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Determination of Liver Enzymes, Lipid Profile, Tumor Necrosis Factor-α and C-Reactive Protein Concentrations in Women in Toxemia of Pregnancy in Tikrit City

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Abstract

Pre-eclampsia is characterized by an increase in blood pressure and proteinuria. The aim of this study was to determine the concentrations of TNF-α in the maternal blood in patients suffering from pre-eclampsia. Patients and methods a cross sectional study was conducted in Sallah Alddin general hospital/Tikrit city from beginning of March to the end of August 2019. The current research focuses on determining of TNF-α level in pregnancy toxemia in Tikrit city- Iraq. Sixty pregnant women were enrolled in the study thirty of them are suffering from hypertension and albumin urea in the third trimester, age (17-36) years and other thirty are healthy pregnant as control age (17-38) years. All blood samples are tested for Tumor Necrosis Factor-α (TNF-α), C- reactive protein (CRP), albumin, uric acid, liver functions, and lipid profile. The results showed a significant increase, for patient's women, in the serum TNF-α, CRP, liver enzymes, LDL, triglyceride (TG), cholesterol. While the HDL show significant decrease and non-significant differences regarding serum albumin and uric acid between patients and controls.

*Key words***:** Pregnancy toxemia; liver function; tumor necrosis factor (TNF-α); C- reactive protein; uric acid.

1. Introduction

In 2004, "Toxemia of Pregnancy" was changed to Pregnancy Induced Hypertension (PIH)" in Japan"[1]. Toxaemia is a condition of multisystem, usually occurring in late pregnancy, with hypertension, proteinuria, oedema, and central nervous system irritability. Sever toxemia may associated with convulsions, the disease has been divided into eclampsia and pre-eclampsia, depending on whether a seizure has occurred. Toxaemia accounts for around 70 % of pregnant women's hypertension [2].

The most common critical condition during pregnancy is pre-eclampsia, occurring in 2-5 % of all pregnancy, worldwide.

Pre-eclampsia is the most common critical condition during pregnancy and pre-eclampsia is characterized by an increase in blood pressure and proteinuria. Pre-eclampsia is defined as high blood pressure condirion following 20 weeks of gestation, [3,4].

A new hypothesis about the etiology of preeclampsia has been targeted on body immune response. Cytokines are immunoregulatory molecules that may take part in pathogenesis of preeclampsia [4]. Type 1 cytokine receptors (interleukin-2), type 2 cytokine receptors (interferon), and type 2 cytokine receptors like tumor necrosis factor alpha-(TNF-α) are generally produced by the pre-eclampsia-induced inflammatory process [5]. Since (TNF-α) is a multifunctional proinflammatory cytokine involved in the pathogenesis of a large number of autoimmune and inflammatory diseases in humans [6]. However, excessive liberation of pro-inflammatory cytokines, in particular the (TNF-α), is responsible for the endothelial activation. Thereby, a fault of trophoblasts invasion demonstrate clinical symptoms of preeclampsia [7].

Furthermore, neutrophils, monocytes, and possibly placenta are the origins of TNF-α synthesis in preeclampsia. One possible mechanism in preeclampsia was that factors derived from the placenta stimulated monocytes and neutrophils to produce TNF-α, contributing to endothelial disruption. It thus appeared that increased serum

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TNF-α could be part of the pre-eclampsia pathology [5].

The objective of the present investigation was to determine the concentration of TNF-α in the maternal blood in patients suffering from pre-eclampsia.

2. Patients and methods:

A cross sectional study carried out at Sallah Alddin General Hospital/Tikrit city from the first of March to the end of August 2019. Sixty pregnant women have been admitted to the hospital, half of them (thirty) are suffering from hypertension and albumin urea. Their ages are (17-36) years, and the other thirty are healthy pregnant women as control group their ages range (17-38) years. All participants were informed by written consent about the study. From all participants, a 5 ml venous blood sample was collected, separated and stored at -20 ° C for later analysis. Serum TNF-α, C- reactive protein (CRP), albumin, uric acid, liver functions serum glutamyl transferase (GGT), alanine transaminase (GPT), serum aspartate transaminase (GOT), and lipid profile were measured according standard procedures and others by using appropriate kits. TNF-α level was determined using enzyme-linked immunosorbent assay according to the manufacturer's instructions (TNF-α Elisa kit, Cayman-USA).

3. Statistical analysis

All data were presented as a mean and standard deviation (SD) by using SPSS version 23. Unpaired student T test was used to compare between variables. P value ≤ 0.05 was used as a significant value.

4. Results:

Table 1 show the concentrations of TNF-α, C-reactive protein and uric acid for pregnancy toxemia patients and normal pregnant women as control. The finding show a significant increase in the concentration of serum TNF-α in pregnant women with toxemia patients as compare with normal pregnant control women, (P≤ 0.05).

Table 1: The mean and SD for TNF-α, C- reactive protein and uric acid for pregnancy toxemia patients and normal pregnant women as control.

Parameters	patients	Control	P value
TNF-α (Pg/µl)	6.96 ± 3.9	4.35 ± 2.3	< 0.05
CRP (mg/L)	11.66 ± 6.5	7.5 ± 2.5	< 0.05
Uric acid (mg/dL)	4.6 ± 1.7	5.4 ± 1.4	NS
Number	30	30	

Also, there is a significant elevation in serum CRP of women with pregnancy toxemia patients as compare with normal control healthy pregnant women (p≤ 0.01). However, regarding uric acid, there is no significant difference in the level of uric acid between patients and control groups, Table 1.

