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RESEARCH ARTICLE
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# "ASSOCIATION OF SERUM HEPATIC ENZYMES WITH METABOLIC SYNDROME AMONG THE NORTH INDIAN POPULATION"

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**Abstract**

**Background:** The rise in metabolic syndrome (MetS) worldwide is mainly because of people's sedentary lifestyles and unhealthy dietary patterns. There is a strong link between MetS and liver problems, which frequently appear as liver inflammation and lead to a higher risk of illness and death. Liver dysfunction is a common sign among people living with MetS, which may show signs of liver injury. The study is designed to examine how metabolic syndrome might contribute to liver injury, and also helps in learning more about the mechanisms involved.

**Aim**: To find if there is any association between the activity of the Hepatic enzymes and MetS.

**Material & Methods:** This is a hospital-based cross-sectional study in 150 patients diagnosed with MetS. It was explained to all participants, who signed consent before the study started, that we would measure their serum liver enzymes ALT, AST, ALP, and GGT, as well as HDL-C, TG, and FBG in their fasting blood, and that we would measure their waistline and blood pressure. All Biochemical parameters (ALT, AST, ALP, GGT, HDL-C, TG, and FBG) were analysed using a MERCK semi-automated analyser in the department of biochemistry. Anthropometric data such as waist circumference and blood pressure were measured independently using standard clinical procedures. Data was analysed using SPSS version 29, and Pearson's correlation test was done to check for a link between Metabolic syndrome and serum liver enzymes. For these results, p-values less than 0.05 were considered statistically significant.

**Results:** Significant changes in the concentration of the estimated liver enzymes were observed in the patients having metabolic syndrome. We observed that serum activity of hepatic enzymes (ALT, AST, ALP, and GGT) was not only associated with components of MetS but also exhibited elevated activity when compared to reference values.

**Conclusion:** Liver enzyme activities were found to be raised in people with metabolic syndrome. Monitoring alterations in liver enzymes may provide critical insights into the pathophysiology of metabolic syndrome and guide the development of more effective therapeutic strategies. Knowing

about liver parameters not only supports the early detection of liver dysfunction but also makes it easier to find and manage both liver dysfunction and MetS.

**Keywords:** Liver enzyme; Metabolic syndrome; liver disorder.

## Introduction

Metabolic syndrome is clinically recognized when a person has a large waistline, high blood pressure, higher than normal blood sugar, elevated triglycerides, or low levels of HDL cholesterol.[1]. Modern lifestyle has contributed to a growing prevalence of metabolic syndrome in many Asian and Indian populations, with studies indicating that individuals with MetS have a twofold increased risk of developing cardiovascular disease within 5–10 years [2] and are also more susceptible to hepatic abnormalities [3]

ALT, AST, ALP, and GGT are the serum biochemical markers that help to find liver injury and show the state of the liver's metabolic status.[4] Higher transaminase values are linked to damage of the liver caused by excess fatty acids and inflammatory substances. New research indicates that changes in transaminase activity in the blood often reflect common features of metabolic syndrome.[5]

A constant difference in calorie intake and the number of calories burned can trigger problems with energy control and lead to metabolic syndrome, the caloric imbalance may cause metabolic changes in adipose tissue. Adipose tissue shows inflammatory changes, and lipolysis occurs, which leads to elevated free fatty acids in the bloodstream that are taken by liver for further metabolism. Overwhelming fatty acids in the liver can cause hepatic steatosis and thereby raise the risk of cardiac illness due to dyslipidaemia.[6]

A cross-sectional analysis was conducted on a north Indian cohort from a tertiary care hospital in Uttar Pradesh to investigate the association between attributes of metabolic syndrome and hepatic enzyme activity. This study aims to fill these gaps by analysing the enzymatic activity of all four hepatic enzymes as there are only few studies comparing prediabetic and diabetic groups to elucidate differences in enzyme activity across glycaemic stages.

## Materials and Methods

There were 150 patients diagnosed with metabolic syndrome, aged between 35 and 70 years, who took part in the study.[7] People with a history of alcohol consumption[8], liver or bone disorders[9], viral hepatitis[8], as well as pregnant women [7], were excluded to minimize confounding factors. Venous blood sample were collected from all participants following the acquisition of written informed consent.

