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Original Article

A Retrospective Multivariate Analysis of Pre and Post Pubertal Onset of Vitiligo in a Tertiary Care Center

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ABSTRACT

Background: Vitiligo is an acquired, progressive depigmenting disorder that presents as depigmented macules or patches. Although it may manifest at any time in life, it usually begins in childhood. There is insufficient data to compare the clinical correlations of prepubertal and post-pubertal onset vitiligo.
Objective: To compile the clinical profiles and sociodemographic parameters of vitiligo patients by the age of onset of vitiligo.
Materials and Methods: Aretrospectivehospital-based study in a tertiary care hospital, the medical records of all patients with vitiligo who attended the OPD over a period of one year were analyzed.
Results: Out of 307 patients, 210 had post-pubertal and 97 had pre-pubertal onsets of vitiligo. There were more females in the prepubertal group than in the post-pubertal group. Only in those with a post-pubertal onset, vitiligo universalis was observed. Segmental vitiligo was seen more in the prepubertal onset group. In univariate analysis, previous episodes of spontaneous re-pigmentation, family history of vitiligo, and canities are commonly associated with prepubertal onset. The association with type 2 diabetes in vitiligo was greater in the post-pubertal group. In multivariate analysis, halo naevi and family history of canities remained statistically significant for prepubertal vitiligo.
Conclusions: Our data present clinical evidence that vitiligo behaves mostly the same way in both groups except that pre-pubertal onset vitiligo is strongly associated with a family history of vitiligo and a personal history of atopy, suggesting that it has a stronger hereditary component and immunological milieu than post-pubertal vitiligo.

Key Words: *Prepubertal vitiligo, post-pubertal vitiligo, univariate, multivariate*

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INTRODUCTION

Vitiligo is a common, acquired, progressive depigmenting disorder resulting from the destruction of melanocytes in the interfollicular and/or intrafollicular region [1]. It is a multifaceted illness with a complex pathophysiology encompassing genetic and autoimmune underpinnings [2]. It frequently coexists with other autoimmune and comorbid illnesses. According to the Vitiligo Global Issues Consensus Conference (VGICC), vitiligo can be divided into three types: non-segmental vitiligo, segmental vitiligo, and mixed vitiligo [3].

Until recently, very few studies have attempted to employ logistic regression techniques to find distinctions between true pediatric vitiligo/prepubertal onset vitiligo (</=12 years of age) and the post-pubertal onset of vitiligo (after the age of 12) [2, 3]. Here we present the outcome of a retrospective observational study that utilized univariate and multivariate logistic regression analysis to determine characteristics related to prepubertal and post-pubertal onset vitiligo.

MATERIALS AND METHODS

In this study, all vitiligo patients who visited the dermatology outpatient clinic over the course of a year in a tertiary care center were considered subjects. Recorded data of each patient, including examination and detailed history, course of the disease, age at onset, site of onset, distribution, presence of halo nevi, presence of the Koebner phenomenon, positive family history, associated autoimmune, any other cutaneous or systemic illnesses, and sociodemographic information, were collected. Laboratory reports, if available, like thyroid profile, antithyroid antibodies, and blood sugar were included.

STATISTICAL ANALYSIS

Data tabulation and analysis were done using Microsoft Excel and Word software. First, descriptive variables were compared between pre-pubertal (</= 12 years old) and post-pubertal (>12 years old) vitiligo onset ages. Population demographics were described using fundamental summary statistics.

Univariate and multivariate unbiased logistic regression comparisons amongst groups were done to find the variables connected to the pre-pubertal onset and post-pubertal onset. Before computing odds ratios (OR), 95% confidence intervals (CIs), and P-values, each putative predictor of pre-pubertal onset and post-pubertal onset was evaluated separately. The Wald chi-squared test was employed to assess the significance of the OR, and predictors with $P < 0.20$ were then evaluated using multivariate analysis and a forward stepwise methodology. The logistic regression model's suitability was verified using the Hosmer and Lemeshows goodness-of-fit test. Statistical software SPSS version 20.0. (IBM Corp., Armonk, New York, 2010) was used to conduct the statistical analyses.

ETHICS

The Institutional Ethics Committee and Protocol Review Board authorized the study.

RESULTS

Clinical and demographic characteristics of patients

A total of 307 vitiligo patient records were collected; 97 (male 38.1%, female 61.8%) belonged to the prepubertal group, and 210 (male 43.8%, female 56.2%) belonged to the post-pubertal vitiligo onset group. In both categories, females were in higher proportion than males.

