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Association of vitiligo and metabolic syndrome: a case control study

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ABSTRACT

Background: Vitiligo is an acquired disorder of depigmentation which involves skin and mucous membranes characterized by development of well-defined white macules on skin, mucosa and overlying hair of the skin can be involved. Systemic nature of the vitiligo might lead to insulin resistance metabolic profile abnormalities. Objective was to study the association between vitiligo and metabolic syndrome.

Methods: The study was done in department of dermatology, venereology and leprosy of Dr. R. P. Government Medical College Kangra (Tanda), Himachal Pradesh. The study included 150 cases and 150 controls. Cases: age above 18 years with a diagnosis of vitiligo were included in the study. Pregnant and lactating women were excluded. Patients who had used medications that could affect the metabolic status (like systemic steroid therapy or cyclosporine or on hormonal replacement therapy). Patients already on lipid lowering agents and antidiabetic drugs. The case group was further subdivided into three subgroups according to VIDA score (group A: 1-0, group B: 1-2 and group C: 3-4). Controls: those visiting outdoor patient department and admitted for minor day care procedures Clinical details of patients were recorded regarding age, sex, smoking/alcohol consumption. General physical examination includes height, weight, body mass index, waist circumference, blood pressure. All the patients and controls were subjected to following tests: fasting blood sugar (FBS), cholesterol (CHOL), triglyceride (TAG), low density lipoprotein (LDL), high density lipoprotein (HDL), very low-density lipoprotein (VLDL), fasting serum insulin level (FSIL). Venous samples were taken after 12 hours of fasting. The participants were screened for metabolic syndrome as per national cholesterol education program adult treatment panel III (NCEP ATP III). Metabolic syndrome rates were compared between case and control groups. **Results:** The mean age was 35.82±12.9 years among cases and 36.97±11.76 years among controls. The M/F ratio of cases being (1:1.6) and controls (1:1). The mean duration of vitiligo was 117.8±105.5 months. Metabolic syndrome was significantly prevalent amid vitiligo cases 74 (49.3%) as compared to controls 23 (15.3%) with OR (95% CI) =5.37 (3.1-9.3). Metabolic syndrome was more frequent in VIDA subgroup 3{71 (47.3%)} and was statistically significant $(p \le 0.001)$.

Conclusions: The study found association of metabolic syndrome among vitiligo patients. In addition, the study also found that in non-segmental vitiligo, frequency of metabolic syndrome was higher as compared to another pattern. Furthermore, frequency of metabolic syndrome increased as activity of vitiligo increased in the study.

Keywords: Vitiligo, Metabolic syndrome, VIDA, Age

INTRODUCTION

Vitiligo is an acquired disorder of depigmentation which involves skin and mucous membranes characterized by development of well-defined white macules on skin, mucosa and overlying hair of the skin can be involved. Any site of the body may be affected but common sites of predilection are areas of chronic pressure/friction/trauma such as knees, dorsal surface of hands and feet, ankles, elbows and buttocks. 1 Recently vitiligo has been classified into non segmental, segmental and undetermined form.² Vitiligo is a heterogenous and multifactorial disease process. Different patho-mechanisms involved in various clinical types of vitiligo are genetic, neural, autoimmune, autocytotoxic, melanocytorrhagy and oxidative stress.³⁻⁸ However, the proinflammatory cytokines involved in pathogenesis of vitiligo have been found to be associated with metabolic syndrome and its complications like atherosclerotic cardiovascular disease.9 Hence, we conducted this study to investigate the association of vitiligo and metabolic syndrome.

METHODS

A case control study was done to find the association of vitiligo and metabolic syndrome. This study was conducted in the department of dermatology, venerology and leprosy, Dr. RPGMC Kangra at Tanda (HP), India, a tertiary care teaching and training hospital. Institutional ethics committee approved the study vide letter no. HFW3 H(DRPGMC)ETHICS/2021-29 dated 28.08.2021. Recruitment took place from September 2021 to November 2022. An informed consent was obtained from each participant.

Sample size

The sample size included 300 patients (150 cases and 150 controls).

Inclusion criteria

A total of one hundred and fifty patients of above 18 years age and with diagnosis of vitiligo were included in the study. Patients already on any anti-vitiligo treatment were given a wash off period of 2 and 4 weeks for topical and systemic therapy respectively prior to sampling.

