Original Article

Path Analysis in PLS for Assessing the Impact of Metabolic Syndrome on Pulmonary Fibrosis in a Rat Model

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Abstract

Background: Metabolic syndrome (MetS) is characterized by obesity, dyslipidemia, hyperglycemia, and insulin resistance, which are associated with increased risk for pulmonary fibrosis. This study investigates the impact of MetS on pulmonary fibrosis in a rat model using Partial Least Squares (PLS) path analysis.

Methods: Sprague Dawley rats were fed a high-fat, high-fructose diet for 37 weeks to induce MetS. Key metabolic parameters, including body weight, lipid profiles, fasting blood glucose, fibrosis markers and Aschroft scores, were assessed. PLS path analysis was conducted to explore the relationships between these variables and their influence on pulmonary fibrosis.

Results: PLS path analysis identified a strong correlation between increased body weight and MetS development (path coefficient=0.977). Dyslipidemia, characterized by elevated triglycerides and reduced HDL cholesterol, was also associated with MetS. A novel association was found between glucose dysregulation and pulmonary fibrosis (R^2=0.908; path coefficient=0.947), suggesting that hyperglycemia contributes to lung fibrosis. Reduced PPARγ expression was associated with insulin resistance and inflammation, implicating it in fibrotic processes.

Conclusion: This study highlights the role of metabolic disturbances in promoting pulmonary fibrosis in MetS. PLS path analysis effectively identified key metabolic pathways, suggesting potential targets for therapeutic intervention to mitigate MetS effects and prevent fibrosis. Further research is warranted to explore these pathways and develop targeted therapies.

Keywords: lung fibrosis, male Sprague Dawley rats, metabolic syndrome, PPARγ,

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INTRODUCTION

Metabolic syndrome (MetS) is characterized by a cluster of interrelated metabolic disorders that elevate the risk of cardiovascular disease (CVD). The primary pathophysiological factors associated with MetS include insulin resistance, central obesity, hypertension, hyperglycemia, and dyslipidemia, particularly elevated triglycerides. The prevalence of MetS is on the rise, with reports indicating that 23% of the population in Indonesia was affected in 2013, and over 20% of adults globally are now diagnosed with this condition.[1]

Metabolic syndrome represents a significant health concern due to its association with an increased risk of developing diabetes and atherosclerotic cardiovascular disease. The pathogenesis of MetS involves both genetic and acquired factors that contribute to inflammation, which is a key pathway leading to CVD. Recent studies have highlighted the importance of lifestyle factors, such as excessive caloric intake and physical inactivity, as major contributors to the development of MetS.[1]

The condition is often defined by the presence of insulin resistance alongside two or more additional risk factors, including obesity, dyslipidemia (characterized by high triglycerides and low high-density lipoprotein (HDL) cholesterol), hypertension, or elevated blood glucose levels. The increasing prevalence of MetS is concerning, as it not only raises the risk of cardiovascular complications but also contributes to other disorders such as non-alcoholic fatty liver disease and polycystic ovary syndrome.[1,2]

Research indicates that metabolic syndrome significantly impacts overall health, leading to respiratory disorders and reduced lung function. This highlights the multifaceted nature of MetS and underscores the need for effective management strategies that include lifestyle modifications and medical interventions aimed at addressing its various components.[2,3]

Recent studies have established a link between severe MetS and alterations in the histological structure of the heart, specifically cardiac fibrosis. Additionally, research over the past decade has indicated that MetS is associated with impaired lung function in both children and adults. The evidence connecting MetS to pulmonary issues continues to grow, with several proposed mechanisms explaining this relationship. One potential mechanism involves the complex interactions between insulin and insulin receptors in the lungs and airways, which are crucial for normal lung development from early life.[3]

The relationship between metabolic syndrome and lung disease is multifaceted, involving various pathophysiological mechanisms. Factors such as obesity, insulin resistance, hypertension, and dyslipidemia significantly affect lung health. Dietary influences, inflammation induced by excess fat, comorbidities like obstructive sleep apnea (OSA), and obesity further contribute to the association between MetS and lung disease.[4]

