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Association of glucose intolerance with liver enzymes and insulin resistance in prediabetic young adult subjects

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ABSTRACT

Aim: The aim of this research was to find out the association of glucose intolerance with liver enzymes and insulin resistance in prediabetic young adult subjects. **Research Design and Methods:** This cross-sectional survey based study was conducted in GRMC, Gwalior. Total 300 prediabetic subjects were selected. The serum samples were removed from the clotted blood for plasma glucose, serum aspartate transaminases (AST), alanine transaminases (ALT), alkaline Phosphatase (ALP), gamma glutamyl transpeptidase (GGT), total cholesterol, triglycerides, HDL-cholesterol were measured by Mindray BS400 Chemistry Analyzer. The VLDL-cholesterol and LDL- cholesterol were measured by Friedwald's Formula: LDL-Cholesterol = TG- (HDL-C + VLDL-C) and VLDL-Cholesterol = TG/5. The serum C-peptide and insulin resistance (HOMA-IR) were measured by ELISA method and HOMA calculator v2.2.3 respectively. **Results:** The serum ALT, GGT and HOMA-IR were positively and significantly ($p \leq 0.01$) correlated with IGT ($r = 0.467, 0.714, 0.794$ respectively) in prediabetic young adult subjects. **Conclusion:** This study confirmed the association between the liver enzymes (ALT and GGT) and insulin resistance with IGT in prediabetic young adult. These enzymes can be used as an inexpensive and easily available early indicator of abnormal glucose metabolism in prediabetic young subjects.

Keywords: Prediabetes, ALT, GGT, Insulin Resistance, HOMA-IR

INTRODUCTION

Prediabetes is defined as having blood sugar higher than normal level but not enough high to be considered as diabetes [1]. The indicators of prediabetes are impaired fasting glucose (IFG) and /or imapired glucose tolerance (IGT) and /or Glycated hemoglobin (HbA1c) 5.7-6.4% which is given in table 1[2]. The prevalence of prediabetes varies from 6.0 % to 14.7% across the different states of India [3]. The liver is the main organ concerning about energy metabolism. The metabolic processes such as glycolysis, gluconeogenesis, glycogenesis, glycogenolysis, ketogenesis, fatty acid synthesis and lipogenesis are taking place in the liver. The substrate for the metabolic reaction is provided by enzyme catalyzed reactions. The liver enzymes are most important concerning about energy metabolism [4]. The metabolic reaction is regulated by insulin and other hormones. The insulin clearance is also taking place in the liver [5]. Various studies indicated that the altered activities of liver enzymes ware associated with prediabetes or impaired glucose intolerance [6-9]. The prediabetes was prevalent in young adults due to many factors like family history, life style factors, obesity etc [10, 11]. Therefore, this study was intended to determine the association of impaired glucose tolerance with liver enzymes and insulin resistance in prediabetic young adult subjects.

Table 1: Categories of increased risk for diabetes or prediabetes [2]

Fasting plasma glucose: 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
or
2-h Plasma Glucose during 75-g OGTT: 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)
or
HbA1C: 5.7–6.4% (39–47 mmol/mol)

RESEARCH DESIGN AND METHODS:

Study population: This cross-sectional survey based study was conducted in the department of biochemistry, Gajara Raja Medical College, Gwalior. The subjects were selected via screening based on the family history of diabetes, obesity, sedentary life style and hypertension. Total 300 prediabetes cases were included in this study. The criterion for prediabetes selection was based on the impaired glucose tolerance (IGT) in which the 2-hours plasma glucose level after 75 gram of glucose intake lies between 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L).

Exclusion Criteria: Any disorders which affect energy metabolism like type I diabetes mellitus (DM), type II DM and the drugs that affect glucose metabolism and pregnant women were excluded from the study.

Survey Procedure: All the anthropometric parameters like age, gender, height, weight etc. were recorded in the study proforma. The consent and written questionnaires were taken from each subject before taking the blood sample. This study was approved by Institutional Ethical Committee, G.R. Medical College, Gwalior. Blood pressure was measured by using sphygmomanometer. The blood samples were taken from antecubital vein after an overnight fast for 10-12 hours. The serum samples were removed from the clotted blood for biochemical analysis. The plasma glucose, serum aspartate transaminases (AST), alanine transaminases (ALT), alkaline Phosphatase (ALP), gamma glutamyl transpeptidase (GGT), total cholesterol, triglycerides, HDL-cholesterol were measured by Mindray BS400 Chemistry Analyzer. The VLDL-cholesterol and LDL- cholesterol were measured by Friedwald's Formula: LDL-Cholesterol = TG- (HDL-C + VLDL-C) and VLDL- Cholesterol = TG/5. The serum C-peptide and insulin resistance (HOMA-IR) were measured by ELISA method and HOMA calculator v2.2.3 respectively.

