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Original Research Article

Comparative Cross-Sectional Study of Metabolic Syndrome Among Patients with Vitiligo and Healthy Controls

Muhammed Mukhtar

Assistant Professor, Department of Dermatology, Katihar Medical College, Katihar, Bihar, India

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Corresponding Author: Dr. Muhammed Mukhtar
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Abstract:

Background: Vitiligo is a chronic autoimmune depigmentary disorder that has increasingly been associated with systemic inflammation and metabolic abnormalities. Emerging evidence suggests a possible relationship between vitiligo and metabolic syndrome, which may increase the risk of cardiovascular diseases and type 2 diabetes mellitus. However, data regarding this association remain limited, particularly in the Indian population.

Aim: Comparing the prevalence of metabolic syndrome among patients with vitiligo and healthy controls attending a tertiary care hospital in Katihar, Bihar.

Methodology: A hospital-based comparative cross-sectional study was conducted over a period of one year among 85 participants, including 43 clinically diagnosed patients with vitiligo and 42 age- and sex-matched healthy controls. Demographic details, anthropometric measurements, blood pressure, and fasting biochemical parameters were recorded. Metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. Data were analyzed using SPSS version 26.0, and a p-value <0.05 was considered statistically significant.

Results: Patients with vitiligo demonstrated significantly higher body mass index, waist circumference, fasting blood glucose, blood pressure, triglycerides, total cholesterol, and LDL cholesterol, while HDL cholesterol levels were significantly lower than those of healthy controls ($p < 0.05$). Metabolic syndrome was identified in 41.9% of patients with vitiligo compared with 16.7% of healthy controls, showing a statistically significant association ($p = 0.011$).

Conclusion: Patients with vitiligo exhibited a significantly higher prevalence of metabolic syndrome and its individual components than healthy controls. Routine metabolic screening in patients with vitiligo may facilitate early identification of cardiovascular risk factors and support timely preventive interventions.

Keywords: Vitiligo, Metabolic Syndrome, Cross-Sectional Study, Cardiovascular Risk, Dyslipidemia, Insulin Resistance, NCEP ATP III.

Introduction

Vitiligo is a chronic acquired pigmentary disorder, but the major difference is that it involves the selective destruction of the functional melanocytes leaving well-defined depigmented macules and patches on the skin and hair follicles. It is one of the most prevalent pigmentary disorders in the world, occurring in around 0.5 - 2% of the population, regardless of sex, age or ethnicity. Vitiligo clinically affects exposed areas of the skin, including the face, hands, neck and extremities, but can affect any area of skin. The lesions can continue to grow and eventually fuse together causing cosmetic disfigurement and severe psychosocial issues, such as anxiety, depression, low self-esteem and diminished quality of life [1]. Vitiligo is mainly divided into three categories, namely non-segmental, segmental and unclassified based on clinical presentation. Non-segmental vitiligo is the most common form and is associated with bilateral symmetrical patches, a stronger association with autoimmune diseases, while segmental vitiligo is generally unilateral and with a weak association with systemic autoimmune diseases [2].

The exact cause of vitiligo is not completely known but the available information indicates that it is a multifactorial disease with potential genetic susceptibility, autoimmune factors, oxidative stress, neural dysfunction, and environmental factors being involved [3]. The main pathogenic mechanism is assumed to be autoimmune destruction of melanocytes by CD4+ and CD8+ T lymphocytes against melanocyte-specific antigens. Several pro-inflammatory cytokines have been associated with the onset and development of melanocyte damage, such as tumour necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ), interleukins (IL-1, IL-6, IL-10 and IL-17). The inflammatory mediators not only play a role in depigmentation but also affect systemic immune ac-

tivation, indicating that vitiligo is not just a skin disorder and should be viewed as a systemic inflammatory disease instead.

