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Reduced Glutathione, Lipid Peroxidation and Malondialdehyde Status in Women with Mild and Severe Preeclampsia for Babylon Governorate

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Abstract

The presented study aims to evaluate the levels of serum reduced. glutamine , lipid peroxidation and malondialdehyde status with Mild, severe preeclampsia and healthy pregnant control in the case – control study. Twenty five patients with severe preeclampsia, twenty five patients with mild preeclampsia and fifty healthy pregnant as control in Babylon province / Iraq were enrolled in this study. Results of this study were shown The median serum reduced GSH concentration in the preeclampsia group was significantly lower than that in the group with normal pregnancy, indicating that there is more extensive oxidative stress in preeclamptic pregnancy. Also In this result, there was increased in malondialdhyde level in preeclampsia pregnant women groups when compared with non-preeclampsia pregnant women group.

Keywords: *Babylon Governorate ; Severe Preeclampsia ; Glutathione, Lipid*

Introduction

Pregnancy complicated by gestational hypertension is managed based on its severity, presence of preeclampsia, and gestational age . Increases in systolic and diastolic blood pressure can be either normal physiological changes or signs of developing pathology. Heightened surveillance permits more prompt recognition of ominous changes in blood pressure, Critical laboratory findings,and clinical signs and symptoms [(1)].

Pre-eclampsia (PE) is defined when BP ≥140/90 mm Hg and proteinuria (≥300 mg per 24 hours) after 20 weeks of gestation with an incidence of 2-8%. Its complications lead to placental abruption, eclamptic fits. Moreover, PE has been strongly associated with increased risk of later-life death due to liver insults and cardiovascular disease (2). It is a major cause of preterm birth, accounting for 15% of all preterm Deliveries [(3)].

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Oedema is no longer included as a diagnostic criterion for preeclampsia because its occurrence is expected in pregnancy and has not been shown to be discriminatory. If untreated, the symptoms get progressively worse [(4)]. Although PE is associated with abnormal trophoblast invasion in the first half of pregnancy, it is not until later in the pregnancy that the clinical syndrome of PE is seen. The timing of onset and the clinical course are unpredictable. In some, hypertension and proteinuria are the only manifestation, while others may present with severe renal or liver impairment, and in yet others the most prominent feature might be intrauterine fetal growth restriction secondary to placental disease.

The term pregnancy- induced hypertension (PIH) suggests a disorder of blood pressure that arises because of the presence of pregnancy. Pregnancy induced hypertension and PE rarely develop before 20 weeks gestation unless associated with trophoblastic disease or fetal triploid [(5)].

Mild and Severe Pre-eclampsia :

Pre-eclampsia is divided into mild and severe forms, depending on the *severity of the hypertension, the*

amount of proteinuria , and the degree to which other organ system are affected [6].

Mild Pre-eclampsia:

Is defined as the presence of hypertension (BP ≥140/90 mm Hg) on 2 occasions, at least 6 hours apart, but without evidence of end- organ damage in the patient [7].

Severe Pre-eclampsia:

Is defined as the presence of the following:[2]

1. Severe hypertension (systolic blood pressure ≥160 mm Hg , or diastolic blood pressure ≥ 110 mm Hg) at rest, on two occasions at least 6 hr apart.

2. Heavy proteinuria (at least 5 g in a 24-hr collection or a qualitative value of 3+ in urine samples collected 4 hr apart.

3. Oliguria (<500 mL in 24 hr).

4. Cerebral or visual disturbances.

5. Pulmonary edema or cyanosis.

6. Epigastric pain.

7. Impaired liver function (elevated liver enzymes).

8. Thrombocytopenia.

9. Fetal growth restriction.

Materials and Method

Ethical Issues

a- Approval by scientific committee of the Clinical Biochemistry Department,

College of Medicine/University of Babylon, Iraq.

b- Approval by Babylon Health Directorate, Ministry of Health and

Information centre for Research and Development of Babylon Province.

c- The objectives and methodology were explained to all subjects and verbal consent had been taken.

Date and Durations

The period extended from October 2018 to April 2019 . This work was done in the Department of Biochemistry, College of Medicine

University of Babylon and in Hilla city . Iraq.

Study Design

This study design was a case – control study.

Patients and control

A total of 50 patients divided to 25 sever and 25 mild with preeclampsia were enrolled in this study.50 subjects who were apparently healthy control group of pregnant.

Exclusion Criteria:

Age over 35 years.

Previous history of PE.

Conditions in which the placenta is enlarged like multiple pregnancy

Pre-existing hypertension or renal disease.

Pre-existing vascular disease (as diabetes or autoimmune vasculitis.

Determination of Serum Reduced Glutathione

Determination of serum reduced glutathione levels in patient and control group were depends on the action of sulfhydryl group [8].

Determination of Lipd peroxidation

Determination of Lipd peroxidation was done by Elabscience (USA)kits and according to Colorimetric method .

Determination of MDA

Determination of MDA was done by Elabscience ELISA kits and according to Competitive-ELISA principle .

Results

According to the clinical and laboratory examination the patients participating in this study divided in to two main groups illustrated below in Table 1

Table 1:- Number of the different stage among preeclampsia patients.

Stage of cancer	No. of Patients
G1 . mild preeclampsia	25
G2 .sever preeclampsia	25

In this study serum reduced glutathione was significantly lower in preeclampsia patients groups compared with normal patients CG (Control group) P-value < 0.001. In this study, the level of (GSH) decreases more with increase the severity of preeclampsia. Serum reduced glutathione was not significantly lower in G2(sever preeclampsia) compared with G1 (mild preeclampsia) P-value > 0.05 Table 3.

