

EVALUATION OF APOLIPOPROTEIN-B LEVELS IN DYSGLYCEMIA

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ABSTRACT

Lifestyle modifications have resulted in an increased prevalence of dysglycemia in young individuals. Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) represent intermediate stages of abnormal glucose regulation that exists between normal glucose homeostasis and diabetes. IFG is considered as a potential indicator of preventive importance for diabetes and cardiovascular diseases. The plasma concentration of apolipoprotein B (apo B) indicates the cumulative number of atherogenic particles. The study group included 50 patients with IFG and 50 euglycemic subjects in the age group of 20-35 years. Apo-B and lipid profile measurements were carried out. As compared to the euglycemic group, in the dysglycemic group the Body Mass Index (BMI) and apo-B levels were significantly elevated while there was no significant difference in Low Density Lipoprotein-Cholesterol (LDL-C) levels. The inclusion of apo-B in atherogenic risk assessment will be beneficial for early identification and intervention strategies.

Keywords: Dysglycemia, Impaired Fasting Glucose, apolipoprotein-B.

INTRODUCTION

Dysglycemia includes Impaired Fasting Glucose (IFG), Impaired Glucose Tolerance (IGT) and diabetes. Pre-diabetes includes IFG and IGT [1]. IFG and IGT represent intermediate stages of abnormal glucose regulation that exists between normal glucose homeostasis and diabetes [2]. IFG is defined as elevated Fasting Plasma Glucose (FPG) concentration ≥ 100 mg/dl and < 126 mg/dl [3]. Patients with IFG or IGT were approximately 5-10 times likely to develop diabetes within 1 year than people without IFG or IGT [4]. IFG has received increasing attention in recent years, because it is an intermediate stage in the development of diabetes and cardiovascular diseases (CVDs) [5, 6, and 7]. In a developing Country like India Obesity and Malnutrition are two ends of spectrum, obesity being an emerging issue which needs closed monitoring [8]. Diabetic dyslipidemia most commonly manifests as elevated triglycerides and low levels of HDL cholesterol, with a predominance of small dense LDL particles amid relatively normal LDL cholesterol levels [9]. Small dense LDL cholesterol is highly atherogenic due to its ability to penetrate the arterial wall and has low affinity for the LDL receptor [10].

Apolipoprotein B is the main structural protein of atherogenic lipoproteins VLDL, IDL and LDL [11]. Therefore the plasma concentration of apo B indicates the cumulative number of atherogenic particles. Modifications of lipoproteins by glycation and oxidation and variations in the size distributions of lipoprotein particles are not reflected in conventional lipid profiles [12]. Apo B levels are more stable than lipid levels particularly in individuals with hyperglycaemia and are not affected significantly by prandial status [13, 14]. Thus, the measurement of apo B provides additional information to that obtained by assessing LDL-C.

Inclusion of this parameter in the standard lipid profile, may aid in risk prediction. The relationship between IFG and markers of dyslipidemia vary in different populations. Numerous longitudinal studies indicate that both IFG and IGT are associated with a modest increase for CVD. Both IFG and IGT are independent risk factors for CVD in some studies but not in others [15-25]. Since IFG is the early stage of diabetes and cardiovascular diseases, identifying preventable risk factors associated with IFG at this early stage is very important in prevention and control of these diseases [26]. Hence we have analysed the levels of apolipoprotein B, along with lipid profile in young individuals with impaired fasting glucose.

MATERIALS AND METHODS

The study was conducted at SRM Medical College Hospital and Research Centre, SRM Nagar, Potheri. Biochemical characteristics of fifty subjects with Impaired Fasting Glucose (IFG) and fifty healthy euglycemic subjects were compared. The study was approved by the Institutional Ethical Committee. An informed consent was taken from all the participants. Individuals with history of ischemic heart disease, clinical evidence of acute infection, renal and hepatic disease, hypo and hyperthyroidism, recent surgery/major trauma and those using lipid lowering and hypoglycemic drugs were excluded from the study.

5 ml of venous blood was collected from the subjects after an overnight 12 hour fast. Serum total cholesterol (TC), triglycerides (TGL), HDL-C and plasma glucose were measured using standard enzyme kits in auto analyser on the same day of sample collection. LDL-C was calculated by Friedewald's formula. The serum was stored at -20°C and apo-B was analysed by immunoturbidimetric method using fully automated Beckmann Coulter analyser.

STATISTICAL ANALYSIS

All data were expressed as the mean and standard deviation. SPSS 20.0 software was used for statistical analysis. The statistical significance of biochemical parameters for subjects with impaired fasting glucose and healthy euglycemic subjects were analyzed by using unpaired students 't' test and $p < 0.05$ was accepted as statistically significant.

RESULTS

Table I shows the laboratory characteristics of the participants. In patients with IFG, the serum levels of apo B [82.65 ± 11.96 vs. 67.9 ± 7.96 mg/dl, $p < 0.01$] was significantly elevated when compared with the euglycemic group. BMI [25.90 ± 3.04 vs. 23.12 ± 1.2 kg/m², $p < 0.01$] was significantly increased in the dysglycemic group when compared with the euglycemic group. The mean levels of TGL and TC were significantly higher in dysglycemic patients. There were no significant differences in LDL-C and HDL-C levels between the two groups.

