Serum γ-Glutamyltransferase and Risk of Metabolic Syndrome and Type 2 Diabetes in Indore

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Abstract
Background & Objectives: To investigate the association between serum γ-glutamyltransferase (GGT) and risk of metabolic syndrome and type 2 diabetes.
Methods: This study included 250 metabolic syndrome free men and 250 nondiabetic men aged 35–59 years who did not have medication for hepatitis, alanine aminotransferase (ALT). We used a customized National Cholesterol Education Program definition of metabolic syndrome with BMI instead of waist border.
Results: With alteration for age, family history of diabetes, BMI, alcohol intake, cigarette smoking, regular physical activity (fasting plasma glucose for the risk of type 2 diabetes) the risk of metabolic syndrome and type 2 diabetes increased in association with the levels of serum GGT, ALT, aspartate aminotransferase (AST), and alkaline phosphatase. Additional modification for all of the other liver enzymes attenuated these relations, but serum GGT remained a significant risk factor for the risk of both metabolic syndrome and type 2 diabetes.
Conclusion: These results point to that serum GGT may be a significant predictor for increasing metabolic syndrome and type 2 diabetes.
Keywords: γ-glutamyltransferase, Cardiovascular, Aspartate aminotransferase (AST).

Introduction
In accumulation to its analytical uses, serum γ-glutamyltransferase (GGT) has extensive epidemiologic implication[11]. Prospective studies[2,3] have shown a significant association between serum GGT and the progress of specific situation with coronary heart disease (CHD) and stroke. In accumulation to alcohol, obesity has been establish[4] to have a major cause on serum GGT, and there is increasing confirmation[4–8] involving raised serum GGT levels with other metabolic disorder, such as glycemic disorder, hypertension, hypertriglyceridemia, and low HDL cholesterol. Excess evidence of fat in liver, usually termed non alcoholic fatty liver disease, is directly related with high serum GGT, obesity, insulin resistance, and hyperinsulinemia[9–11]. The Adult Treatment Panel III of the National Cholesterol Education Program (NCEP) newly proposed a meaning of the metabolic syndrome to aid recognition of individuals at risk for both CHD and type 2 diabetes[12]. The meaning incorporates thresholds for five easily calculated variables connected to insulin resistance: waist circumference,
triglyceride level, HDL cholesterol level, fasting plasma glucose level, and blood pressure. The NCEP-defined metabolic syndrome categorization is triggered when predefined restrictions of any three of these five criteria are exceeded\textsuperscript{[13–15]}. BMI has been lately adopted in its place of waist circumference for analyses of metabolic syndrome \textsuperscript{[16,17]}. Using a modified NCEP description with BMI instead of waist circumference, we examined the relationship of serum GGT with metabolic syndrome and type 2 diabetes (as diagnosed with the 1997 revised criteria of the American Diabetes Association\textsuperscript{[18]} for epidemiological studies) in Indian male office workers and performed a longitudinal study to prospectively examine the association of serum GGT with the development of metabolic syndrome and type 2 diabetes. Probable relations between other liver enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and alkaline phosphatase) and risk of metabolic syndrome and type 2 diabetes were also examined.

**Subjects and Method**

Our study is an ongoing cohort investigation, designed to clarify risk factors for major diseases, including hypertension, dyslipidemia, and diabetes, among Indore men who are office workers at one of the biggest building contractors in India. A total of 500 males office workers aged 35–59 years participated in cardiovascular risk surveys in May 2020, with a participation rate of 99.6%. The Industrial Safety and Health Law in Indore requires the employer to conduct annual health examinations of all employees. The study was approved by the Index Medical College Ethics Committee and informed consent was obtained from patients.

**Statistical Methods**

The X\textsuperscript{2} test and one-way ANOVA were used to analyze the statistical differences among characteristics of the study participants at enrollment in relation to serum GGT levels. Categories of serum GGT comprised the following quintiles: <16, 16–22, 23–32, 33–53, and ≥54 units/l. For calculation of incidence density, person-years of follow-up were calculated from the date of enrollment to the date of the first incidence of the development of the metabolic syndrome or type 2 diabetes or the date of follow-up where either was diagnosed.

