ORIGINAL ARTICLE

SERUM MALONDIALDEHYDE AS A MARKER OF OXIDATIVE STRESS IN GESTATIONAL DIABETES MELLITUS: A COMPARATIVE STUDY

Tallat Naureen, Syeda Fouzia Mazloum*, Laiba Shaukat, Qurat-ul-Ain Fatima, Sadia Mubarak***, Mahvash Khan†**

Department of Physiology, Army Medical College, Rawalpindi, *Bahria University of Health Sciences, Islamabad, **Student, Rawalpindi Medical University, Rawalpindi, ***Islamabad Medical and Dental College, Islamabad, †Akhtar Saeed Medical College, Rawalpindi, Pakistan

Background: Oxidative stress is implicated in causation of many diseases including diabetes mellitus. An abnormally high level of oxidative stress may be involved in development of gestational diabetes mellitus (GDM). We aimed to compare degree of oxidative stress in healthy pregnant, and GDM women by measuring serum malondialdehyde (MDA) levels. **Methods:** This comparative cross-sectional study was conducted on age and gestational age matched 30 healthy pregnant women and 30 patients of GDM at Army Medical College and Pak Emirates Military Hospital, Rawalpindi over a period of one year. The diagnosis of GDM was made during second trimester after oral glucose tolerance test. The subjects with type-1 or type-2 diabetes, past history of gestational diabetes and systemic inflammatory disease were not included. Serum malondialdehyde levels of all subjects were measured with ELISA technique. Data were analysed on SPSS-22. Numerical data were expressed as Mean±SD and the comparison between two groups was done using independent samples *t*-test. The Pearson's correlation coefficient for association between numerical variables was assessed, and $p \leq 0.05$ was regarded statistically significant. **Results:** GDM group had significantly higher mean serum MDA level as compared to healthy pregnant women. Serum MDA had positive correlation with fasting plasma glucose and glycosylated haemoglobin. **Conclusion:** A significantly high MDA in GDM along with positive correlation with fasting glucose and glycosylated haemoglobin indicates the possible role of oxidative stress in GDM.

Keywords: Gestational diabetes mellitus, Hyperglycaemia, Malondialdehyde, Oxidative Stress

Pak J Physiol 2025;21(3):3–6, **DOI:** https://doi.org/10.69656/pjp.v21i3.1836

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as the glucose intolerance that is first identified during second or third trimester of pregnancy and is not overt diabetes.[1] Its prevalence varies greatly in different areas with highest prevalence in South Asian countries.[2] In addition to geographic variance, its prevalence is also affected by criterion used for diagnosis. Highest prevalence of gestational diabetes is observed with International Association for Diabetes and Pregnancy Study Group (IADPSG) criteria of diagnosis and is equal to 34.9%.[3] Gestational diabetes mellitus is linked with adverse pregnancy outcome as well as development of complications in both mother and offspring. It increases the risk of premature labour, pre-eclampsia and premature operative delivery. Moreover, there are high chances of macrosomia, hypoglycaemia and hyperbilirubinemia in foetus in addition to risk of developing diabetes in future.[4] Women with gestational diabetes are also at risk of developing type-2 diabetes and cardiovascular problems.[5]

Pregnancy is associated with development of insulin resistance secondary to secretion of placental hormones. This insulin resistance is compensated by increased beta cell activity. It is suspected that beta cell dysfunction occurs during gestational diabetes due to which they are unable to regulate insulin secretion.[6] A number of factors like autoimmunity, gene mutation, inflammation and oxidative stress play a role in its causation. An abnormal inflammatory response especially occurs in obese women and may be a consequence of oxidative stress.[6] Oxidative stress occurs as a result of imbalance between pro-oxidant and antioxidant species.

The pro-oxidants are reactive oxygen species (ROS) like hydrogen peroxide, hydroxyl radical and superoxide anion. These ROS have damaging effects on various cellular components and can cause destruction of lipids, proteins and DNA, thus affecting their normal physiological functions.[7] During pregnancy, placenta produces a large number of reactive oxygen species. An increased number of lipid peroxidation markers like malondialdehyde, and 8-isoprostane are isolated from placenta of patients of gestational diabetes. An uncontrolled production of reactive oxygen species can lead to exhaustion of antioxidant defence mechanism and may cause cell injury and cell death.[8] The oxidative damage can involve peripheral tissues like pancreatic beta cells which are specifically susceptible to oxidative damage due to lack of antioxidant defence mechanism, thus resulting in increased apoptotic events and suppression of transcription factors involved in regeneration of beta cells. It also abolishes mitochondrial activity and ultimately causes decreased production of insulin. Oxidative stress also reduces the sensitivity of peripheral tissues to insulin by disrupting the process of

insulin signalling via decreasing tyrosine phosphorylation of insulin receptor substrate proteins as well as decreased expression of glucose transporters in muscle and adipose tissue.[9] Malondialdehyde (MDA) is a reactive, toxic aldehyde produced as a result of lipid peroxidation by ROS and is frequently used as a reliable marker of oxidative stress.[10]