Table 1: Comparison of Mean \pm S.D of measured parameters between the euglycemic and dysglycemic groups and the statistical significance of the differences.

Parameters	Euglycemic Group (n=50) Mean \pm S.D	Dysglycemic Group (n=50) Mean \pm S.D	p Value
Fasting Plasma Glucose (mg/dl)	90.8 \pm 5.54	106.9 \pm 4.27	p<0.01
Body Mass Index (kg/m ²)	23.12 \pm 1.2	25.90 \pm 3.04	p<0.01
Apolipoprotein-B (mg/dl)	67.9 \pm 7.96	82.65 \pm 11.96	p<0.01
Total Cholesterol (mg/dl)	154.06 \pm 21.1	171.5 \pm 34.09	p<0.05
Triglycerides (mg/dl)	95.1 \pm 23.97	113.8 \pm 5.94	p<0.01
High Density Lipoprotein-C (mg/dl)	39.4 \pm 5.9	38.2 \pm 6.1	NS
Low Density Lipoprotein-C (mg/dl)	100.6 \pm 23.5	106.98 \pm 29.12	NS

The values are considered statistically significant if the p value is less than or equal to 0.05 (p \leq 0.05). NS = Not Significant

DISCUSSION

Type 2 diabetes is usually considered to be a disease of the middle-aged and elderly. IFG is considered to be a pre diabetic state [1]. Patients with diabetes or IFG have a substantially higher risk of cardiovascular events [27]. Lifestyle modifications have resulted in an increased prevalence of dysglycemia in young individuals. Hence the study group consisted of participants in the age group of 20-35 years. Impaired fasting glucose is considered to be predictive of an increased CAD risk [28]. A graded relationship between plasma glucose and cardiovascular risk is observed in non-diabetic individuals with high glucose levels that are below the diabetic cut-offs [29, 30].

Hyperglycemia due to insulin resistance is characterised by dyslipidemia and inflammation. The role of hormones like leptin, adiponectin and ghrelin have been reviewed in the progression of type-2 diabetes mellitus [31]. According to the consensus statement, the optimum cut-offs for BMI of Asian Indians is Normal BMI: 18.0-22.9 kg/m², Overweight: 23.0-24.9 kg/m², Obesity: >25 kg/m². The mean BMI of individuals with IFG was more than 25 kg/m². BMI was significantly increased in patients with IFG when compared with the euglycemic group. Obesity could result in higher insulin concentration, secretion and resistance. Yun Qian et al in a case control study of IFG in a Chinese population has demonstrated that the BMI is significantly related to FPG, TG, TC, HDL-C, Systolic blood pressure and Diastolic blood pressure. [26]

Drexel et al have reported on the prevalence of angiographic CAD in patients with IFG. The significantly increased levels of total cholesterol and triglycerides in the dysglycemic group of our study support this concept. Measurement of LDL cholesterol is relatively insensitive to the accumulation of small dense LDL particles which are believed to be highly atherogenic [32]. As there is one apo B per LDL particle, apo B detects the presence of these atherogenic particles. Apo B₄₈ concentrations comprise less than 1% of total apo B concentrations in the fasting or post prandial state [33]. In this study the dysglycemic group has significantly elevated apo B levels when compared to euglycemic individuals while there is no difference in LDL-C levels.

Martin et al have found that plasma apo B but not LDL cholesterol levels were associated with coronary artery calcification (CAC) in type 2 diabetes [34]. Apo B is a measure of LDL particle number (LDL-P). Cross-sectional studies of healthy individuals showed that LDL-P was associated with CAC in post-menopausal women [35] and carotid intima-media thickness [36]. The meta-analysis by Sniderman et al has indicated apo B is a more accurate marker of cardiovascular risk than LDL cholesterol [37]. Thus the increased concentration of apo B in IFG group indicates the presence of increased levels of atherogenic particles. Once triglyceride levels exceed 100 mg/dl, the atherogenic small, dense LDL predominate [38]. On the contrary, apolipoprotein-B levels were not associated with the presence of significant stenosis in a group of 750 patients who underwent coronary angiography [39].

Measurement of apolipoprotein levels has methodological advantages over measurement of LDL-C. Apo B can be measured directly, accurately, precisely, does not require fasting samples, is internationally standardized, may be conducted on frozen samples and can be easily automated [40,41,42]. Moreover even in patients

receiving lipid-modifying therapy, determination of subsequent cardiovascular risk is likely to be more accurate if it is based on assessment of apo B level rather than LDL-C [41].

CONCLUSION

The results of the study indicate that IFG is characterised by the presence of cardiometabolic risk factors. The measurement of plasma levels of apolipoprotein-B provides additional information to that obtained by conventional lipid profile. Therefore the inclusion of this parameter for atherogenic risk assessment will be beneficial for early identification and intervention strategies.

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