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Study of glutathione, glutathione reductase, glutathione peroxidase as antioxidant system during pregnancy

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Abstract

Background: *The glutathione system, consisting of glutathione, glutathione reductase, and glutathione peroxidase, plays a significant role in pregnancy by acting as an antioxidant. This article aimed to measure glutathione, glutathione reductase and glutathione peroxidase in pregnant woman during their first, second and third trimesters as antioxidant and malondialdehyde (MDA) as parameter on oxidative stress. compared it with non-pregnant women. So, estimation of oxidant status can predict.*

Methods: *This study includes 120 samples; ninety of them are from pregnant women, divided into three groups based on the term of pregnancy., the first trimester (n=30), from (1-12 week), and the second trimester (n=30) from (13-27 week) and third trimester from (28-40 week) (n=30). For comparison, 30 non-pregnant women involved as the control group. The parameters that used to estimate antioxidant levels in serum were glutathione, glutathione peroxidase, glutathione reductase and MDA to estimate oxidant levels.*

Result: *The current study shows there was a significant difference in serum glutathione levels in the first, second and third trimester (sub groups) when compared to control group (48.21 ±1.13 b pg./ml), (34.01 ±1.02 c pg./mL), (9.76 ±0.34 d pg./mL) vs. (75.24 ±1.29 a pg./mL), (P≤0.01).*

Conclusion: *The decrease in antioxidant levels and increase in MDA level lead us to conclude that pregnancy as a situation produces huge amount of oxidant so reduce capability of body to overcome its effect leading to oxidative stress. based on that pregnant woman need to surg of antioxidants as supplement in food or food fortified by antioxidants.*

Key words: pregnancy, oxidative stress, Antioxidant enzymes, MDA, Glutathione.

INTRODAUCTION:

Even under normal circumstances, pregnancy is linked to a higher degree of oxidative stress (OS) than what happens during the nonpregnant state, posing a metabolic challenge to both the mother and the growing baby [1, 2]. Because of its high metabolic rate and increased mitochondrial activity, the placenta is a significant provider of this OS [3, 4]. The presence of an intrauterine operating system (OS) during pregnancy is a natural reaction to meet the energy needs of the foetus and placenta [5]. During the first trimester, placental tissues have low levels and limited functioning of antioxidant enzymes. As a result, trophoblastic cells are very vulnerable to damage caused by oxygen [6].

The term "antioxidant" can be used to describe any agent that, even in small amounts, slows down or prevents the oxidation of a substrate [7]. There are multiple chemicals involved in antioxidant defense, which can be categorized as either endogenous (produced internally) or exogenous (consumed). Antioxidants get relieve of free radicals, donate electrons and hydrogen, stop singlet oxygen from oxidising, break down peroxides, stop enzymes from working, work together to make other substances stronger, and bind metals together. Antioxidants, both enzymatic and nonenzymatic, can be found inside and outside of cells. They work to fight reactive oxygen species (ROS) and reduce their damages. [8]. Antioxidants are classified into two types based on their mode of action. They possess the capacity to function as either chain-breaking antioxidants or preventative antioxidants.

Glutathione, often known as GSH, is a tripeptide called L-γ-glutamyl-L-cysteinyl glycine, which serves several roles in living organisms [9–12]. It safeguards cells from damage by directly engaging with reactive oxygen and nitrogen species (ROS and RNS) and relocating a thiol group in the form of a cysteine residue. Furthermore, it can act as an electrophile or function as a cofactor for several enzymes [13–16]. Glutathione exhibits considerable stability in the cellular milieu owing to intracellular peptidases that can hydrolyse peptide bonds. It consists of the -carboxyl groups of amino acids, but generally excludes the -carboxyl groups. Glutathione exists in two forms: reduced (GSH) and oxidised (GSSG). These forms, in conjunction with other redox-active molecules such as NAD(P)H, collaborate to regulate and maintain the cellular redox state [17]. The mechanisms for scavenging free radicals include antioxidant enzymes like Glutathione peroxidase (GSH-P) and Glutathione reductase (GSH-R). These enzymes regulate the concentration of free radicals in cells and prevent excessive oxidative damage [18]. Oxidative stress causes many diseases in humans like Epileptic [19], Rheumatoid arthritis (RA) [20], cardiovascular diseases [21]. It is noteworthy to mention that polyunsaturated fatty acids undergo oxidation to synthesize the chemical. Oxidative stress primarily damages lipids, especially polyunsaturated fatty acids that contain several carbon-carbon double bonds. As a biomarker for oxidative stress, MDA a by product made when lipids are oxidised, has been used to check for it in blood, urine, and exhaled breath condensate (EBC) from people with a range of conditions, such as neurodegenerative disorders, cardiovascular diseases, and pulmonary cancer [22, 23]. The levels of the lipid peroxidation indicators MDA can be detected in both pregnant women and non-pregnant women [24-27]. Furthermore, it is worth noting that the levels of MDA are elevated during the initial three months of pregnancy and are much higher compared to non-pregnant women. Additionally, MDA levels continue to rise throughout the course of pregnancy.

