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Research Article

Metamorphic Changes of Liver Enzymes in Prediabetic Young Adult Subjects

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Abstract
Aim: *Liver is the vital organ regarding energy metabolism. Alteration of liver enzymes may be one of the risk factor for altered glucose metabolism. This study aim is to analysis metamorphic changes in liver enzymes in prediabetic young adult subjects.*
Methods: *Total 400 subjects were taken, out of which 300 were diagnosed prediabetic subjects while 100 are normal healthy age and gender match controls (normoglycemic).The anthropometric parameters were measured by standard methods. The serum samples were used for glucose, AST, ALT, ALP and GGT estimation by mindray BS-400 autoanalyser. The plasma HbA1c estimated by boronate affinity chromatography.*
Results: *the prediabetic subjects had higher WC, WHR, BMI, blood pressure, serum AST, ALP and GGT as compared to normoglycemic subjects.*
Conclusion: *The altered liver enzymes (serum AST, ALP and GGT) may be associated with altered glucose homeostasis. Liver enzymes may be used as a cheap and reliable marker in prediabetes subjects. Proper and timely management of prediabetes may prevent the various complications which may appears in future.*
Keywords: *Prediabetes, liver enzymes, young adult, GGT, ALT.*

Introduction

Prediabetes is the previous stage of diabetes mellitus in which the glycemic parameters above the normal level but below the diabetic threshold [1, 2]. Prediabetes is a condition which concerns about impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or altered glycated hemoglobin (HbA1c), each of which posing the person towards high risk complication like diabetes, fatty liver diseases and other diseases[3,4] As per the American Diabetes Association, prediabetes is defined as the condition in which fasting plasma glucose (FPG) lies between 100 mg/dl to 125mg/dl or 5.6 mmol/L to 6.9 mmol/L. This condition is called impaired fasting glucose (IFG). It is also defined on the basis of impaired glucose tolerance (IGT) in which 2

hours plasma glucose (PG) level lies between 140 mg/dl to 199 mg/dl or 7.8 mmol/L to 11.0 mmol/L. On the basis of glycated hemoglobin (HbA1c), the prediabetic subjects should have 5.7 to 6.4% (39-46 mmol/mol) of glycated hemoglobin[1,3]. In India, 77.2 million peoples have prediabetes[5]. National Health and Nutrition Examination Survey (NHANES) conducted in the United States and Korea revealed that the prediabetes was very prevalent among adolescents and young adults due to sedentary life style and change in food habits; the young adults are especially prone to develop prediabetes[6,7]. The deranged metabolism of carbohydrates, lipids and proteins is responsible for prediabetes[8]. The major metabolic pathways are taking place in the liver and the enzymes which regulate glycolysis, gluconeogenesis, glycogen metabolism TCA cycle, urea cycle; lipogenesis and insulin clearance are taking place in the liver [9,10]. Therefore, this study is conducted to determine the liver enzymes in prediabetic young adult subjects.

Materials and Methods

Study Population: The cross-sectional case control survey based study was conducted on prediabetic young adult subjects, selected via screening through survey in the Gwalior and in the Department of Biochemistry, G.R. Medical College & J.A. group of hospitals, Gwalior (M.P.). Total 400 subjects were taken out of which 300 were prediabetes young adult subjects and 100 were being normal age and gender matched healthy control subjects.

Exclusion Criteria: The Subjects with hepatic disorders, type I diabetes mellitus (DM), type II DM, other diseases and drugs that altered glucose metabolism and pregnant women.

Data Collection: All the information pertaining study like physiological parameters such as age, sex, height, weight etc., was noted in study proforma; also the written screening questionnaires and consent of the subjects were taken from the subject prior to analysis of blood. The study was approved by Institutional Ethical Committee, G.R. Medical College Gwalior.

Laboratory Measurements: After overnight fasting for 8-12 hours, blood was taken from antecubital vein. The plasma glucose, serum aspartate transaminases (AST), alanine transaminases (ALT), alkaline Phosphatase (ALP), gamma glutamyl transpeptidase (GGT) were measured by Mindray BS400 Chemistry Analyzer. The plasma glycated hemoglobin was estimated by boronate affinity chromatography.

Statistical Analysis: For the statistical analysis, the data was entered in Microsoft Excel and coding and cleaning was done in same. Mean and standard deviation was compared by using Z-test. The data was analyzed by using the Statistical Package for the Social Sciences, version 23.0 (SPSS software).

