

A Study of Association of Diabetes Mellitus and Vitiligo Patients

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Abstract

The most accepted pathogenesis of vitiligo is autoimmune theory and as a result vitiligo is known to be associated with many autoimmune diseases one of which is diabetes mellitus. A comparative cross-sectional study was done in Department of Dermatology in a tertiary care institute. Eighty patients of vitiligo and eighty controls in the age group of 12-60 years were investigated for fasting blood glucose levels. Five (6.25%) out of eighty patients with vitiligo were found to have diabetes mellitus. This study indicates that all the patients of vitiligo must be screened for diabetes mellitus, for its early diagnosis, to avoid its adverse impact on health status.

Keywords: Autoimmune Theory, Blood Glucose Levels, Diabetes Mellitus, Vitiligo

1. Introduction

Vitiligo is a common, acquired, depigmentary disorder of the skin that affects approximately 1-2% of the general population, without racial or sex differences. The condition occurs when pigmented cells are destroyed, causing patches of skin to lose their normal colour and appear whiter¹.

Numerous studies from abroad have described an association of vitiligo with other autoimmune disorders such as thyroid disease (hashimoto's thyroiditis and grave's disease), Addison's disease, pernicious anemia, insulin dependent diabetes mellitus and alopecia areata^{2,3}.

Although the pathogenesis of vitiligo is not yet fully understood, the autoimmune hypothesis is the most commonly accepted. This theory is supported by the clinical association of vitiligo with autoimmune disorders, the frequent detection of circulating autoantibodies to surface and cytoplasmic antigens of melanocytes. Furthermore, there are findings of activated T cells in the periphery of actively progressing lesions in some vitiligo patients^{1,4}.

Diabetes mellitus is an autoimmune disease and has been reported in association with vitiligo, and it seems that the

incidence of diabetes mellitus is more common in vitiligo patients than healthy subjects⁵. Vitiligo associated diabetes mellitus is seen in 1-7% of vitiligo patients in the world⁶.

In India, however, some studies have focused on association of diabetes mellitus with vitiligo. We therefore undertook this study of prevalence of diabetes mellitus in vitiligo patients.

2. Materials and Methods

Study design was comparative cross-sectional study and was done in the period from June 2015 to December 2017. The study was conducted in the OPD of Department of Dermatology, Medical College and Tertiary Health Care Centre. The sample size taken was of 80 cases and 80 of comparative group.

2.1 Eligibility Criteria

Inclusion Criteria:

- Study group:
 1. Clinically diagnosed cases of vitiligo.

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2. Patients between the age group of 12 years to 60 years.
3. Patients willing to participate in the study.
 - Comparative group:
1. Patients attending hospital OPD without any evidence of vitiligo or any dermatological disorder or any systemic disorder or on any medications.
2. Individuals fulfilling these criteria and ready to participate in the study.

Exclusion Criteria:

- Cases and Comparative group:
1. Known cases of diabetes mellitus.
 2. Those who have severe systemic illnesses.
 3. Pregnant women, lactating women.
 4. Children aged less than 12 years.
 5. Patients not willing to participate in the study.
 6. Patients with any other disease or condition known to alter blood glucose levels.
 7. Patient with known endocrine dysfunction.

2.2 Methodology

The study was conducted in the Department of Dermatology, Venereology and Leprology in a tertiary care centre and medical college. Eighty subjects satisfying the eligibility criteria were taken and eighty age, sex matched controls without vitiligo were taken. Subjects were enrolled for study after taking a written informed consent.

A complete history regarding name, age, gender, age of onset, duration, progression of vitiligo, family history of vitiligo and personal or family history of common systemic diseases associated with vitiligo such as anemia, alopecia, thyroid dysfunction, diabetes mellitus, smoking habits, alcohol consumption, diet, presence of any other systemic illness, past medication for vitiligo, any concomitant medications was taken .

