Medical Science

25(112), June, 2021

Elevated indicators of oxidative stress and hyperlipidaemia in pregnant women at delivery compared to the cord of their new-born babies and non-pregnant women

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ABSTRACT

Oxidation reactions are important in many vital processes of the body, but they are associated with many toxic effects under certain conditions, from insufficient availability of antioxidants to neutralize them and get rid of them. Pregnancy, delivery, and the first period of life of the fetus are critical conditions that increase the risk of oxidative stress. The aim of this study is to evaluate the levels of oxidative stress products, antioxidants, and lipid indices in pregnant women at delivery and their cord blood, and women who are not pregnant. The study included 25 healthy pregnant women at delivery and their cord blood, and 25 healthy non-pregnant women recruited from Prince Mishari Bin Saud Hospital in Baljurashi, SA. The serum was tested for the antioxidants, oxidative stress products, and lipid profile. The results showed a significant increase ($p \leq 0.05$) in reduced glutathione (GSH), superoxide dismutase (SOD), total antioxidant capacity (TAO), and a significant decrease ($p \leq 0.01$) in the advanced oxidation protein product (AOPP), cholesterol, low density lipoproteins (LDL) and triglyceride level in the cord serum compared to the group of pregnant women. The results also showed a significant increase ($p \leq 0.01$) in AOPP, cholesterol, LDL, and triglycerides, and a significant decrease ($p \leq 0.01$) in GSH, catalase (CAT), TAO, and glutathione-s-transferase in pregnant women compared to non-pregnant women. Pregnant women at delivery areincurred to increased oxidative stress, while the cord blood contains a high percentage of antioxidants, which protect the fetus from the risk of free radicals at birth.

Keywords: Oxidative stress, pregnant women, at delivery, oxidation

To Cite:
Al Ghamdi AM, Elsherif H, Kafy SM, Al-Zahrani MH. Elevated indicators of oxidative stress and hyperlipidaemia in pregnant women at delivery compared to the cord of their new-born babies and non-pregnant women. *Medical Science,* 2021, 25(112), 1494-1501

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Peer-Review History
Received: 20 May 2021
Reviewed & Revised: 21/May/2021 to 14/June/2021
Accepted: 14 June 2021
Published: June 2021

Peer-review Method
External peer-review was done through double-blind method.

1. INTRODUCTION

Oxidative stress (OS) occurs due to the imbalance between the powers of pro-oxidant and antioxidant, which causes a total pro-oxidant insult. Reactants, in general called reactive oxygen species (ROS), which are derived from oxygen, are usual side products of cells' metabolism (Shobeiri et al., 2017). To counter this, cells have developed some antioxidant defensive systems. Antioxidants are molecules that can slow down or prevent other molecules' oxidation. Oxidation is defined as a chemical reaction that changes the electrons from a substance into an oxidizing agent. These reactions could result in free radicals that initiate chain reactions, and hence destroy cells. To end these chain reactions, the antioxidants get rid of the free radical agents and include other oxidation reactions by having themselves oxidized. Consequently, antioxidants frequently decrease agents such as thiols or polyphones (Jayashree et al., 2016). Producing reactive oxygen species and activating antioxidant defensive mechanisms are significant elements of the reproduction process for women (Yüksel &Yiğit, 2015). Oxidative stress may affect the whole reproduction span for females, and its effect may continue afterward (Agarwal et al., 2005). OS can play an essential role over the gestational period (Schoots et al., 2018), normal childbirth (Mocatta et al., 2004), and initiation of premature delivery (Wall et al., 2002; Pressman et al., 2003). Moreover, the oxidative stress can be also affects ovarian steroidogenesis, ovulation, oocyte maturation, the formation of blastocyst (Ademuyiwa et al., 2007).

Pregnancy is a period full of stress, during which a lot of physiological and metabolic processes are changed to a reasonably large extent. Recently, the role of reducing antioxidants and raising superoxidase is being considered significant because these are a risk to healthy pregnancy (Shobeiri et al., 2017). The placenta controls the intrauterine oxidative balance, and it is affected by different elements, which include mother's food habits, physical exercises, and the other aspects concerning lifestyle which may change during the gestational period. Furthermore, an adaptive mechanism of the placenta on the side of the mother may affect the maternal oxidative balance (Min et al., 2009). Additionally, over the gestational period, the placenta provides a correlation between the bloodstreams of the mother and the fetus to fulfil the breathing, feeding, and excreting needs of the fetus. The blood flow from the womb must increase in order to enhance the growth of the fetus and the placenta tissue during every part of pregnancy. During the first stages of the gestational period, oxidative stress goes up due to that the increased metabolism of the placenta results in increasing the formation ofROS (Myatt, 2006; Yüksel &Yiğit, 2015).

