

Original Research Article

Oxidative DNA damage in gestational diabetes

mellitus: Correlation with antioxidants in an Iraqi

cohort

ABSTRACT

Aims: This study illustrates an increased oxidative DNA damage in gestational diabetes mellitus associated with a significant rise in serum malondialdehyde and a significant reduction in plasma reduced glutathione when compared to non-diabetic pregnant women.

Methodology: This cross-sectional study included 73 participants attending the Maternal and Childhood Unit, Al-Husayniya Medical Centre, Baghdad, Iraq.

Results: Serum 8-Hydroxy-2-Deoxyguanosine was significantly greater in the gestational diabetes mellitus group compared to control group (57.2 ± 17.6 ng/dl versus 19.8 ± 7.8 ng/dl respectively). The increase in 8-Hydroxy-2-Deoxyguanosine was associated with a significant elevation in serum malondialdehyde level and a significant reduction in plasma reduced glutathione in the gestational diabetes mellitus group compared to the control group at $P = .05$. A significant change in total cholesterol (5.4 ± 1.1 mmol/L) and low density lipoprotein cholesterol (3.3 ± 0.9 mmol/L) were also noted in gestational diabetes mellitus group compared to the control group (4.7 ± 1.3 mmol/L and 2.8 ± 1 mmol/L respectively) at $P = .05$.

Conclusion: An increase in 8-Hydroxy-2-Deoxyguanosine is associated with higher levels of malondialdehyde and a significant reduction in reduced glutathione in gestational diabetes mellitus group, suggesting that significant oxidative stress associated with lipid peroxidation is occurring. Measuring these markers is useful in monitoring gestational diabetes mellitus to prevent the negative outcomes of gestational diabetes mellitus such as increased risk of diabetes and fetal morbidity.

Keywords: Gestational Diabetes, Oxidative DNA damage, Lipid peroxidation, Antioxidants.

1. INTRODUCTION

Gestational diabetes mellitus (GDM) is a clinical disorder characterized by an impaired glucose level which is first detected in pregnancy [1] and it accounts for 3-5% of pregnancy complications [1, 2]. It affects pregnant women predominantly after the first trimester due to placental hormones action on

maternal blood glucose hemostasis [3]. The disorder is associated with high maternal and fetal morbidity [1, 2]. Previous studies have shown that women with a history of GDM are more likely to develop type 2 diabetes (T2DM) mellitus and cardiovascular diseases after pregnancy as compared to women with normal blood glucose level during pregnancy[4]. In addition, type 1 diabetes mellitus (T1DM) is also known to occur following GDM particularly if associated with familial history of T1DM [2].

There are several risk factors for development of GDM including (but not limited to) maternal age, previous multiple births, family history of diabetes mellitus and an abnormal high body weight (overweight and obesity) [1]. Therefore, these factors have regularly been used for screening purposes for GDM [1].

Johnstone et al. in 1990 showed that controlling plasma glucose level is critical in reducing the incidence of microvascular complications due to GDM [5]. However, reducing plasma glucose level has no effect on reducing the rate of congenital anomalies (like macrosomia) [5, 6]. Fetal malformation may occur not only due to maternal hyperglycemia, but also due to an abnormal level of maternal lipids and amino acids which may accompany a badly controlled diabetes mellitus. Elevated low density lipoprotein-cholesterol (LDL-C) and reduced high density lipoprotein-cholesterol (HDL-C) promote lipid peroxidation through free radical activity, which is increased due to the increased plasma glucose levels.

Oxidative stress is common in GDM and occurs due to an imbalance between total free radical production and the body's ability to remove them via its antioxidant systems [7, 8]. Hence previous studies have focused on monitoring a variety of low molecular weight antioxidants and how these are related to GDM [9]. The cumulative action of all antioxidants present in plasma and body fluids is referred to as the total antioxidant status (TAS) which gives an estimation of the sum of measurable antioxidants [3, 10].

In normal pregnancy, the degree of oxidative stress and lipid peroxidation products predominates mostly because of the mitochondria- rich placenta and abundant transitional metals such as iron [6, 11, 12]. However, most body cells are capable of counter acting a small increase in oxidative stress, adequately stimulating the activity of antioxidants such as glutathione (GSH). But, when this capacity gets exhausted, the continuing rise of reactive oxygen species (ROS) may cause a severe irreversible

42 damage to cellular components [13]. Oxidative stress is much higher in GDM due to hyperglycemia
43 that favors generation of high amounts of reactive oxygen species and enhances progression of
44 diabetes [6, 14].