### Blood sample analysis

The antecubital vein was used to obtain a venous blood sample after the patients had fasted for at least 12 hours. After centrifuging the sample, the resulting serum was used for a detailed biochemical study. Blood glucose level was estimated by using the (GOD-POD) method[10]. Triglyceride was measured by the end-point method[11], while HDL-C was tested using an enzymatic colorimetric method[11]. The measurement of serum ALT and AST activities was done according to IFCC standards[12]. ALP levels were estimated using the King and King's method.[13] The specific diagnostic kit was used to measure GGT activity by using the kinetic method.

### Statistical analysis

The data was analysed by using SPSS software in this study. Comparison of parameters between 2 groups was performed by using an independent sample t-test, while associations among the parameters were analysed using Pearson's correlation coefficient. All results were considered significant only if the p-value was less than 0.05.

**Results and discussion**

MetS characteristics include raised blood sugar, raised cholesterol levels, and increased waist circumference. Studies have reported that liver function abnormalities, especially raised liver enzymes, are strongly associated with MetS. Due to variation in genetic and lifestyle factors across different areas, metabolic syndrome affects liver enzymes differently for each group.[1]

In this study, 70 (46.6%) participants were male and 80 (53.3%) participants were female, and all participants were aged between 35 to 70 years. This finding aligns with the 2017 study by Pucci et al. from the Department of Medicine at the University of Perugia in Italy, who reported that females are more likely to suffer from MetS compared to males. Underlying factors such as social factors, hormonal effects, and stress that are mostly present in the post menopause groups may be the cause for this gender difference.[14]

In the study, individuals with MetS were divided into two subgroups: "Prediabetic" and "Diabetic" based on their blood glucose status. The liver enzymatic activity of these subjects was checked and compared with the standard average values given in the literature. Table 1 reveals that liver enzymes increased considerably in both prediabetic and diabetic individuals compared to standard average values ($p < 0.0001$).

**Table 1: 'Comparison of liver enzymes in Pre-diabetic & Diabetic subjects with standard reference value.**

| Enzyme | Reference value | Pre-Diabetic subjects | t-value (Pre-Diabetic) | p-value (Pre-Diabetic) | Diabetic subjects | t-value (Diabetic subjects) | p-value Diabetic subject) |
|---|---|---|---|---|---|---|---|
| ALT (IU/L) | 25 ± 6.6 | 56.8 ± 55.7 | 6.79 | <0.0001* | 59.5 ± 134 | 3.14 | <0.0001* |
| AST (IU/L) | 25 ± 6.6 | 57.2 ± 49.6 | 7.88 | <0.0001* | 42 ± 42.6 | 4.82 | <0.0001* |
| ALP (U/L) | 88 ± 12.6 | 145.2 ± 217 | 3.29 | <0.0001* | 127.5 ± 87 | 5.47 | <0.0001* |
| GGT (U/L) | 34.5 ± 8.8 | 85.3± 141.2 | 4.39 | <0.0001* | 64.7 ± 56.5 | 4.82 | <0.0001* |

The Reference values of ALT[15], AST[15], ALP[16], and GGT[17] given in Table 1.

