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Elevated serum iron levels in pregnant women with preeclampsia

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Abstract
Background: Pre-eclampsia is one of the common medical complications that happened during pregnancy, it affecting 5% to 10% of all pregnancies. It is best termed as a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation, characterized by hypertension and proteinuira that may lead to multisystem involvement including renal, hematological, hepatic and cerebral impairment.
Objective: To assess the elevated serum iron levels in pregnant women with preeclampsia.
Patients and method: A case control study conducted in 2 hospitals in Baghdad city (Al-Immamain Al-Khadimain Medical City, and Abugraib general hospital) in one year duration in the period from the 1st of Jan 2017 to the end of Dec 2017, in which 176 women were enrolled in the current study.
Results: The mean age of the PE group was (30.2±7) years, (28.4±5) years for control group, with no significant association. Highly significant associations were found between case and control groups regarding; gestational age, mean arterial blood pressure, weight of fetus and premature baby (p value <0.001). Highly significant increase were found in PE patients than healthy patients among serum iron and serum ferritin (P<0.001).
Conclusion: Serum iron level was increased in pregnant patients with preeclampsia.

Keywords: Preeclampsia, iron level, ferritin, pregnancy

Introduction
Pre-eclampsia is one of the common medical complications that happened during pregnancy, it affecting 5% to 10% of all pregnancies [1]. It is best termed as a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation, characterized by hypertension and proteinuira that may lead to multisystem involvement including renal, hematological, hepatic and cerebral impairment [2, 3]
Preeclampsia is usually more frequent in primigravids. It is likely that by an immune mechanism, the future mother 'learns' to tolerate the paternal antigens present in the seminal fluid; Limited exposure to sperm would contribute as a risk factor for the patient to develop preeclampsia. This would explain why women with limited exposure to sperm (first intercourse and pregnancy, pregnancy after artificial insemination, multiparous women who change partners) have a higher risk of preeclampsia [4].
Preeclampsia can occur in family groups, suggesting a genetic component [5]. In twin studies, it is estimated that in 22% to 47% 'preeclampsia can be inherited' [6] Previous studies have shown significant associations between preeclampsia and DNA variants in the alpha 1 chain of collagen (COL1A1), interleukin-1 alpha (IL1A), [7] mutation of factor V Leiden, mutations of endothelial nitric oxide synthase, antigen human leukocyte and angiotensin converting enzyme [8]

Abnormal implantation and vasculogenesis
One of the main mechanisms in the pathogenesis of preeclampsia is placental insufficiency due to a poor remodeling of the maternal vasculature of perfusion in the intervillous space. In a normal pregnancy, the fetal cytotrophoblast invades the maternal spiral uterine arteries replacing the endothelium, and the cells differentiate into 'endothelioid' cytotrophoblasts [9].
Until know the precise mechanisms that responsible for the trophoblastic invasion and defective vascular remodeling are not entirely clear [10, 11]. The results have been evident that NOTCH signaling (NOTCH is a transmembrane protein that serves as a receptor for extracellular signals

and that it participates in several signaling pathways with the main purpose of controlling cell fate) is vital in the invasion process. trophoblast and vascular remodeling. The absence of NOTCH2 would be associated with a reduction in vascular diameter and affect placental perfusion. In addition, participants will demonstrate in preeclampsia models that endovascular and perivascular cytotrophoblasts lacked JAG1 (which is a ligand of NOTCH2) [12].

Other studies have to do with the variability in the genes of the immune system that encode the molecules of the histocompatibility complex and the receptors of the natural killer cells can affect the placentation [13]. In this way, factors such as combinations of histocompatibility complex characteristics and natural killer cell receptor genes correlate with the risk of developing preeclampsia, recurrent abortion and fetal growth restriction.

Activation and endothelial dysfunction

The maternal vascular endothelium in the patient predestined to develop preeclampsia is subject to various factors that are generated as a consequence of hypoxia and placental ischemia. The vascular endothelium has important roles, including the control of smooth muscle layer tone through the release of vasoconstrictive and vasodilatory factors, as well as the release of different soluble factors that regulate anticoagulation, and antiplatelet and fibrinolytic functions. Alterations in the circulation concentration of many markers of endothelial dysfunction have been found in women who develop preeclampsia. [14] The maternal state influences the endothelial response to factors derived from ischemia and placental hypoxia in preeclampsia. There is evidence that obesity increases the risk of preeclampsia. A body mass index greater than 39 increases the risk of preeclampsia by 3 times [15].

