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Evaluation of Hepatic Biomarkers in Pregnant Women with Preeclampsia

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Abstract

Preeclampsia is a pregnancy-related disorder and considered as one of the major reasons of infants and mothers death in developed nations. HELLP disorder is a problem related to childbirth that usually happens in women with intense preeclampsia and associated with different features, including hemolysis, elevated liver enzymes, and low platelet count. Due to normal hepatic markers during pregnancy, our purpose is to examine these factors in pregnant women and their association with disorders such as preeclampsia and HELLP syndrome. This case-control study included 99 Iranian pregnant women that were divided into two group including preeclamptic and normotensive pregnant women. Samples were collected from Ahvaz city. We measured liver enzymes activity (ALT, AST, and ALP), total bilirubin and direct bilirubin and blood platelets by calorimeter methods in both groups. The results showed that there was no significant difference in the platelet level in both groups. However, we found a significant difference in the serum level of ALT, AST, ALP and total bilirubin between two groups ($p<0.05$), while the result related to direct bilirubin was not significant at the end of the study. The outcomes related to this study show that hepatic biomarkers in pregnant women with preeclampsia was higher than normal pregnant women, therefore, we can predict more likely to develop HELLP syndrome in pregnant women with preeclampsia.

Keywords: Preeclampsia; HELLP; ALT; AST; Bilirubin

Introduction

Preeclampsia is a pregnancy-related disorder and considered as one of the major reasons of infants and mothers death in developed nations [1]. Some of the risk factors for the development of preeclampsia are diabetes mellitus, hypertension, obesity and antiphospholipid antibody syndrome [2]. Each year, 585,000 women die due to complications related to pregnancy that is 95% of them in developing countries and among them, 30% of cases are due to problems of hypertension during pregnancy and particularly preeclampsia [3]. In the USA, 18% of mortality among women is related to pregnancy period and especially hypertension disorders during this period [4]. Generally, the definition of preeclampsia is complicated due to differences in its diagnosis, but persistence in blood pressure that occurs in 12%-22% of pregnancies and is dependent on the type of population can be one of its reasons [5]. Also, vascular endothelial dysfunction is the final common pathway that causes the mother's system response [6]. For example, one study showed that in women with preeclampsia, increase in the level of soluble fms-like tyrosine kinase 1 (sFlt-1), and a decrease in PlGF levels is higher than the control group, as these changes occur several weeks before the first onset, their measurement can be a good predictor [7]. Researchers have found that men and women, whose mothers during pregnancy have preeclampsia, likely their children develop preeclampsia later that shows the effect of genetic factors in this disorder, although not too much information in this field [8]. In addition, a study was conducted in Iran, winter and urinary tract infection were considered as risk factors for preeclampsia [9]. It has been reported that slight changes occur in biomarkers of the liver during pregnancy, indeed in this period, the level of AST, ALT, GGT, serum bilirubin, and bile acids usually remain within the normal range, therefore any change in their level may indicate a problem [10].

HELLP disorder is a problem related to childbirth that usually happens in women with intense preeclampsia [10,11]. This syndrome occurs mainly in preterm and sometimes in during late gestation and after childbirth [12]. HELLP is expressed as the following three features: hemolysis elevated liver enzymes and low platelet count [13]. This syndrome is a very dangerous situation and leads to serious problems such as hemolysis, epigastria pain, a decrease of liver enzymes and thrombocytopenia in during this syndrome [14].In Iran, a study conducted on preeclampsia was showed that there is a relationship between preeclampsia and vitamin D [15]. In addition, Shahbazian et al, examined the relationship between preeclampsia and hypertension and microalbuminuria [16]. As the women health is important during pregnancy and there are few studies on pregnancy and liver problems in Iran, we studied liver markers in pregnant women and their association with disorders such as preeclampsia and HELLP syndrome. In addition, this study was in line with our recent studies on women health, including cell cycle arrest in ovarian cancer, the effect of purslane extract on antioxidant balance in women with type 2 diabetes, changes in the level of AGEs and β2-microglobulin and imbalance of trace elements in type 2 diabetes [17,18].

Material and Methods

Subjects

This case-control study was performed on 99 Iranian pregnant females, who were divided into two group including preeclampsia and normotensive pregnant women.

Measurements

We measured enzyme activity of liver biomarkers (ALT, AST, and ALP), total bilirubin and direct bilirubin by calorimeter method and blood platelets by Hematology Analyzer-Sysmex KX-21 in pregnant women with preeclampsia (n=50) and normotensive (n=49). HELLP syndrome among woman with preeclampsia by the following criteria: total bilirubin ≥ 0.6 mg/dl for detection of hemolysis, AST ≥ 20 IU /L, ALT ≥ 15 IU /L for the diagnosis of liver damage and blood platelet count less than 50,000 cells/μL.

Statistical analysis

The data were expressed as a mean ± standard deviation. For comparison of groups was used independent t-test and Mann-Whitney test for platelet count and serum ALT, AST, ALP, total bilirubin, direct bilirubin, respectively. The different level was set at $P<0.05$.

