RESEARCH ARTICLE

GLUCOSE-6- PHOSPHATE DEHYDROGENASE ACTIVITIES IN DIABETICS A STUDY AT A TERTIARY CARE TEACHING HOSPITAL IN THE NORTH EAST INDIA

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Abstract

Background and Objectives: Diabetes mellitus is a common metabolic disease leading to various systemic complications in the affected individuals if not properly controlled with timely interventions. There are various studies showing the toxic effects of high blood glucose and its oxidant derivatives in the pathogenesis of various complications of the disease. Glucose-6- phosphate dehydrogenase (G6PD) is the key enzyme of hexose monophosphate shunt which produces NADPH that protects the body from oxidative damage and prevents from development of various complications. Uncontrolled blood glucose level for a longer duration time diminishes the G6PD activity and can lead the body into complications. This study was conducted in North-East India to evaluate the difference of G6PD activity among diabetics and non-diabetics and to study the impact of hyperglycemia on the G6PD activity.

Methodology: Fifty diabetic and fifty non diabetic subjects are selected from participants of age 45 to 76 yrs. Demographic data including age, sex, height, weight, duration of diabetes mellitus, presenting symptoms, medical history was taken. Blood pressure and BMI were also measured. Blood samples from each patients were sent for estimation of FBS and PPBS, G6PD screening test and enzyme kinetic study, blood urea and serum creatinine estimation and serum triglycerides estimation.

Results: G6PD activity was found to be diminished in diabetic patients, mild to moderately in comparison to the control group. It was also found that the deficient activity was dependent upon the duration of diabetes mellitus but not on the severity of the condition.

Introduction:
Diabetes mellitus (DM) is a common metabolic disease leading to various systemic complications in the affected individuals if not properly controlled. Its prevalence is increasing in developing countries. Diabetes mellitus causes a heavy impact on the health and economic status of the society. The common cause of death in diabetics are cardiovascular complications accounting for almost 75-80 % death. There is high incidence of coronary heart disease, cerebrovascular disease and peripheral vascular disease among diabetics. There are various recent studies showing toxic effects of high blood glucose and its oxidant derivatives in the pathogenesis of various complications of the disease. G6PD is the key enzyme of hexose monophosphate shunt (HMP) which is important for prevention

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of oxidative damage of various organs by producing NADPH. The impact of poorly controlled higher blood glucose levels on G6PD activity seems useful for better understanding of pathogenesis of DM and also prediction of its complications based on G6PD activity.\textsuperscript{9} The aim of the present study was to find out the incidence of deficient G6PD activity among diabetic patients and its relation with the duration of diabetes mellitus.

Methodology:

This study was conducted at a tertiary care teaching hospital of North-East India as similar studies was not conducted previously. Fifty diabetic patients were selected from various wards of the hospital from the age group 45 to 76 yrs and fifty non-diabetic subjects were also selected from age group of 45 to 76 yrs. Demographic data including age, sex, height, weight, duration of DM, type of treatment and other medical history were recorded for all patients. Diabetes mellitus was defined as fasting blood glucose (FBG) of 126 mg/dl or 2 hours post prandial blood sugar of 200mg/dl. Non diabetics had FBG <100 mg/dl, PPBG <140 mg/dl and also there was absence of any other major illnesses. Fasting lipid profile and BMI were also measured. Dyslipidemia was defined as fasting plasma triglyceride (TG) more than 250 mg/dl and fasting plasma HDL less than 35 mg/dl. Since BMI above 25 is a risk factor for type 2 DM it was also calculated. Hypertension as comorbidity was defined as systolic blood pressure more than 140 mm of Hg or diastolic blood pressure more than 80 mm of Hg. All patients of our study group were subjected to FBS, PPBS, HDL, G6PD screening test and G6PD enzyme kinetic study. G6PD deficiency was detected by Dye decolourisation test of Motulsky modified by Bernstein (1962). (Brilliant cresyl blue dye) was used by kit method which is a qualitative test for detection of G6PD activity. This test was recommended by WHO (1967) for screening of population for G6PD deficiency. Enzyme kinetic study for G6PD activity was done by spectrophotometry.