45 Malondialdehyde (MDA) is a biomarker of lipid peroxidation, among other by-products such as
46 pentane, ethane, hexanal and thiobarbituric acid reacting substance (TBARS). 8-Hydroxy-2-Deoxy
47 guanosine (8-OHdG) is a known sensitive marker of oxidative DNA damage and of total systemic
48 oxidative stress [15, 16]. Studies have shown that higher levels of this marker in early pregnancy may
49 be associated with increased GDM risk [17].

50 Cells possess a wide variety of antioxidants, which under normal conditions are able to minimise the
51 damaging actions of oxygen free radicals. These include enzymes such as superoxide dismutase
52 (SOD), catalase and glutathione peroxidase (GPX) and small molecules such as vitamin E, vitamin C,
53 carotenoids and glutathione [18]. Antioxidants may be critical to preventing fetal malformations like
54 birth defects in babies of women with diabetes, especially neural tube defects that occur two to five
55 times more often in GDM than in women without diabetes mellitus [6, 19]. Reduced glutathione (GSH)
56 constitutes the principal antioxidant defense system of the body [20] and is a cellular antioxidant
57 found in red blood cells [20]. Patients with diabetes tend to have a smaller amount of GSH and a
58 more oxidized glutathione pool than control subjects of a similar age [21], which weakens the defense
59 against oxidative stress [21].

60 The current study aims to measure the markers of oxidative stress (as expressed by the level of
61 serum MDA and serum 8-OHdG) and correlate their levels with the antioxidants (as expressed by the
62 level of plasma reduced GSH) in an Iraqi cohort of women whom diagnosed with GDM.

63 This study compared the extent of oxidative damage present in GDM women compared to non-
64 gestational diabetic women by measuring 8-OHdG levels, lipids, serum MDA and plasma GSH.

65 **2. METHODOLOGY**

66 *Protocol:* The study protocol was reviewed and approved by the Scientific and Ethical Committee of
67 the College of Medicine, Al-Nahrain University. Informed consent was obtained from each subject.
68 Participants were drawn from the Maternal and Childhood Unit, Al-Husayniya Medical Centre,
69 Baghdad, Iraq during the period of the study between January 2008 and May 2010. Only participants

where complete data was available as required for this study were included in the analysis. Participants were divided into two groups: a) Control group (Control): including pregnant women with normal blood glucose levels and no family history of diabetes. b) Gestational diabetes group (GDM group): including pregnant women who were diagnosed with diabetes mellitus for the first time during the current pregnancy according to the recommendations of the World Health Organization for definition and diagnosis of diabetes mellitus and intermediate hyperglycemia [22]. No exclusions were applied for the GDM group as cardiovascular and/or renal disease occur as a part of disease progression. Participants in the two groups were comparable for age, gender, smoking habit, diet, and physical activity. Women with gestational diabetes were requested not to take any diabetic medication in the morning of the day of the test before blood sampling. All blood samples were collected prior to 10 am to reduce any possible hyperglycemic events in those with GDM.

Measurements of oxidative stress: Serum MDA was measured using the thiobarbituric method of Buege & Aust [23]. Oxidative DNA damage was measured using the serum 8-OHdG ELISA kit (Cayman Chemical, MI, USA) [24]. The test utilizes an anti-mouse IgG-coated plate and a tracer consisting of an 8-OHdG-enzyme conjugate. This format has the advantage of providing low variability and increased sensitivity compared with assays that utilize an antigen-coated plate. The level of plasma GSH was determined using the 5,5-dithiobis-2-nitrobenzoic acid (DTNB) reaction [25, 26].

Statistical analysis: The data was analyzed using SPSS (Version 14) and Microsoft Excel (Office2007, Microsoft). All values were expressed as mean $\pm$ standard deviation (M $\pm$ SD). Statistical analysis was performed using an independent sample t-test, if data was normally distributed; otherwise a Mann Whitney test was applied. In all tests, $p < 0.05$ was considered to be statistically significant.

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93 **3. RESULTS**

Table 1 illustrates the baseline values of the 73 participants. Disease status, fasting blood glucose level (FPG), age, gestational weeks, glycosylated hemoglobin (HbA1c), blood pressure and Body mass index (BMI) are shown.