Moreover, metabolic syndrome has been linked to pulmonary fibrosis, including idiopathic pulmonary fibrosis (IPF), through mechanisms involving cytokines such as RBP4, JAK/STAT signaling pathways, and the formation of advanced glycation end products (AGEs). A comprehensive understanding of these mechanisms is essential for managing and preventing lung diseases related to metabolic syndrome.[5,6]

Peroxisome proliferator-activated receptor gamma (PPARγ), also known as NR1C3, plays a significant role in two distinct health conditions: metabolic syndrome (MetS) and pulmonary fibrosis. In the context of MetS, PPARγ, primarily expressed in adipocytes, is essential for regulating energy metabolism and adipocyte differentiation.[7] Research by Siersbæk, Nielsen, and Mandrup indicates that increased PPARγ activity may be linked to fat accumulation and bone mass loss, while decreased activity may correspond with increased bone mass. Therapy with PPARγ agonists, such as thiazolidinediones (TZDs), has demonstrated hypoglycemic effects in conditions like obesity and diabetes. Additionally, PPARγ reduces leptin expression in adipocytes, aiding energy storage following high-fat meals and regulating genes involved in adipogenesis and glucose metabolism.[8–13]

These findings indicate that PPARγ has a multifaceted role linking metabolic syndrome and pulmonary fibrosis, suggesting that further understanding of its functions could be key to developing therapies for these conditions. Therefore, this study aims to utilize path analysis in Partial Least Squares (PLS) to investigate the impact of metabolic syndrome on lung tissue in a rat model, focusing on the degree of pulmonary fibrosis assessed through histopathology using the Ashcroft score, fibrosis area, and PPARγ levels in plasma and lung tissue.

METHODS

This study employed a true experimental in vivo design with a pre-test and post-test control group, using male Sprague-Dawley rats (Rattus norvegicus). The study was conducted from June 2022 to March 2023, with animal maintenance, treatment procedures, and organ collection performed at the Animal Laboratory of Biomolecular Sciences, Faculty of Mathematics and Natural Sciences, Universitas Brawijaya. Histological preparations were performed at the Biomolecular Laboratory of Universitas Brawijaya. Meanwhile, tissue fibrosis analysis was conducted through histopathological examination, and serum PPARγ assessment was performed using ELISA at the Pathology Anatomy Laboratory and Biomedical Laboratory of Universitas Brawijaya, respectively.

This methodological approach aligns with established practices in metabolic syndrome research, where controlled environments are

essential for ensuring the validity of experimental outcomes. The comprehensive setup facilitates precise monitoring of metabolic changes and allows for accurate assessments of histological alterations associated with metabolic disturbances. Such rigorous methodologies are crucial for generating reliable data that can contribute to a more profound understanding of the pathophysiology of metabolic syndrome and its complications.

The use of male Sprague Dawley rats in this study is consistent with previous research that has effectively utilized this model to investigate metabolic syndrome. For instance, studies have shown that high-fat and high-sucrose diets can induce significant metabolic changes in these rats, mirroring human conditions related to metabolic syndrome. This model is particularly valuable for examining the interactions between dietary factors and metabolic health, as well as for exploring potential therapeutic interventions.

The study utilized healthy male Sprague Dawley rats (Rattus norvegicus), aged 10–12 weeks and weighing approximately 100–250 grams, sourced from BPOM Jakarta. A total of 20 rats were selected based on Festing's formula, which considers the number of observations, interventions, and samples. Inclusion criteria specified male rats aged 10–12 weeks, weighing between 300 and 400 grams, in a healthy condition, and with no prior treatments. Exclusion criteria included inactive rats or those showing signs of illness, physical defects, or rejection of food and water.

The independent variables in this study were the administration of a high-fat, high-sucrose (HFHS) diet and streptozotocin (STZ) injection, while the dependent variables included metabolic profiles and biomarkers such as PPARγ expression in blood and lung tissue, as well as histopathological changes in lung tissue fibrosis. The subjects were divided into two groups: a control group receiving a normal diet and a metabolic syndrome group.