Table 3. Sex-wise distribution in cases and controls

Sex	Cases		Control		Total	
	Frequency	%	Frequency	%	Frequency	%
Male	37	46.25%	37	46.25%	74	46.25%
Female	43	53.75%	43	53.75%	86	53.75%
Total	80	100.00%	80	100.00%	160	100.00%
Chi-Square Tests						
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)		
Pearson Chi-Square	.000 ^a	1	1	1		

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 37.00

P=1 using Chi Square test. Since p value is > 0.05, there is no significant difference between two study groups.

Ratio Male to Female: 1:1.16

A thorough dermatological examination was done in all cases and controls. The patients were instructed to fast overnight and visit next day for collection of blood sample. A blood sample (5 ml) was taken from each case and control for the estimation of serum fasting blood glucose levels in the endocrinology laboratory. A diagnosis of diabetes mellitus was made when fasting blood glucose levels were more than 126mg/dl².

Patients were asked for follow up after one day. The reports were informed to the patient. Patients with abnormal findings were counselled and were referred to appropriate speciality for further investigations and management.

Similar procedures regarding history, examination and investigations were carried out in matched controls. The data collected was evaluated using appropriate statistical methods.

3. Results

Table 1. Age distribution of vitiligo cases

Age Groups in years	Cases	Percentage
12-22	18	22.50%
22-32	25	31.25%
32-42	12	15.00%
42-52	13	16.25%
52-62	12	15.00%
Total	80	100.00%

Table 2. Mean age in the two study groups

Age	Cases	Controls
Age (years)	33.1±14.02	33.21±13.92

P=0.959 using unpaired t test. Since p value is > 0.05 there is no significant difference between two study groups.

Table 4. Showing onset of vitiligo

Onset of Vitiligo (age in years)	No of Cases	Percentage
1-10 years of age	14	17.50%
11 - 20 years of age	33	41.25%
21 - 30 years of age	24	30.00%
31 - 40 years of age	8	10.00%
41 - 50 years of age	1	1.25%
Total	80	100.00%

Table 5. Showing mean age of onset of vitiligo

Parameter	Onset of vitiligo at age in yrs.
Mean	19.25
Std. Deviation	9.21

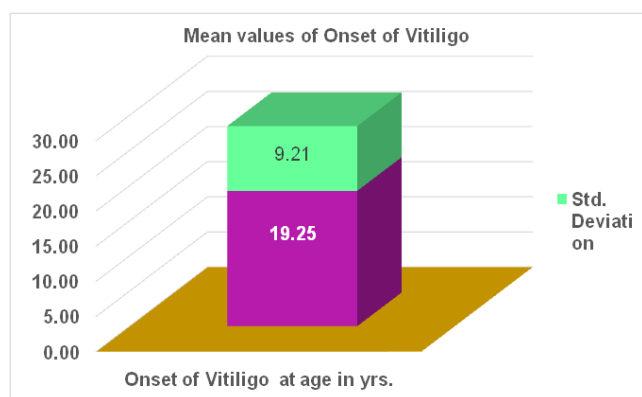


Figure 1. Showing mean values of age of onset of vitiligo.

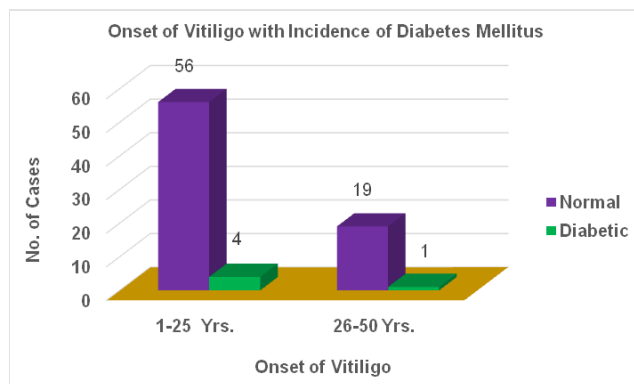


Figure 2. Showing onset of vitiligo with incidence of diabetes mellitus.