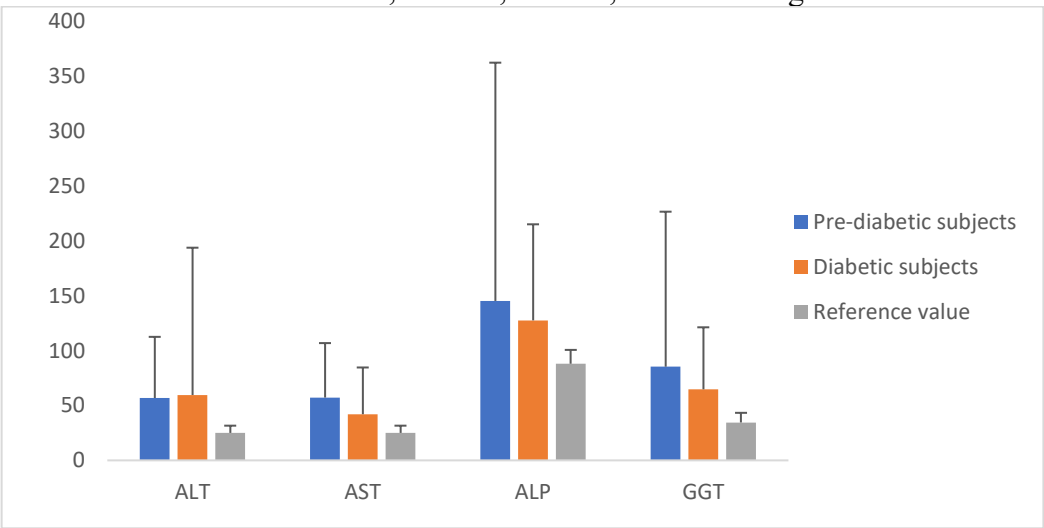


**Figure 1**: Graphical representation of liver enzymes comparing pre-diabetic, diabetic groups with reference values

Serum hepatic enzyme activity was significantly elevated in diabetic and pre-diabetic individuals compared to normal average values, as shown in Table 1 (with $p<0.0001$), consistent with the findings reported by Sakharkar et al. in 2021 at Roosevelt University College of Pharmacy, Schaumburg, IL, USA. Similar increases in enzyme activity were also observed in individuals with impaired glucose tolerance.[18] We found that pre-diabetic individuals generally showed higher average levels of enzyme activity in their blood than those with diabetes, as shown in Figure 1. An altered metabolism often puts added pressure on the liver, which results in liver swelling and extra enzyme activity. Since neither medication use nor diet was determined, it's still possible that the abnormal liver enzymes

found in the pre-diabetic subjects could be due to other, not yet identified factors. To our knowledge, no prior study has specifically compared diabetic and pre-diabetic individuals with metabolic syndrome in this context, making this investigation an important step toward better understanding liver enzyme changes in such patients.

**Table 2: Correlation between liver enzymes and Attributes of Metabolic Syndrome.**

| Parameters | ALT | ALP | AST | GGT |
|---|---|---|---|---|
| **WC** | r = 0.320 | r = 0.107 | r = 0.514 | r = 0.217 |
| | p = **0.001*** | p = 0.194 | p = **0.001*** | p = **0.008*** |
| **SBP** | r = 0.045 | r = 0.090 | r = 0.133 | r = 0.229 |
| | p = 0.587 | p = 0.273 | p = 0.106 | p = **0.005*** |
| **DBP** | r = 0.102 | r = 0.289 | r = 0.287 | r = 0.359 |
| | p = 0.214 | p = **0.001*** | p = **0.001*** | p = **0.001*** |
| **FBG** | r = -0.095 | r = 0.018 | r = -0.191 | r = -0.096 |
| | p = 0.248 | p = 0.831 | p = **0.019*** | p = 0.241 |
| **TG** | r = 0.011 | r = -0.029 | r = -0.051 | r = 0.209 |
| | p = 0.892 | p = 0.722 | p = 0.532 | p = **0.045*** |
| **HDL-C** | r = -0.025 | r = -0.130 | r = -0.167 | r = -0.108 |
| | p = 0.762 | p = 0.114 | p = **0.040*** | p = 0.188 |

This study was performed to find a correlation between liver enzymes and attributes of MetS. The findings observed that serum ALT and waist circumference are strongly correlated, showing a very good and positive association ($p<0.001$) as shown in Table 2 and Figure 2, while no association was seen between ALT and other components of Mets.

A relationship between ALT and waist circumference was found, which suggests that central obesity may be linked to an early rise in liver enzyme activity. The findings of the study by Shuang Chen et al. (2016) in the Department of Cardiology at China Medical University are also consistent with our findings. The findings add to the proof that building visceral fat can increase liver stress or cause early signs of liver dysfunction in those with metabolic risks. [19]