On the other side, the generation of free radicals acts on lipids in order to form lipid peroxidation (Jayashree et al., 2016). The formation of the lipid peroxidation occurs either by a free radical process or through enzymes during arachidonic acid metabolism. Lipid peroxidation is likely to cause damage to cells due to that the uncontrolled self-improving process results in disrupting the membrane lipid and the other essential elements of the cell (Arikan et al., 2001). The cord correlating the fetus inside the uterus to the placenta of the mother is called the umbilical cord, and through which the nutrients are provided, and the wastes are removed. It has a structure similar to a cord, and its length is about 22 inches. It connects the placenta with the walls of the fetus' abdomen. Its principal function is to transfer the blood that carries the nutrients and oxygen through the placenta to the fetus' body and to carry the excretions the opposite way around. The umbilical cord consists of an expansion of the membrane that covers the fetus' body, surrounded by a mucoid jelly. Through this mucoid jelly, one vein takes the blood carrying oxygen to the embryo, and two arteries return it to the placenta. Here the umbilical cord brings the fetus' blood close to the mother's blood. This is how it accomplishes its function (Jayashree et al., 2016).

The process of parturition comes with a high level of OS because childbirth, per se, is a hyperoxic process (Shobeiri et al., 2017). Therefore, the concentrations of oxygen relatively increase after delivery, which could be poisonous to the fetal tissues. The high formation of ROS mediates a likely mechanism of toxicity and pathophysiologic cell alterations (Jayashree et al., 2016). Cells are usually upregulating antioxidant protections and other defensive systems in response to OS. Our objective in the current study is to assess the oxidative stress condition of pregnant mothers at parturition and its influence on their babies (Guržanova-Durnev et al., 2013). It is hard to directly identify the measurement of OS in the human body because the active oxygen species and free radicals live for a brief period (Pryor & Goldber, 1991) and it is impossible to detect them in people using the present methods of detection (Cheeseman, 1990). Therefore, we measure the products of the oxidative process instead (Little & Gladen, 1999).

The aim of the current study is to evaluate the levels of oxidative stress products, antioxidants, and lipid indices in pregnant women at delivery and their cord blood, and women who are not pregnant.

2. SUBJECTS AND METHODS

Study duration

From (28 February 2019) to (10 November 2020).

Subjects

All subjects were recruited from Prince Mishari Bin Saud Hospital in Baljurashi, Saudi Arabia. The study comprised 25 normal pregnant women at delivery and the cord blood of their new-borns (with a total of 50 blood samples from the mothers and their cord blood). The age of the participants ranged from 20 to 35 years. They were between 38 and 40 weeks of gestation. In addition, 25 healthy non- pregnant women who served as a control group and matched for age. Body mass index (BMI) was also included in the study. All the women were subjected to full clinical examination. Women with any complications (pre-eclampsia) and/or any history of chronic diseases (diabetes, hypertension, kidney diseases, and liver diseases) were excluding. All participants' women signed an informed consent.

Anthropometric measurement

Body weight and height were measured for all subjects and body mass index was calculated by dividing the weight (kg) on the [height (m)]^2 (Jamilian et al., 2019). In addition, the birth weight for all the new-borns was recorded.

Samples collection

Blood samples were withdrawn from all subjects on a plain tube after overnight fasting. After delivery of the new-born apiece of umbilical cord was isolated by clamping, and cord blood samples were taken from the vein. The serum was separated, distributed into aliquots and stored at -20 ºC until assay.

Biochemical determination of oxidative stress/antioxidant measures

Reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), total antioxidant capacity (TAO), and glutathione S transferase were determined using the kits of Biodiagnostic Egypt according to the manufacture instructions. Advanced oxidation protein product (AOPP) was quantified using the kit of Cell Biolabs, Inc. (STA-318) according to the manufacture instructions. Lipid profile (cholesterol, triacylglycerol, low density lipoprotein cholesterol (LDL)) was measured using the kits of Biodiagnostic Egypt according to the manufacture instructions.