Results:-

50 nos of non diabetic subjects (40 males and 10 females) and 50 nos of diabetic patients (40 males and 10 females). The age of the patients ranged from 45 to 76 yrs with mean age 60 ± 15 years. 10 patients used insulin, 30 patients used oral hypoglycemic medicines and 10 patients used a combination of insulin and OHA in our study. 20 patients had a history of hypertension. Among diabetic patients 10% patients were of age group 41 to 50 yrs, 54 % patients from age group 51 to 60 yrs, 26 % patients from age group 61 to 70 yrs, and 10 % patients from age group 71 to 80 yrs. In our study 80% patients were male and 20% patients were female. 16 % patients had duration of DM for less than one year, 30 % patient had duration of 1 -5 years, 32 % had duration of 6- 10 yrs and 22 % patient had disease duration of more than 10 years. All diabetic patients of our study was subjected to G6PD screening test by dye decolourisation method. The time of decolourisation recorded after 30 minutes and every 30 minutes till the blue colour of the dye changed to red. Out of 40 male cases 30 cases (75.0%) cases decolourised the dye within 30 minutes, 7 cases (14.5 %) within 30 to 60 minutes, 2 cases (5.0 %) between 120 – 150 minutes and one case (2.5 %) after 240 minutes. Among the control cases 6.6% deficient activity was found being 7.5 % in male and 5.0 % in female. In our study 7 participants were found to be G6PD deficient out of 50 diabetic cases. The incidence of deficient G6PD activity being 14.0 %. Incidence in male being 15.0 % and incidence among female being 10.0 % . The difference between the incidence of male and female is statistically insignificant ( \textsuperscript{P}<.05 ). Among the control cases 6.6 % showed deficiency of G6PD, and diabetic patient showed 14.0 % deficiency of G6PD. ( \textsuperscript{P} <.05 ) which is statistically significant. Out of 50 diabetic cases 7 cases showed deficient G6PD activities. Therefore in the present study incidence of deficiency is 14.0%. In this study incidence of deficiency among male diabetic is 15.0 % and female diabetic is 10.0 % and which is statistically insignificant. The incidence of deficient G6PD activity was found to be lower (10 %) in diabetes mellitus of less than 10 yrs. duration than in diabetes mellitus of more than 10 yrs duration which was 20 % in this study.

Discussion:-

In the present study in the control group the overall incidence of deficient G6PD activity is 6.6 % out of which 1.6 % showed severely deficient activities and 5 % showed mildly deficient activities. In the study group there were altogether 50 cases of which 40 were male and 10 were female subjects. Of the 40 male subjects 34 subjects (85%) showed activities within the normal range, 3 (7.5 %) subjects showed mildly deficient activities and 2 subjects (5%) showed moderately deficient activities and one case (2.5%) showed severely deficient activities. Overall deficient activities was shown by 15.0% of male subjects of the test group. Of the 10 female ( 90% ) 9 subjects showed activities within normal limit and only (10%) one case showed mild deficient activities. The overall deficiency among the test group was 14.0 %. THE FINDINGS OF THIS STUDY IS IN CLOSE PROXIMATE TO THOSE REPORTED BY PREVIOUS STUDIES.\textsuperscript{5} In this study the overall incidence in the control group was 6.6 %,
whereas in the test group the incidence is 14.0 %. It indicates a higher frequency of incidence of G6PD deficiency in diabetes mellitus. The incidence of severe deficiency being approximately equal in both the group i.e. 2.0 % in test group and 1.6 % in the control group. The incidence of mild to moderate deficiency among the control is 5 % whereas the incidence of mild to moderate deficiency among the test group is 12.0 %. It appears that G6PD DEFICIENCY MAY NOT BE A PREDISPOSING CAUSE OF DM BUT A CONSEQUENCE OF DIABETIC STATE. In the present study no significant variation of the incidence of G6PD deficiency was observed. In mild cases it was 13.3 %, moderate cases 15.0 % and in severe cases it was 13.3 %. Similar observation was seen a study with presence of 12.4 % among diabetic patients and 2% in healthy controls. In the present study the relation between the duration of diabetes mellitus with the frequency of deficient G6PD activity was studied. Of the 50 test subjects 30 cases had duration of diabetes mellitus less than 10 yrs and 20 subjects had a diabetic state of more than 10 years duration . Among the 30 diabetic with less than 10 yrs duration 3 (10 %) subjects showed deficient activities and among 20 diabetics with more than 10 yrs duration 4 (20%) subjects showed deficient activities (P value is less than 0.05). From this observation it appears that the incidence of deficiency increases along with the duration of the diabetes state. G6PD deficiency is an inborn error of carbohydrate metabolism. Little effect would be expected on carbohydrate metabolism from an enzyme which is only involved in intracellular metabolism of glucose. The results of these studies confirm a positive association between diabetes mellitus and G6PD deficiency. There is a positive association between diabetes mellitus and G6PD. Hperglycemia has got negative effects on this enzyme as prolonged hyperglycemia may lead to continuous action of G6PD to convert glucose 6 phosphate to 6 phosphogluconate resulting in G6PD deficiency. This explanation is supported by a significant increase in the prevalence of deficiency with increase in the duration of diabetes. Correlation of G6PD deficiency with diabetes is not only of metabolic interest but also has clinical significance as diabetic acidosis may lead to acute self limited hemolyis crisis in G6PD deficient patients or may lead to drug induced haemolysis when diabetic person gets infection. Patients with G6PD deficiency may have a higher risk of developing diabetes. A systematic search on MEDLINE, EMBASE, AMED and CENTRAL database of studies published between 1966 to 2016 assessed the association between G6PD deficiency and diabetes. Current evidence suggests G6PD deficiency may be a risk factor of diabetes with higher odd among men compared to women. Another study showed that G6PD deficiency shows a trend for protection against diabetes with PDR but results are not satisfactorily significant. Studies shows that deficiency of G6PD leads to beta cell dysfunction and cell death in diabetic patients. High blood glucose and diabetes decrease G6PD activity in endothelial cells, kidney, liver and red blood cells which leads to oxidative damage, cellular dysfunction and organ damage.