The mean age of onset of the entire study group was 21.9 years in our study. The mean age of onset in the prepubertal group was 9 years and 27.9 years in the post-pubertal group. The mean age at the time of consultation was 15 years in the pre-pubertal onset group and 42.7 years in the post-pubertal onset group. Disease duration was ≤ 3 years in 63.9% and 15.8% of patients with pre-pubertal and post-pubertal onset disease, respectively. A generalised type of vitiligo (59.9%) was recorded predominantly for both groups. Universal vitiligo was seen only in patients with post-pubertal onset of disease (0.7%). For pre-pubertal onset vitiligo, the trunk (28.9%) was the most common location of lesion onset, whereas for post-pubertal onset vitiligo, the limbs (32.9%) were the most common site of lesion onset.

A significant difference was observed between family history of vitiligo with 48.5% and 32.9% respectively in patients with pre-pubertal and post-pubertal onset disease. We also observed a significant independent correlation between prepubertal onset vitiligo and familial history of canities ($p<0.001\%$). Halo naevi were observed more frequently in patients with pre-pubertal onset (9.3%) compared to individuals with post-pubertal onset (1.9%) in terms of frequency. The previous episode of spontaneous regimentation were 26.8% and 16.7%, respectively, observed in both groups. Thyroid disease was found in 11.3% of patients with the prepubertal onset and 13.8% of those with the post-pubertal onset.

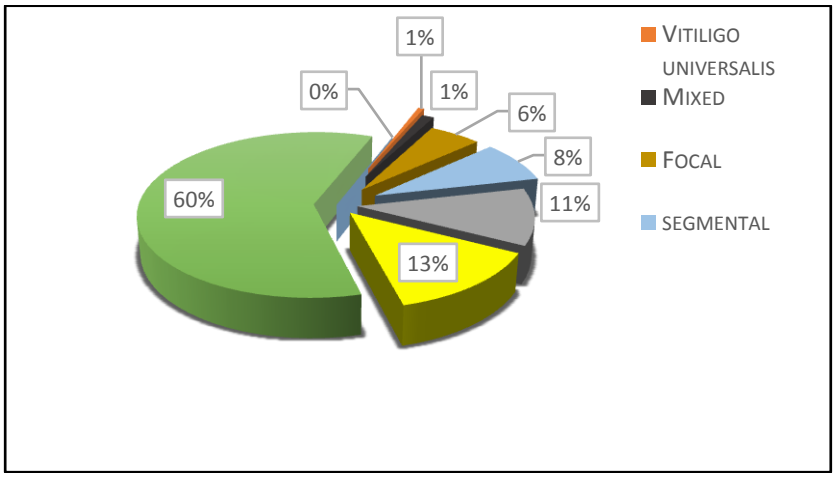

Figure 1: Type of vitiligo at the time of consultation

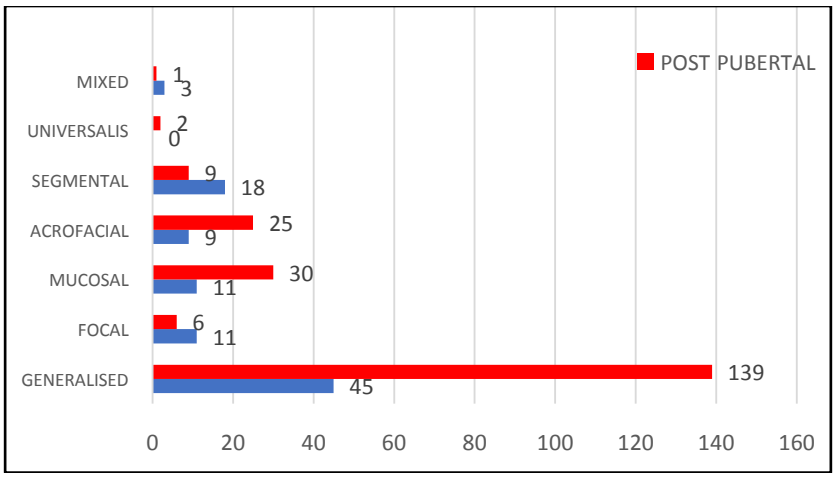

Figure 2: Type of vitiligo at the time of consultation with respect to the age of onset.

