Comparison of the Level of Uric Acid and LDH in Mothers in Early and Late Preeclampsia and Determination of Its Association with the Severity of Preeclampsia

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Abstract

Introduction: LDH and uric acid are two considerable markers in the new researches on the preeclampsia patients. The aim of this study was Comparison of the Level of Uric Acid and LDH in Mothers in Early and Late Preeclampsia and Determination of Its Association with the Severity of Preeclampsia. **Method**: In a descriptive-analytical study, 64 mothers with preeclampsia were studied in two early and late preeclampsia groups, groups was divided into individuals with severe or mild preeclampsia. While examining the demographic data, Hemato-biochemical tests were performed in order to examine the level of uric acid and LDH; the data analyzed by SPSS software version 20. **Results**: The mean age of the total patients was 29.40 ± 5.37 years. The mean of uric acid in the early group was 5.49 ± 1.43 and for late group was 4.63 ± 1.44, that was significantly higher in the early group (P <0.001). The mean LDH in the early group was 362.63 ± 262.29 and for the late group was 427.64 ± 174.59, that was significantly higher in the late group (P = 0.004). In addition, in both early and late groups, the mean LDH of the severe patients was significantly higher than the mild patients (P = 0.004). The correlation between the age of patients with their uric acid level in late patients showed a significant positive correlation (P = 0.015). **Conclusion**: uric acid in pregnant women with preeclampsia significantly increases, so that it is higher in early preeclampsia pregnant women than the late preeclampsia group; and it is higher in severe preeclampsia individuals than those with mild preeclampsia. In addition, LDH of late preeclampsia is more prevalent than tthe early preeclampsia, and it is significantly higher in severe cases compared to the mild patients.

Keywords: Preeclampsia, Uric acid, LDH.

Introduction

Hypertensive diseases with high rates of morbidity and maternal mortality, affect 5.10% of total pregnancies. Accounting for 16% of maternal mortality in advanced countries and the prevalence rate of 53% in the first pregnancy, preeclampsia affects 3.9% of pregnancies. This rate is more prevalent than three other major causes (bleeding, abortion and sepsis), and based on the performed studies, half of maternal deaths due to hypertensive diseases may be prevented (Gibbs et al., 2008; Cuningham, Kenneth and Steven, 2010).

Defined by the traditional triangulation of hypertension, proteinuria and disease symptoms, preeclampsia increases the mortality rate and prenatal consequences by five times. The abnormal trophoblastic invasion, immunological intolerance between the maternal and fetal tissues, genetic effects, incorrect compliance of mother with cardiovascular changes, followed by the activation of symptoms like vascular spasm, endothelial cell activation, prostaglandins, nitric oxide, endothelin, as well as nutritional deficiencies have been proposed as mechanisms for the emergence of preeclampsia (Chappll, 1999).

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The fundamental definition of preeclampsia is the hypertension with proteinuria and, in case that seizure is added, the diagnosis will be eclampsia. Nevertheless, we frequently face with the variable signs of the disease. Hypertension alone will not be always a reliable sign to specify the severity of the disease (Vitoratis et al., 1999; Gandley et al., 2005).

Considered as an important indicator of the disease's severity, proteinuria is usually emerged at the last stages of the disease, and provided that it is apparent and persistent, we encounter with the increased risk for the mother and the fetus (Krainova et al., 2005).

Some researchers believe that coagulation disorder is one of the early symptoms of the disease; it exists in the early stages of the disease due to immune system's impairment, and increased immunological factors including anti-platelet, immunoglobulin, anticardiolipin antibodies, and vascular endothelial as well as decreased platelet level. In some studies, increased serum levels of lactate dehydrogenase (LDH) is believed to be a predictive factor in the onset of HELLP syndrome (hemolysis, elevated liver enzyme levels, and low platelet levels), and as the predictor factor for SGA; it is worth considering in such studies (Tsoi and Zhong, 2001). In addition, uric acid is associated with hypertension. In more than three quarters of the individuals with hypertension, serum uric acid level is higher than normal. This increased uric acid levels may be caused by decreased renal blood flow during the course of the disease that stimulates uric acid recovery (Nasri et al, 2014; Khodadadi, 2015).