97

TABLE 1. Characteristics of the subjects included in this study

	Control Group	Gestational Diabetes Group
Number	44	29
Age (years)	24.4 ± 4.7	24.9 ± 5.2
Gestational Weeks	24.5 ± 3.8	23.3 ± 2.4
Body Mass Index (kg/m²)	25.8 ± 4.3	27.5 ± 2 [*]
Fasting Plasma Glucose (mmol/L)	4.5 ± 0.3	6.1 ± 0.7 ^{**}
HbA1c %	5.7 ± 0.5	7.6 ± 1 ^{**}
Systolic Blood Pressure (mmHg)	116.8 ± 6.3	118.8 ± 6.1
Diastolic Blood Pressure (mmHg)	73.1 ± 7.4	73.2 ± 7.7

98 ^{*}significant difference ($P = .05$)

99 ^{**}significant difference ($P < .001$)

100 Using an independent samples t-test, FPG and HbA1c were significantly different between the Control
101 group and the GDM group ($p < 0.001$). BMI also showed a significant increase in the GDM group ($P =$
102 .05), (Table 1).

103 For serum lipids, there was a statistically significant elevation of total cholesterol (TC), (LDL-C) as well
104 as TC/HDL-C ratio in the GDM group compared to the Control group ($P = .05$) (Table 2).

TABLE 2. Serum lipid profile (mean ± SD) in control and gestational diabetes groups (mmol/L)

Serum Lipid Profile	Control Group	Gestational Diabetes Group
Total Cholesterol	4.7 ± 1.3	5.4 ± 1.1 [*]
Triglycerides	1.7 ± 1	1.7 ± 0.8
HDL-C	1.3 ± 0.3 [*]	1.2 ± 0.4

LDL-C	2.8 ± 1	$3.3 \pm 0.9^*$
TC/HDL Ratio	3.8 ± 1.1	$5.3 \pm 3.3^*$

HDL-C high density lipoprotein cholesterol; LDL-C low density lipoprotein cholesterol.

**significant difference ($P = .05$)*

There was also a significant elevation of serum 8-OHdG in the GDM group compared to the Control group ($P < .001$) (Table 3). This was accompanied by a significant rise in serum MDA in the GDM group (2.1 ± 0.8) compared to the Control group ($P < .001$).

TABLE 3 TABLE 3 Biomarkers of oxidative stress (mean $\pm$ SD) in control and gestational diabetes groups

Oxidative Stress Biomarkers	Control Group	Gestational Diabetes Group
MDA (nmol/ml)	1 ± 0.4	$2.1 \pm 0.8^{**}$
GSH (mg/dl)	24.1 ± 4.4	$20.6 \pm 5^*$
8-OHdG (ng/dl)	19.8 ± 7.8	$57.2 \pm 17.6^{**}$

**significant difference ($P = .05$)*

***significant difference ($P < .001$)*

MDA (serum malondialdehyde); GSH (plasma reduced glutathione); 8-OHdG (8-OH-2-deoxy-Guanosine).

The statistical analysis also showed a significant positive correlation between serum 8-OHdG and serum MDA in our participants ($r=0.67$, $P = .05$), (Figure 1).

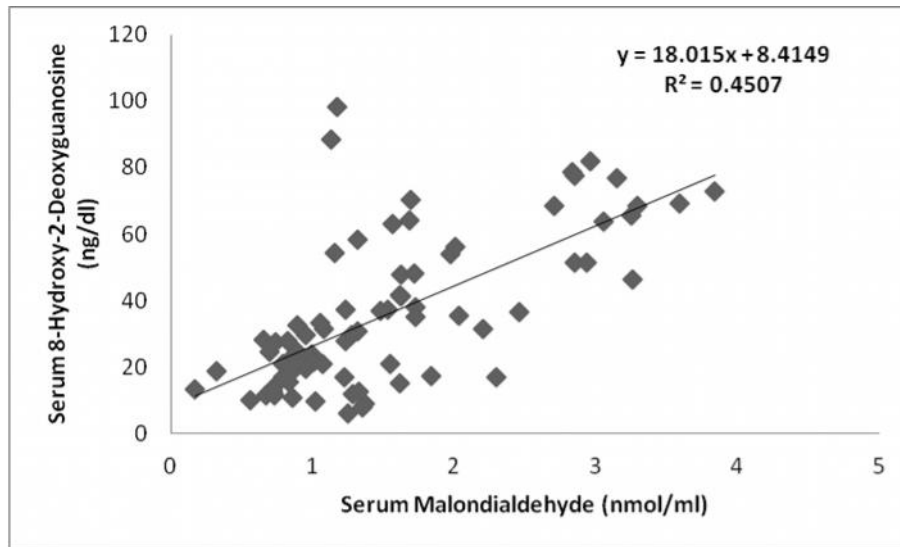


FIGURE 1 Significant positive correlation between serum 8-hydroxy-2-deoxyguanosine and serum malondialdehyde among all participants of the study ($r=0.67$, $P= .05$)

A reduction in the plasma GSH levels was observed in the GDM group compared to the control group ($P = .05$) (Table 3) and is associated with a significant negative correlation to serum 8-OHdG ($r=0.36$, $P = .05$), (Figure 2).