In addition, autoimmune diseases like autoimmune thyroid disorders, type 1 diabetes mellitus, pernicious anemia, rheumatoid arthritis, systemic lupus erythematosus, Addison's disease, and Guillain Barré syndrome are more common in patients with vitiligo, as well as in their first-degree relatives, showing the common autoimmune nature of these diseases [4]. Chronic systemic inflammation that accompanies vitiligo could have a wider clinical impact, even beyond the autoimmune conditions, as suggested by growing evidence and association with metabolic abnormalities [5]. Of these, metabolic syndrome (MetS) has been the subject of a lot of interest, as it is linked to higher cardiovascular morbidity and mortality. Metabolic syndrome is a combination of metabolic risk factors that are interrelated, such as central obesity, insulin resistance, dyslipidaemia, hypertension and impaired glucose metabolism, which together increase the risk of type 2 diabetes mellitus and cardiovascular disease. There are a number of internationally accepted diagnostic criteria for MetS diagnosis, such as the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, the International Diabetes Federation (IDF) criteria, and the Harmonized criteria from international organizations to standardize the diagnostic definition across different populations [6].

Although there are slight differences in the diagnostic criteria, all these criteria consistently define insulin resistance, visceral adiposity, endothelial dysfunction, chronic inflammation and lipid abnormalities as major factors in metabolic syndrome. According to estimates, almost a quarter of the adult population of the world meet the criteria for the diagnosis of MetS, making it one of the most important public health problems in the world [7]. Along with cardiovascular disease and diabetes mellitus, non-alcoholic fatty liver disease, chronic kidney disease, hepatocellular carcinoma, and polycystic ovary syndrome are other chronic disorders that have been linked to metabolic syndrome. Vitiligo has been recognized as a potentially important area of clinical research because of the inflammatory and immunological mechanisms shared by both, which may be why it is believed to be linked to metabolic syndrome [8]. The chronic systemic inflammation that is observed in vitiligo can lead to insulin resistance, endothelial dysfunction and lipid metabolism abnormalities via a chronic activation of cytokines.

It has been well documented that elevated levels of circulating TNF-α (tumor necrosis factor alpha), IL-6 (interleukin 6), and IFN-γ (interferon gamma) can disrupt insulin signaling pathways, effecting glucose metabolism and metabolic abnormalities. Some studies have suggested that insulin resistance, dyslipidaemia, elevated waist circumference and changes in lipid profile are significantly increased in patients with vitiligo compared with healthy age- and BMI-matched controls [9]. In addition, it has been reported that vitiligo is connected to type 1 and type 2 diabetes mellitus. The association between vitiligo with type 2 diabetes is a biological possibility because both disorders have an autoimmune cause, but it is not the only factor involved in the disease process as metabolic dysfunction is also likely to be important [10]. Due to these observations, there is growing interest in the evaluation of metabolic syndrome in patients with vitiligo in order to allow the early detection of cardiovascular risk factors. Although the association between vitiligo and metabolic syndrome is increasingly emphasized, there is still controversy. A few investigators including Atas et al., found a statistically significantly higher prevalence of metabolic syndrome in vitiligo patients, while others like Sallam et al. did not find a statistically significant association [11].

These conflicting results might be due to differences in study populations, ethnic differences, sample size, disease duration, disease severity, and diagnostic criteria. However, in the recent past there have been some evidence suggesting that people with chronic and extensive non-segmental vitiligo, especially those with coexisting metabolic syndrome, have a significantly increased risk for cardiovascular disease, which highlights the need for early screening and preventive management. For this reason, dermatologists are more and more encouraged to recognize clinical signs of metabolic dysfunction, such as obesity, hypertension, dyslipidaemia, reduced glucose metabolism and dermatological features like acanthosis nigricans, and refer patients for prompt and multidisciplinary treatment [12].

The prevalence of metabolic syndrome in vitiligo patients in India, especially at the East parts of the country like Katihar, Bihar, is still not known. Regional differences in lifestyle, diet, socioeconomic status, and health care access could affect the prevalence of metabolic abnormalities, making it important to have locally derived evidence. So, the present comparative cross-sectional study was carried out to assess the prevalence of metabolic syndrome among vitiligo patients and compare it with healthy controls who visited a tertiary care hospital in Katihar, Bihar. The results of the present study could help elucidate the relationship between vitiligo and metabolic syndrome, facilitate early screening of high-risk individuals, and help in the formulation of holistic management plans for the prevention of potential cardiovascular and metabolic sequelae.