Statistical analysis*:* The significance of association of glucose intolerance with liver enzymes and insulin resistance in prediabetic young adult subjects was analyzed by using Statistical Package for the Social Sciences, version 23.0 (SPSS software). The graphs were prepared by using Excel and graph pad prism7.

RESULT:

The mean and standard deviation (±SD) of anthropometric and biochemical characteristics in prediabetic young adult subjects was given in the table 2. The serum ALT, GGT and HOMA-IR were positively and significantly correlated with IGT (r= 0.467, 0.714, 0.794 respectively) in prediabetic young adult subjects shown in table 3. Figure 1,2,3,4 and 5 showing the graphical presentation of the association of IGT with liver enzymes and HOMA-IR.

Table 2: Anthropometric and biochemical characteristics in prediabetic young adult subjects

Parameters	Mean	± SD
Age (Yr)	25.51	5.17
Weight (Kg)	67.93	6.06
Height (m)	1.65	0.1
BMI (Kg/m^2)	24.94	2.77
Waist (cm)	83.18	5.5
Hip (cm)	98.37	5.23
W/H Ratio	0.85	0.03
Pulse	71.25	3.14
Systolic BP (mmHg)	121.01	3.78
Diastolic BP (mmHg)	80.74	2.7
IGT (mg/dl)	153.95	7.81
AST (IU/L)	28.92	3.52
ALT (IU/L)	33.6	4.28
ALP (IU/L)	71.65	8.77
GGT (IU/L)	35.4	4.61

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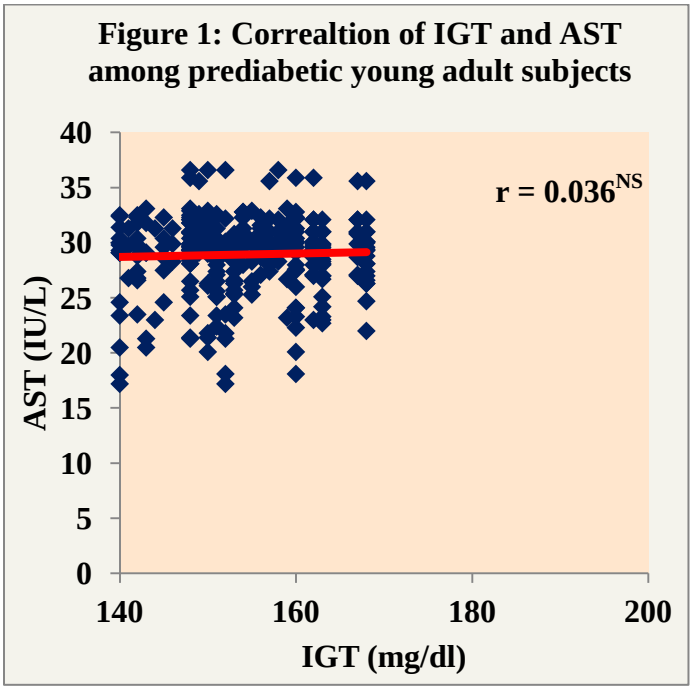
Total Cholesterol (mg/dl)	154.71	12.64
Triglycerides (mg/dl)	146.93	16.21
HDL- Cholesterol (mg/dl)	42.8	6.14
VLDL- Cholesterol (mg/dl)	29.39	3.24
LDL- Cholesterol (mg/dl)	82.52	14.24
C-peptide (ng/ml)	2.00	0.42
HOMA-IR	1.59	0.36