Few previous studies show positive association between oxidative stress markers and development of GDM. However, studies elucidating the role of oxidative stress in gestational diabetes are scarce in our set up. To fill this gap, we compared the level of oxidative stress in normal pregnancy and in gestational diabetes by measuring serum levels of MDA. Identifying the association of oxidative stress and gestational diabetes may help us take steps in the direction of prevention of GDM development.

METHODOLOGY

This cross-sectional study was conducted at Army Medical College and Pak Emirates Military Hospital, Rawalpindi. The study was conducted over a period of one year from 1st Aug 2019 to 31 Jul 2020. Formal approval was obtained from ethical review board of the institution. The sample size was estimated using WHO calculator. Considering the estimated prevalence of GDM in Pakistan as 3.5%[11] and 95% confidence level, a sample size of 60 was calculated. Subjects were selected through non-probability convenient sampling after informed consent. The subjects were divided into two groups. Group I consisted of 30 healthy pregnant women at 24 weeks onwards gestation with normal glucose tolerance test (GTT). Group II consisted of 30 pregnant women at 24 weeks onwards gestation with diagnosis of gestational diabetes mellitus. The diagnosis of gestational diabetes was made after performing oral GTT on basis of IADPSG criterion approved by American Diabetes Association (ADA).[2] The women with type-1 or type-2 diabetes, previous history of gestational diabetes and systemic inflammatory disease were excluded from study. The baseline demographic data and relevant history and examination were recorded for all subjects.

Blood samples of subjects were collected after an 8 hour overnight fast. Oral GTT was performed. After determining concentration of haemoglobin and glycosylated haemoglobin (HbA1c), HbA1c/ haemoglobin ratio was expressed as percentage (% HbA1c). Serum malondialdehyde levels of the subjects were determined using Enzyme Linked Immunosorbent Assay (ELISA Kit Cat No. 10798-Glory Bios).

Data were analysed by using IBM SPSS-22. The quantitative variables were expressed as Mean±SD. For assessment of association of quantitative variables, Pearson's correlation was used and $p \leq 0.05$ was taken as significant.

RESULTS

Thirty healthy pregnant women and thirty patients of GDM were matched for age and gestational age. The groups did not show a significant difference regarding body mass index (BMI). The HbA1c levels of both groups were found to have significant differences (p=0.012). Serum MDA levels of GDM group were significantly higher as compared to healthy pregnant women. (Table-1). There was a significant positive correlation of serum MDA with HbA1c and fasting plasma glucose (FPG). (Table-2).

Table-1: FPG, HbA1c, serum MDA and BMI of the subjects

Variable	Control	GDM	*p*
FPG (mmol/L)	4.52±0.47	5.98±1.04	<0.001
HbA1c (%)	5.3±0.59	5.8±1.05	<0.05
MDA (ng/mL)	424.0±278.0	872.64±767.94	<0.01
BMI (Kg/m^2)	27.34±1.56	27.46±1.94	0.9

Table-2: Correlation of serum MDA with HbA1c, fasting plasma glucose

Parameter correlated	*r*	*p*
HbA1c	0.400	<0.001
Fasting plasma glucose	0.449	<0.001

*p is significant at ≤0.05

DISCUSSION

We conducted a study recruiting thirty healthy pregnant women and thirty women with GDM and compared serum MDA levels as marker of oxidative stress during 24–28 weeks of pregnancy. We found a significant increase in serum MDA in GDM group in addition to raised levels of HbA1c, fasting and postprandial plasma glucose levels. Serum MDA levels also correlated positively with HbA1c and fasting plasma glucose level.

Our results are in coherence with previously conducted similar studies. Qin Z *et al*[12] conducted a prospective study in China taking 130 GDM cases and 260 controls. They found a significant elevated mean level of serum MDA in GDM group as compared to healthy adults. They also found a positive correlation of MDA with fasting plasma glucose but a significant correlation was not found with HbA1c. The reason they didn't find a significant correlation with HbA1c may be because they measured HbA1c in second trimester and MDA in first trimester.

A study by Ayse Arsalan[13] also showed similar results. In that study, 40 GDM patients and 37 healthy controls were compared for assessment of degree of oxidative stress and antioxidant mechanisms by measuring serum MDA, glutathione peroxidase and catalase levels at 24–28 weeks of gestation. They observed a high mean serum MDA level along with low glutathione peroxidase level in GDM group.