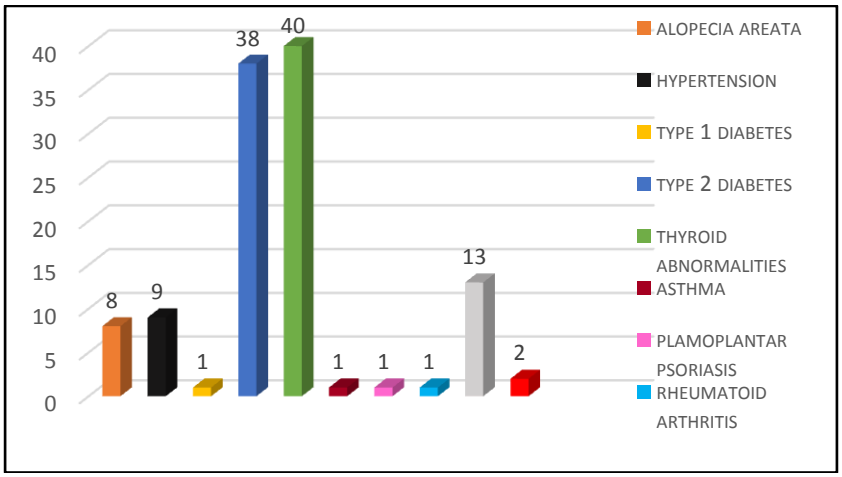

Figure 3: Various associated disorders

Table 1: Univariate analysis of patient's characteristics according to the age of onset of vitiligo

		prepubertal onset of vitiligo n=97		post-pubertal onset of vitiligo n=210		OR (95%CI)	P-value
		n	%	n	%		
Gender	Male	37	38.1	91	43.3	1.2 (0.75-2.02)	0.39
	Female	60	61.9	119	56.7		
Family history	Yes	47	48.5	69	32.9	0.52 (0.31-0.85)	0.009
	No	50	51.5	141	67.1		
Duration of disease	≤3 years	62	63.9	32	15.2	0.10 (0.05-0.17)	<0.001
	>3 years	35	36.1	178	84.8		
Previous episode of Spontaneous re-pigmentation	Yes	26	26.8	35	16.7	0.54 (0.30-0.97)	0.039
	No	71	73.2	175	83.3		
Koebner's phenomenon	Yes	43	44.3	73	34.8	0.66 (0.41-1.09)	0.10
	No	53	54.7	137	65.2		
Personal History 0f Autoimmune Thyroiditis	yes	11	11.3	29	13.8	1.25 (0.59-2.62)	0.55
	No	86	88.7	181	86.2		
Halo nevus	Yes	9	9.3	4	1.9	0.19 (0.05-0.63)	0.003
	No	88	90.7	206	98.1		
Family history of canities	Yes	13	13.4	2	1.0	0.06 (0.01-0.28)	<0.001
	No	84	86.6	208	99.0		

Logistic regression analysis

Results of the univariate logistic regression of pre- vs post-pubertal onset disease for patient characteristics are presented in Table 1.

There was statistical significance for family history of vitiligo (OR 0.52, P = 0.009), disease duration (OR 0.10, P < 0.001), previous episode of re-pigmentation (OR 0.54, P = 0.039), presence of halo naevi (OR 0.19, P < 0.003), and family history of canities (OR 0.06, P=<0.001) in the prepubertal onset of vitiligo. Personal history of autoimmune thyroiditis and Vitiligo universalis was positively related to post-pubertal onset vitiligo. The distribution of gender and the occurrence of the Koebner phenomena did not show any statistically significant variations.

When all of the patient characteristics were included simultaneously in the logistic regression analysis, duration of the disease (OR = 0.08; 95% CI: 0.04-1.57, P<0.001), family history of canities (OR =0.03; CI 0.007-0.18, p<0.001), and Halo nevus (OR = 0.14; 95% CI 0.03-0.57), P = 0.006) remained statistically significant (Table 2).

Table 2: **Multivariate logistic regression analysis of patient's characteristics according to the age of onset of vitiligo**

VARIABLE	Adjusted OR	95%CI	P- value
Family history (Yes/no)	0.62	0.33-1.15	0.13
Duration of disease (≤3 years />3 years)	0.08	0.04-1.57	<0.001
Previous episode of spontaneous re-pigmentation (Yes/no)	0.47	0.23-0.97	0.04
Koebner's phenomenon (Yes/no)	0.52	0.28-0.98	0.04
Halo nevus (Yes/no)	0.14	0.03-0.57	0.006
Family history of Canities (Yes/no)	0.03	0.007-0.18	<0.001

DISCUSSION

Vitiligo affects 1% of the world's population, and Indians reportedly have the highest incidence of vitiligo. It creates a significant appeal in a country like India, where most of the population has dark skin.