The rats were subjected to a high-fat, HFHS diet combined with STZ injection to induce metabolic syndrome. The HFHS diet was administered to rats aged 10–12 weeks over a duration of 37 weeks, while the STZ injection was given to rats weighing over 500 grams, which was targeted to be achieved by week 18 and administered over a period of 10 weeks.

Previous studies have established similar methodologies for inducing metabolic syndrome in rat models. For instance, research has shown that a combination of high-fat and high-sucrose diets can effectively induce metabolic syndrome features such as increased fasting blood glucose, triglycerides, and altered lipid profiles.[7] In one study, male Sprague Dawley rats were subjected to an HFHS diet for eight weeks, resulting in significant metabolic changes, including elevated triglyceride levels and reduced HDL cholesterol.[7,10]

The approach taken in this study aligns with established protocols that demonstrate the effectiveness of using a high-fat diet alongside STZ injection to mimic the pathophysiological characteristics of metabolic syndrome. This model is crucial for understanding the underlying mechanisms of MetS and its associated complications, providing insights that could inform future therapeutic strategies.[2,7]

Following the 10-week induction period, pre-test assessments were conducted to measure fasting blood glucose, triglycerides, HDL cholesterol, and body weight. Post-test measurements were taken after an additional 9 weeks of intervention, after which the rats were euthanized for tissue collection and further analysis. Serum and lung tissue PPARγ levels were assessed using ELISA, while lung histopathology was evaluated through hematoxylin-eosin staining, with fibrosis scored by two experts using the modified Ashcroft scale.

The Ashcroft scale is a widely recognized method for quantifying pulmonary fibrosis in histological samples, utilizing a numerical scoring system that typically ranges from 0 to 8. This scale evaluates the extent of fibrosis based on visual assessment of stained lung sections. Studies have shown that while the Ashcroft scale is effective, it can be subject to variability among different observers, which may affect the reliability of the results. Modifications to this scoring system have been

proposed to enhance its consistency and accuracy in quantifying lung fibrosis.

Path analysis was conducted using Smart PLS to assess the impact of metabolic syndrome on lung tissue fibrosis, focusing on the Ashcroft score and PPARγ levels. The effectiveness of the model was evaluated through goodness-of-fit measures, utilizing R-square for the latent dependent variable and Q-square predictive relevance for the structural model. In particular, the role of PPARγ in this context is noteworthy. PPARγ is involved in regulating various metabolic processes and has been shown to influence fibrogenesis through its effects on inflammation and cell differentiation.

The outer model delineates the relationships between latent variables and their indicators, illustrating how each indicator correlates with its associated latent variable. This analysis emphasizes the outer loading values of each variable within the PLS model, which reflect the extent to which indicators effectively represent their corresponding latent variables. High outer loading values indicate that an indicator serves as a strong representative of its associated latent variable.

To assess the significance of these outer loading values, bootstrapping was performed using 500 subsamples, with a significance threshold set at 5%. This statistical technique allows for the estimation of the stability and reliability of the outer loadings by generating confidence intervals and significance levels for each indicator. By applying this method, researchers can determine which indicators significantly contribute to their respective latent variables, thereby enhancing the validity of the measurement model.

Convergent validity was assessed using two criteria, the outer loading coefficients and the average variance extracted (AVE) values. Reflective indicators are considered valid if their loading factor is greater than 0.7, although a loading value of 0.5-0.6 is considered acceptable.

The structural model (inner model) was evaluated using R-square (R^2) values, reflecting the predictive power of the model. R-square values were calculated based on data processing with PLS. Meanwhile, the model's goodness-of-fit was evaluated using the Q-square value, which functions similarly to R-square in regression analysis. A Q-square value greater than zero suggests that the model possesses good predictive relevance. In this study, the Q-square value for the overall model was calculated to be approximately 99.9999958%, indicating exceptional predictive capability.

The strong relationship between metabolic syndrome and its effects on various metabolic parameters demonstrates the model's effectiveness in capturing these dynamics. The high R-square and Q-square values reinforce the validity of using this rat model to study metabolic syndrome and its implications for understanding related health issues.

