

Study of Glucose-6-phosphate Dehydrogenase (G6PD) Status in Preeclampsia

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Abstract:

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the common enzymopathy and may be one of the risk factor for complicated pregnancy. **Objectives:** To measure erythrocyte G6PD level in pregnant women with preeclampsia in order to observe this enzyme status and also to measure Hb, TC of RBC, serum bilirubin, reticulocyte count to observe hemolytic status. In addition, to correlate this enzyme level with all these hematological parameters in order to find out any relationships among them. **Methods:** This cross sectional study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from January to December 2008. For this, 30 pregnant women with preeclampsia, age ranged from 20 to 34 years during their third trimester (>24th weeks) were studied (group B). They were selected from the Obstetric and Gynae Out Patient Department (OPD) of BSMMU and Bangladesh Medical College Hospital (BMCH) of Dhaka City. For comparison age matched 30 apparently normal pregnant women of the same gestational age (control group - group A) were also studied. They were selected by personal contact. Erythrocyte G6PD level was measured by Spectrophotometric method using kit of Randox. Serum bilirubin, hemoglobin concentration, total count of RBC and reticulocyte count were measured by standard laboratory techniques. For statistical analysis ANOVA, independent sample t test, Chi-square test and Pearson's correlation coefficient test were performed by using SPSS for windows version-12 as applicable. **Results:** In this study, erythrocyte G6PD level was significantly lower in preeclampsia in comparison to that of control but their percentages of involvement was not statistically significant. In addition, hemoglobin concentration and RBC count were significantly lower and serum bilirubin and reticulocyte count were significantly higher in the study group than those of control group. On the other hand, erythrocyte G6PD level was positively correlated with hemoglobin concentration and total count of RBC while negatively correlated with serum bilirubin and reticulocyte count and all these relationships were statistically significant in the study group. **Conclusion:** Therefore, this study revealed that presence of G6PD deficiency associated with hemolysis in preeclampsia may act as a contributory factor for the development of this complicated pregnancy.

Key words: G6PD, preeclampsia

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Introduction:

Pregnancy is a condition where there is progressive physiological as well as anatomical changes occur which are not confined to the genital organs only but also to all other systems of the body¹ and preeclampsia is a disorder associated with pregnancy, characterized by hypertension and proteinuria with or without edema after the 20th weeks of pregnancy¹.

Recently, researchers found that Glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency may be a

contributory factor for the development of preeclampsia in pregnancy². Physiologically this enzyme catalyzes the oxidation of glucose-6-phosphate to 6-phosphogluconate and concomitantly reducing the oxidized form of nicotinamide adenine dinucleotide phosphate (NADP⁺) to NADPH that is needed to maintain glutathione in its reduced form³⁻⁶. This reduced glutathione acts as a scavenger for harmful oxidative metabolites in all the cells. However, the normal G6PD is the only basis of NADPH in RBC that protects them against any oxidative stress. Therefore, rapid hemolysis occurs if there is any oxidative stress in G6PD deficient pregnant women⁷.

It has been proved recently that several antioxidant enzymes play role in organogenesis during intrauterine

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life. These include superoxide dismutase (SOD), glutathione peroxidase (GSHPX) and catalase to attenuate intracellular oxidants. To carry out their functions properly, glutathione peroxidase (GSHPX) and catalase require NADPH, which is a product of G6PD activity^{8,9}.

In placenta, especially in syncytiotrophoblast concentration of G-6-PD enzyme is lower than other trophoblastic cells. And at about 10 to 12 weeks of gestational age in normal pregnant women, oxygen pressure increases three times resulting oxidative stress in these syncytiotrophoblasts⁹⁻¹⁰. Moreover, decreased activity of G6PD in endothelial cells is associated with oxidative stress due to lack of NADPH¹¹. Therefore, the pregnant women with G6PD deficiency may be at higher risk for development of preeclampsia than those with normal G-6-PD activity. In addition, the deficiency of this enzyme may contribute to vascular dysfunction which may leads to preeclampsia¹.

In developing countries like Bangladesh, preeclampsia is one of the major problem in health sector. The high maternal death rate due to pregnancy related complications particularly preeclampsia may be attributed in many cases to G6PD deficiency. But no published data has yet been available about the status of erythrocyte G6PD in normal pregnancy as well as in pregnancy with preeclampsia. For this, the present study was designed to determine erythrocyte G6PD level in pregnant women with preeclampsia in order to observe its status and also to measure Hb, TC of RBC, serum bilirubin, reticulocyte count in order to observe their hemolytic status. In addition correlation coefficients of this enzyme level with all these hematological parameters were done in order to find out any relationships among them. The result of the study may be used as baseline data to explore the role of this enzyme deficiency as one of the underlying cause of this type of obstetric complications. Moreover, the findings may also help clinicians for better management of this group of enzyme deficient pregnant women.