Iron level in pregnancy

The normal level of the haemoglobin in healthy women is 12 g/dl. The ideal level of Hb that recommended by World Health Organization should be ≥11.0 g/dl, and should not be ≤10.5 g/dl in the second trimester. Iron was required by pregnant women more than in non- pregnant and the net needed approximately for pregnancy are 840 mg [16].

Deficiency of iron can be defined as that time when iron stores in the body become depleted with apparent restriction of iron supply to the various tissues [17].

Iron deficiency also puts the pregnant women at risk for developing abruptio placenta, postpartum haemorrhage, which can be disastrous. Globally, 20% of maternal deaths are due to anemia; furthermore, anaemia contributes partly to half percent of all maternal deaths [18].

Aim of the study: To assess the elevated serum iron levels in pregnant women with preeclampsia

Patients and method: A case control study conducted in 2 hospitals in Baghdad city (Al-Immamain Al-Khadimain Medical City, and Abugraib general hospital) in one year duration in the period from the 1st of Jan 2017 to the end of Dec 2017, in which 176 women were enrolled in the current study (56 women with preeclampsia and 120 healthy pregnant women). At the time of the delivery the researchers collected blood and put it in the centrifuge for 10 minutes at 1,500×g for 10 so as to extract serum samples and then serum was stored before used.

Ethical consideration: Verbal consent was taken from the respondents before the beginning of the study and patients was informed that all data in the current study were used confidentially and for the purpose of the study only.

Statistical analysis: After data entering, then it analyzed by using the IBM-SPSS version 25. All data were presented as mean ± standard deviation. Statistical significance was established at $p<0.05$.

Results

176 women were enrolled in the current study, 56 were with preeclampsia and 120 were normal healthy pregnant women. The mean age of the PE group was (30.2±7) years, while (28.4±5) years for control group and with no significant association. Highly significant associations were found between case and control groups regarding; gestational age, mean arterial blood pressure, weight of fetus and premature baby (p value <0.001) (table 1).

Table 1: Relation between demographic criteria of the studied groups

	PE (n=56)	Normal (n=120)	P value
Maternal age (years)	30.2±7	28.4±5	0.052
Gestational age (weeks)	35±3	38±3	<0.001
Mean arterial blood pressure (mmHg)	135±10	85±5	<0.001
Weight of fetus	2.3±0.3	3.09±0.7	<0.001
Premature baby	46	7	<0.001

As shown in table 2, highly significant increase were found in PE patients than healthy patients among serum iron and serum ferritin ($P<0.001$). No significant associations were found between the studied groups among hemoglobin, hematocrit, and platelet count ($P<0.05$).

Table 2: Association between different hematological parameters

	PE (n=56)	Normal (n=120)	P value
Serum iron µg/dL	220.7±60.3	150.2±60.1	<0.001
Serum ferritin	109.2±18.9	30.3±7.1	<0.001
Hemoglobin (g/dl)	10.8±1.2	10.9±0.8	NS
Hematocrit (%)	37±3.9	38±4.2	NS
Platelet count	189±66	208±75	NS

Discussion

The current study shows that there is highly significant association were found regarding the gestational age and preeclampsia, when the decrease gestational age were noticed in preeclampsia group than the healthy group. This is not in agreement with that found in Adam B, *et al*. study when no significant association was found [19].

In a study carried by Kim J *et al*., [20] revealed that there is a significant association regarding weight of fetus and premature baby, which is same that found in the present study.

There is a significant increase of S. Ferritin in women with preeclampia than that in normal healthy pregnancy, which is similar to that found by Maitra S *et al*., study to evaluate serum ferritin and iron level and its probable causal role in pre eclampsia [21].

The most important finding in the current study is the elevated level of Serum iron and there is a significant increase in serum iron level in preeclampsia than in normal pregnant women which is in agreement with that mentioned by Siddiqui I in Saudi Arabia, in a study carried at King Abdulaziz Medical City

in the period between February 2009 and January 2010 [22]. Moreover it is in agreement with Liu JX *et al*. in his meta-analysis found that the serum iron levels in patients with preeclampsia are significantly higher than those found in healthy pregnant women [23].

Conclusion

Serum iron level was increased in pregnant patients with preeclampsia.

Conflicts of interest: No

Source of funding: Self

Ethical clearance: Was taken from the scientific committee of the Iraqi Ministry of health

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