RESULTS

The study involved 20 experimental animals with an average age of 260.5 days, ranging from 259.0 to 269 days. The average body weight of these animals was 454.9 grams, with a range from 319 to 570 grams. Regarding the observed variables, the average fasting blood glucose (FBG) level was 195.95 mg/dL, with values ranging from 70.0 to 420 mg/dL. The average triglyceride (TG) level was recorded at 190.29 mg/dL, ranging from 67.07 to 436.62 mg/dL. The average HDL cholesterol level was found to be 39.59 mg/dL, with a range of 22.34 to 63.77 mg/dL.

Additionally, the average plasma PPARγ level was measured at 37.15 ng/mL, with values ranging from 10.73 to 64.82 ng/mL, while the average PPARγ level in lung tissue was reported as 48.23 ng/mL, with a range from 20.88 to 73.15 ng/mL. These findings provide important baseline data for understanding the metabolic and biochemical profiles of the experimental animals, which are crucial for evaluating the effects of interventions related to metabolic syndrome and pulmonary health in this study.

The average Ashcroft score for lung histopathology among the 20 experimental animals was 3.95, with a range from 2 to 6. According to the Ashcroft scoring system, 65% of the animals

exhibited normal histopathological results (scores <5), while 35% showed signs of fibrosis (scores ≥5). The average fibrosis area was measured at 37.15 units, ranging from 5 to 80 units.

In this study, the distribution of Ashcroft scores indicates that a significant majority of the experimental animals maintained relatively normal lung histology, while a notable portion exhibited fibrotic changes. These findings contribute valuable insights into the effects of metabolic syndrome on lung health, highlighting the relevance of histopathological assessments in understanding disease mechanisms and potential therapeutic targets.

Table 1. The outer loading values and p-values for each variable

Variable	Outer Loading	*P*
Body Weight (BW)	1.000	-
Glucose Plasma (GDP)	1.000	-
High-Density Lipoprotein (HDL)	1.000	-
Aschroft Score (HistoPA_Score) → Fibrosis	0.990	0.0001
Control and Mets Group	1.000	-
Lung Fibrosis Area → Fibrosis	0.868	0.0001
PPARγ Tissue	1.000	-
PPARγ Plasma	1.000	-
Triglycerides (TG)	1.000	-

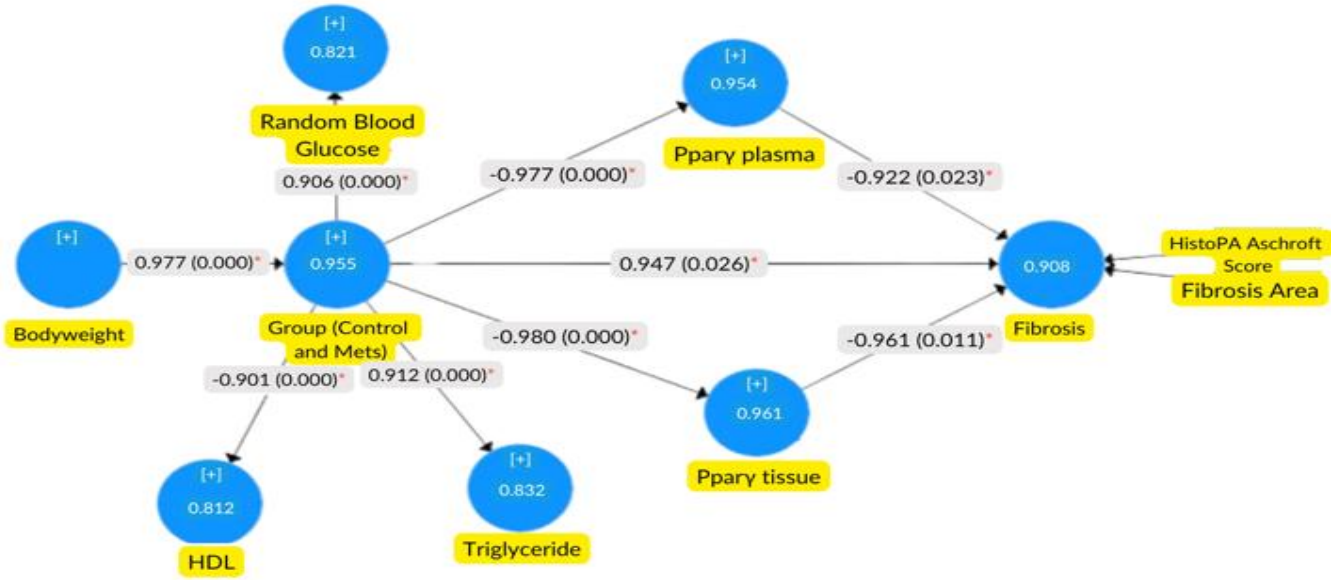
The outer loading values indicate that BW, HDL, FBG, TG, PPARγ plasma, and PPARγ tissue each have a loading factor of 1.0, indicating high validity. The lung fibrosis area and Aschroft score have loading factors of 0.868 and 0.990, respectively, both greater than 0.7, confirming their validity in measuring the variables in the model of metabolic syndrome in a rat model (Table 1).