The result of the liver enzymes indicate a significant elevation in (GGT), (GPT) and highly significant increase in (GOT) activities in patients as compare with controls Table 2.

Table 2: The mean and SD of liver functions (GGT, GPT, GOT, albumin), for pregnancy toxemia patients women and normal control pregnant women.

Parameters	patients	Control	P value
GGT (UI/L)	29.13 ± 10.5	20.1 ± 6.2	< 0.05
GPT (UI/L)	38.8 ± 4.2	26. 6 ± 7.4	< 0.05
GOT (UI/L)	40.4 ± 13.7	23.2 ± 5.9	< 0.05
Albumin (g /dL)	181.6 ± 33	189.4 ± 33	NS
No.	30	30	

However, regarding albumin concentrations, there is no significant differences between pregnancy toxemia patients and normal pregnant control women Table 2.

On the other side, a significant reduction in HDL levels in preeclamptic women comparing to the control group was found Table 3. None the less, there are significant elevations in the concentrations of serum LDL, triglyceride (TG) and cholesterol in preeclamptic pregnant women in comparing with normal pregnant women.

Table 3: The mean and SD of lipid profile for patients and control groups

Parameters	patients	Control	P value
HDL (mg/dL)	25.5 ± 7.4	30.4 ± 8.4	< 0.05
LDL (mg/L)	133.8 ± 20	114.1 ± 17.4	< 0.05
TG (mg /dL)	271.1 ± 49	174.2 ± 48.6	< 0.05
Cholestrol (mg/dL)	242.6 ± 43.1	176 ± 57	< 0.05
No.	30	30	

5. Discussion:

In the present study, a significant increase in the concentration of serum TNF-α in toximic pregnant women as compare with normal pregnant control women, (P≤ 0.05). This finding agrees with previous study that found a serum

TNF-alpha level in preeclamptic patients was increased as compare to normotensive nonpregnant women [8,9]. Recently, two separate studies, maternal serum levels of TNF-alpha have been shown to rise significantly in preeclamptic patients such that higher levels were seen in severe to moderate preeclampsia patients, [10,11].

In another study, attempts to explain these findings have shown that the fractional secretion of TNF-α in preeclamptic women is significantly reduced and therefore indicate that decreased clearance and altered TNF-α renal excretion may lead to preeclampsia [12]. In addition, another study based on their results concluded that cytokine-dependent preeclampsia screening such as IL-6 or TNF-α is not suggested [13]. Previous studies not agree with the present study, which failed to detect an association between maternal serum levels of TNF-α and preeclampsia, [14,15].

Endothelial dysfunction is characterized by elevated rates of inflammatory markers, which are higher in women with preeclampsia relative to normal pregnancy; one of these markers is CRP, recruited in response to stress, tissue injury and other inflammatory stimuli, [16]. Because early detection of patients with an elevated risk of preeclampsia is one of the important objectives in obstetrics, the association between these inflammatory markers and the occurrence of preeclampsia has been attempted,[17]. The association between the high CRP rates and preeclampsia was recorded in the present study, which is in agreement with other previous works, [16,17].

In regarding to the uric acid, the present examination show no significant differences between preeclamptic pregnant women and normal control pregnant women. A previous study shows elevation in serum uric acid in preeclampsia women [18]. In addition, a research on the association between uric acid and preeclampsia indicates that the concentration of maternal serum tends to be a predictor for severity of preeclamptic syndrome. However, the severity of hypertension had a positive correlation with the concentration of serum uric acid [19], which is not in the line with current findings.

In the present study, a significant elevation in the activities of GGT and GPT and GOT enzymes in patients as compare with control subjects. There are a variety of physiological changes that occur during pregnancy to support fetal growth and development. This can result in anticipated improvements in some laboratory results, including minimal to minor decreases in hepatic transaminases and alkaline phosphatase levels [20]. In women who develop preeclampsia and hemolysis, elevated liver enzymes, and low platelet count syndrome, there is a shift toward increased complement activation and decreased complement regulation[21]. Pregnant women with preeclampsia have higher statistically significant GOT and GPT activities as compared to healthy pregnant women. The effect of hypoxia on the liver during preeclamptic pregnancy is explained by elevated serum levels of GOT in preeclampsia [19]. During preeclampsia various mediators are released from the endothelium of the liver and blood vessels (fibronectin, thrombomodulin, endothelin-l, thromboxane), which induces vasoconstriction and hypoxia of the liver which raises the GPT rate and other liver enzymes [22]. These findings are in a good agreement with that achieved previously [19,22].

Albumin declines and improves over time during pregnancy. It is explained by an increase in plasma and interstitial volume, and likely by an increase in metabolism of albumin. This finding seems to be partly responsible for increased capillary permeability secondary to endothelial damage [23].

Various lines of evidence indicate that abnormal lipid metabolism is not just a manifestation but also involved in disease pathogenesis [24]. Preeclamptic pregnant females were found to possess significantly lower levels of HDL cholesterol than normal pregnant females in this study. In preeclamptic females the concentration of total cholesterol, LDL, VLDL & triglycerides was found to be significantly increased compared with normal pregnant females. In this study the noted dyslipidemia was consistent with many studies carried out worldwide [25-27].

Therefore, taking into account the present findings of this research compared with the various other different studies, it can be safely concluded that dyslipidemia is substantially evident in preeclampsia and plays an important pathological function.

6. Conclusion:

The present study concludes that preeclampsia shows an increase in maternal inflammatory cytokines TNF-α, and C- reactive protein. Such inflammatory cytokines can also be used as predictive indicators for preeclampsia.

7. Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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