Table 7. Duration of vitiligo in months

Duration in months	Cases	Percentage
<12 months	2	2.50%
12-24 months	14	17.50%
25-36 months	5	6.25%
37-48 months	2	2.50%
49-60 months	5	6.25%
>60 months	52	65.00%
Total	80	100.00%

Table 6. Onset of vitiligo in relation to raised blood sugar levels (BSL)

Onset of vitiligo	BSL				Total	
	Normal		Diabetic			
	Fre-quency	%	Fre-quency	%	Fre-quency	%
1-25 years of age	56	74.67%	4	80.00%	60	75.00%
26-50 years of age	19	25.33%	1	20.00%	20	25.00%
Total	75	100.00%	5	100.00%	80	100.00%
Chi-Square Tests						
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)		
Pearson Chi-Square	0.071	1	0.79	1		
Continuity Correction	0	1	1			
Fisher's Exact Test				1		

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.25.

P Value = 1.000 > 0.05 by applying Chi square test with Continuity Correction implies there is no significant association between onset of disease and incidence of diabetes.

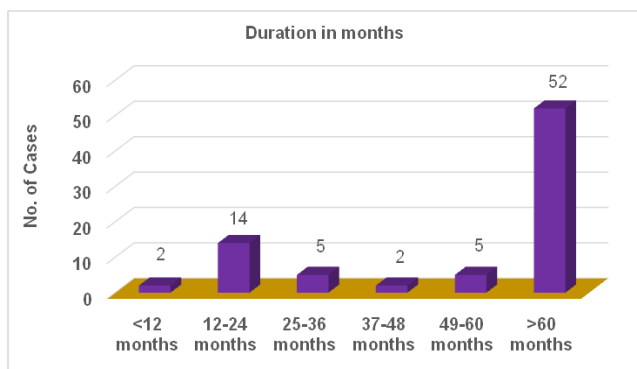


Figure 3. Showing duration of vitiligo in months.

Table 9. Presence of family history of vitiligo

Family History	No of Cases	Percentage
Positive	24	30.00%
Negative	56	70.00%
Total	80	100.00%

Table 11. Type of vitiligo-wise distribution of cases in the study

Type of Vitiligo	No of Cases	Percentage
Acrofacial	22	27.50%

Table 8. Duration of vitiligo in relation to raised Blood Sugar Levels (BSL)

Duration	BSL				Total	
	Normal		Diabetic		Fre-quency	%
	Fre-quency	%	Fre-quency	%		
<=60 months	28	37.33%	0	0.00%	28	35.00%
>60 months	47	62.67%	5	100.00%	52	65.00%
Total	75	100.00%	5	100.00%	80	100.00%
Chi-Square Tests						
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)		
Pearson Chi-Square	2.872a	1	0.09			
Continuity Correction	1.465	1	0.226			
Fisher's Exact Test				0.156		

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.75.

P Value = 0.226 > 0.05 by applying Chi square test with Continuity Correction implies there is no significant association between duration of vitiligo and incidence of diabetes

Table 10. Presence of family history of vitiligo in relation to raised blood sugar level (BSL)

Family History	BSL				Total	
	Normal		Diabetic		Fre-quency	%
	Fre-quency	%	Fre-quency	%		
Positive	22	29.33%	2	40.00%	24	30.00%
Negative	53	70.67%	3	60.00%	56	70.00%
Total	75	100.00%	5	100.00%	80	100.00%
Chi-Square Tests						
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)		
Pearson Chi-Square	.254a	1	0.614			
Continuity Correction	0	1	1			
Fisher's Exact Test				0.633		

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.50.

P Value = 1.000 > 0.05 by applying Chi square test with Continuity Correction implies there is significant association between family history and incidence of diabetic mellitus.

