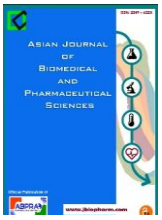
Asian Journal of Biomedical and Pharmaceutical Sciences
ISSN : 2249 - 622X



RESEARCH ARTICLE

Received on: 16-02-2014
Accepted on: 25-02-2014
Published on: 15-03-2014

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Conflict of Interest: None Declared !

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Association between Serum Lipid Profile and Glycated Hemoglobin in Pre-diabetic Individuals

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Abstract

Background: Pre-diabetes is a condition in which the blood glucose level is above normal but below the diagnostic threshold for diabetes mellitus. Impaired lipid profile i.e dyslipidemia is commonly associated with CVD in type 2 diabetes and can also occur in pre-diabetics.

Material and method: The present study was conducted on 50 patients with no sign and symptoms of diabetes mellitus with HbA1c level between 5.7% – 6.4%. Pre-diabetic individuals were categorized into 2 groups according to their fasting blood sugar level, FBS < 110 mg/dl as normal and for impaired fasting glucose between 110 – 125 mg/dl. HbA1c was analyzed by high pressure liquid chromatography (Biorad D10). Fasting blood sugar and lipid profile were analyzed on Vitros 250 dry chemistry fully autoanalyzer.

Result: There was no significant difference in total cholesterol, triglyceride, HDL-c, VLDL, LDL, TC/HDL and LDL/HDL in patients with normal and impaired fasting glucose level with HbA1c between 5.7% – 6.4%

Conclusion: Relationship between high risk range of HbA1c (5.7% - 6.4%) and CVD mortality is still not clear. Studies on large population are required to find out whether estimation of lipid profile in pre-diabetic should be used routinely or not in pre-diabetic patients..

Keywords: Cholesterol, Cardiovascular diseases, Diabetes, Dyslipidemia

Cite this article as:
Kalpana Singh, Neha Srivastava, Ram Lakhan Singh, Abbas Ali Mahdi. Association between Serum Lipid Profile and Glycated Hemoglobin in Pre-diabetic Individuals. Asian Journal of Biomedical and Pharmaceutical Sciences; 04 (29); 2014; 30-33.

INTRODUCTION

In Indian population, 61.3 million people had diabetes in 2011, which is expected to reach 101.2 million by 2030 (International Diabetes Federation) now placing India at second position in world diabetic prevalence [1]. Diabetes mellitus has become a global pandemic, generating overwhelming costs and burdens upon patients as well as health care providers. Its pathological complications are associated with increased mortality and morbidity [2-4]. The defining diagnostic feature of diabetes is an abnormal glucose metabolism, categorized as 'pre-diabetes' in its early stage [5]. Pre-diabetes is a condition in which the blood glucose level is above normal but below the diagnostic threshold for diabetes mellitus [6]. According to National diabetes fact sheet 2011, in United States 79 million people were in pre-diabetic phase. The American Diabetes Association reports that approximately 11% of people with pre-diabetes who receive no treatment or intervention will develop type 2 diabetes every year [7]. A recent study conducted by Anjana RM et al, (2011) reported that 77.2 million populations in India fall in pre-diabetic group or the risk group [1].

Impaired glucose metabolism included two conditions: Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT). IFG a condition when fasting blood glucose levels are higher than normal but below the cut off used for diagnosing diabetes mellitus i.e 110-125 mg/dl (5.6-6.9 mmol/l) while IGT, a condition when 2 hr post prandial blood sugar level are higher but still below the cut off used for diagnosing diabetes between i.e 140-199 mg/dl (7.8-11.0 mmol/l). Pre-diabetes are characterized by either impaired fasting glucose and impaired glucose tolerance or glycated haemoglobin (HbA1c) level between 5.7%-6.4% or both [8].

Pre-diabetes is multifactorial and common risk factors includes being overweight especially those who have excess weight around the waistline, physically inactive, dyslipidemia (high triglycerides and low high density lipoprotein cholesterol and/ or high total cholesterol), high blood pressure, polycystic ovarian syndrome, gestational diabetes, family history of type 2 diabetes and/or heart disease. Pre-diabetes occurs 73.4% more frequently in people with family history of diabetes as compared to those without family history and are at higher risk of developing diabetes and its complications [9].

Pre-diabetics are at higher risk of having low level of high density lipoprotein cholesterol (HDL-c), increased level of low density lipoprotein cholesterol (LDL-c), high triglyceride (TG), and hence are at higher risk of cardio vascular disease (CVD). Impaired lipid profile i.e dyslipidemia is commonly associated with CVD in type 2 diabetes and can also occur in pre-diabetics. There are evidences which show that pre-diabetics are at higher risk of developing type 2diabetes. According to Saudek CD et al, (2008) macrovascular and microvascular complications can start in pre-diabetic individuals with IFG or IGT [10]. Early detection of impaired lipid profile in pre-diabetic phase will reduce the risk of CVD and its complications.