Results

The outcomes of the present study were reported for 99 pregnant women including preeclampsia (n=50) and normotensive (n=49) case. The summary of these results is presented in Table 1.

Factor	Group	
	Preeclampsia (n=50)	Normotensive (n=49)
Blood platelet (cell/μL)	223.80 ± 72.63	216.45 ± 47.48
ALT (IU/L)	34.34 ± 12.77*	14.51 ± 3.93
AST (IU/L)	41.10 ± 10.61*	20.55 ± 6.82
ALP (IU/L)	397.20 ± 174.49*	180.02 ± 46.72
Direct bilirubin (mg/dl)	0.23 ± 0.08	0.15 ± 0.4
Total bilirubin (mg/dl)	0.99 ± 0.91*	0.42 ± 0.13

Table 1: Comparison factors related to preeclampsia in both groups.

The current data shows that there was no significant difference in the platelet levels between normotensive pregnant and preeclampsia pregnant women. However, we obtained a significant difference in the ALT serum level between normotensive pregnant women and preeclamptic pregnant women at the end of study ($P<0.05$) also there was a significant difference in the AST level between two groups ($P<0.05$). The evaluation of serum ALP serum level was also indicated that its level in preeclamptic pregnant women was significantly higher than normotensive pregnant women (about 2-fold) ($P<0.05$). In relation to bilirubin level (either direct or total), the result was confirmed that direct bilirubin level in preeclamptic pregnant women had not obvious difference compared to normotensive pregnant women, while the level of total bilirubin in preeclamptic pregnant women was higher than normotensive pregnant women so that it was significant ($P<0.05$).

Discussion

Liver function tests are abnormal in 20% to 30% of pregnancies that are associated with preeclampsia, [19,20] and are related to poor motherhood and embryonic result. [21,22] Preeclampsia is a disorder with three features: proteinuria, hypertension, and edema that occur during last trimester of 5%-10% of pregnancies. Although the liver problem is infrequent in this disorder, nevertheless intense preeclampsia is related to perinatal illness and death. In fact, it is the most common reason of hepatic sensitivity and liver impairment in gestation period and 2%-12% of cases will suffer from HELLP syndrome that this syndrome is expressed as the following three features: hemolysis, elevated liver enzymes, and low platelet count. Liver involvement of preeclampsia requires no specific therapy, although the involvement is an indicator to prevent more serious disorders such as eclampsia, hepatic rupture, or necrosis [22].

We studied hepatic markers and liver damage in pregnant women in both normotensive and preeclamptic group. In agreement with studies conducted by Weinstein [12] and Shukla [23] our data showed that there was a significant difference in the serum ALT level between normotensive pregnant women and preeclampsia pregnant women ($P<0.05$). In addition, line with Cerutti [24] Weinstein [12] and Shukla [23] our data indicated that there was a noticeable difference in the AST level between two groups ($P<0.05$). Surprisingly, the current data showed that there was no significant difference in the platelet level between normotensive pregnant and preeclampsia pregnant women. But there was a significant difference in the serum ALP level and total bilirubin level between the two groups ($P<0.05$). The various investigations have been examined the evaluation of liver function tests and liver damage in pregnant women with preeclampsia and normal pregnant women so that obtained different results. For example; in a study by Girling et al, stated that the rate of liver function tests are less in normal gestation than the scope of reference presently used [25]. The results of our project also revealed that more hepatic markers such as total bilirubin, ALT and ALP in pregnant women with preeclampsia were higher than normal pregnant women. In another study on the HELLP syndrome was indicated that AST, ALT, and bilirubin were abnormal [12]. We as well as found that total bilirubin and ALT level were more in pregnant women with preeclampsia, but direct bilirubin level had no significant difference compared to the normal group. It has been reported AST level abnormality more than 18 U/L, [26] 30 U/L 52 to 57 U/L (20) 70 U/L [24,27]. In normal gestation, ALT and AST are lower than non-pregnant age-matched women, however, AST changes to the lesser amount [23]. Based on a study of Cerutti et al, 1976 AST, ALT and GGT significantly increase during the sixth month of pregnancy, however, it is not obvious whether this is compared with early gestation [24]. The primary fluctuations in liver function evaluation may be due to red cell demolition and ultimately happens liver injury [28]. The results showed that liver damaged in pregnant women with preeclampsia. Although platelet count was nearly equal in both group, other biomarkers were higher in pregnant women with preeclampsia compared with normal pregnant women.

Conclusions

At the end of the study, we conclude that pregnancy with preeclampsia likely results in HELLP syndrome. We suggest further studies to understand the exact mechanism of the problem.

Declarations

Acknowledgment

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Conflict of interest statement

The authors declare that there is no conflict of interest regarding this study.

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Contribution of authors

This work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article was borne by the authors named in this article.

Ethical approval

This research does not contain any studies with human participants or animals and was performed by the authors alone.

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