Focal	23	28.75%
Segmental	5	6.25%
Vitiligo vulgaris	30	37.50%
Total	80	100.00%

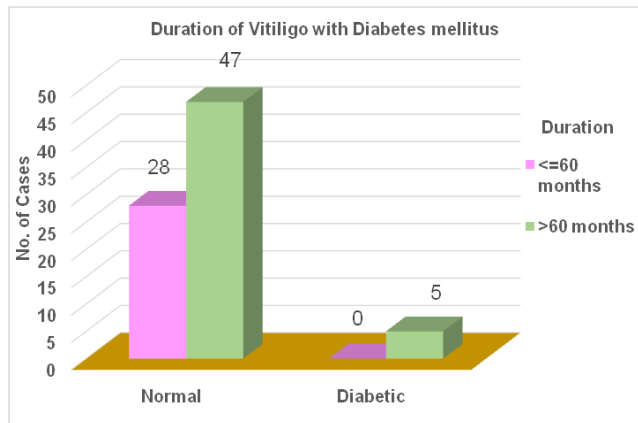


Figure 4. Showing duration of vitiligo with diabetes mellitus.

Table 12. Type of vitiligo

Type of Vitiligo	Frequency	Percentage
Generalised	52	65.00%
Localised	28	35.00%
Total	80	100.00%

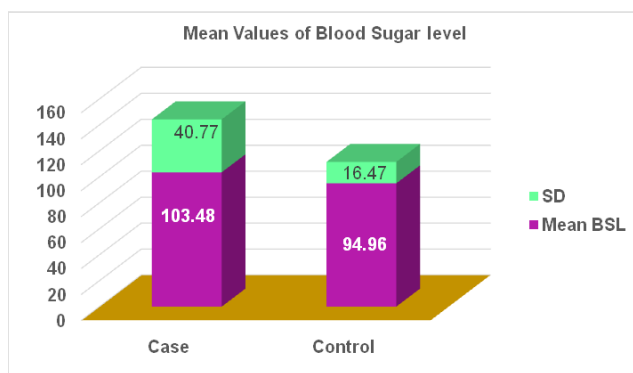


Figure 5. Showing mean values of blood sugar fasting levels in cases and controls.

4. Discussion

Vitiligo is a common, acquired hypomelanotic disorder of the skin, in which there is destruction of the pigment cells. Autoimmunity has a crucial role in the pathogenesis of vitiligo, and vitiligo is found to be associated with many autoimmune diseases like diabetes mellitus. Thus, screening of patients of vitiligo for blood sugar levels is relevant and important to detect early changes in the health status.

We therefore undertook this study, to determine whether vitiligo is statistically significantly associated

Table 13. Type of vitiligo in relation to raised blood sugar levels (BSL)

Type of Vitiligo	BSL					Total	
	Normal		Diabetic				
	Frequency	%	Frequency	%	Frequency	%	
Generalised	47	62.67%	5	100.00%	52	65.00%	
Localised	28	37.33%	0	0.00%	28	35.00%	
Total	75	100.00%	5	100.00%	80	100.00%	
Chi-Square Tests							
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)			
Pearson Chi-Square	2.872	1	0.09				
Continuity Correction	1.465	1	0.226				
Fisher's Exact Test				0.156			

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.75.

P Value = 0.226 > 0.05 by applying Chi square test with Continuity Correction implies there is no significant association between type of vitiligo and incidence of diabetes mellitus.

with diabetes mellitus. We evaluated the prevalence of the association between vitiligo and diabetes mellitus in the patients of vitiligo and the various factors which can possibly affect the prevalence of diabetes mellitus like age of onset, duration, family history and type of vitiligo.

Table 14. Mean values of blood sugar fasting levels in cases and controls

Characteristic	Case	Control
Fasting blood sugar levels	103.48 ± 40.77	94.96 ± 16.47

P=0.085 using unpaired t test

Since p value is >0.05, there is no significant difference in both study groups

4.1 Age Distribution

In our study, total 80 patients of vitiligo and 80 controls were included. The age wise distribution of patients with vitiligo shows 22.50% below the age of 22 years, 46.25% in the age group of 22-42 years and 31.25% above the age of 42 years (Table 1). Larger number of cases was found in 22-42 years of age group, this could be due to increased awareness and consciousness regarding cosmetic appearance among younger age group.

