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Original Research Article

# Relationship of Metabolic Syndrome and Insulin Resistance in Papulosquamous Diseases

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**Abstract:**

**Background and Aim:** There is a significant connection between metabolic syndrome (MetS), insulin resistance (IR), and papulosquamous diseases. These conditions share a common pathophysiology and contribute to the accumulation of risk factors for non-communicable diseases such as cardiovascular disease (CVD) and type 2 diabetes (T2D). This has resulted in a high mortality rate globally. This cross-sectional study aimed to analyze the relationship between MetS and IR in papulosquamous diseases.

**Material and Methods:** A total of eighty patients, aged between 20 and 50 years, who were seeking treatment for papulosquamous diseases, were included in this study conducted at the dermatology outpatient department. A group of eighty control subjects, who were matched in terms of age and sex, were selected for this study. These individuals had no personal history of dermatological disorders and were either hospital employees or patients' attenders. The diagnosis of MetS was made using the criteria from the National Cholesterol Education Program's Adult Treatment Plan III, with the Asian modification for measuring abdominal circumference. FI was utilized as a surrogate marker of insulin resistance, commonly used in health journalism.

**Results:** The results showed no significant statistical difference in age, sex, height, and weight between the cases and controls. The mean serum HDL-C level was found to be low and statistically significant ($p<0.05$). The fasting plasma glucose level in patients was found to be significantly higher ($p<0.05$). The mean FI level showed a significant difference between the cases and controls ($p<0.05$). In 74% of cases, IR was found, which was significantly higher than in controls ($p<0.05$). The prevalence of MetS was found to be 30% in cases and 20% in controls, but this difference did not reach statistical significance.

**Conclusion:** Cases with papulosquamous diseases were found to have MetS and IR. In our study, we found that there were several significant parameters to consider. These included an increased fasting glucose level, raised FI, and low HDL-C. There is a positive correlation between IR and MetS. Having elevated FI levels can indicate insulin resistance, which in turn can increase the likelihood of developing metabolic syndrome.

**Keywords:** Insulin Resistance, Metabolic Syndrome, Papulosquamous Diseases, Type 2 Diabetes Mellitus.



## Introduction

Metabolic syndrome (MetS) is linked to a collection of unfavorable metabolic risk factors, such as excess body fat around the waist, glucose intolerance, pre-morbid hypertension, and dyslipidemia. [1-3] Several studies have found a link between MetS and an increased risk of developing type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and other health issues.

MetS is characterized by a combination of metabolic risk factors, such as excess body fat around the waist, glucose intolerance, pre-morbid hypertension, and dyslipidemia. Metabolic syndrome (MetS) is a significant concern among non-communicable diseases (NCDs), affecting a considerable percentage of the global population, ranging from 12.5% to 31.4%. MetS, also referred to as "insulin resistance syndrome" or "syndrome X," is a collection of conditions that includes dyslipidemia, hypertension, abdominal obesity, and high blood glucose. These factors combined increase the likelihood of developing various severe health issues, including cardiovascular diseases, type 2 diabetes, and even mortality. [4,5]

There are various criteria used to diagnose MetS, including those utilized by the World Health Organization, National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP

III), and the International Diabetes Federation (IDF). These criteria may have slight differences from one another. Several studies have highlighted the link between Metabolic Syndrome (MetS) and an increased risk of developing type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and various other non-communicable diseases (NCDs). Metabolic syndrome, a condition affecting many individuals, poses a significant threat to personal well-being. There are 8-12 communicable diseases (NCDs). [6,7] The increasing occurrence of MetS presents a concerning obstacle to individual well-being. [8,9] One widely used criterion is the ATP III with Asian modification for abdominal circumference, which is commonly used worldwide. You need to have at least three of the following: Abdominal obesity is a condition that many people struggle with. For men, a waist circumference of 90 cm or more, and for women, a waist circumference of 80 cm or more, is considered a cause for concern. Triglyceride levels of 150 mg/dl or higher are considered elevated, while HDL cholesterol levels below 40 mg/dl for men and below 50 mg/dl for women are considered reduced. Blood pressure is considered elevated if the systolic reading is 130 mmHg or higher, or if the diastolic reading is 85 mmHg or higher. Fasting blood glucose levels of 100 mg/dl or higher are considered elevated. [10]

