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Brief Report

Possible Association between Glucose-6-Phosphate Dehydrogenase Deficiency and the Development of Preeclampsia

Omid R. Zekavat[1], Maryam Eskandary[2], Behia Namavar Jahromi[3], Athar Rasekh[4], Sara Barzegar[1], Nasrin Ized Panahy[1], Mehran Karimi[2]

Abstract

Glucose-6-Phosphate dehydrogenase (G6PD) deficiency is a common enzyme deficiency in the world. It's Prevalence in Iran is about 12% in male & about 1% in female. The present study did examine the relation between the development of preeclampsia and G6PD deficiency. It was investigated whether or not the risk of preeclampsia in G6PD deficient women is higher than that in normal pregnant women.

A total of 400 pregnant patients with an age range of 20-34 years were selected in the cities of Shiraz and Jahrom, Iran, They were on 24 weeks inside their first or second pregnancy. There were 4 cases of G6PD deficiency in preeclamtic women compared to two cases in normal pregnant women. (OR=2.02, CI: 0.37-11.02). Although the relation between G6PD deficiency and preeclamsia did not reach statistical significance, the higher incidence of the deficiency in preecclamtic women might suggest that the test for G6PD deficiency might be used as a screening tool for preeclamsia.

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Keywords ● G6PD deficiency ● preeclampsia ● pregnancy

Introduction

Glucose-6-Phosphate dehydrogenase (G6PD) deficiency is the most common X-chromosome linked enzyme pathway in human.[1] Its Prevalence in Iran is about 12% and 1% in male and female, respectively.[2] The deficiency leads to the collection of oxidants in cells, and finally to cell destruction.[3]

Preeclampsia is a kind of specific pregnancy-related condition in which the blood circulation is decreased because of the vascular spasm and endothelium activation.[4] Preclampsia is defined by hypertension, proteinurea, and other symptoms.[5] One of the causes of the preeclampsia is an ischemia of the placenta due to a defect of in cavitation.[6] Several factors such as the lack of immunological conformity, genetic and vascular factors cause the defect in cavitation.[6] There are a number of vascular conditions that cause the human to be in danger of preeclampsia. One of such conditions is oxidant stress such as peroxidation of lipids. The rate of lipid peroxidation in the placenta of the patients with severe preeclampsia is more than that in the placenta of the patients with normal pregnancy.[7]

The syncitiotrophoblast membrane of placenta that regulates the passage of nutrients from mother's blood into the embryo's blood is exposed to the danger of oxidative agents by the oxygen free radicals.[7] In research, it has been observed that at the syncitiotrophoblast cells, which have been derived

[1]Department of Pediatrics,
[4]Department of Gynecology,
School of Medicine,
Jahrom University of Medical Sciences,
Jahrom, Iran.
[2]Hematology Research Center,
[3]Department of Gynecology,
School of Medicine,
Shiraz University of Medical Science,
Shiraz, Iran.

Correspondence:
Mehran Karimi MD,
Hematology Research Center,
Department of Pediatrics,
Nemazee Hospital,
Shiraz University of Medical Sciences,
Shiraz, Iran.
Tel/Fax: +98 711 6473239
Email: karimim@sums.ac.ir
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from trophoblast in the women with preeclampsia, the activity of the glutathione peroxidase is less than the normal range. The glutathione peroxidase enzyme uses the reduced glutathione as the initial elements (substrate). It has been observed that the sensitivity of the syncitiotrophoblast membrane is increased due to the oxidant stresses in women with preeclampsia. Such an increase in the sensitivities is related to the decrease in antioxidant systems and or to the abnormality of the lipids components of the membrane.[6]

The aim of the present study was to investigate the incidence of G6PD deficiency in pregnant women with preeclampsia in order to evaluate whether or not the risk of preeclamsia in G6PD-deficient women was more than that in nonG6PD-deficient women.

Materials and Methods

Study Design

The study was a prospective clinical trial recruiting a case and a control groups aiming at investigating whether or not G6PD deficiency was a risk factor for preeclampsia in women. Considering an α=0.05, a prevalence of G6PD in normal female=1%, an expected prevalence of G6PD in women with preeclampcia=5% and a power=70%, a sample size of 200 for each group was calculated. The study protocol was approved by medical and ethical committees of Shiraz and Jahrom Universities of Medical Sciences.

