: a retrospective study from a tertiary care centre of North India. Ind Dermatol Onl J. 2019;10(1)38-44. doi: 10.4103/idoj.IDOJ_124_18 [Crossref]

16. Mogawer RM, Elmasry MF, Mostafa WZ. New insights into leucotrichia in nonsegmental vitiligo- A crossesctionalstudy. Ind J Dermatol Venereol Leprol. 2019;85(4)374-379. doi: 10.4103/ijdvl.IJDVL_49_18 [Crossref]

17. Sehgal VN. A clinical evaluation of 202 cases of vitiligo. Cutis. 1974;439-445. [Crossref]

18. Datta AK, Mondal SB. A clinical study of 650 vitiligo cases and their classification. Ind J Derm. 1969;14(3)103-111. [Crossref]

19. Norlund JJ. Vitiligo- A Review of Some Facts Lesser Known About Depigmentation. Indian J Dermatol. 2011;56(2)180-189. doi: 10.4103/0019-5154.80413 [Crossref]

20. Goudie RB, Soukop M, Dagg JH, Lee FD. Hypothesis- Symmetrical cutaneous lymphoma. Lancet. 1990;335(8685)316-318. doi: 10.1016/0140-6736(90)90607-7 [Crossref]

21. Kanwar AJ, Mahajan R, Parsad D. Effect of age at onset on disease characteristics in vitiligo. J Cutan Med Surg. 2013;17(4)253-258.
doi: 10.2310/7750.2013.12075 [Crossref]

22. Euphemia W Mu, Brandon E Cohen, BS, Seth J Orlow. Early-onset childhood vitiligo is associated with a more extensive and progressive course. J Am Acad Dermatol. 2015;73(3)467-470.
doi: 10.1016/j.jaad.2015.05.038 [Crossref]

23. Chun WH, Hann SK. The progression of nonsegmental vitiligo- clinical analysis of 318 patients. Int J Dermatol. 1997;36(12)908-910.
doi: 10.1046/j.1365-4362.1997.00320.x [Crossref]

24. Barona MI, Arrrunatehui A. An epidemiologic case-control study in a population with vitiligo. J Am Acad Derm. 1995;33(4)621-625.
doi: 10.1016/0190-9622(95)91282-7 [Crossref]

25. Soo Min Kim, Han-Seung Lee, Seung-Kyung Hann. The efficacy of low-dose oral corticosteroids in the treatment of vitiligo patients. Int J Dermatol. 1999;38(7)546-550.
doi: 10.1046/j.1365-4362.1999.00623.x [Crossref]