Papulosquamous diseases encompass a diverse range of conditions that are characterized by the presence of scaly papules and plaques. There are several skin conditions that fall under this category, such as psoriasis, lichen planus (LP), pityriasis rubra pilaris (PRP), parapsoriasis, lichen nitidus, and lichen striatus (LS). [1] Several chronic dermatological conditions, such as psoriasis and LP, often involve common underlying mechanisms, including persistent inflammation, oxidative stress, and endocrine imbalances. [11]

The impaired metabolic response of insulin results in a failure to stimulate glucose uptake into skeletal muscle and adipose tissue, as well as a failure to suppress hepatic gluconeogenesis and glucose release into circulation. [12] The role of serum insulin in the homeostasis and physiology of the skin is significant. Previous research has found a connection between insulin resistance and conditions such as acanthosis nigricans, acne, and psoriasis. [13] In recent years, there has been a concerning rise in the worldwide prevalence of MetS. Metabolic syndrome affects a significant portion of the adult population in developed countries, with around one-third being affected. In India, approximately 18.3% of the population is affected by MetS. There is a lack of clinical trials focusing on papulosquamous diseases other than psoriasis and their connection to MetS. Therefore, examining the link between MetS and IR in papulosquamous diseases is crucial for identifying the early risk of cardiovascular disease and type 2 diabetes. Conducting a cross-sectional study, we aimed to examine the correlation between MetS and IR in papulosquamous diseases.

## Material and Methods

Conducted at a prestigious Tertiary Care Teaching Institute in India, this hospital-based case-control study spanned duration of one year. A total of 80 patients between the ages of 20 and 50, who were seeking treatment for papulosquamous diseases, were included in the study. A group of eighty healthy control subjects, matched for age and sex, were recruited for the study. These individuals had no personal history of dermatological disorders and were either hospital employees or patients' attenders. All the recruited subjects provided written informed consent. Individuals undergoing treatment for skin diseases, diabetes, hypertension, dyslipidemias, as well as pregnant and lactating women were not included in the study. A pre-validated, semi-structured questionnaire was used to collect socio-demographic and clinical profile data from the subjects. Diagnosing papulosquamous diseases primarily relied on a comprehensive clinical history and examination. A skin biopsy was performed if there was any uncertainty regarding the lesion. The study received approval from the institutional research and ethical committee.

The diagnosis of MetS was determined using the national cholesterol education program's- adult treatment plan III with Asian modification for abdominal circumference criteria.4 There are various ways to diagnose IR, and in this case, we utilized fasting serum insulin levels as a means to measure it.

### Measurement of various parameters

The height measurement was taken by attaching a measuring tape to the wall. The weight in kilograms was measured using an electronic weight scale, while the waist circumference in centimeters was measured at the level of the iliac crest using a measuring tape. The measurements were taken by a single observer while the subject was standing. The calculation for body mass index (BMI) involves dividing weight in kilograms by the square of height in meters. According to the Asia-Pacific guidelines, obesity is classified based on different ranges. The normal range is 18.5-22.9, while the overweight range is 23-24.9. Anything equal to or above 25 falls into the obesity category.[14]

Patient was seated and their blood pressure was measured using a sphygmomanometer. The subjects' venous blood was collected after a 12-hour fasting period. The fasting plasma glucose was measured using the Glucose oxidase-

peroxidase (GOD-POD) method, while total triglycerides (TG) were measured using an enzymatic method. Measuring serum high density lipo-protein-C (HDL-C) involves using phosphotungstate precipitation, followed by an enzymatic method. The parameters were analyzed using a fully automated analyzer. FI was determined using a hormone analyzer in a clinical laboratory improvement amendments (CLIA) compliant facility.

**Statistical analysis**

The recorded data was organized and inputted into a spreadsheet computer program (Microsoft Excel 2019) and then transferred to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described using statistical measures such as means and standard deviations, or median and interquartile range, depending on their distribution. The presentation of qualitative variables was in the form of counts and percentages. Confidence level and level of significance were set at 95% and 5% respectively for all tests.