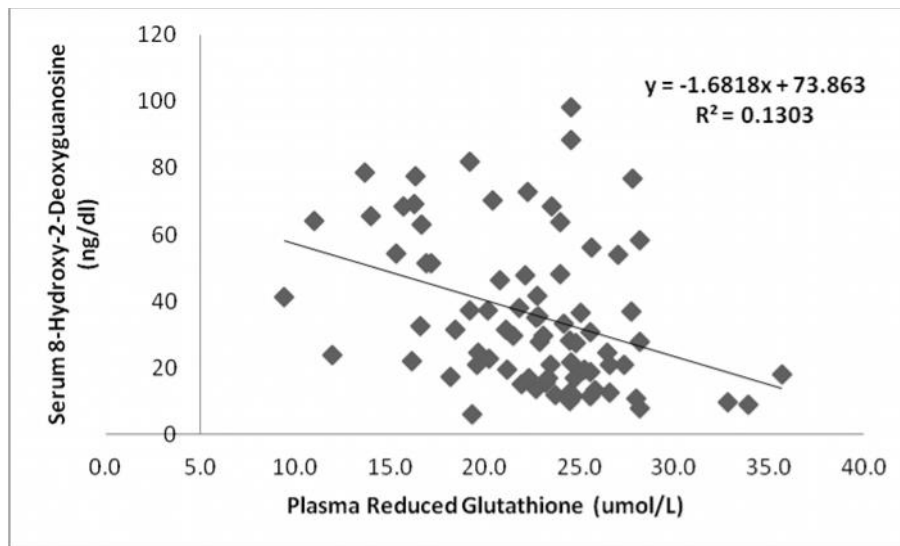


FIGURE 2 Significant negative correlation between serum 8-hydroxy-2-deoxyguanosine and plasma reduced glutathione among all participants of the study ($r=0.36$, $P = .05$)

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135 **4. DISCUSSION**

136 This research has demonstrated the efficacy of using emerging biomarkers as a multi-marker
137 approach to characterize GDM in the first trimester of pregnancy. Increased 8-OHdG combined with
138 increased MDA and a decrease in GSH provides a unique picture of the health state of the patient
139 and can be used as an indicator for individualized treatment. The significant correlation between 8-
140 OHdG with MDA and GSH indicates the extent of lipid peroxidation and oxidative DNA damage.

141 Gestational diabetes mellitus need to be diagnosed early during pregnancy for optimum control of
142 maternal blood glucose level which is a critical step to minimize the risk on the developing fetus [1, 2].
143 Although the oral glucose tolerance test can confirm gestational diabetes mellitus, this test is not
144 appropriate during the first trimester of pregnancy, as gestational diabetes is not quite developed at
145 this stage [27]. However early treatment is necessary to prevent fetal pathology. Previous studies
146 agreed that GDM is characterized by a disturbance in the redox balance [28]. This redox imbalance
147 can be measured by the extent of impaired enzymatic antioxidant activities [29], reduced circulatory
148 antioxidants [30], and increased levels of lipid and protein oxidation [28]. But there is still controversy
149 about the most reliable oxidative stress markers for clinical use in GDM.

150 The increased serum MDA observed in our study in the GDM group compared to the Control group is
151 in accordance with a study reported by Grissa et al [29] and confirms that the reactive oxygen species
152 generated during GDM react with the free lipid and lead to lipid peroxidation products that cause toxic
153 stress to cells such as MDA. Similarly Suhail et al. (2010) and others have reported a significant
154 increase in lipid peroxidation and oxidative stress in GDM [31, 32]. However Karb (2000) reported a
155 statistically non-significant rise of this biomarker in GDM with a much smaller cohort [33]. An
156 association between MDA and 8-OHdG has previously been demonstrated in various pathologies
157 suggesting the involvement of oxidative stress as a major component of disease progression [34].