Zhang C *et al*[14] carried a study on 93 patients of GDM and 82 healthy pregnant women. They found a

significantly increased serum MDA in GDM group compared to control group.

Contrary to above researches, a study[15] conducted on 200 subjects didn't show a significant difference regarding MDA between healthy pregnant women and those with GDM, although it revealed a high serum MDA in non-pregnant diabetic women compared to non-pregnant healthy women. A study[16] conducted on 51 pregnant women revealed no significant differences in serum MDA although it showed a significant difference in salivary MDA. Salivary MDA may be more sensitive than serum MDA to measure oxidative stress level as more free radicals are neutralized by plasma as compared to saliva.[16]

Pregnancy is a state of oxidative stress characterized by increased production of reactive oxygen species (ROS). This is the result of enhanced metabolism, increased consumption of oxygen and fatty acid utilization. ROS cause damage to biomolecules resulting in production of different by-products. One of the damaging effects of ROS is peroxidation of lipid molecules which results in formation of malondialdehyde.[8]

The damaging effects of this oxidative stress is counterbalanced by increased production of antioxidants. Excess production of glucose in GDM results in its auto-oxidation and increased production of reactive oxygen species. Depletion of antioxidant mechanisms in GDM further worsens the condition.[17] A previous study has shown increased oxidative stress shown as elevated levels of MDA and thiobarbituric acid reactive substances (TBARS) in GDM patients and decreased levels of antioxidants such as glutathione peroxidase and superoxide dismutase.[18] Another study did not reveal a significant difference in antioxidant levels in GDM despite increased levels of oxidative stress markers.[19]

Shang M *et al*[20] did a study on 68 pregnant women and assessed the levels of a number of oxidative stress markers as well as antioxidants in maternal, cord and placental blood. They also compared these levels in GDM patients diagnosed with different diagnostic criteria. They found increased levels of oxidative stress indicators like MDA, xanthine oxidase (XO) and 8-isoprostane, and decreased levels of antioxidants such as superoxide dismutase and total antioxidant capacity.

We found a positive correlation between MDA and HbA1c as well as fasting plasma glucose which is comparable to study of Shang *et al*[20]. This supports the hypothesis that hyperglycaemia and poor glycaemic control are associated with higher degree of oxidative stress.[21] Obesity as well as increased age results in increased oxidative stress.[22] Level of oxidative stress varies with the gestational age and is usually at peak in second trimester. In our study, GDM subjects were matched with controls regarding age, gestational age and BMI. The results of our study suggest the role of oxidative stress in hyperglycaemia and development of GDM. Measurement of oxidative stress markers like serum MDA may be helpful in early identification of gestational diabetes risk.

The limitations of our study include small sample size and one time measurement of biochemical markers. Moreover, it is a cross-sectional study measuring the oxidative stress markers at the time of diagnosis of GDM. Future prospective studies involving a variety of oxidative stress markers along with antioxidants are recommended to establish the link between oxidative stress and development of GDM.

CONCLUSION

A significantly high serum MDA level in GDM patients and a positive correlation between serum MDA and maternal glycaemic levels suggest role of oxidative stress in gestational diabetes. Identification of oxidative stress early in pregnancy may be helpful in better management of gestational diabetes.