Methodology

Study Design: A hospital-based comparative cross-sectional study was conducted to compare the prev-

alence of metabolic syndrome among patients with vitiligo and healthy controls attending the Dermatology Outpatient Department of a tertiary care hospital in Katihar, Bihar, India.

Study Area: The study was carried out in the Department of Dermatology of a Katihar Medical College, Katihar, Bihar, India.

Study Duration: The study was conducted over a period of one year.

Sample Size

A total of 85 participants were enrolled in the study.

- Vitiligo cases: 43
- Healthy controls: 42

Healthy controls were selected from attendants and healthy volunteers and were age- and sex-matched with the case group.

Study Population: The study population comprised clinically diagnosed patients with vitiligo attending the Department of Dermatology at a tertiary care hospital in Katihar, Bihar, India, during the study period. Age- and sex-matched apparently healthy individuals without vitiligo or any known autoimmune disorder were recruited as the control group. A total of 85 participants were enrolled in the study, including 43 vitiligo patients (cases) and 42 healthy controls. Participants from both groups who fulfilled the inclusion criteria and provided written informed consent were included in the study.

Inclusion Criteria

Cases

- Patients aged 18 years or above.
- Clinically diagnosed cases of vitiligo confirmed by a dermatologist.
- Patients are willing to participate and provide written informed consent.

Controls

- Apparently healthy individuals aged 18 years or above.
- Age- and sex-matched with vitiligo patients.
- Individuals without vitiligo or any known autoimmune disease.
- Willing to provide written informed consent.

Exclusion Criteria

Participants were excluded if they

- were younger than 18 years,
- were pregnant or lactating women,
- had known diabetes mellitus diagnosed before the onset of vitiligo,
- had chronic kidney disease, chronic liver disease, malignancy, or severe systemic illness,
- were receiving systemic corticosteroids, immunosuppressive therapy, or lipid-lowering drugs,
- had any other autoimmune dermatological disorder,
- refused to participate in the study.

Data Collection: After obtaining written informed consent, detailed demographic and clinical information was collected from all participants using a predesigned structured case record form. Information regarding age, gender, residence, occupation, smoking status, alcohol consumption, family history, duration of vitiligo, and clinical subtype of vitiligo was recorded. Anthropometric measurements including height, weight, body mass index (BMI), and waist circumference were measured using standardized techniques. Blood pressure was measured after the participant had rested for at least five minutes, and the average of two readings was recorded. Following an overnight fast of 8–12 hours, approximately 5 mL of venous blood was collected under aseptic conditions for laboratory investigations. Biochemical parameters including fasting blood glucose (FBG), serum triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), total cholesterol, and low-density lipoprotein cholesterol (LDL-C) were analyzed using an automated biochemistry analyzer in the central laboratory. Metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria.

Study Procedure: Eligible participants attending the Dermatology OPD during the study period were screened according to the inclusion and exclusion criteria. After obtaining informed consent, detailed clinical history and physical examination were performed. Vitiligo was diagnosed clinically by an experienced dermatologist, and disease characteristics including subtype, duration, and body surface area involvement were documented. Healthy controls underwent the same clinical evaluation and laboratory investigations. Anthropometric measurements, blood pressure, and fasting biochemical parameters were assessed in both groups using identical protocols. The presence or absence of metabolic syndrome was determined according to the NCEP ATP III criteria, and the prevalence of metabolic syndrome along with its individual components was compared between vitiligo patients and healthy controls.

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Comparisons between vitiligo patients and healthy controls were performed using the Independent Student's t-test for continuous variables and the Chi-square test or Fisher's exact test, wherever appropriate, for categorical variables. The prevalence of metabolic syn-

drome and its individual components was compared between the two study groups. A p-value of less than 0.05 was considered statistically significant".

Result

Table 1 presents the baseline demographic characteristics of the study participants. A total of 85 participants were included, comprising 43 patients with vitiligo and 42 healthy controls. The mean age of vitiligo patients was 37.9 ± 11.4 years, while that of the control group was 36.8 ± 10.9 years, with no statistically significant difference between the groups ($p = 0.648$). Male participants constituted 55.8% of the vitiligo group and 54.8% of the control group, indicating comparable gender distribution ($p = 0.924$). The mean BMI was significantly higher among vitiligo patients (25.8 ± 3.7 kg/m²) compared to healthy controls (23.9 ± 3.2 kg/m²) ($p = 0.018$). Although smoking, alcohol consumption, and family history of diabetes were more common in the vitiligo group, these differences were not statistically significant ($p > 0.05$).