Statistical analysis

Results were described in a box-and-whisker plot utilizing version 5 of the Graphpad Prism. Every box contained the average of all values between the 25th and 75th percentiles, and the median was shown as a horizontal line among each box. Comparison between results was conducted using one-way analysis of variance (ANOVA) followed by Tukey's HSD post hock test to see comparison between different groups. The level of significance was settled $p \leq 0.05$.

3. RESULTS

Anthropometric measurements of study groups

The anthropometric measurements of the study groups were presented in Table 1. There wasn't any significant difference in body weight between the women in the non-pregnant group compared to the women in the pregnant group. On the other hand, there was a statistically significant difference between the two groups in both the height and BMI ($p \leq 0.05$). Concerning the new-born babies included in the present study, there was 2 out of the 25 babies were preterm babies while the rest were full-term babies. The average body weight, height, head circumference, and gestational age were in the normal range.

Table 1 anthropometric measurement of study groups

Group / Biomarker	Mean ± SDM			*P* value
	Non-Pregnant Women	Pregnant Women	New-Born Babies	
Body Weight (kg)	64.24 ± 15.5	69.33 ± 14.5	2.9912 ± 0.44	0.237
Height (cm)	160.1 ± 6.1	155.9 ± 5.7 [a]	50.32 ± 2.17	0.016**
BMI	24.9 ± 5.2	28.3 ± 4.6 [a]	-	0.019**
Head Circumference (cm)	-	-	33.7 ± 1.64	-
Gestational Age (week)	-	-	38.76 ± 1.61	-
Preterm (Number; Percentage)	-	-	2; 8%	-
Term (Number; Percentage)	-	-	23; 92%	-

Data were presented as mean ± standard deviation of the mean (SDM), number or percentage.
[a]significantly different compared to the non-pregnant women group ($p \leq 0.05$).