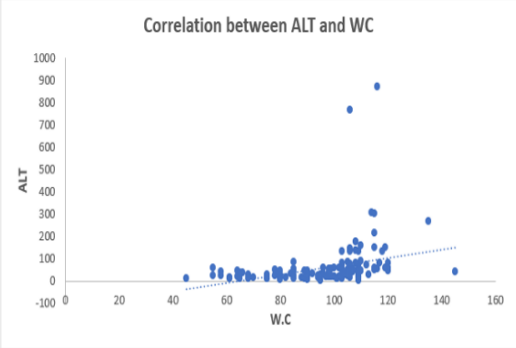


**Figure 2: Correlation between ALT and WC**

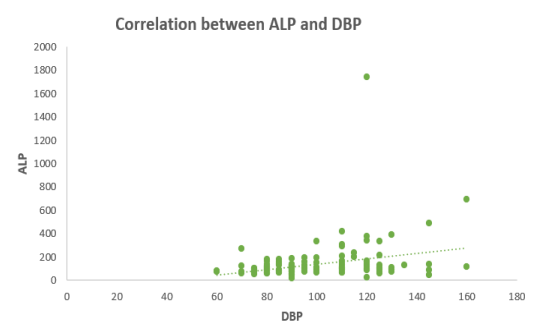


**Figure 3: Correlation between ALP and DBP**

As shown in Table 2, a positive relationship was observed between ALP and diastolic blood pressure ($p < 0.001$), as further illustrated in Figure 3, while no significant correlation was observed between ALP and other components of MetS which may indicate that an increase in ALP is associated with metabolic syndrome through high vascular resistance and low-grade systemic inflammation. Krishnamurthy V. R. et al. have observed similar results, suggesting that ALP could show future risk of cardiac and metabolic disorders [20]

Higher ALP levels may indicate that there is sometimes low-grade inflammation that is hard to detect. Since inflammation often happens with obesity eventually leads to insulin resistance and alterations

of blood glucose levels. It in turn can lead to a rise in cholesterol levels, damage endothelial cells, and thereby lose integrity of blood vessel walls, which could cause many cardiovascular complications.

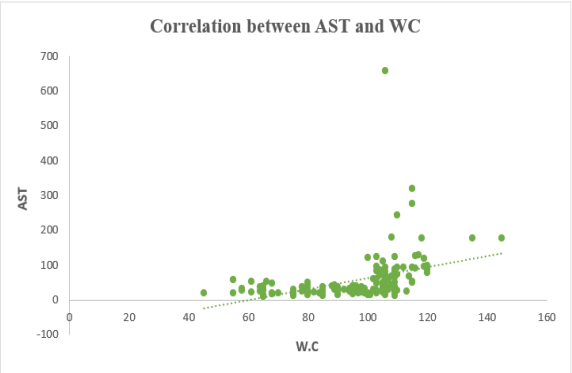


**Figure 4: Correlation between AST and WC.**

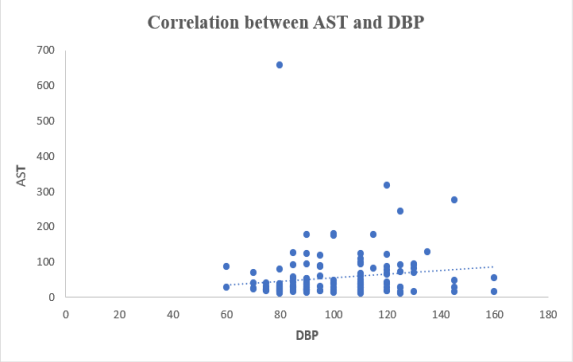


**Figure 5: Correlation between AST and DBP.**

The link between serum AST and the attributes of metabolic syndrome was measured. A positive association was found between AST, WC, and DBP ($p<0.001$). At the same time, AST showed a negative correlation with high-density lipoprotein cholesterol and fasting blood glucose, which was significant at ($p<0.04$ and $p<0.019$), as shown in Table 2.

