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CORRELATION STUDY OF BLOOD G6PD LEVELS WITH DYSLIPIDEMIA IN TYPE 2 DIABETES MELLITUS

Biochemistry

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ABSTRACT

Glucose -6-phosphate dehydrogenase (G6PD) is the rate limiting enzyme of pentose phosphate pathway which produce NADPH , involved in lipid biosynthesis. Insulin is an anabolic hormone having profound influence on various key enzymes involved in lipid metabolism. The current study was designed to evaluate serum G6PD activity and its association with dyslipidemia in Type 2 DM. Total 100 diabetic patients and 100 age and sex matched healthy controls were included in the study. Blood G6PD was measured by chemical method. Estimation of cholesterol , TG , HDL, LDL was done in autoanalyzer . Statistical analysis was done by SPSS Version 20 software. Mean G6PD levels was significantly higher in diabetic cases . Increased G6PD levels correlates positively with TC,TG,LDL, however HDL shows a negative correlation. Increased activity of G6PD in diabetic cases, alters lipid homeostasis which leads to atherogenic abnormalities. Estimation of serum G6PD & its correlation with dyslipidemia can highlight its role in regulating lipid status in diabetes mellitus patients .

KEYWORDS

G6pd, Dyslipidemia, NADPH

INTRODUCTION -

According to International Diabetes Federation(IDF) 415 million people worldwide were suffering from Type 2 DM in 2015 which is projected to increase to 642 million in 2040[1]. Diabetic dyslipidemia is a complex cluster of potentially atherogenic lipid and lipoprotein abnormalities involving both quantitative and qualitative changes. Chronic hyperglycemia exerts a deleterious effect on the vascular wall and, by glycation of apolipoproteins , interferes with the normal pathways of lipoprotein metabolism. Increased plasma triglycerides, is linked to an active reductive synthesis pathway which involves increased G6PD activity being the major pathway for generation of NADPH.

Glucose -6-phosphate dehydrogenase (G6PD) is the rate limiting enzyme of pentose phosphate pathway which produce NADPH the cells principal reductant involved in reductive biosynthesis of lipids. Insulin is an anabolic hormone having profound influence on various key enzymes involved in lipid metabolism. The excess free fatty acid is ultimately stored in non-adipose depots leading to increased intramyocellular lipids , which causes insulin resistance[2,3].

AIMS AND OBJECTIVES -

The current study was designed to correlate serum G6PD activity which produces NADPH and its association with dyslipidemia in Type 2 DM

MATERIAL AND METHODS-

It is a Case Control hospital based study. Total 100 patients (76 males 24 females) with history of Type 2DM were selected from Medicine & Endocrinology OPD of MKCG Medical College. Equal age & sex matched healthy individuals were taken as controls. The study was approved by Institutional Ethical Committee . This study includes Type 2 DM patients, Non-smokers with or without complications where as Smokers and patients with autoimmune disorders were excluded from the study.

A morning sample of venous blood (5ml) was collected after overnight fast. The sample was analysed for G6PD, FPG , Fasting insulin and lipid profile. G6PD was measured by chemical method in semiauto analyzer. Estimation of cholesterol, triglyceride, HDL, VLDL and LDL was done in autoanalyzer . For serum lipid level , National Cholesterol Education Programme(NCEP) Adult Treatment Panel(ATP III) guidelines were referred[4]. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentrations. Fasting insulin (FI) levels were analysed in Roche Cobas e411 by electrochemiluminescence method.

Statistical analysis was done by SPSS Version 20 software. Analysis of data was done using independent sample't'test(2-tailed) and correlation was calculated by using the Pearson's correlation method. p value of <0.05 was considered significant.

RESULTS -

In this study the mean age of diabetes mellitus patients is 52yrs as it is more common in middle age group. The anthropometric attributes like age , BMI , waist circumference , BP were elevated but not stastistically significant in diabetic patients when compared to healthy subjects ($p>0.05$). The levels of FPG level was found to be higher in diabetic cases which is stastistically significant . The mean of FI & HOMO-IR levels are higher in controls when compared with cases.

Table 1 - Anthropometric and metabolic characterstics of Type-2 diabetics and controls

Parameters	Diabetics(N=100)	Controls(N=100)	p value
Age (yrs)	52.6±8.5	51.5±10.2	0.416
BMI(kg/m2)	28.2±4.9	28.5±4.0	0.690
Waist ciruumference (cm)	99.7±9.93	100.2±10.5	0.295
SBP(mm of Hg)	132.3±16.21	131.2±31.6	0.862
DBP(mm of Hg)	81.6±10.8	82.1±10.1	0.295
FPG(mg/dl)	146.64±25.55	96.39±10.29	0.000
Fasting Insulin (µIU/ml)	16.35±7.72	6.29±1.15	0.00
HOMO-IR	5.83±2.79	1.49±0.33	0.00

The levels of TC , TG , LDL and VLDL were significantly higher in patient group as compared to controls, ($p<0.05$) . The levels of HDL Cholesterol was found to be significantly lower in diabetics as compared to control group. Dyslipidemia is most frequently seen in diabetics and they are at greater risk of developing atherosclerotic diseases.