**Results**

The study included a total of 80 subjects, with cases and controls matched for age and sex. The enrolled subjects had a male-to-female ratio of 1.4:1. The average age of the cases and controls was 44.5±4.5 and 43.8±3.4, respectively. There were no notable statistical differences in age, sex, height, and weight between the cases and controls. The average BMI and waist circumference in cases was similar to that of controls ($p>0.05$) (Table 1). The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) of the cases were 120.5±9.2 mm Hg and 80.5±7.1 mmHg, respectively.

These values were not statistically significant compared to the controls, which had mean SBP and DBP of 118.4±9.1 mmHg and 79.8±6.2 mmHg, respectively. The mean serum HDL-C level was found to be significantly lower compared to the control group. The serum triglyceride levels were slightly higher in the control group compared to the cases, but this difference did not reach statistical significance. Patients had significantly higher fasting plasma glucose levels compared to controls. FI level was used as a surrogate marker for insulin resistance. The mean FI levels showed a significant difference between the cases and controls, as indicated in Table 1. In 74% of cases, IR was found, which was significantly higher than in controls ($p<0.05$). The prevalence of MetS was found to be 30% in cases and 20% in controls, but this difference was not considered statistically significant ($p>0.05$; Table 1).

The mean age of patients in the papulosquamous groups did not show any significant difference. The mean BMI showed no significant differences among the different groups ($p>0.05$; Table 2). There were no significant differences in waist circumference, SBP and DBP, and serum TG levels among the papulosquamous groups ($p>0.05$, Table 2). The mean plasma glucose levels among groups showed significant differences ($p>0.05$; Table 2). After conducting post hoc testing, it was found that the average plasma glucose level was higher in the LP group compared to the PRP group ($p>0.05$). The groups showed statistically significant differences in mean serum HDL-C levels. The FI level showed a notable difference between the groups, as indicated by the statistical analysis ($p>0.05$; Table 2). After conducting post hoc testing, it was found that the mean FI level was higher in the LP group compared to the PRP group ($p<0.05$).

The incidence rate (IR) was highest in psoriasis at 28.5%, followed by LP at 22.5%, PRP at 18.5%, and LS at 6%. These differences were found to be statistically significant ($p<0.05$). MetS was most commonly observed in individuals with psoriasis (16.5%), followed by LP (8%), and was least prevalent in individuals with PRP and LS (2% and 1% respectively). Nevertheless, there were no notable variations observed among the papulosquamous groups ($p>0.05$; Table 2). There appears to be a direct link between insulin resistance (IR) and metabolic syndrome (MetS). The statistical significance level was found to be less than 0.05.

**Table 1: Study parameters in cases and controls, (n=80)**

| Variables | Cases | Controls | P value |
|---|---|---|---|
| Age (years) | 44.5 | 43.8 | 0.1 |
| BMI (kg/m2 ) | 22.2 | 23.2 | 0.22 |
| Waist circumference (cm) | 89.5 | 87.8 | 0.12 |
| Insulin resistance (%) | 74 | 26 | 0.02* |
| Metabolic syndrome assessed by NCEPATP III (%) | 30 | 20 | 0.45 |

**Statistically significance at p≤0.05**

**Table 2: Parameters in Papulosquamous group of diseases**

| Parameters | Psoriasis, (n=24) | Lichen planus, (n=18) | Pitirisis rubra pilaris (n=6) | Lichen stria-tus, (n=2) | P value |
|---|---|---|---|---|---|
| Age (years) | 42.5 | 42.8 | 41.5 | 38.4 | 0.09 |
| BMI (kg/m2 ) | 23.1 | 23.2 | 22.4 | 22.8 | 0.12 |
| Waist circumference (cm) | 87.5 | 87.9 | 87.2 | 88.5 | 0.88 |
| Serum HDL (mg/dl) | 45.3 | 39.7 | 43.4 | 44.7 | 0.02* |
| Insulin resistance (%) | 28.5 | 22.5 | 18.5 | 6 | 0.04* |
| Metabolic syndrome assessed by NCEPATP III (%) | 16.5 | 8 | 2 | 1 | 0.40 |

*** Indicate statistically significance at p≤0.05**

## Discussion

Given the rising global impact of MetS as a major health concern, researchers have conducted more studies in recent years to explore the connection between MetS and skin diseases. [14] MetS is a widely recognized non-communicable disease characterized by its adverse effects, including damage to vital organs, increased levels of glucose and blood lipids, and elevated blood pressure.50 Patients are at risk of developing type 2 diabetes and cardiovascular diseases, including atherosclerosis and hypertension. Insulin resistance is widely recognized as the fundamental pathophysiology of MetS. [13]