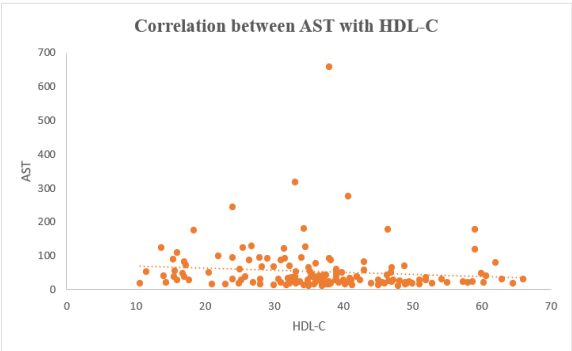


**Figure 6: Correlation between AST and HDL-C.**

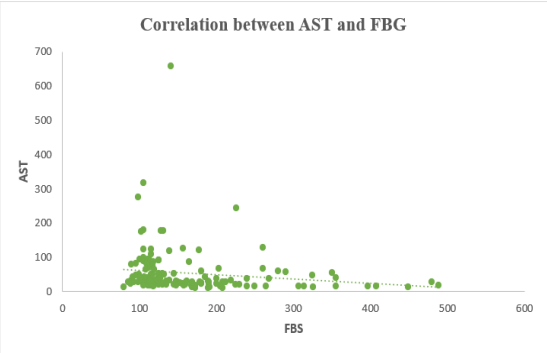


**Figure7: Correlation between AST and FBG.**

In our study, the enzymatic activity of AST demonstrated a positive correlation with WC and DBP, as illustrated in Figures 4 and 5. The findings of our investigation were consistent with those observed by Shuang Chen et al. in 2016 from the Department of Cardiology in a Chinese medical hospital, which found that AST, a hepatic enzyme, may reflect underlying hepatic stress or injury.[19] Such findings can be due to similar processes, such as altered metabolism, inflammation, and organ damage. A large waist circumference can suggest abdominal obesity, which is commonly linked to hepatic steatosis, where lipids are stored in more than 5% of hepatocytes.

Paschos P and Paletas K mentioned in 2009 that obesity is associated with excessive intracellular lipid accumulation in hepatic cells and displaces normal cellular components, potentially leading to cellular rupture and an elevation in AST activity. Abdominal obesity further leads to issues like chronic low-grade inflammation and oxidative stress that harm the linings of arteries and make the arteries stiffer, which raises diastolic blood pressure. Blood pressure is also regulated by hormones from the liver, such as aldosterone and angiotensin, which reinforces the connection between liver disease and vascular problems.[21]

A decrease in HDL-C in the liver increases AST enzyme activity, as revealed in Figure 6, and may indicate a connection between liver abnormalities and lipid metabolism. HDL-C may guard the liver and reduce liver inflammation and oxidative stress. The results are aligned with what Deb S, Puthanveetil P, and their team found in 2018 at the Department of Pharmaceutical Sciences, College of Pharmacy, Larkin University, USA, who discovered lower HDL-C in people who had high AST levels.[22]

Several studies have reported that AST levels tend to be mildly elevated in individuals with metabolic syndrome, although the increase is often less pronounced than that of ALT. For instance, Esteghamati et al. In 2010 found significantly higher AST levels in diabetic patients with MetS compared to those without, even in the absence of fatty liver disease.[23] However, in our study, a negative correlation between AST and fasting blood glucose was observed as shown in Table 2. This unexpected relationship might be attributed to the lack of detailed patient history, particularly regarding the use of medications such as insulin sensitizers, statins, or hepatoprotective drugs, which can influence liver enzyme levels and potentially mask expected elevations.

However, AST didn't show a significant correlation with SBP and TG.

Gamma Glutamyl Transferase is a powerful antioxidant and also transfers amino acids across the membrane of cells. Naidu B. T. K. et al. have reported in previous studies that GGT plays a significant role in various pathological processes of the liver.[24]

Elevated serum gamma-glutamyl transferase activity was strongly linked to major aspects of metabolic syndrome, such as excess abdominal fat, high blood pressure, and unusual lipid profiles, as shown in Table 2. These findings are aligned with Naidu B T K et al. from the Department of General Medicine, Maharajah's Institute of Medical Science in India, published in 2023, showing that GGT is a key sign of metabolic imbalances and can increase the risk of heart disease in people with metabolic syndrome.