Exclusion criteria

Pregnant and lactating women. Patients who had used medications that could affect the metabolic status (like systemic steroid therapy or cyclosporine or on hormonal replacement therapy). Patients already on lipid lowering agents and antidiabetic drugs.

Controls

One hundred and fifty healthy controls visiting outdoor patient department and admitted for minor day care

procedures were recruited after taking informed consent assuring confidentiality and freedom of choice of participation. Clinical details of patients were recorded regarding age, sex, smoking/alcohol consumption. General physical examination includes height, weight, body mass index, waist circumference, blood pressure. Waist circumference was measured as the smallest circumference of the trunk at the midpoint between the lowest margin of 12th rib and the highest point of iliac crest at the end of normal expiration. It was ensured that the tape measurement was horizontal and did not compress skin. The measurements were performed in standing position of the patients with a relaxed abdomen, arms at sides and feet joined together. All the patients and controls were subjected to following tests: fasting blood sugar (FBS), cholesterol (CHOL), triglyceride (TAG), low density lipoprotein (LDL), high density lipoprotein (HDL), very low-density lipoprotein (VLDL), fasting serum insulin level (FSIL). Venous samples were taken after 12 hrs of fasting. The participants were screened for metabolic syndrome as per national cholesterol education program adult treatment panel III (NCEP ATP III) (if any 3 of the following were present).¹⁰

Table 1: National cholesterol education program ATP III criteria.

Abdominal obesity	Waist circumference ≥88 cm (35 inch) in women ≥ 102 cm (40 inch) in men		
Impaired glucose	FBS ≥100 mg/dl (5.6		
tolerance	mmol/l)		
Hypertriglyceridemia	TAG≥150 mg/dl (1.7		
	mmol/l) or drug treatment		
	for high TAG		
Low levels of HDL	HDL <40 mg/dl (1 mmol/l)		
	in men, HDL <50 mg/dl		
	(1.3 mmol/l) in women or		
	drug treatment for low HDL		
III ah blaad maaanna	≥130/85 mmHg or drug		
High blood pressure	treatment for hypertension		

Vitiligo patients were evaluated for family history, site, age of onset, duration, progression, subtype and mean duration of vitiligo. VIDA score was used for the activity of vitiligo. Additionally, the cases were divided into 3 subgroups according to their VIDA score values (group A: -1-0, group B: 1-2 and group C: 3-4) metabolic syndrome rates were compared between study and control groups.

Statistical analysis

The data was statistically analyzed using EPI-INFO version 7. Qualitative data were described using numbers and percentages. Quantitative data were described using minimum and maximum values, mean and their SD, and medians. Comparison between different groups regarding categorical variables was performed using chi square tests, and for continuous parametric data t-tests and analysis of

variance were used. P is the calculated probability and it was considered significant if less than 0.05.

RESULTS

Demographic characteristics

The study included 150 cases and 150 controls. The mean age was 35.82±12.9 years among cases and 36.97±11.76 years among controls. The M/F ratio of cases being (1:1.6) and controls (1:1). The mean duration of vitiligo was 117.8±105.5 months. Thirty-four vitiligo patients and 31 patients from control group had history of smoking (p=0.39), while 20 vitiligo patients and 21 patients from control group had history of alcohol consumption (p=0.5). Hence risk factors such as smoking and alcohol consumption were not significantly different among cases and controls.

Characteristics of metabolic syndrome and its components

Metabolic syndrome was higher in the case group 74 (49.3%) as compared to controls 23 (15.3%) (Table 2). Comparison of the various components of metabolic

syndrome was done among both groups. As shown in table 2 there was no significant difference between the mean WC, BMI, HDL and DBP of two groups. The cases had higher mean SBP, TAG, FBS and LDL values (p<0.001) as compared to controls.

Comparative analysis of metabolic syndrome and its components in cases and controls

Metabolic syndrome was significantly prevalent amid vitiligo cases 74 (49.3%) as compared to controls 23 (15.3%) with OR (95% CI) =5.37 (3.1-9.3). In our study vitiligo patients had higher prevalence of abnormal TAG {OR (95% CI) =9.3(0.286-0.963)}, and HDL{OR (95% CI) =2.45 (1.52-3.92)}, FBS {OR (95% CI) =3.46 (1.87-6.38)}, WC {OR (95% CI) =2.54 (1.53-4.19)}, SBP OR (95% CI) =2.68 (1.47-4.87) and DBP OR (95% CI) =1.9 (1.03-3.5)} levels as compared to healthy controls (Table 3)

Association of metabolic syndrome and vitiligo duration

In our study the duration of vitiligo was statistically insignificant w.r.t. metabolic syndrome {OR (95% CI) =0.635 (0.317-1.27)} (p=0.133) (Table 4).