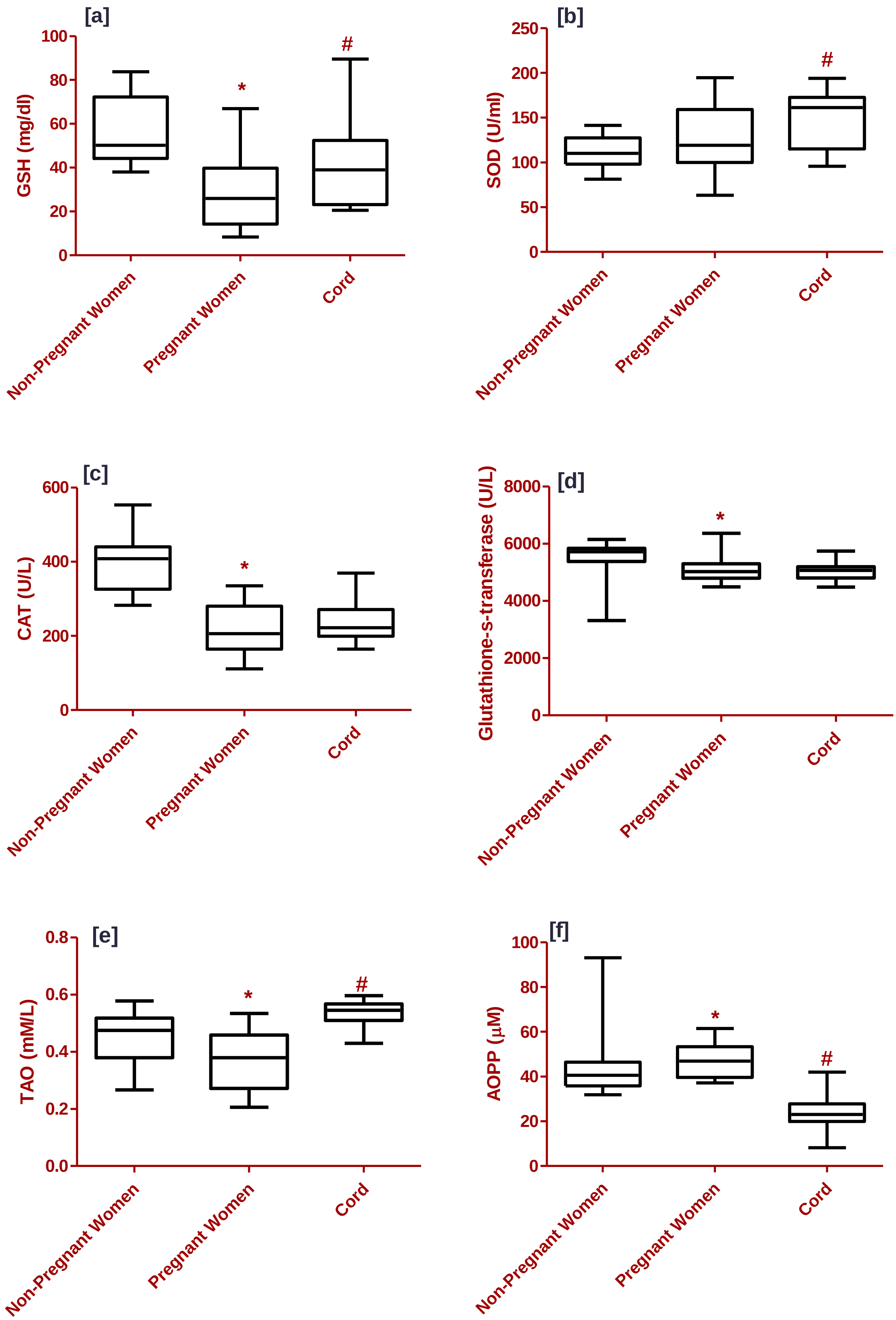

Figure 1 Oxidative stress / antioxidant measures determined in serum of non-pregnant women, pregnant women, and cords of their new-born babies. (a) GSH, (b) SOD, (c) CAT, (d) glutathione-s-transferase, (e) TAO, and (f) AOPP.* significant compared to non-pregnant women, #significant compared to pregnant women, ($p \leq 0.05$). Results were described in a box-and-whisker plot. Every box contained the average of all values between the 25th and 75th percentiles, and the median was shown as a horizontal line among each box.

Oxidative stress / antioxidant measures determined in serum of non-pregnant women, pregnant women, and cords of their new-born babies

The results indicated to a significant ($p \leq 0.01$) increase in AOPP, and a significant ($p \leq 0.01$) decrease in GSH, CAT, TAO, and glutathione-s-transferase in pregnant women compared to non-pregnant women. Concerning the cord blood of new-born babies compared to their mothers the results also showed a significant ($p \leq 0.05$) increase in GSH, SOD, TAO, and a significant ($p \leq 0.01$) decrease in AOPP (Figure 1 a-f).

Lipid profile determined in serum of non-pregnant women, pregnant women, and cords of their new-born babies

The results indicated toa significant ($p \leq 0.01$) increase in cholesterol, LDL, and triglycerides in pregnant women compared to non-pregnant women. Concerning the cord blood of new-born babies compared to their mothers the results also showed a significant ($p \leq 0.01$) decrease in cholesterol, LDL, and triglycerides (Figure 2 a-c).