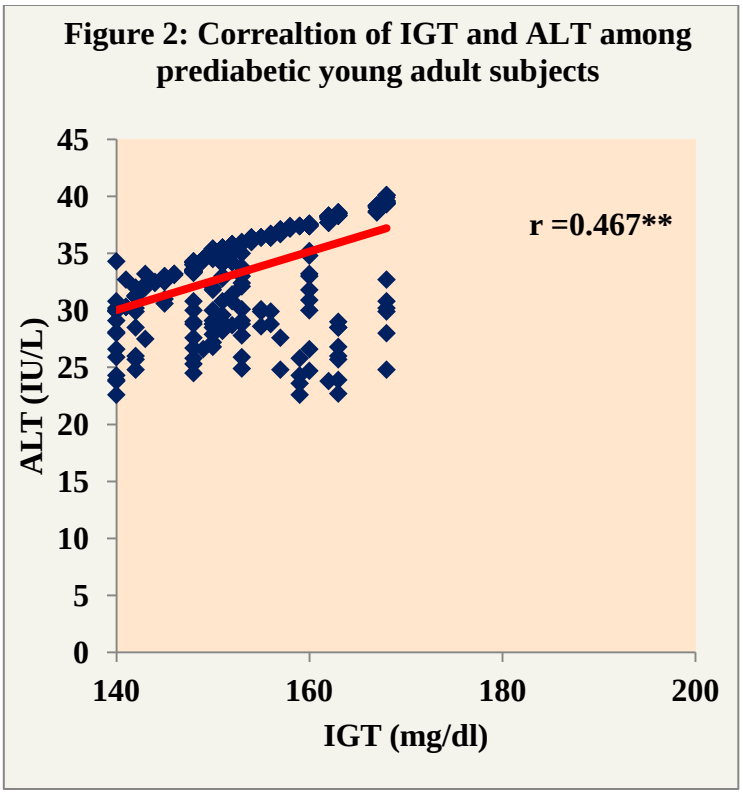
Table 3: Showing the correlation of IGT with liver enzymes and HOMA-IR

Parameters	**IGT**
AST	$r = 0.036^{NS}$
ALT	r = 0.467**
ALP	$r = 0.004^{NS}$
GGT	r = 0.714**
HOMA-IR	0.794**

** Correlation is highly significant at the 0.01 level.

^{NS} Non-significant





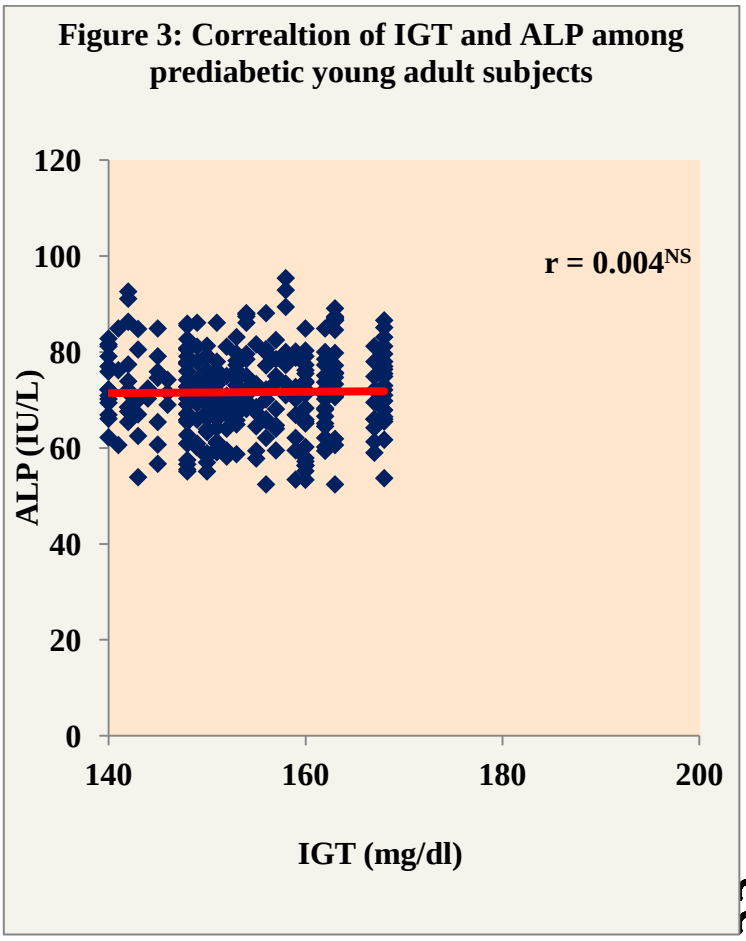


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Figure 4: Correaltion of IGT and GGT among prediabetic young adult subjects