REFERENCES

1. Saucedo R, Ortega-Camarillo C, Ferreira-Hermosillo A, Díaz-Velázquez MF, Meixueiro-Calderón C, Valencia-Ortega J. Role of oxidative stress and inflammation in gestational diabetes mellitus. Antioxidants 2023;12(10):1812.
2. Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D. Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. Diabetes Res Clin Pract 2021;172:108642.
3. Gyasi-Antwi P, Walker L, Moody C, Okyere S, Salt K, Anang L, *et al*. Global prevalence of gestational diabetes mellitus: a systematic review and meta-analysis. New Am J Med 2020;1(3):1–10.
4. Moon JH, Jang HC. Gestational diabetes mellitus: diagnostic approaches and maternal-offspring complications. Diabetes Metab J 2022;46(1):3–14.
5. Reitzle L, Heidemann C, Baumert J, Kaltheuner M, Adamczewski H, Icks A, *et al*. Pregnancy complications in women with pregestational and gestational diabetes mellitus. Dtsch Arztebl Int 2023;120(6):81.
6. Phoswa WN, Khaliq OP. The role of oxidative stress in hypertensive disorders of pregnancy (preeclampsia, gestational hypertension) and metabolic disorder of pregnancy (gestational diabetes mellitus). Oxid Med Cell Longev 2021;2021(1):5581570.
7. Caturano A, D'Angelo M, Mormone A, Russo V, Mollica MP, Salvatore T, *et al*. Oxidative stress in type 2 diabetes: impacts from pathogenesis to lifestyle modifications. Curr Issues Mol Biol 2023;45(8):6651–66.
8. Lappas M, Hiden U, Desoye G, Froehlich J, Hauguel-de Mouzon S, Jawerbaum A. The role of oxidative stress in the pathophysiology of gestational diabetes mellitus. Antioxid Redox Signal 2011;15(12):3061–100.
9. Zheng ZX, Feng X, Zhuang L. The effect of oxidative stress and antioxidants treatment on gestational diabetes mellitus outcome: a scoping review. Cell Biochem Biophys 2024;82(4):3003–13.
10. Halliwell B, Gutteridge JM. Free radicals in biology and medicine. Oxford University Press, USA; 2015.
11. Qadir SY, Yasmin T, Fatima I. Maternal and foetal outcome in gestational diabetes. J Ayub Med Coll Abbottabad 2012;24(3-4):17–20.
12. Qin Z, Du Y, Wang Z, Qin X, Wu H, Yu X, *et al*. Serum ferritin levels in pregnancy and their association with gestational diabetes

mellitus: A prospective longitudinal study. Diabetes Metab Syndr Obes 2025:413–22.
13. Arslan A. Serum ischemia modified albumin and oxidative stress levels in patients with gestational diabetes mellitus. East J Med 2022;27(4):507–12.
14. Zhang C, Yang Y, Chen R, Wei Y, Feng Y, Zheng W, *et al*. Aberrant expression of oxidative stress related proteins affects the pregnancy outcome of gestational diabetes mellitus patients. Am J Transl Res 2019;11(1):269–79.
15. Akinjiyan MO, Atiba AS, Asaolu MF. Effects of gestational diabetes mellitus and diabetes mellitus on lipid profile, antioxidants, hormones and electrolytes status in a population of Nigerian women. Cardiovascular Diabetology-Endocrinology Reports 2025;11(1):1.
16. Bulut A, Akca G, Aktan AK, Akbulut KG, Babül A. The significance of blood and salivary oxidative stress markers and chemerin in gestational diabetes mellitus. Taiwan J Obstet Gynecol 2021;60(4):695–9.
17. Sudharshana Murthy KA, Bhandiwada A, Chandan SL, Gowda SL, Sindhusree G. Evaluation of oxidative stress and proinflammatory cytokines in gestational diabetes mellitus and their correlation with pregnancy outcome. Indian J Endocrinol Metab 2018;22(1):79–84.
18. Ibrahim A, Khoo MI, Ismail EHE, Hussain NHN, Zin AAM, Noordin L, *et al*. Oxidative stress biomarkers in pregnancy: a systematic review. Reprod Biol Endocrinol 2024;22(1):93.
19. López-Tinoco C, Roca M, García-Valero A, Murri M, Tinahones FJ, Segundo C, *et al*. Oxidative stress and antioxidant status in patients with late-onset gestational diabetes mellitus. Acta Diabetol 2013;50:201–8.
20. Shang M, Zhao J, Yang L, Lin L. Oxidative stress and antioxidant status in women with gestational diabetes mellitus diagnosed by IADPSG criteria. Diabetes Res Clin Pract 2015;109(2):404–10.
21. Nishikawa T, Edelstein D, Du XL, Yamagishi S, Matsumura T, Kaneda Y, *et al*. Normalizing mitochondrial superoxide production blocks three pathways of hyperglycaemic damage. Nature 2000;404(6779):787–90.
22. Davì G, Guagnano MT, Ciabattoni G, Basili S, Falco A, Marinopiccoli M, *et al*. Platelet activation in obese women: role of inflammation and oxidant stress. JAMA 2002;288(16):2008–14.

Address for Correspondence:
Dr Tallat Naureen, Department of Physiology, Army Medical College, Rawalpindi, Pakistan. **Cell:** +92-331-5154167
Email: naureentallat@gmail.com

Received: 25 Mar 2025 **Reviewed:** 1 Jul 2025 **Accepted:** 6 Jul 2025

Contribution of Authors:
TN: Concept of study and data interpretation and final write-up
LS: Literature review, data analysis and draft of manuscript
SM: Drafting of manuscript and literature review
SFM: Data analysis, interpretation and literature review
QAF: Data analysis and critical review
MK: Final draft and critical review

Conflict of Interest: None
Funding: The study was partially funded by research grant from National University of Medical Sciences, Rawalpindi