A study by Nilendu Sarma S et al showed the institutional prevalence of vitiligo in India was 0.89% [1]. In our OPD clinic, a nearly similar prevalence was observed 0.66% over a year. Considering the fact that autoimmune illnesses often afflict more females than males, in our study, there is a female gender preponderance of 61.9% and 56.7% respectively, in both pre-and post-pubertal onset vitiligo. Other studies also reported a similar female preponderance of 57- 66% [2] but few studies expressed an equal frequency of patients for both genders [3]. We also noticed more female gender predilection in the prepubertal onset group. At the consultation, the mean age of our patients was 15 and 42.7 years, respectively, in pre and post-pubertal onset, comparable to Ezzedine et al study 16 and 41.6 years, thus supporting the vitiligo's gradual development and asymptomatic nature.

Another noteworthy result of this study is it reinforces the notion that vitiligo onset age is impacted by genetic background. We noticed that pre-pubertal vitiligo is strongly associated with a family history of the illness, contributing to the concept that it has a stronger hereditary component than post-pubertal vitiligo. In our study, 48.5% of the patients with pre-pubertal onset vitiligo and 32.9% of the patients with later-onset vitiligo had a positive family history of the disease. However, studies by Khurrum et al. show 49.1% and 45.1% respectively.

Halder et al found that patients with childhood-onset vitiligo had a higher rate of family history of premature hair graying than did patients with adult-onset vitiligo [5]. We also found a significant independent correlation between prepubertal onset vitiligo and familial history of canities (p<0.001%), which in this context questions the relationship between vitiligo and premature hair graying as it pertains to oxidative stress or autoimmunity. In a previous study, a significant correlation between halo nevi-associated non-segmental vitiligo and premature graying of hair was observed, raising the possibility that it is a result of an autoimmune process [2]. This may be supported by the finding that halo nevus was more frequently seen in our cohort of vitiligo patients with prepubertal onset (p=0.003).

Ezzedine et al study suggests pre-pubertal onset vitiligo is strongly associated with a personal and family history of atopy, similarly, we observed in our study 5.8% of prepubertal onset vitiligo had a personal history of atopy indicating that immunological milieu predisposes to vitiligo and is not just autoimmunity [3].

The trunk (28.9%) was the most common initial presentation site for prepubertal onset vitiligo, whereas the lips and genitalia (8.2%) were the least common. Our results conflict with those of previous studies, which suggested that the head and neck were the most frequent site whereas the upper extremities were the least frequent site of onset. Only in the post-pubertal onset group of individuals vitiligo universalis was found, and the mucosal form of vitiligo was found to be

more common in this group. Also, we observed that the prepubertal group had more proportions of segmental vitiligo (18.5%) than the post-pubertal group (4.28%). A similar observation was recorded by Khurrum et al [2] and Pajvani et al [4] in their studies. In our study, associations with thyroid abnormalities and insulin-independent diabetes mellitus are more in the post-pubertal group, comparable to Ezzedine et al study, but few are conflicting with this as in Khurrum et al [2].

It is generally known that therapy for vitiligo is more effective in new lesions compared to older lesions. We observed that patients with pre-pubertal onset of vitiligo had a higher probability of spontaneous re-pigmentation 26.8%, and alike 22.8% was reported in the [3] Ezzedine et al study, hence this may argue for early treatment of children with vitiligo.

The drawbacks of this study are it is retrospective, observational, hospital-based, and descriptive in design, the study may not accurately reflect the characteristics of the general population, and chances of duplicate registration of outpatient attendance. Patients with prepubertal onset of vitiligo may find it difficult to recollect the exact time the disease first appeared, therefore a potential for false recall bias cannot be completely ruled out. Strong elements of this study can be the sample size and the advanced statistical methods used in the analysis.

CONCLUSIONS

Our analysis unequivocally demonstrates that vitiligo, regarding the age of onset, has different clinical characteristics and perhaps a separate genetic foundation. There is a significant correlation between prepubertal onset vitiligo with halo nevus, episodes of spontaneous re-pigmentation, familial history of vitiligo, and canities. To establish the relationship between the various causes of vitiligo and steer clinicians toward an appropriate target therapy, further epidemiological studies are necessary, particularly genetic studies. Also, early screening for thyroid issues and diabetes mellitus in all vitiligo patients would be very beneficial.

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Conflicts of interest: There are no conflicts of interest.

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