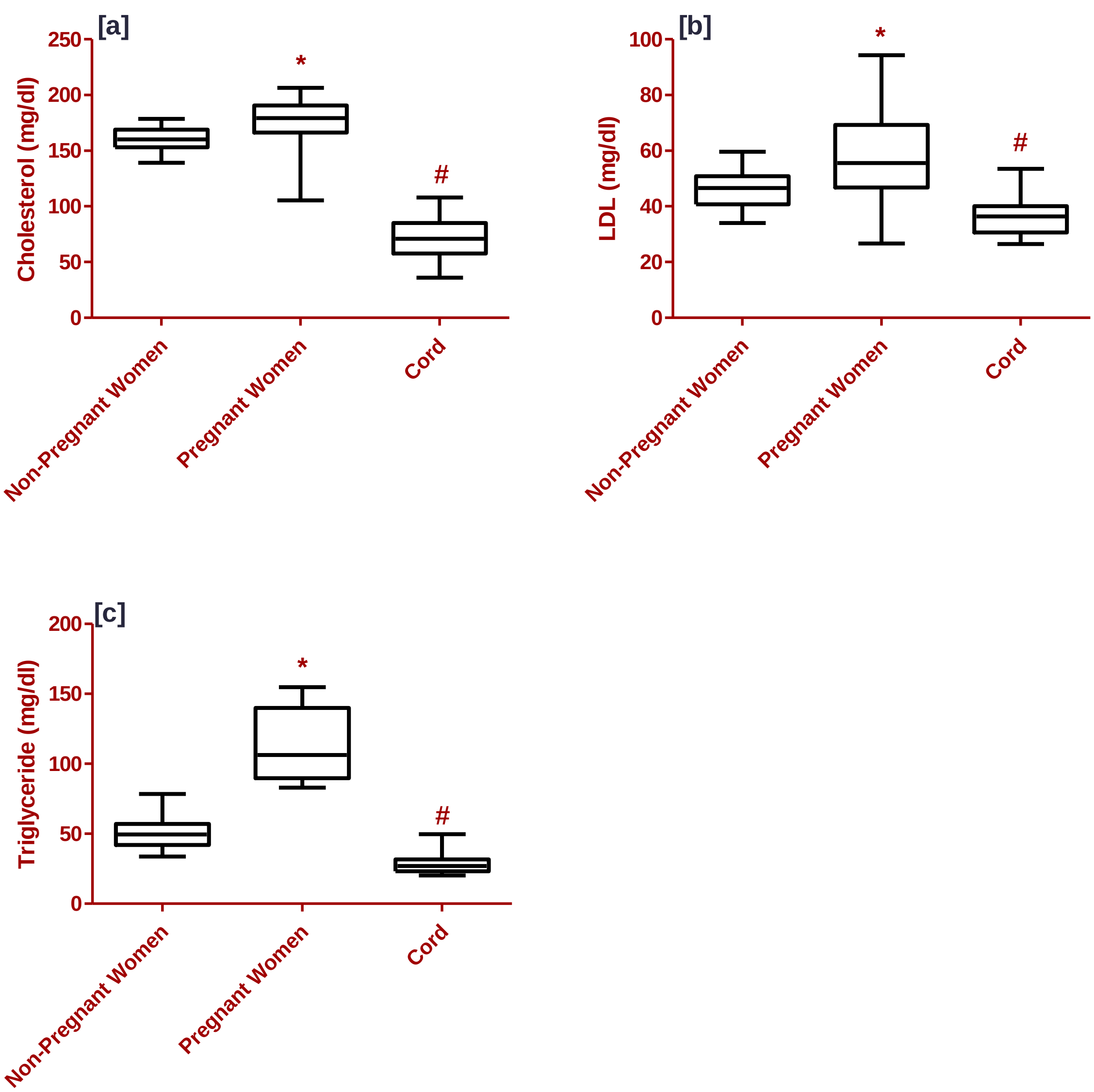

Figure 2 Lipid profile determined in the serum of non-pregnant women, pregnant women, and cords of their babies. (a) cholesterol, (b) LDL, and (c) triglyceride. *significant compared to non-pregnant women, #significant compared to pregnant women, ($p \leq 0.05$). Results were described in a box-and-whisker plot utilizing version 5 of the Graphpad Prism. Every box contained the average of all values between the 25th and 75th percentiles, and the median was shown as a horizontal line among each box.

4. DISCUSSION

The results of the present study showed a significant increase in the index of oxidative stress-AOPP- in the blood of pregnant women at birth compared to the group of non-pregnant women. A significant deficiency was observed in non-enzymatic and enzymatic antioxidants, besides the TAO in the pregnant group compared to the non-pregnant group. The results of the current study were in agreement with the results of former studies that support the occurrence of oxidative stress during pregnancy, even this, which is not accompanied by complications (Wang et al., 1991; Little & Gladen, 1999; Toescu et al., 2002; Argüelles et al., 2006; Ademuyiwa et al., 2007; Mannaerts et al., 2018).

The oxidative stress that occurs in pregnant women may be due to the pregnancy itself as well as the circulation of the placenta, which causes the release of free radicals and the lack of their scavengers during this critical period (Leal et al., 2011). Some researchers attributed the increased oxidative stress during pregnancy to the increased metabolism in the placenta mitochondria and the concomitant decrease in the scavenging strength of different antioxidants (Wu et al., 2015). This could also be linked to the increased concentration of free radicals forming enzymes, such as xanthine oxidase and nicotinamide adenine dinucleotide phosphate oxidase in the placenta (Jiang & Zhang, 2011; Dröse & Brandt, 2012; Sánchez-Aranguren et al., 2014).