Physicians are using fasting plasma glucose test and 2hr post prandial test from decades for screening diabetes. The glycated hemoglobin (HbA1c) provides information about a person's average levels of blood glucose over the past 8 – 10 weeks. Glycated hemoglobin was first identified in 1968 as novel hemoglobin associated with diabetes [11]. In 1977 it was recognized as potential indicator of glycaemic control [12]. HbA1c estimation is based on the attachment of glucose to hemoglobin, the protein in red blood cells that carries oxygen. In the body, red blood cells are constantly forming and dying, but typically they live for about 120 days. Thus, the HbA1c test reflects the average of a person's blood glucose levels over the past 2 - 3 months. According to American Diabetes Association (ADA) an HbA1c level of ≥ 6.5% is recommended as the cut off point for diagnosing diabetes but a value less than 6.5% does not exclude diabetes. HbA1c level below 5.7% is considered as non-diabetic while between 5.7% - 6.4% are pre-diabetics and they are at higher risk of developing diabetes. Previous studies have taken IFG or IGT to categorize patients in pre-diabetic or diabetic phase. In this study we have taken ADA criterion of HbA1c level between 5.7% – 6.4% as pre-diabetes and estimated the fasting lipid profile in same patients. Very few literature are available, to our knowledge no such study is available in India where diabetes is now declared as an epidemic and prevalence of pre-diabetes is also high especially in urban population. The aim of this study was to compare total cholesterol, triglyceride, HDL-c, VLDL and LDL cholesterol levels in pre-diabetic subjects with HbA1c between 5.7% - 6.4%.

MATERIALS AND METHODS

The present study was conducted on 50 patients with no sign and symptoms of diabetes mellitus with HbA1c level between 5.7% – 6.4%, aged between 35 – 70 years presented to the OPD of King George's Medical University, Lucknow Uttar Pradesh over a period of 3 months. After obtaining informed consent from the patients, venous blood sample were taken and analyzed in Department of Biochemistry, King George's Medical University, Lucknow Uttar Pradesh, India. In our study for selection of pre-diabetic patients we have taken American Diabetes Association criteria of

glycated hemoglobin. Pre-diabetic individuals were categorized into 2 groups according to their fasting blood sugar level, FBS < 110 mg/dl as normal and for impaired fasting glucose between 110 – 125 mg/dl. HbA1c was analyzed by high pressure liquid chromatography (Biorad D10). Fasting blood sugar and lipid profile were analyzed on Vitros 250 dry chemistry fully autoanalyzer. NECP ATP III (National Cholesterol Education Program Adult Treatment Panel III) guidelines for dyslipidemia were also used to calculate the percentage of individuals with abnormal lipid profile. Variables were represented in mean ± SD and n (%). Student test't' test, Fisher Exact test and chi square test was used to test the significance. P value ≤ 0.05 was taken as statistically significance.

RESULTS AND DISCUSSION

Out of 50 pre-diabetic patients enrolled in our study 37 were having normal fasting blood glucose and 13 were in impaired fasting glucose range. The difference between males and females was not statistically significant (χ^2= 0.04; P value > 0.05). There was no significant difference in total cholesterol, triglyceride, HDL-c, VLDL, LDL, TC/HDL and LDL/HDL in patients with normal and impaired fasting glucose level with HbA1c between 5.7% – 6.4% as shown in Table1. When NECP ATP III guidelines for dyslipidemia were considered, there was no significant difference in lipids profile levels among pre-diabetics with normal and impaired fasting blood glucose level as shown in Table 2.

Lipids Variables	Normal Fasting Glucose (n=37)	Impaired Fasting Glucose (n=13)	't'	'P value'	Significance
TC(mg/dl)	155.40 ± 42.68	153.84 ± 49.91	0.10	0.91	NS
TG(mg/dl)	124.35 ± 45.77	141.53 ± 60.16	1.07	0.28	NS
HDL-c(mg/dl)	40.18 ± 15.05	39.69 ± 15.58	0.10	0.92	NS
VLDL(mg/dl)	24.89 ± 9.19	28.30 ± 11.90	1.06	0.29	NS
LDL(mg/dl)	88.75 ± 34.55	86.53 ± 33.57	0.20	0.84	NS
TC/HDL-c	4.29 ± 1.55	4.33 ± 1.69	0.076	0.94	NS
LDL/HDL-c	2.38 ± 0.90	2.44 ± 1.07	0.21	0.83	NS