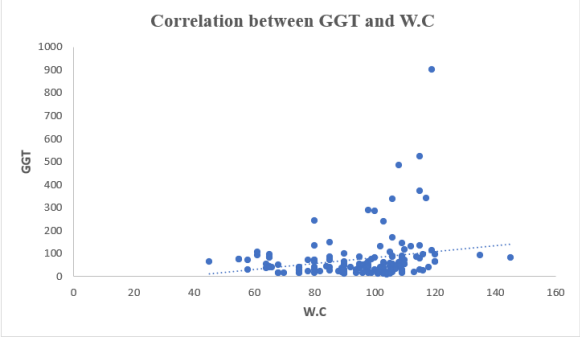


**Figure 8: Correlation between GGT and WC**

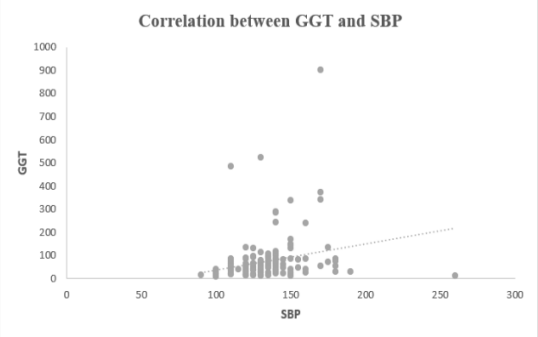


**Figure 9: Correlation between GGT and SBP**

Elevated GGT activity increases when individuals have central obesity, as shown in Figure 8. High values of GGT may boost oxidative stress and damage fat cells, which can cause visceral fat to build up. An insufficient amount of glutathione causes ROS, which makes it easier for fat to build up in the abdomen.[24]

Somehow, an increase in GGT levels is closely connected to an increase in blood pressure, as shown in Figures 9 & 10. It is clear from studies that stress and inflammation inside the body may lead to it due to the relationships with C-reactive protein and fibrinogen levels. Vessels and blood pressure can be affected by inflammation pathways being turned on.[25]

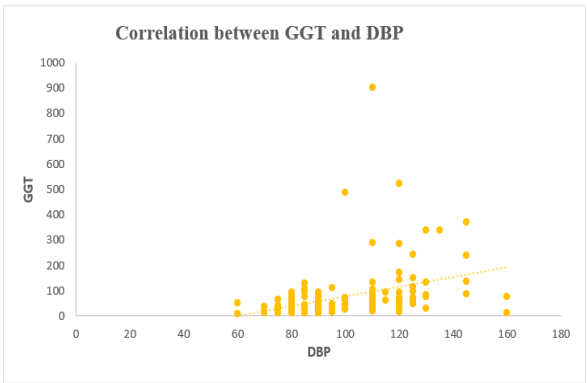


**Figure 10: correlation between GGT and DBP**

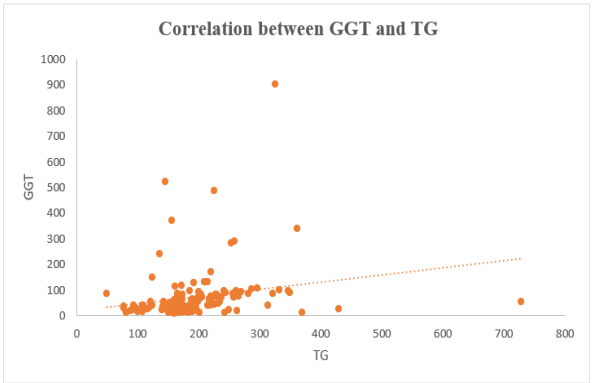


**Figure 11: correlation between GGT and TG**

High levels of gamma-glutamyl transferase (GGT) are typically linked with unhealthy lipid levels, as shown in Figure 11, revealing increased triglycerides might lead to lipid peroxidation and oxidative stress in cells, which in turn harms the action of lipase and upsets lipid metabolism. These processes may indicate that GGT is a contributor to the development of dyslipidemia, the main feature of MetS.[24]
While no correlation was observed between GGT with FBG and HDL-C.

## Conclusion

The outcomes of this research indicate that hepatic enzymes (ALT, AST, ALP, and GGT) have a strong association with the MetS. From these, AST or GGT were more associated with waist circumference, high blood pressure, and dyslipidaemia, though both ALT and ALP displayed less connection to metabolic factors. Females were found to have MetS more often than male participants. Liver enzyme activity was found to be much higher in prediabetic and diabetic subjects as compared to the reference value. The findings prove that analysing liver enzymes, which is not invasive, can be used to detect and stratify the early stages of MetS among North Indian individuals.

## Limitation

- Conducted in a single tertiary care hospital in North India, the findings may not be generalizable to the broader Indian population or to other ethnic groups due to regional, genetic, and lifestyle differences.
- The study relied solely on liver enzyme activity as a marker of liver function. Imaging or liver biopsy, which could have confirmed hepatic steatosis or fibrosis, was not performed.
- The study did not include longitudinal follow-up, so we could not observe how liver enzymes or MetS parameters changed over time or with treatment.

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