The R-square values indicate the degree to which metabolic syndrome influences various parameters in the rat model. For instance, the R-square for glucose-dependent insulinotropic polypeptide (GDP) is 0.821, meaning that 82.1% of the variability in GDP can be attributed to the metabolic syndrome model in rats, while the remaining 17.9% is influenced by other factors.

Table 2. R-square values

Variable	R^2
FBG	0.821
HDL	0.812
TG	0.832
Control and Mets Group	0.955
PPARγ Plasma	0.954
PPARγ Tissue	0.961
Fibrosis	0.908

The direct effect analysis examines the direct impact of exogenous variables on endogenous variables without involving mediating variables. The direct path coefficients and their significance levels are presented in Table 3.



Note: *=significant effect; ts = no significat effect; Blue circle = construct variable; yellow box = indicator; number outside the sign "()" = loading factor coefficient; number inside the sign "()" = p-value; number inside the blue circle = R-square

Figure 1. Path analysis diagram for PLS output results

The results indicate significant direct effects, such as the direct impact of body weight on the control and mets groups with a path coefficient of 0.977 (*P*=0.0001), suggesting a positive relationship between body weight and metabolic syndrome in the rat model.

Table 3. The Direct Effect Path Coefficient

Direct Effect	Path Coefficient	*P*
BW→Control and Mets Group	0.977	0.0001
Control and Mets Group→FBG	0.906	0.0001
Control and Mets Group→HDL	-0.901	0.0001
Control and Mets Group→TG	0.912	0.0001
Control and Mets Group→PPARγ Tissue	-0.980	0.0001
Control and Mets Group→PPARγ Plasma	-0.977	0.0001
Control and Mets Group→Fibrosis	0.947	0.026
PPARγ Tissue→Fibrosis	-0.961	0.011
PPARγ Plasma→Fibrosis	-0.922	0.023

Indirect effects were also analyzed to determine the mediating effects between variables. The coefficients and significance levels for indirect effects are presented in Table 4.

Table 4. The Indirect Effect Path Coefficient

Indirect Effect	Path Coefficient	*P*
BW→Control and Mets Group→Fibrosis	0.926	0.026
Control and Mets Group→ PPARγ Tissue→Fibrosis	0.942	0.011
BW→Control and Mets Group→ PPARγ Tissue→Fibrosis	0.921	0.011
Control and Mets Group→ PPARγ Plasma→Fibrosis	0.901	0.024
BW→Control and Mets Group→ PPARγ Plasma→Fibrosis	0.880	0.024
BW→Control and Mets Group→GDP	0.886	0.0001
BW→Control and Mets Group→HDL	-0.881	0.0001
BW→Control and Mets Group→ PPARγ Tissue	-0.958	0.0001
BW→Control and Mets Group→ PPARγ Plasma	-0.955	0.0001
BW -> Control and Mets Group -> TG	0.892	0.0001