Table 2: Demographic characteristics and comparison of laboratory parameters between cases and controls.

Characteristics	Cases (n=150)	Controls (n=150)	P value
	Mean±SD		
Age (years)	35.82±12.9	36.97±11.76	0.419
Gender (F M)	F>M	F=M	
Total duration (months)	117.88±105.58		
Smoking	34	31	0.39
Alcohol consumption	20	21	0.5
BMI (kg/m ²)	23.61±4.7	23.82±3.03	0.584
WC (cm)	90.71±10.89	89.15±6.7	0.136
SBP (mmHg)	124.98±8.49	122.36±6.6	0.003
DBP (mmHg)	80.71±5.59	80.31±4.63	0.501
TAG (mg/dl)	187.47±62.37	135.99±35.74	< 0.001
HDL (mg/dl)	49.25±11.53	50.88±8.24	0.159
CHOL (mg/dl)	174.98±55.97	177.41±42.93	0.673
VLDL (mg/dl)	38.18±14.98	38.08±12	0.951
LDL (mg/dl)	111.33±42.83	89.61±21.18	< 0.001
FBS (mg/dl)	97.86±16.61	92.36±6.9	< 0.001
FSIL (μU/l)	15.13±9.41	13.39±4.92	0.046
Metabolic syndrome	74 (49.3%)	23 (15.3%)	< 0.001

Table 3: Comparative analysis of metabolic syndrome and its components in cases and controls.

Characteristics	Cases (%)	Controls (%)	OR (95% CI)	P value
Metabolic syndrome	74 (49.3)	23 (15.3)	5.37 (3.1-9.3)	< 0.001
TAG≥150 mg/dl	110 (73.3)	34 (22.6)	9.3 (5.5-15)	< 0.001
FBS≥100 mg/dl	46 (30.7)	17 (11.3)	3.46 (1.87-6.38)	< 0.001
HDL (mg/dl) <40 males, <50 females	78 (52)	46 (30.7)	2.45 (1.52-3.92)	< 0.001
SBP ≥130 mmHg	42 (28)	19 (12.7)	2.68 (1.47-4.87)	0.001
DBP ≥85 mmHg	34 (22.7)	20 (13.3)	1.9 (1.03-3.5)	0.025
WC ≥102 cm males, ≥88 females	64 (72.7)	34 (71.3)	2.54 (1.53-4.19)	< 0.001

Table 4: Association of metabolic syndrome and vitiligo duration.

Metabolic syndrome	Total duration (years)		OR (95%	P value	
	<5	≥5		value	
Yes	20	54	0.635	0.133	
No	28	48	(0.317-1.27)	0.133	

Metabolic syndrome and vitiligo activity

Among vitiligo cases mean VIDA score was 3.3 ± 1.1 . Metabolic syndrome was more frequent in VIDA subgroup 3 {71 (47.3%)} and was statistically significant (p \leq 0.001) (Figure 1).

Components of metabolic syndrome and its comparison with different clinical vitiligo patterns

In our study the predominant pattern was vitiligo vulgaris in 123 (82%), segmental vitiligo in 12 (8%), acrofacial vitiligo in 9 (6%), focal vitiligo in 4 (2.6%) and vitiligo universalis in 2 (1.3%). Majority, 62 (83.7%) patients with metabolic syndrome had vitiligo vulgaris as the most common pattern. This was followed by segmental vitiligo 6 (8.3%), acrofacial (AF) vitiligo 4 (5.5%) and 1 patient

each having metabolic syndrome with focal vitiligo (FV) as well as vitiligo universalis (U) pattern 1 (1.3%). The mean age of the patients with different pattern of vitiligo was comparable amongst all groups. The mean SBP (125.57±9 mm of Hg) was statistically significantly raised among vitiligo vulgaris pattern (p=0.017). Also, the triglycerides and LDL were significantly raised in vitiligo universalis pattern (Table 5).

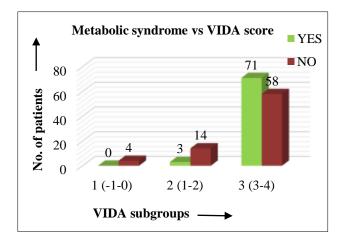


Figure 1: Metabolic syndrome among VIDA subgroups.