**Conclusion:**

Deficiency of G6PD of erythrocyte is present in Assamese population. There is a close association of G6PD deficiency with diabetes mellitus as is evident from the observation of increased incidence of G6PD deficiency among diabetic population. G6PD deficiency was observed to be a consequence of the diabetic state rather than a predisposing cause for diabetes mellitus as incidence of severe deficiency was found to be almost equal among both the population i.e. control non diabetic and diabetic population and also incidence of mild to moderate deficiency is found to be higher among diabetic population. It has also been observed that G6PD deficiency increases along with the duration of diabetis. Most recent studies shows that diabetic hyperglycemia may lead to serious complications and decrease G6PD activity through glycation process and oxidative stress. This issue itself aggravates diabetic injury due to inappropriate anti oxidation process. Simultaneous dyslipidemia and obesity may intensify the effect of hyperglycemia and oxidative stress. Thus the G6PD activity level can reflect the glycemic control and even predict subsequent complications while they are not present. It is essential to screen all diabetic patients for G6PD activity. The end product of HMP shunt NADPH protects the cells from oxidative damage as high glucose level inhibits the GPPD activity leading to oxidative damage of pancreatic beta cells. As G6PD deficiency has a role in the apoptosis of pancreatic beta cells therefore it's screening can help to define the state of insulin requirements in a patient with type 2 diabetes mellitus.

**References:**

1. Diabetes mellitus : in : Braunwald E. Fauci AS, Longo DL, Kasper DL, Jamesh DL, Editors : Harrison’s Principle of internal medicine , 15 th ed, New York : MC Grow Hill ; 2005 ; 2015 – 2179.
2. Abnormal oral glucose tolerance response erythrocyte G6PD deficiency, D. Chanmugam, Abraham M. Frumin MD ; New England J Med. 1964 ; 271 : 1202-1204.
3. Genetics of Diabetes , DA Pyke , vol 6 issue 2 july 1977 pages 285 -303.
4. The occurrence of Diabetes in tropics , J A Tallock ; article ( pubmed ) SAGE journals.
5. Glucose 6 phosphate dehydrogenase deficiency and diabetes mellitus, GA Niazi; Int. J. Hematol 1991 Aug 54 (4) 295-298.

6. G6PD Deficiency Its role in the high prevalence of hypertension and diabetes mellitus, R.S Gaskin, D. Estwink, R. Peddi Ethn Dist Fall 2001; 11(4) 749– 754 , PMID : 11763298.

7. G6PD Deficiency and risk of diabetes, A systematic review and meta analysis, Yin key Lai, Nai ming Lai, swaun wen aueg lee, Annals of hematology 96 839- 845 14 Feb 2017.

8. G6PD Deficiency and Diabetes mellitus with severe Retinal Complication in Sardinian population, Italy; Int. J. Med science 2013 : 10 (13) 1907-1913.

9. Erythrocyte Glucose 6 phosphate Dehydrogenase activity in diabetic patients, Hamaira Rashidi, Maryam Shufiei, Reza Hamaidian, Pakistan Journal of MEDICAL Science vol. 25, July – Sept 2009; 25 (4) : 665 – 668.

10. Deficiency of erythrocyte G6PD and sickle cell trait, A survey of Mahar students at Aurangabad, Maharastra, VV Deshmukh et. al., Indian Journal of Res. 1968 Jun

11. Association of G6PD with Diabetes Mellitus, Th Kh Saeed et al, Diabetic Medicine, vol 2 issue 2, March 1985.

12. High glucose inhibits glucose 6 phosphate dehydrogenase leading to oxidative stress and beta cell failure, ZhuoyunZhang et al FASEB J. 2010 May; 24 (5):1497-1505.