Table 3: The mean ±SD of (GSH) in preeclampsia compared to control group.

Parameter	Subjects	No.	Mean ± SD
Reduced Glutathione (ng/ml)	**G1** sever preeclampsia	25	15.6±5.5
	G2 mild preeclampsia	25	18.4±4.9
	CG Control	50	26.3±6.3
P-value	mild preeclampsia versus Control group (P < 0.001) sever preeclampsia versus Control group (P < 0.001) mild preeclampsia versus sever preeclampsia group (P > 0.05)		

In this study MDA was significantly higher in preeclampsia patients groups compared with normal patients CG (Control group) P-value < 0.05. In this study, the level of MDA increase more with increase the severity of preeclampsia. Serum MDA was significantly higher in G2(sever preeclampsia) compared with G1 (mild preeclampsia) P-value < 0.05 Table 3.

Table 4: The mean ±SD of MDA in preeclampsia patients compared to control group.

Parameter	Subjects	No.	Mean ± SD
Malondialdehyde (ng/ml)	**G1** sever preeclampsia	25	477.5±33.1
	G2 mild preeclampsia	25	418.2±23.6
	CG Control	50	203±27.2
P-value	mild preeclampsia versus Control group (P <0.05) sever preeclampsia versus Control group (P < 0.01) mild preeclampsia versus sever preeclampsia group (P < 0.05)		

In this study Lipid peroxidation was significantly higher in preeclampsia patients groups compared with normal patients CG (Control group) P-value < 0.05. In this study, the level of Lipid peroxidation increase more with increase the severity of preeclampsia. Serum Lipid peroxidation was not significantly higher in G2(sever preeclampsia) compared with G1 (mild preeclampsia) P-value >0.05 Table 3.

Table 4: The mean ±SD of Lipid peroxidation in preeclampsia patients compared to control group.

Parameter	Subjects	No.	Mean ± SD
Lipid peroxidation (ng/ml)	**G1** sever preeclampsia	25	4.2±0.69
	G2 mild preeclampsia	25	4.0±0.82
	CG Control	50	3.7±0.76
P-value	mild preeclampsia versus Control group (P > 0.05) sever preeclampsia versus Control group (P < 0.05) mild preeclampsia versus sever preeclampsia group (P > 0.05)		

Discussions

The median serum reduced GSH concentration in the preeclampsia group was significantly lower than that in the group with normal pregnancy, indicating that there is more extensive oxidative stress in preeclamptic pregnancy. Reactive oxygen species cause decreases in antioxidants. In patients with preeclampsia placental angiogenc activity is significantly lower than in the placenta of normal pregnancy[9]. Other studies are similar, as shown by the significant decreases in the mean value of endogenous antioxidants such as GSH, superoxide dismutase, and glutathione peroxidase in preeclampsia cases as compared with normotensive pregnant women .

In this study extremely low level of reduced glutathione in sever preeclampsia go with the idea that says increase production of ROS In conjunction to increase the severity of preeclampsia the matter that will extremely increase the consumption of glutathione to neutralize the ROS and other free radicals. Glutathione plays essential roles in T cell function and proliferation [10]. Reported that Activation of T helper cell results in decreased levels of reduced glutathione (GSH) and production of ROS. In sever preeclampsia there is a demand to increase activation of T helper cell, that may contribute the consumption of reduced glutathione pool in the serum of preeclampsia

Lipid peroxidation is oxidative degradation of lipid by which, free radicals steal electron from lipid in cell membrane and resulting in cell damage [11]. Lipid peroxidation represent a crucial and causative role in the pathogenesis of atherosclerosis and it involve also, in the oxidative modification of LDL which lead to initiation of hypertensive and preeclampsia [12]. Excessive lipid peroxidation occurring in preeclampsia can be attributed to hypercholesterolemia. Hypercholesterolemia promotes the formation of free radicals.

Increased oxygen demand to meet the bodily functions in pregnancy is also a contributory factor for the oxidative stress that results in the formation of free radicals. Thus, lipid alterations observed may promote oxidative stress, leading to endothelial dysfunction in preeclampsia.[13]

In this result, there was increased in malondialdhyde level in preeclampsia pregnant women groups when compared with non-preeclampsia pregnant women group. Products of lipid peroxidation are the candidate factor that mediate disturbance of the maternal vascular endothelium and may inhibit prostacyclin synthesis and also stimulate smooth muscle contraction that lead to widespread vasospasm, a prominent feature of preeclampsia[14]. The decrease of red cell deformability due to the increase of plasma malondialdehyde level may be the underlying mechanism of pregnancy induced hypertension[15].

Conclusion

Preeclampsia patients in Babylon province have low reduced glutathione level comparing to normal subjects and this level decrease more as the preeclampsia progress to advance severity .As regard to glutathione antioxidant and immune supporting properties, glutathione consumed during elimination of ROS that produced by lipid peroxidation processes . Also, preeclampsia patients in Babylon province have high Malondialdehyde and Lipid peroxidation level comparing to normal subjects and this level increase more as the the preeclampsia progress to advance

severity. The oxidative stress underlying the occurrence of systemic inflammation in patients with preeclampsia indicates that there is an imbalance between free radicals and the antioxidant defense mechanism in the course of pregnancy.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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