Table 5: Components of metabolic syndrome and its comparison with different clinical vitiligo patterns.

n=150	AF (9)	FV (4)	SV (12)	U (2)	VV (123)	P
	Mean±SD					value
Age (years)	31±13.45	32±6.16	30±8.16	34.5±14.8	36.95±13.19	0.297
VIDA	2.56±1.59	3±0.81	3.08±1.44	4±00	3.37±1.03	0.189
SBP (mmHg)	122.22±4.52	119±2.58	123.16±5.14	124±8.48	125.57±9	0.017
DBP (mmHg)	80.22±4.41	78±4.32	81.5±6.37	76±5.65	80.83±5.65	0.599
BMI (kg/m ²)	23.5±6.3	23.77±4.98	22.93±6.43	25.2±4.94	23.65±4.46	0.034
WC (cm)	85.33±15.36	89.5±15.41	90.75±11.34	86.5±16.26	91.21±10.35	0.282
HDL (mg/dl)	46.88±6.56	64±16.65	44.33±7.5	49±9.89	49.43±11.69	0.14
CHOL (mg/dl)	151.11±47.2	146.5±34.54	176.91±74.69	168.5±17.67	177.56±55.39	0.561
TAG (mg/dl)	169.56±63.07	174.5±63.14	179.2±40.57	224.5±112.43	190.21±63.67	< 0.001
VLDL (mg/dl)	46.55±14.94	63.6±41.15	41.66±18.26	33±1.41	36.49±12.53	0.001
LDL (mg/dl)	117.77±26.29	75.29 ± 24.83	123.16±25.64	138±86.26	110.44±44.58	< 0.001
FBS (mg/dl)	98.11±7.76	99.25±11.14	95.08±10.99	97±1.41	98.08±17.84	0.014
Metabolic syndrome	4 (5.4%)	1 (1.3%)	6 (8.1%)	1 (5.4%)	62 (83.7%)	< 0.001

DISCUSSION

Metabolic syndrome is complex of risk factors for cardiovascular, diabetes mellitus, stroke and myocardial infarction. In addition to the fact that the melanocytes are present in the skin and hair follicles, they are also found in adipose tissue. Melanocytes of adipose tissue participate in anti-inflammatory reactions in conjunction with abatement of ROS. Here they act as a scavenger of free radicals. Thus, drop in melanocyte number and decline in the process of melanogenesis in adipose tissue impart in increased production of oxidative species which plays a significant role in pathogenesis of metabolic disturbance

in vitiligo patients. Pietrzak et al in their investigative report found lipid disturbances among young vitiligo children. Noël et al found out that statins impede the production of IFN γ and expression of major histocompatibility complex in vitiligo patients. Thus, they illustrated that statins (immune modulating medications) may contribute in the treatment of vitiligo patients. The endogenous melanogenic peptide i.e., α -melanocyte stimulating hormone (α -MSH) bind to melanocortin 1 receptor (MC1R) on human adipocytes and triggers melanogenesis in them. The serum levels of endogenous melanogenic peptide are higher in obese individuals. The serum levels of endogenous melanogenic peptide are higher in obese individuals.