Result

Table 1 showing the comparative changes of anthropometric parameters **(**Mean ±SD) in normoglycemic subjects and prediabetic young subjects. The weight, body mass index (BMI), Waist circumference (WC) and waist/hip circumference ratio (WHR) were statistically extremely significantly ($p<0.001$) increased and systolic blood pressure were statistically highly significantly ($p<0.01$) increased while diastolic blood pressure was statistically significantly increased in ($p<0.05$) prediabetic young subjects as compared to normoglycemic subjects. Table 2 showing the comparative changes of glycemic parameters and liver enzymes parameters **(**Mean ±SD) in normoglycemic subjects and prediabetic young subjects. The serum FBS, IGT, HbA1c, ALT, GGT were statistically extremely significantly ($p<0.001$) while serum ALP was statistically significantly ($p<0.05$) increased in prediabetic young adult subjects as compared to normoglycemic subjects. The serum AST level was non-significant in prediabetic young adult subjects as compared to normoglycemic subjects. The graphic representation of metamorphic changes of liver enzymes in prediabetic young adult was shown in the figure 1.

Table-1: Showing the comparative changes of anthropometric parameters in normoglycemic subjects and prediabetic subjects

Parameters	Normoglycemic subjects	Prediabetic subjects
	Mean ±SD	Mean ±SD
Weight (Kg)	61.57 ±7.94	67.93 ±6.06***
Height (meter)	1.64 ±0.12	1.65 ±0.10 ^{NS}
BMI (kg/m^2)	22.93 ±1.21	24.94 ±2.77***
Waist circumference (Cm)	79.17 ±4.6	83.13 ±5.50***
Hip circumference (Cm)	98.07 ±4.42	98.37 ±5.23 ^{NS}
Waist/Hip Ratio	0.81 ±0.05	0.85 ±0.03***
Systolic Blood Pressure (mmHg)	119.8 ±3.54	121.01 ±3.78**
Diastolic Blood Pressure (mmHg)	79.96 ±2.63	80.74 ±2.70*

* Statistically significant at 0.05 ($p<0.05$) ** Statistically highly significant at 0.01 ($p<0.01$)
*** Statistically extremely Significant at 0.001 ($p<0.001$) ^{NS}Non significant

Table-2: Showing the comparative changes of glycemic parameters and liver enzymes of normoglycemics and prediabetic subjects

Parameters	Normoglycemic subjects	Prediabetic subjects
	Mean ±SD	Mean ±SD
FBS (mg/dl)	87.41 ±6.13	115.77 ±7.69***
IGT (mg/dl)	123.78 ±7.7	153.95 ±7.81***
HbA1c (%)	4.56 ±0.22	5.96 ±0.18***
AST (IU/L)	28.41 ±3.96	28.92 ±4.52^{NS}
ALT (IU/L)	31.78 ±5.22	33.6 ±4.28***
ALP (IU/L)	68.7 ±8.6	71.65 ±8.77**
GGT (IU/L)	28.54 ±4.25	35.4 ±4.61***