Table 2 – Comparative analysis of lipid profile parameters in healthy control subjects & diabetic patients

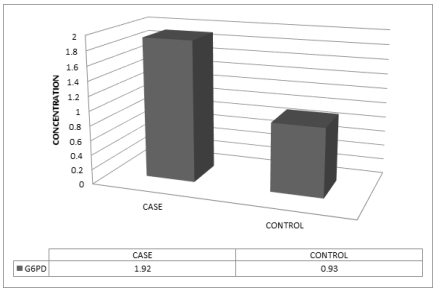
Parameters(mg/dl)	Case	Control	p value	t
TC	204.37±40.27	129.04±25.82	0.000	15.74
TG	207.95±114.85	127.74±31.69	0.000	6.73
HDL	31.78±6.64	35.09±13.39	0.028	-2.21
LDL	116.12±34.19	76.16±18.56	0.000	10.27
VLDL	41.58±22.92	25.56±6.33	0.000	6.72

Table 3 shows the Mean ± SD of G6PD the control and patient groups was **0.09 ± 0.06 and 1.92± 0.55** respectively. In our study the levels of G6PD was found to be higher in diabetic patients as compared to controls which is statistically significant. (Graph-1)

Table 3- Comparison of Glucose-6-phosphate Dehydrogenase (G6PD) activity in diabetics and controls

	Case	control	p	t
G6PD(mU/mL)	1.92±0.55	0.09±0.06	0.00	32.59

Graph 2 - Mean of G6PD Activity in Cases and Control



G6PD is positively and significantly correlated with Total Cholesterol ($R^2 = 0.680$) , Total Triglyceride ($R^2 = 0.358$) , LDL cholesterol ($R^2 = 0.549$) , VLDL Cholesterol ($R^2 = 0.385$) but it is negatively correlated with HDL Cholesterol ($R^2 = -0.151$ p= 0.033).(Table 4)

Table 4: - Correlation of Glucose –6- phosphate Dehydro ge nase (G6PD) with Lipid Profile in diabetic patients

	TC		TG		HDL		LDL		VLDL	
	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p
G6PD	0.680	<0.001	0.358	<0.001	-0.151	0.033	0.549	<0.001	0.385	<0.001

FBS is positively and significantly correlated with Fasting insulin(R^2 = 0.483) and HOMA-IR (R^2 = 0.676) . On comparision it was observed that as the FBS level rises there is increase in Insulin Resistance (Table 5).

Table 5: - Correlation of Fasting plasma glucose with Insulin Resis tan ce in diabetic patients

Parameters	Fasting Insulin		HOMA-IR	
	R^2	p	R^2	p
FPG(mg/dl)	0.483	<0.001	0.676	<0.001

DISCUSSION-

G6PD is an intracellular enzyme and barely shows any serum activity[5]. But in our study we have found that serum activity is increased in diabetic patients as compared to healthy individuals . Joshi et al.,2001[6] observed a slight increase in the activity of G6PD in patients with Type 2 DM.

Lipid metabolism in type 2 diabetes is modulated by the degree of glycemic control and the presence of insulin resistance , the two most prominent players. Insulin resistance is the basis of the pathophysiologic mechanisms of diabetic dyslipidemia, being closely linked to hypertriglyceridaemia and postprandial lipemia .Lipid & lipoprotein abnormalities in type2 diabetes are due to the effects of insulin deficiency & insulin resistance on key metabolic enzymes. Patient populations in our study shows statistically significant relationships between changes in glucose and changes in the various components of the lipid panel over the same time period. The only component that did not show statistical significance in both groups was that of HDL, but there was a somewhat inverse relationship between those two variables in the glucose intolerant patient group. This helps to reinforce the idea that decreasing HDL is associated with insulin resistance. Overproduction of VLDL alter the composition of HDL through the actions of CETP(cholesteryl aster transfer protein) and hepatic lipase, leading to the formation of small dense HDL and increased catabolism of these particle resulting in reduced amount of circulating HDL particles. Triglycerides in HDL are a good substrate for hepatic lipase and the hydrolysis produces smaller HDL particles and free apoAI which is excreted by the kidneys. The protective effect of HDL is attributed mainly to its role in reverse cholesterol transport but other HDL properties (anti-inflammatory, antioxidant, antithrombotic, etc) may also be involved. This ultimately leads to atherosclerotic coronary artery disease[7].

Low HDL-C was a common finding associated with raised serum TG, serum cholesterol and LDL- C. Our study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C , high VLDL-C and low HDL-C levels which are well known factors for dyslipidemia in diabetes mellitus. Insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein[8,9,10,11]. Dessi et al.,1992[12] reported that G6PD deficient patients showed a decreased lipogenic rate and serum lipoprotein concentrations, implying the importance of G6PD in fatty acid synthesis .G6PD produces cellular NADPH which is required for the biosynthesis of fatty acids & cholesterol.G6PD is regulated by the NADPH/NADP ratio , as the ratio decreases, activity increases to provide more NADPH. G6PD is activated following exposure of cells to various extracellular oxidants that lead to decrease in the level of NADPH. Since NADPH is indispensible for synthesis of fatty acids and cholesterol , it is plausible to speculate that NADPH producing enzymes might be associated with lipid metabolism such as hyperlipidemia and lipid peroxidation in metabolic diseases like diabetes mellitus.

CONCLUSION -

G6PD is an intracellular enzyme .The increased activity of G6PD in type 2 diabetics is associated with dyslipidemia resulting in failure of lipid homeostasis . Lipogenic activity of G6PD is regulated by nutritional signals and hormonal signals like insulin, glucagon, thyroid & glucocorticoids . Further study can highlight the role of G6PD in regulating the lipid homeostasis.

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