MATERIALS AND METHODS

Patients: About 120 samples (90 pregnant woman and 30 non- pregnant woman). enrolled in the current study. All patients were collected in the Al-Karkh Maternity Hospital, Baghdad, Iraq in a period from January 2024 to May 2024. The age range of patients was (20-45) years. Patients were divided into three groups according to their trimester: 1st trimesters: (n=30), 2nd trimesters: (n=30), 3rd trimesters (n=30). For comparison, thirty healthy non pregnant woman were inserted in the present study as the control group.

Assessment of serum MDA, Glutathione and its related enzymes.

Each blood sample from participants (in both control and patient groups) was treated to obtain serum which was used to assess glutathione, glutathione peroxidase, glutathione reductase and MDA using the ELISA technique with reagents provided by Elab Science, USA.

RESULTS

Table (1): Means ±SE of Serum anti -Oxidant parameter Levels for all studies group

Subgroups	Means ±SE		
	GSH (pg./mL)	GPX (pg./mL)	GR (pg./mL)
First trimester (No. =30)	48.21 ±1.13 b	492.32 ±24.04 b	1235.08 ±48.77 b
Second trimester (No. =30)	34.01 ±1.02 c	494.87 ±52.89 b	1018.51 ±37.24 c
Third trimester (No. =30)	9.76 ±0.34 d	43.13 ±6.23 c	365.21 ±4.75 d
Control (No. =30)	75.24 ±1.29 a	1082.72 ±18.91 a	1418.98 ±36.80 a
L.S.D.	2.481 **	86.019 **	100.44 **
P-value	0.0001	0.0001	0.0001
Means having with the different letters in same column differed significantly. ** (P≤0.01).			

In this study, the number of participants was 120 healthy women. They were divided into two groups: the first group was(n=90) pregnant women, and the second group was a control group of (n= 30) non pregnant woman. Then we divided the first group into three subgroups according to the term of pregnancy (1st, 2nd and 3rd).

The current study shows that there was a notable disparity in serum glutathione levels in sub groups when compared to control group (48.21 ±1.13 b pg./ml), (34.01 ±1.02 c pg./ml), (9.76 ±0.34 d pg./ml) vs. (75.24 ±1.29 a pg./mL), (P≤0.01) as show in Figure (2).

Noteworthy, there was a difference in serum glutathione reductase (GR) levels in sub groups when compared to control group (1235.08 ±48.77 b pg./mL), (1018.51 ±37.24 c pg./mL), (365.21 ±4.75 d pg./mL) vs. (1418.98 ±36.80 a pg./mL), (P≤0.01) as show in Figure (3)

There was also a notable difference in serum glutathione peroxidase (GPX) levels in subgroups when compared to control group (492.32 ±24.04 b pg./mL), (494.87 ±52.89 b pg./mL), (43.13 ±6.23 c pg./ml) vs. (1082.72 ±18.91 a pg./mL), (P≤0.01) as show in Figure (4)