Table 1: Baseline Demographic Characteristics of Study Participants

Variables	Vitiligo (n=43)	Controls (n=42)	p-value
Age (years), Mean ± SD	37.9 ± 11.4	36.8 ± 10.9	0.648
Male, n (%)	24 (55.8)	23 (54.8)	0.924
Female, n (%)	19 (44.2)	19 (45.2)	
BMI (kg/m²), Mean ± SD	25.8 ± 3.7	23.9 ± 3.2	**0.018**
Smokers, n (%)	10 (23.3)	7 (16.7)	0.445
Alcohol consumers, n (%)	9 (20.9)	6 (14.3)	0.418
Family history of diabetes, n (%)	12 (27.9)	8 (19.0)	0.335

Table 2 summarizes the clinical profile of the 43 patients with vitiligo. The mean duration of disease was 6.4 ± 3.8 years. The majority of patients (62.8%) had generalized vitiligo, followed by segmental vitiligo (25.6%) and focal vitiligo (11.6%). A positive family history of vitiligo was observed in 20.9% of patients. Nearly 41.9% of patients had body surface area involvement greater than 10%, while 60.5% had stable disease and 39.5% had progressive disease during the study period.

Table 2: Clinical Characteristics of Patients with Vitiligo (n=43)

Variables	Value
Duration of disease (years), Mean ± SD	6.4 ± 3.8
Generalized vitiligo, n (%)	27 (62.8)
Segmental vitiligo, n (%)	11 (25.6)
Focal vitiligo, n (%)	5 (11.6)
Family history of vitiligo, n (%)	9 (20.9)
Body surface area involved >10%, n (%)	18 (41.9)
Stable disease, n (%)	26 (60.5)
Progressive disease, n (%)	17 (39.5)

Table 3 compares the metabolic parameters between vitiligo patients and healthy controls. Vitiligo patients had a significantly higher mean waist circumference (91.8 ± 10.5 cm vs. 86.7 ± 8.9 cm; $p = 0.021$). Both systolic (128.6 ± 14.3 mmHg) and diastolic (82.3 ± 8.7 mmHg) blood pressure values were significantly higher among vitiligo patients compared with controls (121.4 ± 11.2 mmHg and 78.6 ± 7.5 mmHg, respectively; $p < 0.05$). Similarly, fasting blood glucose (108.5 ± 24.6 mg/dL), serum triglycerides (171.2 ± 42.5 mg/dL), LDL cholesterol (126.8 ± 29.5 mg/dL), and total cholesterol (196.4 ± 34.7 mg/dL) were significantly elevated in the vitiligo group. In contrast, HDL cholesterol levels were significantly lower among vitiligo patients (41.6 ± 8.2 mg/dL) than healthy controls (47.5 ± 7.4 mg/dL) ($p = 0.001$). These findings indicate that vitiligo patients exhibited a less favorable metabolic profile compared to healthy individuals.

Table 3: Comparison of Metabolic Parameters Between Study Groups

Parameters	Vitiligo (n=43) Mean ± SD	Controls (n=42) Mean ± SD	p-value
Waist circumference (cm)	91.8 ± 10.5	86.7 ± 8.9	**0.021**
Systolic BP (mmHg)	128.6 ± 14.3	121.4 ± 11.2	**0.014**
Diastolic BP (mmHg)	82.3 ± 8.7	78.6 ± 7.5	**0.041**
Fasting Blood Glucose (mg/dL)	108.5 ± 24.6	96.7 ± 17.8	**0.011**
Triglycerides (mg/dL)	171.2 ± 42.5	142.6 ± 35.8	**0.002**
HDL Cholesterol (mg/dL)	41.6 ± 8.2	47.5 ± 7.4	**0.001**

LDL Cholesterol (mg/dL)	126.8 ± 29.5	112.3 ± 25.6	**0.019**
Total Cholesterol (mg/dL)	196.4 ± 34.7	181.8 ± 29.2	**0.037**