**Result**

**Table 1: Relation to serum GGT levels**

| Characteristics                        | <16          | 16–22        | 23–32        | 33–53        | ≥54        | P value |
|----------------------------------------|--------------|--------------|--------------|--------------|------------|---------|
| Age (years)                            | 39.4±0.6     | 48.2±0.3     | 48.0±0.2     | 48.0±0.1     | 48.7±6.8   | <0.001  |
| Family history of diabetes             | 6.5          | 10.2         | 10.7         | 8.6          | 10.4       | 0.315   |
| BMI (kg/m\(^2\))                       | 21.1±1.1     | 24.1±2.3     | 24.8±2.0     | 25.5±3.8     | 25.4±3.1   | <0.001  |
| Current drinkers                       | 70           | 82           | 87.6         | 92.4         | 94.5       | <0.001  |
| Current smokers                        | 42.5         | 47.2         | 52.6         | 54.3         | 57.4       | <0.001  |
| Regular physical activity at least once a week | 50.2         | 52.5         | 53.6         | 58.6         | 58         | 0.132   |
| Systolic blood pressure (mmHg)         | 121.4±142    | 127.2±14.4   | 128.8±14.3   | 131.2±16.2   | 134.5±16.4 | <0.001  |
| Diastolic blood pressure (mmHg)        | 72.4±10.4    | 77.3±10.5    | 79.4±10.2    | 81.1±10.9    | 83.5±10.9  | <0.001  |
| Total cholesterol (mmol/l)             | 4.58±0.70    | 4.85±0.72    | 6.02±0.79    | 6.19±0.84    | 6.22±0.98  | <0.001  |
| HDL cholesterol (mmol/l)               | 1.52±0.31    | 1.49±0.33    | 1.47±0.37    | 1.48±0.37    | 1.51±0.35  | 0.035   |
| Triglycerides (mmol/l)                 | 0.96 (0.74–0.29) | 1.30 (0.951.74) | 1.35 (1.00–2.04) | 1.35 (1.00–2.04) | 1.70 (1.14–2.54) | <0.001 |
| Fasting plasma glucose (mmol/l)        | 4.03±0.72    | 5.20±0.60    | 5.300±0.98   | 5.32±0.96    | 5.41±1.11  | <0.001  |
| AST (units/l)                          | 16 (15–20)   | 20 (17–22)   | 21 (17–24)   | 23 (20–27)   | 28 (23–35) | <0.001  |
| ALT (units/l)                          | 13 (11–17)   | 18 (14–23)   | 22 (16–28)   | 25 (18–33)   | 32 (24–42) | <0.001  |
| Alkaline phosphatase (units/l)         | 162          | 162          | 165          | 165          | 173        | <0.001  |
| Metabolic syndrome                     | 5.4          | 10.0         | 15.6         | 24.2         | 29.0       | <0.001  |
| Type 2 diabetes                        | 4.2          | 6.8          | 8.0          | 10.5         | 12.3       | <0.001  |
The distinctiveness of the study sample in relation to serum GGT levels are shown in Table 1. Tests for difference in distinctiveness diagonally the five serum GGT level groups were considerable except for family the past of diabetes and regular physical activity. Age, BMI, current drinking, current cigarette smoking, systolic and diastolic blood pressures, total cholesterol, triglyceride, fasting plasma glucose, AST, ALT, and alkaline phosphatase showed a linear trend in relation to serum GGT. The proportion of those who had the metabolic disease and type 2 diabetes also increased in association with an increase in serum GGT. HDL cholesterol showed a U-shaped association with serum GGT.

Discussion
Our study has several limitations. First, serum GGT during follow-up was not incorporated in the analysis. In this study, serum GGT at study entry was strongly linked with that at the date of diagnosis of metabolic syndrome and type 2 diabetes or at the end of follow-up (Spearman’s rank correlation coefficient 0.751 and 0.750, respectively; \( P < 0.001 \) for both). This indicates that those who had the higher serum GGT at study entry tended to continue to do so during follow-up. The observed associations between serum GGT at baseline and the increased risk of metabolic syndrome and type 2 diabetes may thus reflect the effects of serum GGT during a given observation period.

Conclusion
Our findings, which were obtained from a cohort of middle-aged Indian men, support the conclusion that elevated, although still normal, serum GGT is associated with a higher risk of the metabolic syndrome and type 2 diabetes.

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