This study aimed to assess the relationship between components of MetS and IR in a group of papulosquamous diseases. No significant statistical differences were found in BMI, waist circumference, blood pressure, and serum TG between the cases and controls. There were no notable differences in the above parameters among the groups with papulosquamous diseases. In our study, the control group had slightly higher weight compared to the cases, although this difference was not found to be statistically significant. According to a study by Hashba et al, it was found that among patients without MetS, 28.8% were overweight and none were obese. [15] In the current scenario, it's worth noting that even patients who are not obese can be diagnosed with MetS. These individuals are often referred to as metabolically obese because they have a higher amount of visceral fat. [16]

The prevalence of MetS in different regions of India ranges from 11% to 41%. [17] According to a study by Wilson et al, it was found that a significant number of patients with Metabolic Syndrome (MetS) developed Coronary Artery Disease (CAD) and Type 2 Diabetes (T2D) during an 8-year follow-up period. [18] According to a study conducted among the urban population in South India, it was found that MetS had a prevalence rate of 27%. The study also revealed that the prevalence rate was slightly higher in females (28.1%) compared to males (26.4%). [19] These findings align with a recent systematic review and meta-analysis performed by Qiu et al. that examined the association between AGA and the risk of MetS across [19] studies. The pooled odds ratio was 3.46 (95% CI: 2.38-5.05, p<0.01). [20]

Metabolic syndrome was observed in 16.5% of individuals with psoriasis, 8% with LP, 2% with PRP, and 1% with LS. However, these findings did not reach statistical significance. On the other hand, research conducted by Kokpol et al and Owczarczyc-Suczonek et al discovered a higher occurrence of MetS in individuals with psoriasis compared to the general population. [21,22] According to a study conducted by Hashba et al, they examined 70 patients diagnosed with LP for a year and discovered a prevalence of MetS in 35.7% of the participants. Patients exhibited a higher prevalence of central obesity, increased fasting blood sugar, and low HDL-C. [15]

Insulin, a pancreatic hormone, is synthesized by islets of Langerhans. It has a molecular weight of 5808 Da and is made up of 51 amino acid residues. [23] Basal insulin makes up around 45% to 50% of the total daily insulin dose, and the fasting insulin level is similar to the amount of basal insulin. [24] IR refers to the decreased physiological response of peripheral tissues to insulin. IR is observed in approximately 20 to 25% of the general population. Identifying individuals at risk of insulin resistance is crucial for preventing non-communicable diseases.

According to the study, the levels of FI were found to be significantly higher in cases compared to controls. The incidence rate was higher in psoriasis, with a prevalence rate of 18.5% for LP and 6% for LS. In papulosquamous diseases, we discovered a positive correlation between IR and MetS. Research conducted by Cho et al reveals a positive association between a higher IR index, as assessed by the HOMA-IR value, and an increase in abnormalities in each component of MetS. [25] In a study conducted by Sung et al, it was found that 8.5% of healthy Asian subjects developed Metabolic Syndrome (MetS) over a span of 5 years. Interestingly, the study also revealed that elevated fasting insulin (FI) levels were predictive of the development of MetS, even in individuals who did

not have MetS at the beginning of the study. [26] In addition to being an independent risk factor for MetS, a cohort study conducted by Sung et al revealed that elevated FI can also predict the future incidence of MetS. There could be a potential explanation for the connection between the FI level and insulin resistance, which plays a crucial role in MetS. In the present study, the mechanism by which FI may represent insulin resistance was not investigated. However, previous studies have demonstrated that FI can serve as a reliable surrogate marker for insulin resistance. [27,28] This can be calculated using the fasting insulin resistance index (FIRI) or the homeostasis model assessment of insulin resistance (HOMA-IR). Insulin resistance is commonly observed in patients with impaired fasting glucose, and it is worth noting that a higher FI level may not be a reliable marker in diabetics with poor glycaemic control. There is a strong correlation between the FI level and MetS, according to reports.