In our study we found that the mean age of patients of vitiligo was 33.1 ±14.02 years (Table 2). Found the mean age to be 37.14 years in a study of 97 patients of vitiligo⁸. Reported mean age of 34.41± 13 in a study of 109 patients⁹. Reported a mean age of 35.96 in a study of 100 patients¹⁰. The mean age found in our study is in accordance with other studies.

4.2 Sexual Preponderance

In this study, we found that the number of male patients of vitiligo is 37 (46.25%) and females is 43 (53.75%) (Table 3). Showed female preponderance in their study^{8,11}. The male: female ratio is 1:1.16. On reviewing various studies conducted on vitiligo by various authors, reported this ratio to be 1:1, 57:76 and 1.19:1¹²⁻¹⁴. Our study is in accordance with other studies. There was a slight female preponderance seen in our study, could be due to the greater social consequences to women and girls affected by this condition prompting women to seek consultation more often than men.

4.3 Onset of Vitiligo

The most common age of onset of vitiligo in our study was found to be in the age group of 11-20 years. 41.25%

cases had their onset between 11-20 years of age (Table 4). The mean age of onset in our study was 19.25 years (Table 5 and Figure 1). The mean age of onset in other studies was found to be 37.74¹⁵, 34.12 in a study¹⁰ and 41.2¹³ this data upholds that vitiligo can occur at any age.

The onset of vitiligo in the cases found with diabetes mellitus was classified into age group of 1-25 and 26-50 years. In the patients diagnosed with diabetes it was 4/5 and 1/5 patients who had the onset of vitiligo from the age group of 1-25 and 26-50 years respectively (Table 6 and Figure 2). A study^{16,17} states that onset of vitiligo in diabetic patients was before the age of 40 years. In our study there was no significant association between onset of disease and incidence of diabetes mellitus.

4.4 Duration

In our study, we classified duration of vitiligo in cases into less than 12 months, 12-36 months, 37-60 months and more than 60 months. Two (2.50%) patients had duration less than 12 months, nineteen (23.75%) patients and seven (8.75%) patients had duration between 12-36 months and 37-60 months respectively (Table 7 and Figure 3). A higher number of patients that is 52 (65%) were found to have duration of vitiligo more than 60 months.

For statistical analysis of duration of vitiligo with diabetes we classified into less than 60 months and more than 60 months (Table 8 and Figure 4). In duration of vitiligo with diabetes all the cases 5/5 (100%) were found to have duration of more than 60 months. Reported that there is no significant relation in duration of vitiligo and diabetes^{18,19}. In our study, though all the vitiligo patients who were diagnosed with diabetes mellitus were found to have long duration of vitiligo, however we did not find statistically significant association between duration incidences of diabetes. This data concludes that more the duration of vitiligo, more is the frequency of presence of diabetes.

4.5 Family History

We found in our study that family history of vitiligo was positive in 30% of the cases (Table 9). Positive family history ranged from 34% to 38.7% in studies by^{20,21} and 20% in a study²² family history was positive in 40% of vitiligo cases with diabetes mellitus (Table 10). There are very less studies comparing family history of vitiligo with and without thyroid dysfunction and diabetes mellitus. Our findings conclude that there is significant association between family history and incidence of diabetes mellitus

in our study. This data shows that diabetes mellitus is commonly seen in patients with positive family history of vitiligo.

4.6 Type of Vitiligo

In our study, all vitiligo cases were classified into four classes: focal, segmental, acrofacial and vitiligo vulgaris. Amongst these vitiligo vulgaris type was seen in 37.50% patients and was the most common type seen in our study (Table 11). 48%, 41.8%, 67%²³⁻²⁵1565 (41.8%) also found vitiligo vulgaris as the most common type in their study. For statistical analysis, focal and segmental vitiligo was considered under localized vitiligo whereas acrofacial and vitiligo vulgaris were included under generalized vitiligo (Table 12). All the cases (100%) cases who were diagnosed as diabetic belonged to generalized vitiligo group (Table 13). That there was higher prevalence of diabetes mellitus in generalized vitiligo¹⁸. Though all the cases diagnosed with diabetes, belonged to generalized type, our study shows no statistically significant association between type of vitiligo and incidence of diabetes mellitus. This shows that generalized type of vitiligo is frequently associated with diabetes mellitus.