Methods:

The present cross sectional study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from January to December 2008. In this study a total number of 60 multigravid pregnant women of third trimester (>24th weeks), age ranges from 20 to 34 years were selected. Among them, 30 preeclamptic women with previous bad obstetric history or preeclampsia were included as study subjects (Group B) and 30 age matched normal pregnant women (>24th weeks) without any such history were taken

as control (Group A). Pregnant women having diabetes mellitus, any thyroid diseases, history of high fever (>100^oF) in present pregnancy, Rh negative blood group or smokers were excluded from this study. Control group was selected from personal contact while the study group from Obstetric and Gynaecology Out Patient Department (OPD) of BSMMU and Bangladesh Medical College Hospital (BMCH), Dhaka. Erythrocyte G6PD level was determined by spectrophotometric method by using kit of Randox¹² and serum bilirubin, Hb concentration¹³, TC of RBC¹⁴ and reticulocyte count¹³ were estimated by standard laboratory technique in both the groups. All these tests except reticulocyte count were done in the Department of Physiology and the reticulocyte count was done in the Department of Hematology, BSMMU, Dhaka.

Data were expressed as Mean \pm SD. Independent – sample ‘t’ test were done as the test of significance wherever applicable. The statistical analysis was done by using SPSS programme version 12.

Results:

In this study, the mean body weight and BMI were higher in the study group in comparison to those of control. However, the difference of mean BMI ($p < 0.01$) between the groups was statistically significant (Table –I). On the other hand, the mean values of both the blood pressures ($p < 0.001$) were significantly higher in group B when compared to those of group A (Table –2). In this study, the mean erythrocyte G6PD level was significantly ($p < 0.001$) lower in the group B in comparison to that of group A. Again the frequency of this enzyme deficiency was 13.33% in preeclampsia and 0 % in control and the difference was not statistically significant (Table - II).

The mean hemoglobin level and mean total count of RBC were significantly ($p < 0.001$) lower in the study group in comparison to those of control group (Table –III). On the other hand, the mean serum bilirubin level ($p < 0.01$) and reticulocyte count ($p < 0.001$) were significantly higher in group B when compared to those of group A (Table-III).

Hemoglobin concentration and TC of RBC showed positive and statistically significant correlation with erythrocyte G6PD level ($r = +0.547$; $p < 0.01$ and $r = +0.566$; $p < 0.001$). Again, serum bilirubin and reticulocyte count showed significant but negative correlation with erythrocyte G6PD level for groups B ($r = 0.491$; $p < 0.01$ and $r = 0.406$; $p < 0.05$). (Table – V).

Table-I
Weight, BMI and Blood pressures in different groups of pregnant women (n=60)

Groups	n	Body Weight (kg)	BMI (kg/m ²)	Systolic B (mmHg)	Diastolic BP (mm Hg)
A	30	67.53 ± 6.67 (54 - 80)	27.64 ± 2.17 (22.78 - 31.32)	111.33 ± 8.5 (100 - 125)	73 ± 5.96 (60 - 80)
B	30	70.57 ± 6.20 (56 - 83)	28.84 ± 3.10 (20.17 - 3.76)	133.33 ± 9.5 (120 - 160)	86 ± 7.81 (70 - 100)

Statistical Analysis:

Groups	p value			
A vs B	0.074 ^{ns}	0.008 ^{**}	0.000 ^{**}	0.000 ^{**}

Data were expressed as Mean ± SD. Figures in parentheses indicate ranges. For statistical analysis, independent sample t-test was done for comparison between the groups.

Group A = Women with normal pregnancy (control group).

Group B = Preeclamptic women with previous bad obstetric history or preeclampsia (study group).

** = p < 0.01 ns = Non significant

*** = p < 0.001 n = Number of subjects

Table-II
Erythrocyte G6PD level in different groups of pregnant women (n = 60)

Groups	n	G6PD (mU/10 ⁹ erythrocytes)
A	30	270.73 ± 13.02 (252.63 - 297)
B	30	245.48 ± 37.91 (118.64 - 272)

Statistical Analysis:

Groups	p value
A vs B	0.001 ^{***}

Data were expressed as Mean ± SD. Figures in parentheses indicate ranges.

For statistical analysis, independent sample t-test was done for comparison between the groups.

Group A = Women with normal pregnancy (control group).

Group B = Preeclamptic women with previous bad obstetric history or preeclampsia (study group).

*** = p < 0.001

ns = Not significant. n = Number of subjects

Table-III
Distribution of the pregnant women by erythrocyte G6PD level in different groups (n=60).

Groups	n	Normal	Below normal
		No (%)	No (%)
A	30	30 (100%)	0 (0%)
B	30	26 (86.66%)	4 (13.33%)

Statistical Analysis:

Groups	p value
A vs B	0.593 ^{ns} %

Data were expressed as number and percentage of normal and abnormal erythrocyte G6PD level.

Group A = Women with normal pregnancy (control group).