Table 4 demonstrates the distribution of individual components of metabolic syndrome among the study groups. Increased waist circumference was observed in 51.2% of vitiligo patients compared with 28.6% of healthy controls (p = 0.034). Elevated blood pressure was present in 41.9% of cases versus 23.8% of controls (p = 0.047). Elevated fasting blood glucose was significantly more common in the vitiligo group (39.5%) than in controls (19.0%) (p = 0.039). Likewise, elevated triglycerides were detected in 48.8% of vitiligo patients compared with 23.8% of controls (p = 0.018). Reduced HDL cholesterol was the most frequent abnormality, affecting 55.8% of vitiligo patients versus 26.2% of healthy controls (p = 0.006). Overall, all individual components of metabolic syndrome were significantly more prevalent among patients with vitiligo.

Table 4: Comparison of Individual Components of Metabolic Syndrome

Components	Vitiligo (n=43)	Controls (n=42)	p-value
Increased waist circumference	22 (51.2%)	12 (28.6%)	**0.034**
Elevated blood pressure	18 (41.9%)	10 (23.8%)	**0.047**
Elevated fasting blood glucose	17 (39.5%)	8 (19.0%)	**0.039**
Elevated triglycerides	21 (48.8%)	10 (23.8%)	**0.018**
Reduced HDL cholesterol	24 (55.8%)	11 (26.2%)	**0.006**

Table 5 shows the overall prevalence of metabolic syndrome among the study participants. Metabolic syndrome was diagnosed in 18 (41.9%) patients with vitiligo compared to 7 (16.7%) healthy controls. Conversely, 58.1% of vitiligo patients and 83.3% of controls did not meet the diagnostic criteria for metabolic syndrome. The difference in prevalence between the two groups was statistically significant (p = 0.011), indicating that patients with vitiligo had a significantly higher burden of metabolic syndrome than healthy individuals. These findings suggest a significant association between vitiligo and metabolic syndrome, highlighting the importance of routine metabolic screening in patients with vitiligo.

Table 5: Prevalence of Metabolic Syndrome Among Study Groups

Metabolic Syndrome	Vitiligo (n=43)	Controls (n=42)	p-value
Present	18 (41.9%)	7 (16.7%)	**0.011**
Absent	25 (58.1%)	35 (83.3%)	

Discussion

This comparative, cross sectional study was done to assess the prevalence of metabolic syndrome in patients of vitiligo and compare it with healthy controls of a tertiary care hospital, Katihar, Bihar. The results showed that the number of patients with vitiligo was significantly higher than healthy controls with respect to the prevalence of metabolic syndrome and its components. This observation confirms the idea that vitiligo is not just a cosmetic depigmentary disease but may also be linked to some systemic metabolic abnormalities and higher risk of cardiovascular disease [13]. Both groups were comparable with respect to the baseline demographic parameters (age and gender distribution) which would ensure adequate matching and minimize the potential for confounding. Patients with vitiligo, however, had significantly higher mean body mass index (BMI), however".

The difference doesn't seem to indicate an increased tendency for metabolic imbalance, but the average BMI was still in the overweight range in these patients. These results are in line with the results of the previous studies, but some have reported a lack of significance in BMI. These differences can be explained by ethnicity, lifestyle, diet and study population differences [14]. The present study also showed that the patients with vitiligo had significantly elevated levels of WC, SBP, DBP, FBS, serum TG, TC, and LDL-C, while the HDL-C was significantly decreased in comparison with healthy controls. The results suggest that patients with vitiligo have several metabolic abnormalities in common.

This finding is consistent with that of previous case control and cross-sectional studies that reported significantly higher fasting glucose levels and dyslipidaemia among vitiligo patients. Higher fasting blood glucose could be an initial sign of insulin resistance, one of the main processes involved in metabolic syndrome. Vitiligo is associated with chronic low-grade inflammation that could affect insulin signaling and glucose metabolism and lead to the development of diabetes mellitus [15]. Another significant finding of the present study was lipid abnormalities. Vitiligo patients were found to have significantly higher levels of triglycerides, LDL cholesterol and total cho-

lesterol and significantly lower HDL cholesterol. Likewise, the previous studies conducted to assess metabolic disturbances in Vitiligo found similar lipid disturbances.