This study had measured the indicators of OS in the cord blood for new-borns immediately after birth and had compared it with its concentrations in the blood of their mothers at birth. The results revealed a marked decrease in the protein oxidation index-AOPP- and a marked increase in TAO, SOD, and GSH compared to their mothers. As previously mentioned in the research, new-borns have a protection mechanism against OS, which is to maintain biomolecules, reduce the production of reactive oxygen molecules, as well as mechanisms to repair and adapt to the formation of free radicals (Mátyás & Zaharie, 2018). In the pathology of new-borns, many conditions accompanied by increased oxidative stress, such as premature birth and a lack of antioxidant defense mechanisms (Sullivan, 1988).

In harmony with the results of the current study, early research mentioned an increase in the concentrations of some antioxidants in the plasma of full-term and preterm new-borns compared to adults. The researchers also adopted that the total radical trapping capacity of the antioxidants in plasma (TRAP) works to compensate for the deficiency that may occur in some antioxidants in these babies. The study also mentioned reduced measured TRAP compared to the calculated TRAP, and this means that there are anti-oxidation indicators that were not estimated in their study (Lindeman et al., 1989). These indicators could be GSH and SOD that was increased in our study. Contrary to our findings, many studies are documenting increased oxidative stress in new-borns. That may be because their studies of pregnancy conditions associated with some diseases, preeclampsia, or mothers who smoke (Buonocore et al., 2002; Argüelles et al., 2006).

The results of the current study included a statistically significant increase in the levels of different lipids as cholesterol, LDL, and triglycerides in pregnant women compared to non-pregnant women. Measurements of the same types of lipids appeared at a lower level in cord blood for new-borns compared to their mothers. The results of this work are in agreement with the findings of many previous studies, which concluded increased lipid profile measures over the last trimester of pregnancy (Grimes & Wild, 2000; Parchwani & Patel, 2011; Wang et al., 2019).

Previous results indicated that the high increase in the level of triglycerides provides pregnant women with energy and passes glucose to the fetus. LDL is also important for the formation of placental steroid hormones. The rise in the level of LDL during the last months of pregnancy coincides with the high levels of lactogen and insulin in the placenta (Herrera, 2000). Studies attribute the cause of decreased cholesterol in the plasma of new-borns to reduced LDL. The lack of LDL is also due to its rapid consumption by the adrenal gland to produce steroid hormones (Diaz et al., 1989; Atiy et al., 2018).

5. CONCLUSION

In conclusion, the results of this study showed an increase in OS as well as indicators of hyperlipidemiain pregnant women at delivery and low antioxidants levels. On the contrary, the oxidative stress in the cord blood of new-borns decreased, as well as the lipid levels, and increased antioxidants level. As a result of the current study, we infer that the women at delivery are exposed to a high oxidative stress, and this may be because a shortage in the antioxidants system in the body. On the contrary, the low oxidative stress, and high antioxidants level in the cord blood provide protection to the fetus from the damage of oxidative stress at delivery.

Recommendations

The study recommends to eat food rich in antioxidants, such as dark chocolate, blueberry, strawberry, tea, spinach, broccoli and whole grain during pregnancy and especially in the prenatal period or take micronutrients supplementation can increase the efficiency of the antioxidants system and protect the fetus from the damage of oxidative stress. Also, we recommended that the study must be repeated using larger sample size and measuring new indicators of antioxidants to determine the mechanism of the reduced oxidative stress observed in new-borns and the causes of elevated oxidative stress present in the blood of the pregnant women at delivery.

Limitations of the study

There is no limitation in the design or methodology that impacted or influenced the interpretation of the findings in this project.

Conflicts of interest

The authors declare that the manuscript is original, not published before, and not being considered for publication elsewhere. There is no conflict of interest among the authors of the article.

Funding

This work was supported by the Deanship of Scientific Research (DSR), King Abdulaziz University, Jeddah, under grant No. (247-25-DG1441).

Author Contributions

All the authors contributed evenly with regards to data collecting, analysis, drafting and proofreading the final draft.

Ethical approval

The study was approvedby the Unit of Biomedical Ethics Research Committee of King Abdulaziz University, Jeddah, Saudi Arabia (Reference No 170-19).

Acknowledgements

This work was supported by the Deanship of Scientific Research (DSR), King Abdulaziz University, Jeddah, under grant No. (247 - 25 - DG1441). The authors, therefore, gratefully acknowledge the DSR technical and financial support.

Data and materials availability

All data associated with this study are present in the paper.

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