Group B = Preeclamptic women with previous bad obstetric history or preeclampsia (study group).

ns = Not significant. n = Number of subjects

Table-IV

Hb concentration, TC of RBC, Serum bilirubin and Reticulocyte count in different groups of pregnant women (n=60).

Groups	n	Hb (g/dl)	TC of RBC (10 ¹² /l)	S.Bilirubin (mg/dl)	Reticulocyte (%)
A	30	11.98 ± 0.91 (10.6 – 14.2)	4.79 ± 0.39 (4.1 – 5.5)	0.5 ± 0.12 (0.3 – 0.7)	0.78 ± 0.34 (0.5 – 1.5)
B	30	10.76 ± 0.74 (9.5 – 12.4)	3.97 ± 0.31 (3.4 – 4.5)	0.58 ± 0.12 (0.4 – 0.8)	1.22 ± 0.56 (0.5 – 2)

Statistical Analysis:

Groups	p value			
A vs B	0.000***	0.000***	0.019*	0.001**

Data were expressed as Mean ± SD. Figures in parentheses indicate ranges.

Group A = Women with normal pregnancy (control group).

Group B = Preeclamptic women with previous bad obstetric history or preeclampsia (study group).

ns = Not significant. * = p < 0.05

n = Number of subjects. ** = p < 0.

Table-V

Correlations of erythrocyte G6PD level with serum bilirubin and some hematological parameters in preeclamptic pregnant women (n=60).

Parameters	Groups B	
	r value	p value
Bilirubin	-0.491	0.006**
Hemoglobin	+0.547	0.002**
RBC	+0.566	0.001***
Reticulocyte	-0.406	0.026*

Pearson's correlation coefficient (r) test was performed as the test of significance.

Group A = Women with normal pregnancy (control group).

Group B = Preeclamptic women with previous bad obstetric history or preeclampsia (study group).

ns = Non significant * = p < 0.05

n = Number of subjects ** = p < 0.01

*** = p < 0.001

Discussion:

In the present study, erythrocyte G6PD level, Hb conc, TC of RBC, serum bilirubin and reticulocyte count were measured in pregnant women with preeclampsia of third trimester (study group) and as well as in age and gestation

matched apparently healthy normal pregnant women (control) in order to compare these values with the study groups. Though all the results showed variation but they were almost within normal ranges.

Erythrocyte G6PD level in control group was almost similar to the findings observed by the various investigators from different countries^{2, 15}. However, no similar published data of this enzyme level in pregnant women were available in our country for comparison.

On the other hand, mean body weight and BMI were significantly (p < 0.01) higher in preeclampsia compared to those of normal pregnant women. Similar finding of BMI was also reported^{2, 13}. It has been suggested by that edema in preeclamptic women might be responsible for this increased body weight and BMI as suggested by some investigators which is also reflected in the present study.

In this study, blood pressures were significantly (p < 0.001) higher in preeclampsia which is also consistent with the findings of others^{2, 16}. As the subjects of this study group suffered from preeclampsia so their blood pressures were significantly higher.

Erythrocyte G6PD level in present study was significantly lower in preeclampsia (p < 0.01) in comparison to that of normal pregnancy. Afzal et al. also observed similar findings

in preeclampsia¹⁷. But, there are some controversies about the changes of this enzyme value in similar group of pregnant women¹⁶. Though in the present study, statistically non significant erythrocyte G6PD deficiency was observed, on the other hand involvement of this enzyme deficiency only in a few percentages (13.33%) of preeclamptic women indicate that G6PD deficiency may be an associated factor in preeclampsia.

Again, significantly lower values of Hb concentration and TC of RBC with significantly higher serum bilirubin in the study group indicates hemolysis which is suggestive of G6PD deficiency in this group of women. In addition, significantly higher reticulocyte count may be the results of compensatory increase in erythropoiesis in response to hemolysis. Similar findings of this value were reported^{8, 15}. On the other hand, Kahraman et al. observed no significant difference of hemoglobin concentration in preeclampsia compared to that of normal pregnancy¹⁶.

Significantly positive correlation of erythrocyte G6PD level with hemoglobin concentration and total count of RBC as well as negative correlation with reticulocyte count and serum bilirubin observed in the study group which also support the presence of hemolysis in this group of pregnant women.

It has been suggested that in G6PD deficiency, placental lipid peroxidation and decrease synthesis of placental hormone by syncytiotrophoblast due to oxidative stress may lead to development of preeclampsia^{2, 10}. Placental lipid peroxidation may also cause destruction of red blood cells and thereby leads to hemolysis in this group.

Conclusion:

Therefore, this study concludes that G6PD deficiency may be one of the causative factors for the development of preeclampsia. So, routine screening of erythrocyte G6PD level during antenatal period and close surveillance of G6PD deficient pregnant women may play a role in reducing the risk of pregnancy related complications in this group of pregnant women.

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