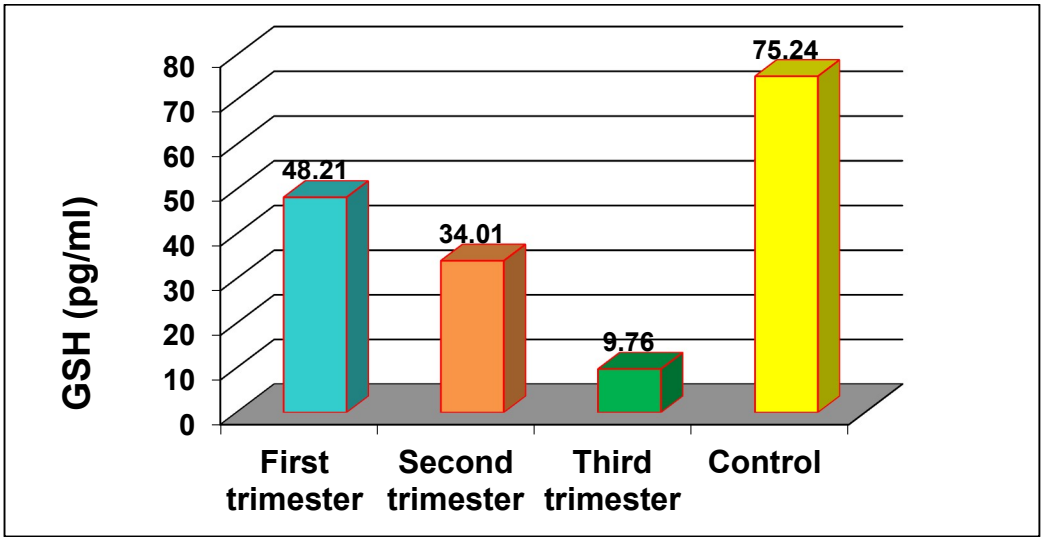

Figure (1) Comparison between Sub-groups in GSH

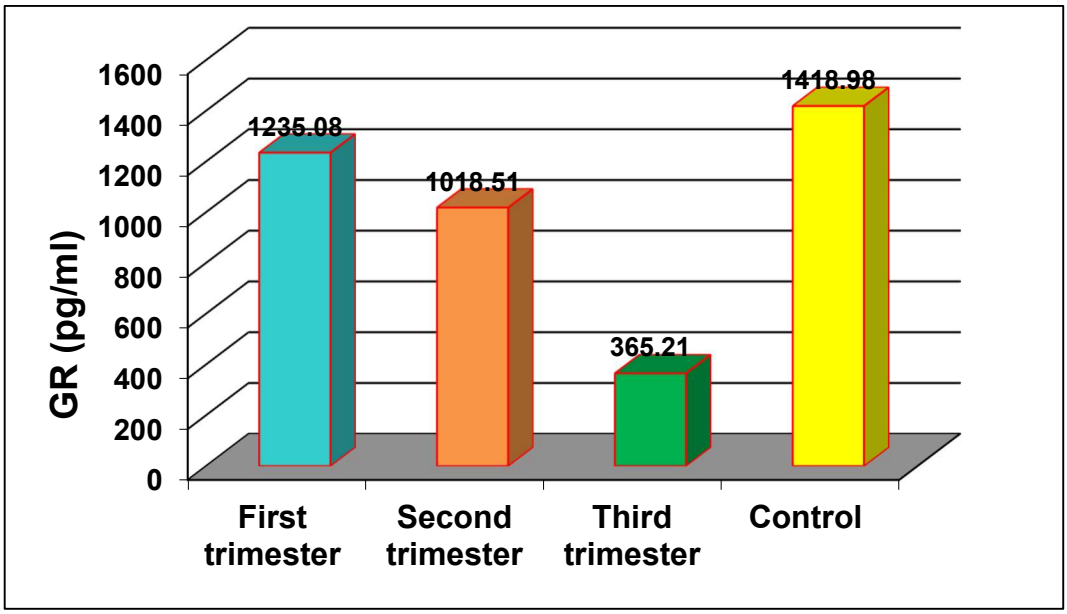

Figure (2): Comparison between Sub-groups in Glutathione reductase

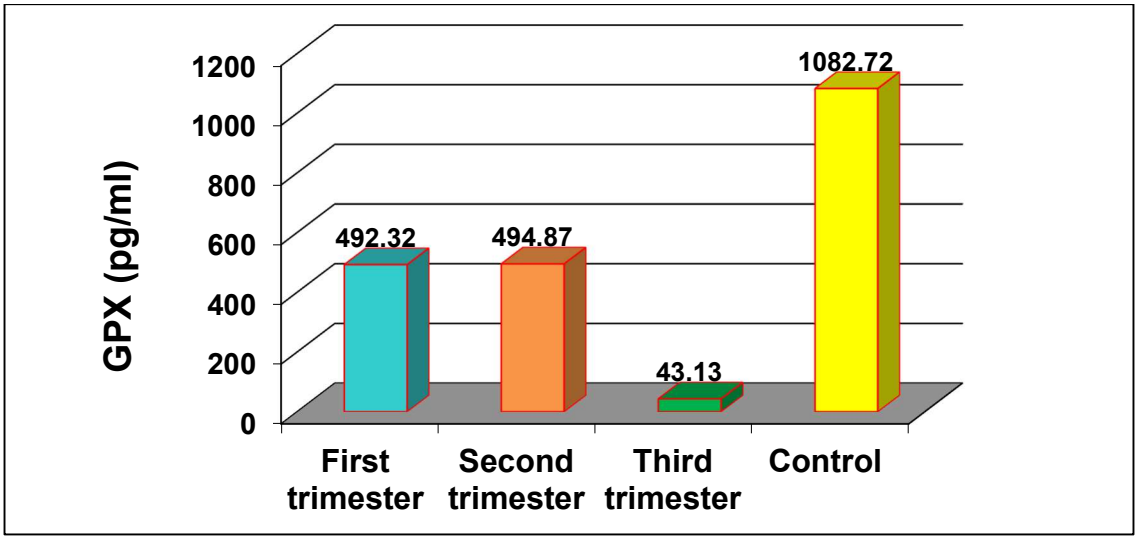

Figure (3): Comparison between Sub-groups in Glutathione peroxidase

Table (2): mean ±SE of Serum Malondialdehyde Levels for all studies group

Sub groups	Means ±SE
	MDA (ng/mL)
First trimester (No. =30)	277.56 ±17.24 b

Second trimester (No. =30)	290.14 ±16.50 b
Third trimester (No. =30)	695.70 ±14.54 a
Control (No. =30)	141.43 ±6.37 c
L.S.D.	40.148 **
P-value	0.0001
Means having with the different letters in same column differed significantly. ** (P≤0.01).	

The present investigation demonstrates a remarkable disparity in serum malondialdehyde (MDA) levels in subgroups when compared to control group (277.56 ±17.24 b ng/mL), (290.14 ±16.50 b ng/mL), (695.70 ±14.54 a ng/mL) vs. (141.43 ±6.37 c ng/ml), (P≤0.01) as demonstrated in Figure (4) and Table (2)