Just one study in Iran has so far examined the serum LDH and the severity of hypertension (Kadkhodaeiyan, 2003). Several studies in this field have been performed abroad (Brown et al., 2001; American College of Obstetricians and Gynecologists, 2013), which are associated with the severity of preeclampsia; and according to the research team, this study was the first study to examine the association between mother's uric acid and plasma LDH and early and late preeclampsia. Given the prevalence and complications of preeclampsia, this study is aimed at comparing the level of uric acid and LDH in early and late preeclampsia and determining its association with the severity of preeclampsia.

Method

This is a descriptive-analytic study aimed at comparing the level of uric acid and LDH in the early and late preeclampsia and determining its association with the severity of preeclampsia on pregnant women referring to obstetrics and gynecology clinics in Ahvaz city, Iran.

In this study, after getting permission from ethical committee of university, pregnant women qualified for inclusion criteria referred to the selected research centers for prenatal care were included. The studied population included pregnant women at their 24th week of pregnancy referring to health centers in Ahvaz city.

The inclusion criteria of the study included single-pregnant mothers, gestational age greater than 24 weeks, systolic hypertension 140 mmHg and diastolic hypertension of 90 mmHg or higher (two times in 4 hours intervals) and proteinuria of oneplus. Exclusion criteria included any known maternal and fetal disorder, underlying diseases (cardiac, blood, renal, liver, dyslipidemia, diabetes diseased, etc.), alcoholic mothers and pre-pregnancy hypertension, as well as BMI above 30.

The study population included the pregnant women referring to the centers with preeclampsia suspicion. The studied pregnant women were assigned to two groups. The first group was the pregnant women with early preeclampsia (up to 34 weeks), the second group was the pregnant women with late preeclampsia (34 weeks and more), and they all were examined in each group under the title of severe and mild conditions. The final sample size in the present study was determined after the initial pilot study.

The method of the study was that after obtaining the permission from the University's Ethics Committee, an appropriate size cuff was employed for measuring the blood pressure. The blood pressure was recorded in the sitting position after at least 10 minutes of rest. Blood samples were taken after six hours of fasting and after hospitalization. A researcher-made questionnaire and laboratory tests were used in order to collect data. The questionnaire was completed by the researcher by interview method. For each participant of the study, a profile form was collected including personal-social and midwifery characteristics (including age, BMI, educational level, income level, parity, gestational age, number of live and dead children, number of abortions, number and type of deliveries), blood pressure, maternal clinical symptoms, underlying diseases, and routine tests to confirm the early or late preeclampsia, serum LDH and uric acid levels and the findings were collected. Moreover, the serum LDH level of more than 600 mg/l and the uric acid level of more than 5.6 mg/l were considered abnormal.

The mean and standard deviation (or median and interquartile domain) were used to describe the data in quantitative variables; and frequency and percentage were employed to describe them in qualitative variables. T-test (Mann-Whitney test, if necessary) and Chi-square test were used to analyze the data. Two-way analysis of variance was used to compare the groups. All analyzes were conducted by means of SPSS 20 statistical software.

Results

The mean age of the patients was 29.4 ± 5.37 years; their mean weight was 82.24 ± 10.34 kg; and their mean height was 163.48 ± 5.12 cm. Furthermore, their mean BMI was 25.01 ± 3.01. Their mean gestational age was 33.16 ± 3.86 weeks. Their mean systolic blood pressure was 127.77 ± 18.00 mmHg and their mean diastolic blood pressure was 79.84 ± 11.70 mmHg. Their mean hemoglobin level was 11.75 ± 0.93, their hematocrit was 35.40 ± 2.83, their total platelet count was 203.76 ± 64.76 and the total pt patient was 12.70 ± 1.78, the mean ptt was 27.62 ± 9.17, the bun was 12.18 ± 11.60; their Cr was 0.68 ± 0.18, their sgot was equal to 83.72 ± 184.86, sgpt equaled to 85.62 ± 192.72, and finally, Bs equaled 98.33 ± 18.69.

In addition, the mean uric acid was 5.07 ± 1.49 and the mean LDH serum level of the patients was 369.90 ± 298.30. Generally, 19.6% of the patients were illiterate, 37% of whom had a high school degree and 43.5% of whom had a university degree, 88.4% were urban and 11.6% of patients were rural residents. 3.1% of them were employed and others were unemployed (housewives). In addition, 12.5% of the patients had extra income, 56.3% had equal income, and 31.3% had low income. Furthermore, 17 patients (26.6%) had systemic diseases that out of the 17 patients with systemic disease, four had diabetes, six had hypertension, one had pulmonary disease, one had hyperthyroidism, three had diabetes associated with hypertension, and two persons had hypertension associated with pulmonary disease and 35.9% of patients used drug following other diseases.