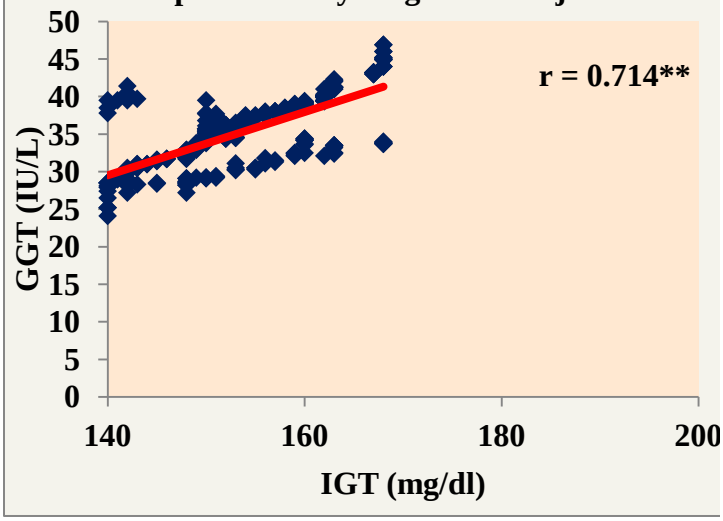
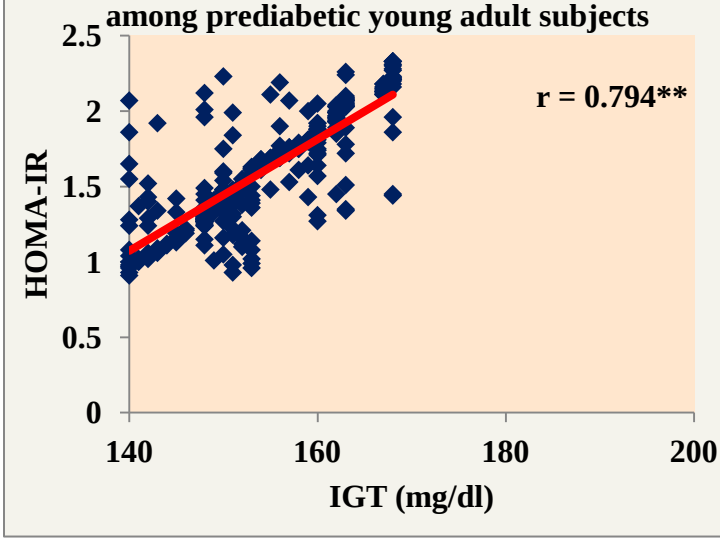


Figure 5: Correaltion of IGT and HOMA-IR among prediabetic young adult subjects



DISCUSSION:

In the present study, we found the association of ALT, GGT and HOMA-IR with IGT in prediabetic young adult subjects. The increased ALT, GGT and HOMA-IR correlated positively with increased IGT in prediabetic young adult subjects. Various other research studies also supported the finding of this study [12-16]. Numerous studies also had proved that the liver enzymes are not only the marker for liver function, but also serve as a surrogate indicator for prediction of diabetic risk in future[17,18,13]. Various Research conducted at Louisiana, South Korea, Shanghai, Thailand, Seoul and Mexico also revealed that the altered serum ALT and GGT were risk factor for diabetes and prediabetes [6, 19-23]. These are the important liver enzymes concerning in the metabolic reaction of carbohydrates specially. The exact mechanisms by which these enzymes are increased are still not very clear. One of the possible mechanisms is that the obesity, fatty liver, insulin resistance, and adiposity leads to the elevation of free fatty acid flux from fat depots that causes lipogenesis and triglycerides rich lipoprotein secretion. This increased free fatty acid flux causes deposition of lipids in the liver, heart, muscles and β-cells of pancreas. This deposition leads to generation of free radicals that causes cellular damage and apoptosis. This event induces increased liver enzymes [6, 24-26]. Obesity is one of the risk factors for altered of liver enzymes specially ALT and GGT. These enzymes are closely related to the fat depots of the body. Increased in the body fats promotes hepatic insulin resistance and ultimately leads to systemic insulin resistance which may be one of the factors for the association of increased liver enzymes, IGT and insulin resistance [12, 27, 28]. Adipose tissues also express large numbers of cytokines and adipocytokines as inflammatory markers. The expression of TNF-α and adipocytokines escort to the insulin resistance [27, 29]. Shimomura I et al., proved the association of increased ALT with IFG and insulin resistance on the experiment in animal model. In animal model the under expression of mRNA for IRS-2 leads to liver gluconeogenesis and stimulated expression of SREBP-1c, results in the activation of fatty acid synthesis which might be the reason for increased ALT and insulin resistance in prediabetic subjects[30, 31]. Serum GGT is an early marker of oxidative stress. GGT is important for glutathione transport into the cell of the organ system and protect the cell from oxidative damage and low grade systemic inflammation. This is the reason for association of increased GGT with IGT and insulin resistance [32, 33].

CONCLUSION:

This study confirmed the association between the liver enzymes (ALT and GGT) and insulin resistance with IGT in prediabetic young adult. These are the routine enzymes used for liver function test. These enzymes can be used as an inexpensive and easily available early indicator of abnormal glucose metabolism in prediabetic young subjects.

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