4.7 Diabetes Mellitus

The mean value of blood sugar fasting levels in our study was 103.48 ± 40.77 mg/dl (Table 14 and Figure 5). Prevalence of raised blood sugar fasting in vitiligo cases is 6.25% and in healthy controls is 2.50% in our study. However, there is no statistically significant difference found in both study groups (Table 14 and Figure 5). After fasting plasma glucose examination, found 16% patients of vitiligo with diabetes mellitus. Previous studies^{12,17,18,20} had findings of association of vitiligo and diabetes mellitus. A study²⁶ showed a significant difference in impaired fasting blood glucose in vitiligo patients.

Vitiligo and diabetes share a common theory of autoimmunity and a common risk factor of familial predisposition. Diabetes is often present in close relatives of patients with vitiligo. Insulin dependent diabetes is a slow autoimmune disease that include HLA-linked genetic predisposition, association with other autoimmune disorders, circulating islet cell and insulin autoantibodies. Both diabetes and vitiligo are associated with HLADR3 and HLADR4. Mutations in insulin receptor cause severe insulin resistance. Multiple genes are involved in diabetes mellitus and its development needs an inheritance of

complements of genes to grant susceptibility HLA region on chromosome 6 hold on the major susceptibility gene. This location posses gene that encode the classic 11 MHC molecules that present antigens to helper T cell that initiate an immune response. Therefore, genetic predisposition is linked with autoimmunity, and same patient may have a genetic predisposition to both vitiligo and diabetes.

In vitiligo, melanocyte dysfunction occurs because there is primary disturbance in immunological mechanisms due to which there is inhibition of melanin production. The occurrence of vitiligo in diabetes may be a result of an autoimmune disturbance in the same patient affecting two organ systems. It is estimated that an injury to melanocytes resulting in the release of an antigenic substance, antimelanocyte antibody formation, inhibition of melanogenesis and occurrence of vitiligo, may be due to long standing diabetes mellitus. It is known that depigmentation may be an important cutaneous marker for immunological diseases. According to self destructive theory apoptosis may play a role in mechanism causing vitiligo in diabetes and the study of factors leading to the development of apoptosis may give a way to find vitiligo and diabetes association¹⁶.

5. Conclusion

We studied the association of diabetes mellitus in vitiligo patients. Findings of fasting plasma glucose examination reported diabetes mellitus in 5 cases out of 80, while in only 2 controls out of 80. The presence of raised blood sugar levels were unrelated to age, sex, onset, duration and type of vitiligo, but showed statistically significant association to positive family history of vitiligo. Prevalence of raised blood sugar fasting in vitiligo cases in our study was 6.25%.

In present study, we indeed found diabetes mellitus in more number of cases than controls, however there was no statistically significant difference found between fasting blood sugar levels in cases and controls. Though we did not get a statistically significant result, this does not outweigh the fact of association between vitiligo and diabetes. Diabetes mellitus can be commonly present in vitiligo patients and screening for the same should be encouraged. More number of studies with larger sample size is required to establish the association of vitiligo and diabetes.

Our study shows that there is a positive correlation between the existence of autoimmune disease and severity of vitiligo. We hereby conclude that, all the above findings

establish a clear association between vitiligo and diabetes. These associations reveal that vitiligo has a common genetic etiologic link with autoimmune disease.

Hence, screening of vitiligo patients for diabetes mellitus will be very useful for early diagnosis of autoimmune disease to avoid its adverse impact on growth and health status. Also, timely treatment in all diagnosed cases will prevent long term morbidity and complications. A more number of researches on the presence of diabetes mellitus in patients with vitiligo should be done conspicuously. The limitations of this study were less duration of time and less number of patients. More studies with more number of patients are welcomed.

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