Examination of clinical symptoms revealed that totally 39 patients had clinical symptoms, nine had headache, four had blurred vision, nine had epigastric syndrome and three had lung edema. Moreover, five had headache associated with blurred vision, three had epigastric syndrome, one had headache and lung edema and one person had blurred vision and epigastric syndrome, two had headaches, blurred vision and epigastric syndrome, and one person had nausea and vomiting. There were SGA infants for 15 (23.4%) patients. Ultimately, seven patients (10.9%) were with HELP; two (6.1%) in the early group, and five (16.1%) in the late group.

The statistical comparison of the study's findings in both early and late groups as well as the separation of each group in subjects with mild and severe symptoms revealed that in the early group, the height of the severe group was significantly more than that of the mild group ($P = 0.02$). The mean gestational age was significantly higher in the patients of late group than that of the early group ($P < 0.001$). Of course, in both early ($P = 0.04$) and late ($P = 0.001$) groups, the average gestational age in severe subjects was more than that of the mild cases. Moreover, the mean systolic ($P = 0.005$) and diastolic ($P = 0.01$) blood pressure in the late group was significantly higher than that of the early group. Furthermore, in the early group, the mean diastolic blood pressure in severe patients was significantly more than that in the mild cases ($P = 0.005$).

From the laboratory findings, the mean hematocrit ($P = 0.07$), pt ($P = 0.06$) and sgot ($P < 0.001$) in the late group were significantly higher than those in the early group. The mean ptt ($P < 0.001$), Cr ($P = 0.004$), and platelet of the late group were significantly lower was than early group. Moreover, the mean ptt ($P = 0.03$) of the late group and Cr ($P = 0.03$) of the early group in the severe cases were significantly higher than those in the mild group. The mean bun of the patients in the early group indicated a significant increase in the severe cases compared to the mild ones ($P = 0.005$) and the mean sgot in the early group in severe patients was significantly more than that in the mild ones ($P = 0.001$).

The mean uric acid score of the patients indicated a significantly higher rate in the early group ($P < 0.001$), and in this group, it was significantly higher than that in the mild cases ($P < 0.001$).

Furthermore, the mean LDH level showed a significantly higher rate in patients of the late group ($P = 0.004$), and in both early and late groups, it was significantly higher in severe cases ($P = 0.004$) compared to the mild ones. Moreover, investigation of the prevalence of systematic diseases showed that the prevalence of these diseases was significantly higher in the early group ($P = 0.01$) and drug use was significantly higher in this group ($P = 0.007$), too.

Continuation of studies revealed that the number of SGA infants was significantly higher in the early mothers ($P = 0.01$); however for HELP, although it was more in the late patients, this difference was not statistically significant ($P = 0.2$).

Finally, correlation analysis of variables showed that the correlation between the age of patients and their uric acid level in the late patients had a significant positive correlation; so that the uric acid level increased with increasing age.

Discussion

Recently, no effective clinical screening test has been conducted to identify women with this disease. Accordingly, finding predictor markers for a more promising prognosis in identifying mothers as well as the severity of preeclampsia has attracted the attention of researchers. LDH and uric acid are two considerable markers in the new researches on the preeclampsia patients that have been

addressed in patients with early and late preeclampsia in the present study.

As the results of the present paper suggested, LDH in pregnant women with late preeclampsia was more than that in mothers with late preeclampsia. Also in severe patients, it was significantly more than that in the mild patients. However, in order to further understand the findings of the current study, in the following, we will examine and compare the findings of other studies with those of the present study. In a study in Iran in order to investigate the relationship between maternal serum LDH and the severity of gestational hypertension, Kadkhodaeian et al. with the publication of a paper stated that the serum LDH level of mothers with preeclampsia was significantly higher than that of the control group. Also in severe preeclampsia, it was significantly higher in indicate that all findings are consistent for serum LDH in patients with severe and mild preeclampsia, since also in our study, the LDH level of patients with severe preeclampsia in both early and late groups was significantly higher and this is consistent with the study of Kadkhodaeian. Of course, in the present study, the early and late patients have been separated, while in their study, the patients had been only separated in the severe, mild, and control groups.