Patients

A total of 400 pregnant women referring for prenatal care to two obstetrics clinics at Shiraz and Jahrom Universities of Medical Sciences in Fars Province located in the south of Iran were evaluated from the middle of 2005 to the end of 2006. The case group consisted of 200 pregnant women with an age range of 20-34 years. They were in the course of their first or second pregnancy with a gestational age of 24 weeks or more, when their discomforts were diagnosed as preeclampsia without any positive past medical history. Moreover, they did not have any previous history of the disease.

The control group consisted of 200 healthy pregnant women who were matched the case group for age and gestational age of pregnancy. Women in both case and control groups were followed and under a close observation until the end of pregnancy.

A questionnaire was filled for all pregnant preeclamptic patients. The questionnaire comprised of questions in regards to demographic information of the patients as well as their medical history including a table for chart regarding the information about the severity of preclampsia such as blood pressure, headache, proteinuria, vision problem, abdominal pain, oligouria and seizer disorders as well as paraclinical data like blood urea nitrogen, creatinin, liver function test, sodium, potassium, fasting blood sugar, complete blood count with platelets, prothrombin time (PT) and partial thromboplastin time (PTT). A questionnaire comprising questions in regards to demographic information of women with normal pregnancy as well as their medical history was also completed.

Paraclinic

After obtaining the informed consents from all patients, blood samples were taken and sent to the laboratory. Fluorescent spot test has been introduced as a more reliable and specific method with specificity of 99%.[7] In this test, the false negative results are rare and less than two in two thousands. But the false positive results are seen only in heterozygote women and hemi-zygote men after severe bleeding that caused increase in the young RBC.[8] The intensity of the fluorescent is high at the blood of the women with natural pregnancy and low or even negative in the patients with G6PD deficiency. The reports of G6PD test in pregnant women have shown that when the enzyme activity is sufficient, the optical fluorescence is strong, when there is partially deficiency a weak fluorescence is observed, and when the sample has severe deficiency no fluorescence is observed.

Data Analysis

Statistical analysis was done using Statistical Package for Social Sciences (SPSS v. 15 SPSS Inc, Chicago IL). The ratio of G6PD deficient patients between the two groups were compared with Chi-square test (Fisher's exact test). Odds ratio was calculated to show whether G6PD deficiency could be a risk factor for preeclampsia in pregnant women. A P value of $\leq$0.05 was considered statistically significant.[9]

Results

The study showed that of 200 normally pregnant women, 2 cases (1%) were G_6PD deficient, but of 200 pregnant women with preeclamsia, 4 cases (2%) were G6PD deficient. (OR=2.02, CI: 0.37-11.02) (figure 1).

Preeclamtic women group were divided into two severities, namely mild (76%) and severe (24%) preeclamsia. Of 4 G6PD deficient preeclamtic women, 2 cases (1.3%) were from mild subgroup and 2 cases (4.2%) were from severe subgroup (OR=3.26, CI: 0.45-23.57) (figure 2). There was no statistically relationship between G6PD deficiency and preclampsia (P=0.343). All the paraclinical data were normal in both groups and no significant difference was found between them.

Discussion

Every year more than five million women die from complications of pregnancy. Up to 10%-15% of obstetric morbidity is due to hypertension. Preclampsia is one of the obstructive morbidities. Therefore, the early diagnosis of this disease can prevent some economic burden and social injuries.[10]

According to the hypothesis that has been proposed by Abdul Hadi et al. in 2004 there is a significant relationship between G6PD deficiencies and the incidence of preeclampsia in pregnant women.[11]

The prevalence of favism is high (12% in male and about 1% in female),[2] in Iran, especially in the southern regions. The findings of the present study indicate that there is no rela-