Table 1: Comparison of Lipids Profile variables in pre-diabetics with normal & impaired fasting blood glucose level

DISCUSSION

In this study we enrolled 50 individuals having no history of diabetes mellitus with HbA1c level between 5.7% - 6.4%. We divided the subjects into 2 groups according to their fasting blood glucose level, 37 subjects were having normal fasting blood sugar while 13 were having impaired fasting glucose levels. Mean age in both the groups were not significantly different (t= 0.08, P= 0.92). No significant difference seen in number of males and females in both the groups (χ^2= 0.04, P> 0.05). There was no significant difference in mean levels of total cholesterol, triglyceride, HDL-c, VLDL and LDL cholesterol (P= 0.91, 0.28, 0.92, 0.29, 0.84) between subjects with normal and impaired fasting glucose. Also no significant difference in TC/HDL-c and LDL-c/HDL-c ratios observed between two groups as shown in Table 1. Mean levels of TC, TG, HDL-c and LDL-c of both the groups were also compared with the guidelines provided by NCEP-ATP III for dyslipidemia as shown in Table 2. Group with normal fasting glucose, elevated levels of TC, TG and LDL-c was found in 18.92%, 29.73%, 43.24% subjects and in IFG group it was 23.08%, 46.15% and 30.76%. Though, the number of subjects with hypertriglyceridemia was more in IFG as compared to subjects with normal fasting glucose but it was not statistically significant. HDL-cholesterol was low in 43.24% and 46.15% subjects with normal fasting glucose and IFG levels.

Lipids Variables	Normal fasting glucose (n=37)	Impaired fasting glucose (n=13)	Fisher Exact Test	Significance
TC	7 (18.92%)	3 (23.08%)	0.72	NS
TG	11 (29.73%)	6 (46.15%)	0.32	NS
HDL-c (low)	16 (43.24%)	6 (46.15%)	1.0	NS
LDL-c	16 (43.24%)	4 (30.76%)	0.52	NS
TC/HDL	10 (27.03%)	4 (30.76%)	1.0	NS
LDL/HDL	12 (32.43%)	4 (30.76%)	1.0	NS

Table 2: Comparison of abnormally raised lipids profile variables in patients with normal & impaired fasting glucose level according to NCEP ATP III

In our study no significant difference in lipid profile variable was observed in pre-diabetic patients with normal fasting glucose and impaired glucose tolerance having HbA1c in high risk range as suggested by American Diabetes Association. Our findings are contrary to the findings of Anjaneya PV et al, but in their study cut off used for fasting blood glucose was > 100 mg/dl for pre-diabetics [13]. We observed no significant difference in HDL-c while Botnia-study showed low HDL-c in pre-diabetics with IFG [14]. There are few factors which may have affected our data firstly, we used cut off for selecting pre-diabetic group i.e HbA1c 5.7% - 6.4% as suggested by American Diabetes Association. We recommend a study to decide whether the cut off provided by American Diabetes

Association can be used on Indian population as it may be affected by race/ethnicity. Secondly, we took cut off for normal fasting sugar < 110mg/dl because in India it is commonly used by the biochemists and clinicians. Cut off for fasting blood sugar should be reduced as now diabetes is declared as an epidemic worldwide and India is among the developing countries with increasing prevalence of diabetes and obesity. Thirdly, sample size of our study was very small, similar study on large sample size is required to find out whether dyslipidemia is associated with pre-diabetes or not. Lastly, we recommend a study which can compare IFG, IGT and HbA1c as a test to diagnose pre-diabetics. On long term follow up approximately one-third pre-diabetics convert to type 2 diabetes, one-third remain in pre-diabetic phase while one-third convert back to normoglycemia. We would like to recommend long term study for dyslipidemia which focus on one-third pre-diabetics who progress to diabetes and also to find out association between dyslipidemia and IFG and a normal fasting blood glucose level.

CONCLUSION

Relationship between high risk range of HbA1c (5.7% - 6.4%) and CVD mortality is still not clear. Other factor which increases the risk of diabetes like smoking, BMI, genetic factor and dyslipidemia should be taken into consideration to identify pre-diabetic patients who actually are at risk and can prevent their progression to diabetes and its complications by treating them at early stages. Studies on large population are required to find out whether estimation of lipid profile in pre-diabetic should be used routinely or not in pre-diabetic patients.

ACKNOWLEDGMENT

We are thankful to patients for giving their consent for this study. We would also like to thank our technicians for helping us in analysis of samples.

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