The common point of the present study with other studies is the importance of LDH and uric acid as appropriate prognostic factors for preeclampsia. The very important finding of the current study is the importance of increased LDH in severe patients, and it has been addressed in other studies, too. For example, a study was done by MOHD. SABIULLAH et al. (2015) entitled "The study of serum lactate dehydrogenase LDH) and uric acid in preeclampsia", and the results revealed that serum LDH levels and uric acid levels significantly increased in women with preeclampsia compared to the control group (Mohd et al., 2015). One of the findings of the present study is the significant changes in LDH and uric acid levels and its association with hypertension in the patients. It is noteworthy that not only in the mothers with preeclampsia, but also in other patients, hypertension even in male sex has a significant association with LDH and uric acid. For instance, a study conducted by Madole M. B. et al. (2016) entitled " The study of uric acid and serum lactate dehydrogenase in hypertension" showed a significant association between serum LDH and uric acid in both sexes (male and female) with increased hypertension. This study concludes that serum LDH and uric acid levels in hypertensive patients have significantly increased with a significant positive correlation between serum uric acid and systolic and diastolic hypertension (Madole et al., 2016). Furthermore, uric acid levels may be useful not only for predicting preeclampsia, but also for screening PIH; since in a study by Apessha et al. (2017) entitled "The importance of serum uric acid in hypertension added to the preeclampsia pregnancy", the results suggested that the uric acid level in pregnant women with PIH was higher than that in the control group. Researchers have introduced uric acid measurement as an affordable method to diagnose PIH severity (Apeksha et al., 2017). In general, the present study indicated that LDH and uric acid may be reliable markers for patients with preeclampsia and LDH levels show a better prognosis for the severity of preeclampsia. Other similar studies also confirm this finding, including the study by Qublan et al. (2005) who concluded that lactate dehydrogenase is a useful biochemical marker for indicating the severity and complications of preeclampsia. In addition, Liggy et al. (2016) stated that serum LDH are significantly associated with the severity of the disease and maternal-fetal complications in patients with preeclampsia-eclampsia; and Mansi et al. (2015) concluded that the serum LDH and uric acid levels are reliable and inexpensive markers for prediction of the severity and outcome of hypertensive disorders in pregnancy.

Conclusion

The results of the present study suggested that uric acid in pregnant women with preeclampsia significantly increases, so that it is higher in early preeclampsia pregnant women than the late preeclampsia group; and it is higher in severe preeclampsia individuals than those with mild preeclampsia. In addition, LDH of late preeclampsia is more prevalent than tthe early preeclampsia, and it is significantly higher in severe cases compared to the mild patients.

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Table 1. laboratory markers comparison by early and late groups

Variable	Group	Indices			p-value
		Number	Mean	SD	
Hg	Early	33	11.70	0.92	0.68
	Late	31	11.80	0.95	
HCT	Early	33	34.98	2.87	0.07
	Late	31	36.30	2.64	
Plt	Early	33	223.78	57.36	0.01
	Late	31	183.75	66.49	
Pt	Early	33	12.19	0.46	0.06
	Late	31	13.66	2.80	
PTT	Early	33	32.86	2.67	<0.001
	Late	31	16.55	8.06	
BUN	Early	33	10.73	4.13	0.96
	Late	31	13.53	15.63	
Cr	Early	33	0.73	0.16	0.04
	Late	31	0.65	0.19	
SGOT	Early	33	56.75	154.39	P<0.001
	Late	31	124.18	220.68	
SGPT	Early	33	52.78	145.86	0.06
	Late	31	133.40	241.44	
Bs	Early	33	97.65	15.09	0.64
	Late	31	98.95	21.79	

Table 2. Uric Acid and LDH markers comparison by early and late groups and mild or sever divisions

Variable	Group	Severity	Indices			p-value
			Numbe	Mean	SD	
Uric acid	Early	Mild	13	4.09	1.30	<0.001
		Sever	20	6.40	0.43	
	Late	Mild	17	4.81	1.43	0.78
		Sever	14	4.42	1.48	
LDH	Early	Mild	13	275.90	77.33	0.04
		Sever	20	406.00	309.96	
	Late	Mild	17	365.75	115.66	0.04
		Sever	14	493.66	204.79	