Our vitiligo patients had mean age of 35.82±12.9 years (102 (68%) found in age between 21-40 years) and control group had mean age of 36.97±11.76 years. Also, the predominant age group among our vitiligo cases having metabolic syndrome was 21-40 years (i.e., in 49 out of 74). Hence our findings concluded that age less than 40 years was a predisposition for metabolic syndrome among vitiligo patients. In our study 57 females and 17 males had metabolic syndrome with F:M=3.3:1. We observed female preponderance in vitiligo patients with metabolic syndrome. Ataş et al also reported higher female prevalence in their subjects with metabolic syndrome. 16 The mean WC of cases (90.71±10.89 cm) was not statistically different from that of controls (89.15±6.7cm) (p=0.136) which was in agreement with Sharma et al and Karadag et al. 17,18 A case control study done by Ataş et al found significantly increased mean level of TAG (157.9±70.02 mg/dl) among vitiligo cases having metabolic syndrome.¹⁶ In our study participants serum triglycerides were significantly raised (187.47±62.37 mg/dl) compared to controls (135.99±35.74 mg/dl). We delineated higher mean LDL levels (111.33±42.83 mg/dl) in cases as compared to controls (89.61±21.18 mg/dl) however, mean cholesterol (174.98±55.97 mg/dl) and VLDL (38.18±14.98 mg/dl) did not show statistical significance when compared with healthy controls (177.41±42.93) and (38.08±12) respectively. In our study mean HDL was 49.25±11.53 mg/dl in cases and 50.88±8.24 mg/dl in controls did not show statistically significant difference which was in congruence with the study done by Tancan et al.¹⁹ Dysfunction of sympathetic nervous system affect production of melanin; thus, sympathetic efflux may develop hypertension in vitiligo patients.²⁰ Our vitiligo participants had statistically significant mean SBP (124.98±8.49 mm of Hg) versus controls (122.36 \pm 6.6 mm of Hg) (p=0.003). Singh et al had observed prevalence of hypertension among vitiligo patients (40%) as compared to controls (3.3%).²¹ We found significant elevation in SBP (≥130 mmHg) {OR=2.68; 95% CI (1.47-4.87); p=0.001} and DBP (≥85 mmHg) {OR=1.9; 95% CI (1.03-3.5); p=0.025} in patients with vitiligo as compared to controls. The mean FBS was (97.86±16.61 mg/dl) statistically significantly higher among vitiligo cases as compared to controls (92.36±6.9 mg/dl) (p=0.002). We also found statistical significant association of FBS (≥100 mg/dl) in vitiligo cases having as compared to controls {OR 3.46; 95% CI (1.87-6.68); p<0.001}. Our findings were in congruence with Sharma et al.17 We observed that metabolic syndrome was associated with vitiligo (74 (49.3%) versus 23 (15.3%) {OR 5.37; 95% CI (3.1-9.3)}. Ataş et al demonstrated increased prevalence of metabolic syndrome among patients with vitiligo 24 (38.1%) as compared to controls 14 (21.5%) (p=0.04). 16 Sixty-two (87.3%) patients of metabolic syndrome had vitiligo vulgaris as the commonest pattern in our study. Moreover, the frequency of metabolic syndrome increased as the activity of vitiligo increased as evident by presence of 71 (47.3%) vitiligo patients in the VIDA subgroup C (VIDA score 3-4) (p=0.002). Thus, our findings were congruous with

previous studies.^{16,19} We did not observed association between segmental vitiligo and metabolic syndrome on the other hand various previous studies reported that segmental vitiligo was associated with increased risk of developing metabolic syndrome.¹⁶

Metabolic syndrome is a global epidemic and established risk factor for atherosclerotic and nonatherosclerotic cardiovascular disease. Various stimuli culminating in a state of chronic inflammation seem to be the main pathophysiological drivers for metabolic syndrome.²² TNF-α, IL-6 and IL-1 are the proinflammatory cytokines playing a role in the vitiligo pathogenesis and are similarly associated with insulin resistance, atherosclerosis and other metabolic complications. 11 We found association of metabolic syndrome among vitiligo patients. In addition, our study also found that in non-segmental vitiligo frequency of metabolic syndrome was higher as compared to another pattern. Furthermore, frequency of metabolic syndrome increased as activity of vitiligo increased in our study. Therefore, screening of the vitiligo patients for metabolic syndrome should be considered. Targeting younger population to control risk factors thus preventing development of metabolic syndrome and long term follow up of vitiligo should be the target of dermatologist dealing with vitiligo patients. Early diagnosis and treatment of metabolic syndrome may help in reducing cardiovascular morbidity and mortality in vitiligo patients.

Limitations

The study is limited by small number of patients and case control design. Additional studies are needed to establish role of vitiligo severity and activity as an independent risk factor for developing metabolic syndrome, atherosclerosis and myocardial infarction. Long term clinical follow up was not part of our study. Also, the role of vitiligo treatment in altering the risk of developing these serious co-morbidities needs to be evaluated.

CONCLUSION

The study shows that association of metabolic syndrome among vitiligo patients has now increased attention in understanding its oxidative stress pathogenesis. In addition, the study also found that in non-segmental vitiligo, frequency of metabolic syndrome was higher as compared to another pattern. Furthermore, frequency of metabolic syndrome increased as activity of vitiligo increased in the study. Thus, early evaluation of metabolic syndrome in vitiligo patients may aid in appropriate management and improved quality of life. However, better designed, more systematic and large prospective studies are needed for further understanding.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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