DISCUSSION

This study investigated the metabolic effects of a high-fat, high-fructose diet combined with diabetes induction in Sprague Dawley rats, aiming to model the pathophysiology of MetS. Over 37 weeks, significant changes were observed in metabolic and biochemical parameters, including body weight, lipid profiles, fasting blood glucose, and markers of fibrosis. These findings align with and expand upon previous research on diet-induced metabolic disturbances, offering deeper insights into the multifactorial nature of MetS.[7]

Research has shown that high-fat and high-fructose diets can effectively induce MetS in various rodent models. For instance, studies involving Wistar rats have demonstrated that such diets lead to significant weight gain, insulin resistance, and dyslipidemia—key characteristics of MetS.[11] Our findings of increased fasting blood glucose levels and altered lipid profiles corroborate these observations, highlighting the relevance of our model in studying the complex interactions between diet and metabolic health.

The correlation between dietary fat intake and body weight further emphasizes the importance of managing lipid profiles to mitigate cardiovascular risks associated with MetS. The insights gained from this study contribute to a better understanding of how high-fat, high-fructose diets influence metabolic health and highlight potential avenues for therapeutic intervention in managing MetS.

The strong correlation identified between increased body weight and the development of MetS in our study supports findings from earlier research. Rohman et al reported significant weight gain in Sprague Dawley rats fed a high-fat, high-fructose diet, which resulted in insulin resistance and obesity—both of which are key components of MetS. Their work demonstrated that dietary fat intake is directly linked to increased adiposity and the subsequent onset of glucose intolerance.[7,11,12]

Our study builds on these findings by showing that body weight alone can account for up to 95.5% of the variance in MetS outcomes, underscoring its critical role as a predictor of metabolic health. The direct path coefficient of 0.977 for body weight's effect on metabolic syndrome further reinforces the importance of managing obesity to prevent MetS.[13]

The significant alterations in lipid profiles observed in our study, particularly the marked increase in TG levels and the decrease in HDL cholesterol, are consistent with the dyslipidemic patterns documented in prior studies involving MetS

models. These studies have indicated that rodents subjected to high-fat diets exhibit elevated TG levels and diminished HDL levels, which are characteristic features of MetS and precursors to cardiovascular diseases. Our findings revealed a TG level of 300.66 mg/dL in the MetS group compared to 79.93 mg/dL in the control group (*P*=0.0001), reflecting the lipid dysregulation commonly seen in human patients with MetS.[7,9]

Moreover, the high R-squared values for HDL is 0.812 and TG is 0.832 in our study further emphasize the influence of diet-induced metabolic disturbances on lipid metabolism. This is in alignment with existing literature that identifies dyslipidemia as a prevalent component of MetS, characterized by elevated triglycerides and low HDL cholesterol levels, both of which are critical risk factors for cardiovascular disease.[1]

The relationship between dietary fat intake and adiposity, along with the subsequent development of glucose intolerance, highlights the necessity of managing lipid profiles to reduce cardiovascular risks associated with MetS.

This study also investigated the effects of MetS on glucose homeostasis and tissue fibrosis, offering new insights into the metabolic complications linked to high-fat, high-fructose diets.[2,3] The significant rise in fasting blood glucose levels and fibrosis scores observed in our MetS model group is consistent with previous research indicating that hyperglycemia and insulin resistance are critical factors in tissue damage and fibrosis associated with metabolic disorders.

The R-squared value of 0.908 for fibrosis in our study, along with a direct path coefficient of 0.947 (*P*=0.026), suggests that glucose dysregulation not only contributes to metabolic disturbances but also plays an essential role in fibrotic processes. This finding is corroborated by Wang et al, who reported that AGEs, which form under conditions of hyperglycemia, promote fibrosis and organ dysfunction.[9]

The correlation between glucose dysregulation and fibrosis is further supported by evidence indicating that elevated glucose levels stimulate the proliferation of hepatic stellate cells, leading to increased collagen production and subsequent fibrosis. This aligns with findings from other studies that have shown a link between metabolic syndrome and severe fibrosis in various contexts, including chronic liver disease.[4]

Additionally, the interaction between hyperglycemia and the activation of fibrogenic pathways highlights the importance of managing glucose levels to mitigate fibrotic complications associated with MetS. The significant impact of metabolic syndrome on both glucose homeostasis and tissue fibrosis reinforces the necessity for targeted interventions to address these interconnected metabolic disturbances.