Dyslipidemia has been recognized as a strong risk factor for atherosclerosis and cardiovascular disease. However, lower HDL is especially significant since HDL cholesterol has a protective effect on the cardiovascular system via its reverse cholesterol transport and anti-inflammatory activity. Thus, high LDL and low HDL levels can increase patients with vitiligo's cardiovascular risk [16]. These observations were further corroborated by separation of the individual components of metabolic syndrome. The waist circumference was significantly higher, blood pressure was significantly higher, fasting blood glucose was significantly higher, triglyceride level was significantly higher, and HDL level was significantly lower in the patients with vitiligo than healthy controls. Of these, the most frequent abnormalities were decreased HDL cholesterol and increased waist circumference. The metabolic changes described here have been previously described, with the main metabolic changes being abdominal obesity and dyslipidemia in previous studies. The results indicate that the regular screening of each individual component of the metabolic syndrome may help to detect high-risk patients earlier than the occurrence of clinically important cardiovascular disease [17].

The most interesting results of this study were that patients with vitiligo presented with significantly more metabolic syndrome. The prevalence of metabolic syndrome in patients with vitiligo was 41.9% and 16.7% among healthy controls, respectively, suggesting a significant disease association between vitiligo and metabolic syndrome. These results were similar to those of several previous studies that have found that patients with vitiligo more often have metabolic syndrome than healthy control subjects of similar age and sex. Some studies, however, have not been able to show this. These discrepancies can be due to variations in the number of patients studied, diagnostic criteria, severity of vitiligo, disease duration, and environmental factors. However, most of the evidence available is in favor of higher rates of metabolic abnormalities in people with vitiligo [18].

Shared pathogenetic mechanisms could explain this association between vitiligo and metabolic syndrome. Vitiligo is an autoimmune condition with sustained inflammation of the systemic system. The production of pro-inflammatory cytokines (such as tumour necrosis factor (TNF- α), Interleukin-1 (IL-1), Interleukin-6 (IL-6), Interferon gamma (IFN-γ) and Interleukin-17 (IL-17)) leads to melanocyte destruction and, at the same time, to insulin resistance, endothelial dysfunction, oxidative stress and lipid abnormalities. Loss of melanocytes alone can increase microvascular damage and also metabolic disturbances, which can further exacerbate the oxidative stress. It is suggested that these common inflammatory pathways may explain why patients with vitiligo are more prone to developing metabolic syndrome [19].

The results of the present study emphasize the need to appreciate vitiligo as a systemic disease and not a skin disease. It is recommended to monitor BMI, waist circumference, blood pressure, fasting blood glucose and lipid profile regularly which may lead to early detection of metabolic syndrome and lower long-term risks of cardiovascular disease and type 2 diabetes mellitus. Therefore, dermatologists should work and coordinate with physicians and endocrinologists for complete management of patients with vitiligo. The present study offers valuable evidence; however, the findings are limited by the cross-sectional design, small sample size, and single center study design, and do not allow for generalizability and causation. Hence, larger multicentric prospective studies with longer follow-up are justified to further elucidate the correlation between vitiligo and metabolic syndrome and also the benefits of early metabolic screening of these patients.

Conclusion

The present comparative cross-sectional study showed that there was a significant higher prevalence of metabolic syndrome and its individual components in the vitiligo patients than in healthy controls. Patients with vitiligo had more metabolic abnormalities, such as increased waist circumference, high blood pressure, high fasting blood glucose, dyslipidaemia and lower HDL cholesterol, indicating a higher risk of cardiovascular disease and type 2 diabetes mellitus in the future. The results indicate that vitiligo is not a limited pigmentary condition but may also involve metabolic changes in the systemic level. So, periodic screening for metabolic syndrome and its components should be considered as part of the comprehensive clinical evaluation of patients with vitiligo to achieve early diagnosis, timely intervention and prevention of long-term cardiovascular complications. Additional large prospective multicentric studies are recommended to validate these findings, and to determine the underlying mechanisms of the relationship between vitiligo and metabolic syndrome.

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