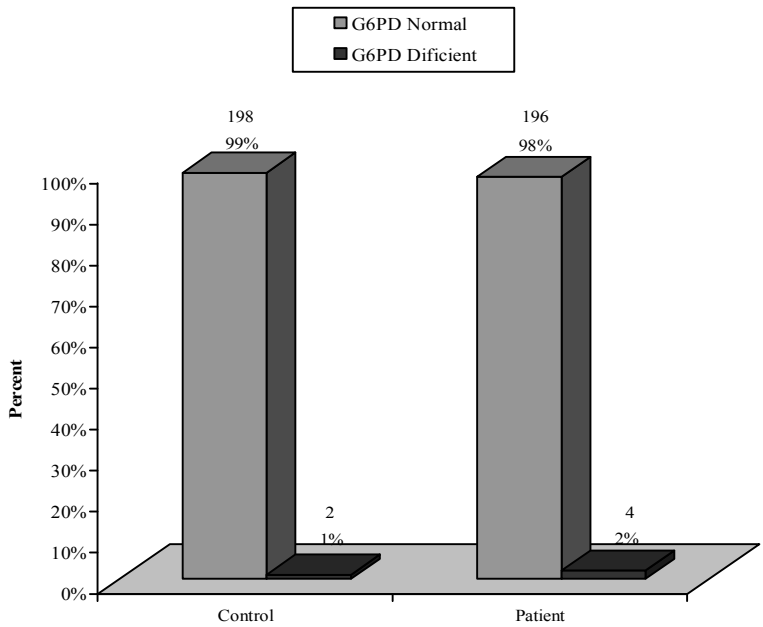

Figure1: The number and percentage of normal and preeclamptic women with and without G6PD deficiency.

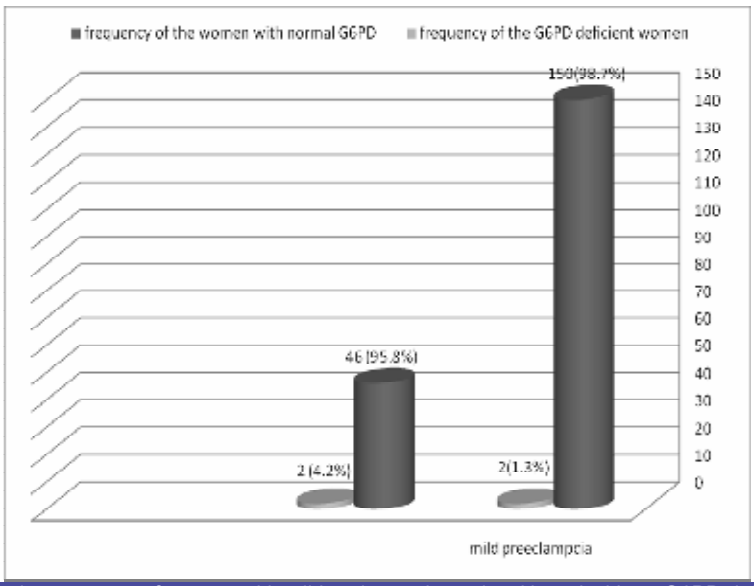

Figure 2: The number and percentage of women with mild and preeclampsia with and without G6PD deficiency.

tionship between G6PD deficiency and preeclampsia. To the best of our knowledge, this is the first clinical study recruiting two hundred women with normal pregnancy and two hundred pregnant women with preeclampsia.

In this study all cases with confounding factors such as systematic diseases including diabetes mellitus, thyroid diseases, liver or renal diseases and previous history of systemic hypertension were excluded in both groups.

As there was no statistical information about the distribution of preeclampsia severity in the country, therefore the compare and contrast with other studies was not possible. Moreover, it was not possible to suggest how the incidence of preeclamptia reported in this region is ranked compared with other regions of the country.

The findings of the study indicate that there was no relationship between G6PD deficiency and preecclamsia. The G6PD deficiency is a X-linked trait, which may underlie the overall low incidence of the deficiency in the present study. Alternatively, the findings of the present study should be assessed in the light of low sample size in both groups. Therefore, a study with a larger sample size might be necessary to examine whether there is a relationship between G6PD deficiency and the occurrence of preeclamsia.

Although the relationship between the occurrence of G6PD and preecclamsia did not reach statistical significance, a comparison of occurrence of the deficiency in normal pregnant and preeclamtic women indicate that there might be trend to a positive relationship, which might be possible to verify using a higher sample size. Therefore, it might be possible to suggest that a test for G6PD deficiency might be used as a screening tool to identify women who might develop preeclamsia later in the pregnancy.

Conclusion

Although the relation between G6PD deficiency and preeclamsia did not reach statistical significance, the higher incidence of the deficiency in preecclamtic women might suggest that the test for G6PD deficiency might be used as a screening tool for preeclamsia.

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Conflict of Interest: None declared

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