Our results indicate significantly lower levels of PPARγ in the MetS group compared to the control group, which aligns with previous research emphasizing the importance of PPARγ in glucose and lipid metabolism, as well as inflammatory responses. PPARγ functions as a nuclear receptor that regulates processes such as adipogenesis, insulin sensitivity, and lipid homeostasis. The reduced expression of PPARγ observed in our study may lead to insulin resistance and heightened inflammatory responses, as suggested by Lefterova et al. This finding is consistent with earlier studies demonstrating that PPARγ activity is linked to anti-inflammatory effects in adipose tissue.[6,10,13]

The therapeutic potential of PPARγ agonists, including thiazolidinediones, has been established in their ability to reduce insulin resistance and inflammation. This suggests that strategies aimed at targeting PPARγ could help alleviate some of the metabolic disturbances associated with MetS.

The association between metabolic syndrome and pulmonary health, particularly regarding fibrosis, is an area that has not been extensively studied.[4] Nevertheless, emerging evidence suggests that metabolic disturbances, such as hyperglycemia and dyslipidemia, may contribute to the remodeling of lung tissue and the development of fibrosis.

Our findings indicate increased fibrosis scores in the metabolic syndrome group, along with elevated fasting glucose levels, which support this hypothesis. This is consistent with prior research indicating that

conditions associated with metabolic syndrome can exacerbate lung injury and fibrosis in adults. The mechanisms underlying this relationship may involve elevated levels of inflammatory cytokines and oxidative stress, both of which are known to occur in metabolic syndrome and pulmonary fibrosis.[5]

Future studies should concentrate on elucidating the molecular pathways that connect metabolic syndrome to lung health, as this could uncover new therapeutic targets for preventing or treating fibrosis in individuals with metabolic syndrome.

LIMITATION

This study is subject to several limitations: it exclusively involved male animals, which precluded the evaluation of metabolic syndrome effects in female rats; the analysis was restricted to a single inflammatory marker, PPARγ; and the research primarily addressed the influence of metabolic syndrome on pulmonary fibrosis without investigating potential treatment and prevention strategies for this condition.

CONCLUSION

This study validates and builds upon earlier research by demonstrating the significant effects of a high-fat, high-fructose diet on metabolic and biochemical parameters that contribute to the onset of MetS in a rat model. It highlights the essential roles of body weight, lipid profiles, glucose regulation, and PPARγ in the development of MetS. Our path analysis using PLS revealed strong direct relationships, particularly with body weight and glucose dysregulation, which are significant predictors of MetS outcomes. These findings underscore the importance of weight management and lipid regulation in the prevention and treatment of MetS.

Additionally, the study suggests a possible connection between metabolic syndrome and pulmonary fibrosis, an area that has received limited exploration. The use of PLS path analysis facilitated a deeper understanding of this relationship, showing a significant path coefficient between metabolic disturbances and the extent of fibrosis. This indicates that metabolic syndrome may contribute to fibrotic processes in the lungs. The high R-square value for fibrosis in our model suggests that a considerable portion of the variance is accounted for, reinforcing the robustness of our findings in this context. This emphasizes the value of PLS path analysis in clarifying complex, multifactorial relationships within biological models, enabling the identification of critical pathways for potential therapeutic intervention.

Given these results, future research should investigate the therapeutic potential of targeting PPARγ and other metabolic pathways to mitigate the effects of MetS and its associated complications, including pulmonary fibrosis. The insights gained from our path analysis could guide targeted interventions aimed at addressing underlying metabolic disturbances, potentially decreasing the risk or severity of fibrosis. Further studies are warranted to confirm these findings and to explore the mechanisms by which metabolic syndrome may predispose individuals to pulmonary fibrosis, thereby identifying new therapeutic targets for preventing or treating fibrosis in patients with MetS.

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CONFLICT OF INTEREST

There are no conflicts of interest that may arise in the conduct of research and the writing process.

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