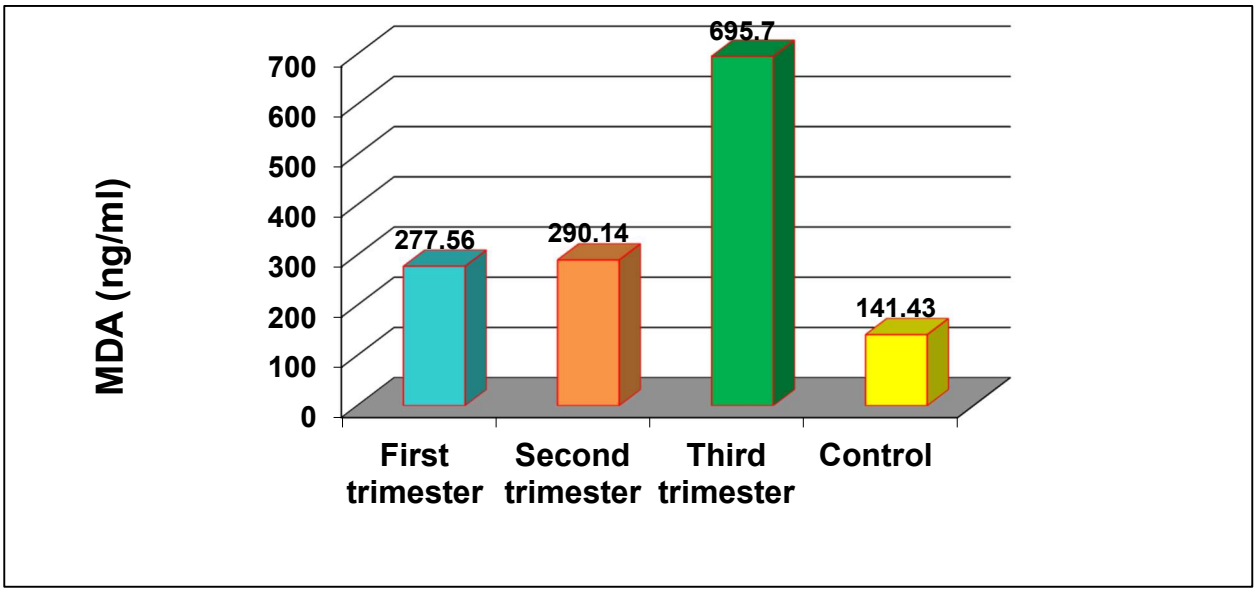

Figure (4) Comparison between Sub-groups in MDA

DISCUSSION

The current study was designed to evaluate the serum levels of MDA, glutathione and glutathione related enzyme, (reductase and peroxidase) in pregnant woman and compared with non-pregnant women to estimate the need for antioxidants. The concentration of glutathione was decreasing gradually from first to third trimester and highly decreasing in third trimester it was in disagreement with **Balasubramanian and Birundha (28)** and their study showed the highly decrease of glutathione in the second trimester. Furthermore, it demonstrated the importance of measuring glutathione levels (a prominent antioxidant) during pregnancy. Supplementation with GSH and antioxidants can reduce the occurrence of birth abnormalities and protect both women and the fetus from the negative and potentially lethal consequences of pregnancy problems [29]. This study displayed the crucial significance of assessing glutathione levels throughout pregnancy to mitigate the occurrence of deleterious consequences such as congenital malformations, spontaneous abortions, and miscarriages.

The present study also showed there was a considerable decreasing glutathione reductase (GR) and glutathione peroxidase was gradually from 1st to 3rd trimester compared with control group which agreement with **30- Lekharu et al. (30).** Both glutathione reductase and glutathione peroxidase exhibited a statistically significant decrease. According to Yu (31), Reduced glutathione is a powerful reducing agent It is crucial to several detoxifying processes. Glutathione reductase is a crucial enzyme that is responsible for replenishing and preserving optimal levels of reduced glutathione in living organisms. Our study revealed a progressive decline in glutathione reductase levels during all three trimesters of pregnancy due to the rise in oxidant levels. The placenta is essential for supplying this oxidative material because of its elevated metabolic rate and enhanced mitochondrial activity.

The concentration of MDA significantly increases gradually in first trimester to third trimester compared to control group, the mean of MDA in 1st and 2nd trimester its, have a no significant difference when compared together but a have a Hight significant differences when compared with control group. In the 3rd trimester the mean of MDA has a highest significant difference when compared to 1st,2nd and control group. This finding is in disagreement with **Saikumar and his colleagues (32).** The average serum MDA levels in the prenatal participants throughout the second trimester are substantially greater than those during the first trimester. Due to their inherent instability and fleeting nature, accurately measuring free radicals is a challenging task. Researchers have used their propensity to cause lipid peroxidation as an indirect measurement. Levels of lipid peroxidation markers, specifically malondialdehyde (MDA), have been observed to rise as normal pregnancy progresses (33). **Ishihara** (34) conducted a study on the levels of lipid peroxides in non-pregnant women and women in different stages of pregnancy (I, II, and III trimesters). The research noted a significant rise in lipid peroxidation product levels throughout the second and third trimesters of pregnancy compared to non-pregnant women.

Conclusion

Through this study, it was shown that pregnancy is a period in which oxidative stress increases, such that antioxidants (in this study, glutathione and its related enzymes) in the body cannot treat this matter. Therefore, it is recommended that antioxidants as supplements be among the most important things that a pregnant woman takes to avoid the damage resulting from this situation**.** Pregnancy is a state of physiological stress and increased blood flow. Oxidative stress escalates during pregnancy as a result of the heightened demand for oxygen and the enlarged size of the foetus. The level of oxidative stress increases during the second and third trimesters. Elevated oxidative stress is characterized by an increase in oxidant markers, such as MDA levels, and a decrease in antioxidant markers, such as glutathione and its associated enzymes (glutathione peroxidase and glutathione reductase). Identifying individuals who exhibit indications of oxidative stress can activate antioxidants.

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