Psoriasis is a condition that impacts a significant portion of the population, causing chronic inflammation of the skin. [29] In recent studies, researchers have discovered a link between psoriasis and various co-morbidities such as cardiovascular diseases, diabetes, Metabolic Syndrome (MetS), and malignancies. [30] According to previous research, the prevalence of MetS is higher in psoriatic patients compared to the general population, with estimates ranging from 15-25%. Several studies, including those by Gisondi et al and Cohen et al, have discovered a noteworthy link between Metabolic Syndrome (MetS) and individuals with psoriasis. [31,32] Praveen Kumar et al examined the connection between MetS and its components in a group of 30 individuals with chronic plaque psoriasis. Metabolic syndrome was found to be more prevalent in individuals with psoriasis compared to the control group, although the difference was not statistically significant. The cases showed a higher prevalence of elevated blood glucose levels and a larger waist circumference compared to the controls. There was a notable difference in the occurrence of low HDL levels between the cases and controls. [29] On the other hand, the occurrence of MetS, IR, and lipid abnormalities in individuals with psoriasis between the ages of 30 and 49 is comparable to that of the overall adult population in Poland. [22] Studies have shown inconsistent findings when it comes to the link between psoriasis and MetS. In our study, we found that psoriasis was associated with a higher prevalence of risk factors such as altered lipid and glucose levels, as well as insulin resistance. However, it's important to note that these differences were not statistically significant.

LP is a chronic inflammatory disorder that affects a small percentage of the global population. When inflammation occurs in LP, it can disrupt lipid metabolism, leading to elevated serum TG levels or decreased HDL-C levels. This can potentially increase the risk of cardiovascular disease. [33] Past research conducted by Lowe et al, Seyhan et al, and Atefi et al has revealed notable changes in glucose levels in LP, which aligns with the findings of our study. [34,35] In 22% of LP cases, we observed elevated FI levels, indicating the presence of insulin resistance. There is a lack of case control studies regarding dyslipidemia and MetS in LP, and there is limited research on IR. This theory is widely accepted as the leading explanation for the pathophysiology of IR. There is a disruption in glucose absorption from the bloodstream as the muscle, fat, and liver cells fail to respond to insulin. The pancreas' beta cells work to increase insulin production in order to maintain normal blood sugar levels. Over time, the pancreas becomes unable to meet the body's growing need for insulin, resulting in a build-up of excess glucose in the bloodstream.

Th1 and Th17 lymphocytes, along with pro-inflammatory cytokines like TNF-α, IL-1, IL-6, and IL-17, have a significant impact on the development of papulosquamous diseases, insulin resistance, and the formation of atherosclerotic plaques. It is believed that chronic systemic inflammatory disease can lead to insulin resistance by reducing the activity of insulin receptors. Furthermore, a notable consequence of reduced expression of insulin receptors in endothelial cells is a decrease in nitric oxide (NO), which serves as a vasodilatory agent. As a health journalist, it is important to note that vasoconstriction can result in increased arterial stiffness, which has been linked to the occurrence of myocardial infarction (MI) and stroke. There is a strong connection between chronic inflammation and atherosclerotic and metabolic disorders, with each influencing the other. Thus, the idea of the "inflammation march" has been put forward.

Chronic inflammation of papulosquamous diseases, combined with genetic and lifestyle factors, can result in the down regulation of insulin receptors. This, in turn, increases the risk of insulin resistance and metabolic syndrome. Screening patients for risk factors can help identify even poorly managed cases of cardiovascular disease and type 2 diabetes. The main limitation that affects the interpretation of our results is the use of a cross-sectional design, which means we cannot establish a causal relationship between the FI level and MetS. In addition, it is worth noting that our study had a relatively small sample size and the participants were recruited from a regional community.

## Conclusion

MetS and IR was found in cases with papulosquamous diseases. Increased fasting glucose level, raised FI and low HDL-C were the significant parameters in our study. IR has a positive correlation with MetS. High FI levels indicate IR which in turn increases susceptibility to MetS. MetS is associated with insidious onset of symptoms with varied presentation depending on topography and ethnic origins leading to delayed detection. So, papulosquamous diseases can be considered as an external marker for tracing IR and MetS. It aids in detection of subclinical cases, early intervention with lifestyle modifications leads to reduction in mortality.

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