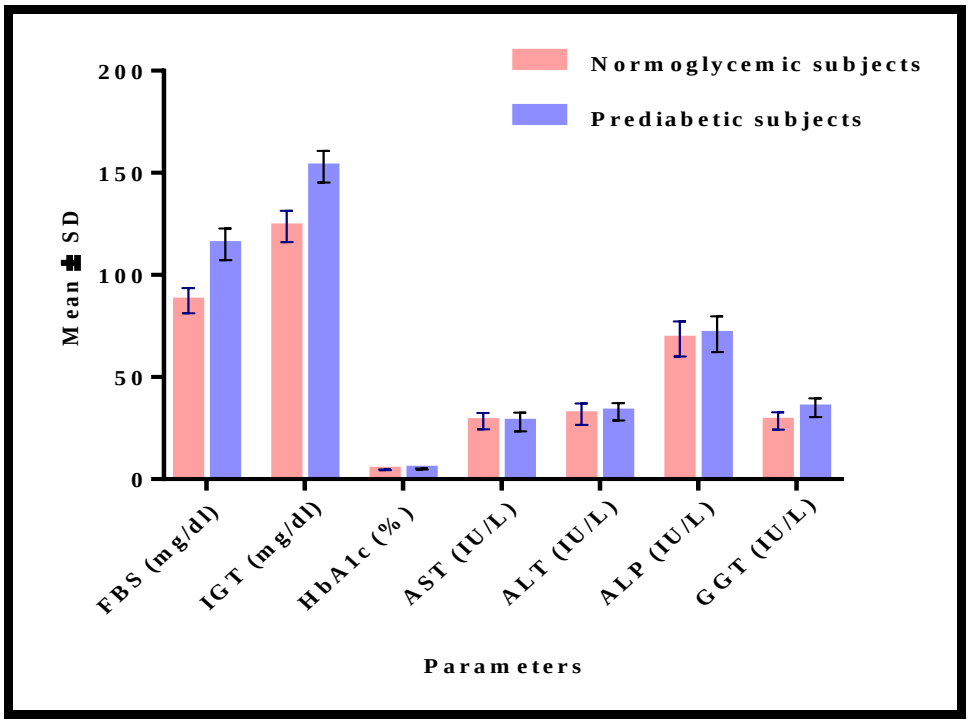

Figure 1: graphical representation of metamorphic changes of liver enzymes in prediabetic subjects as compared to normoglycemic subjects

Discussion

Prediabetes is the risk factors for various diseases and complications[8,11,12]. It may affect various metabolic pathways which are taking place in the liver[13]. So, in this study we compare the metamorphic changes of livers enzymes in prediabetic young adult subjects and normoglycemic subjects taken from cross-sectional survey. The statistical analysis showed that the prediabetes subjects had more weight, BMI, WC, WHR, blood pressure and liver enzymes (ALT, ALP and GGT). Other scientific evidences also supported that prediabetic subjects have higher BMI, WC and WHR[14-16]. Haghighatdoost F et al., concluded that the WC, WHR, BMI was not a significant predictors for prediabetes[17] which is not similar with our finding. The probable reasons for increased WC, WHR and BMI (measures of obesity) are decreased glucose tolerance, alterations in glucose insulin homeostasis, reduced metabolic clearance of insulin, and decreased insulin-stimulated glucose disposal[18]. Various researches supported that the prediabetic subjects had pre-hypertension or hypertension because of the alteration of the endothelial cell structure and function by altered glucose metabolism[19-21] which is consistent with our finding. Liver is vital organ for metabolism. The majority of the metabolic reactions taking place in the liver is regulated by liver enzymes. The liver enzymes (AST, ALP, and GGT) are elevated in our study which is consistent with the various researches on the liver enzymes [22 - 25].The impaired glucose homeostasis is likely to be characterized by altered liver enzymes[26,23]. The liver is a vital organ for insulin clearance[27,28] and generation of inflammatory cytokines[29]. The possible mechanism of altered liver enzymes in prediabetic subjects can be accomplished by accumulation of visceral fats which causes visceral obesity[30,31]. Non-alcoholic fatty liver diseases (NAFLD) and hepatic insulin resistance intervened by raised hepatic free fatty acid flux from visceral fats which brings increased lipogenesis and TG-rich lipoprotein secretion in the liver [23,32,33]. Over accumulation of unoxidized long chain fatty acid exceeds the storage capacity of lipids in adipose tissue which brings overflow of lipid from other tissues such as liver, heart muscles and pancreas. The lipid infiltration causes metabolic disturbances which may induce abnormal liver enzymes concentration[23,34] The GGT and insulin resistance are connected to each other due to oxidative stress and production of reduced glutathione by the GGT [25]. The serum GGT may be one of the main indicators of insulin resistance [35]. The serum GGT is associated with decreased hepatic insulin clearance, peripheral as well as hepatic insulin resistance[25]. The increased expression of GGT indicates increased production of reactive oxygen species[36] which is much more than the antioxidant capacity of GGT, leading to oxidative stress[37]. The oxidative stress is responsible for altered glucose metabolism and prediabetes or increased risk for diabetes[38]. The GGT is an index of insulin resistance linked to NAFLD which is the risk factor for prediabetes[39]. The insulin metabolism is inhibited in the liver by inflammatory cytokines produced from the liver due to chronic inflammation caused by raised GGT involved in NAFLD[40]. These mechanisms lead to alteration of liver enzymes in prediabetic young adult subjects.

Conclusion

The liver enzymes could be used as cheap and readily available early diagnostic markers for deranged metabolism in prediabetic young adult subjects. It is very important to regularly follow up liver enzymes in prediabetic young adult subjects to prevent the onset of disease and related complication.

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