158 Serum 8-OHdG was significantly higher in GDM group compared to the Control group. This indicates
159 that oxidative DNA damage is already occurring in GDM where hyperglycemia is prominent compared
160 to the non-gestational diabetes pregnancies. These finding are generally consistent with a relatively
161 large body of literature documenting positive associations of 8-OHdG with hyperglycemia, impaired
162 glucose intolerance, and type 2 diabetes in men and non-pregnant women [35-37]. In addition, the

rise in serum 8-OHdG appeared to be consistent with the increase in serum MDA among all our participants (GDM group and control group) indicating an overall disturbance in oxidative stress as illustrated by an increase in lipid peroxidation and protein damage (nucleic acid damage), (Figure 1). Increased 8-OHdG may occur due to cellular processes associated with ROS and lipid peroxidation [38].

In addition, the GDM group showed a decreased plasma concentration of reduced GSH in comparison with healthy pregnant mothers (Table 3). Not many studies have measured GSH in diabetic pregnancies [39, 40], but these agree with our results. The low level of plasma GSH in GDM can be explained by the higher activities of glutathione peroxidase enzyme to counteract the high level of lipid hydro-peroxidation and protein damage produced as a result of hyperglycemia compared to the non-gestational diabetes mothers[40]. This is evident by the significant negative correlation between serum 8-OHdG and the plasma GSH among all participants of this study (Figure 2).

5. CONCLUSION

Our study showed that measuring the biomarkers of oxidative stress (as expressed by serum MDA and serum 8-OHdG) and antioxidants (as expressed by plasma GSH) is an important step in managing cases of gestational diabetes mellitus in early pregnancy to help monitor disease progression and reduce the risk of hyperglycemia-associated pathology on pregnant women and their fetuses.

COMPETING INTERESTS

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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192 **CONSENT**

193 All authors declare that 'written informed consent was obtained from the patient (or other approved
194 parties) for publication of this study. A copy of the written consent is available for review by the
195 Editorial office/Chief Editor/Editorial Board members of this journal.

196 **ETHICAL APPROVAL**

197 All authors hereby declare that all experiments have been examined and approved by the appropriate
198 ethics committee and have therefore been performed in accordance with the ethical standards laid
199 down in the 1964 Declaration of Helsinki.

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201 **REFERENCES**

- 202 1. Enquobahrie DA, Williams MA, Qiu C, Luthy DA. Early pregnancy lipid concentrations and
203 the risk of gestational diabetes mellitus. *Diabetes Res Clin Pract.* 2005 Nov;70(2):134-42.
- 204 2. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International
205 Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee.
206 *Diabetes Care.* 1998 Aug;21 Suppl 2:B161-7.
- 207 3. Karacay O, Sepici-Dincel A, Karcaaltincaba D, Sahin D, Yalvac S, Akyol M, et al. A
208 quantitative evaluation of total antioxidant status and oxidative stress markers in
209 preeclampsia and gestational diabetic patients in 24-36 weeks of gestation. *Diabetes Res*
210 *Clin Pract.* 2010 Sep;89(3):231-8.
- 211 4. Davis CL, Gutt M, Llabre MM, Marks JB, O'Sullivan MJ, Potter JE, et al. History of
212 gestational diabetes, insulin resistance and coronary risk. *Journal of diabetes and its*
213 *complications.* 1999 Jul-Aug;13(4):216-23.
- 214 5. Johnstone FD, Nasrat AA, Prescott RJ. The effect of established and gestational diabetes
215 on pregnancy outcome. *British journal of obstetrics and gynaecology.* 1990
216 Nov;97(11):1009-15.
- 217 6. Omu AE, Al-Azemi MK, Omu FE, Fatinikun T, Abraham S, George S, et al.
218 Butyrylcholinesterase activity in women with diabetes mellitus in pregnancy: correlation with
219 antioxidant activity. *Journal of obstetrics and gynaecology : the journal of the Institute of*
220 *Obstetrics and Gynaecology.* 2010 Feb;30(2):122-6.
- 221 7. Granot E, Kohen R. Oxidative stress in childhood—in health and disease states. *Clinical*
222 *nutrition (Edinburgh, Scotland).* 2004;23(1):3-11.
- 223 8. Al-Shebly MM, Mansour MA. Evaluation of oxidative stress and antioxidant status in
224 diabetic and hypertensive women during labor. *Oxidative medicine and cellular longevity.*
225 2012;2012:329743.

- 226 9. Kharb S. Total radical-trapping antioxidant potential in gestational diabetes. *International*
 227 *journal of gynaecology and obstetrics: the official organ of the International Federation of*
 228 *Gynaecology and Obstetrics*. 2008 Dec;103(3):257-8.
- 229 10. Serafini M, Del Rio D. Understanding the association between dietary antioxidants, redox
 230 status and disease: is the Total Antioxidant Capacity the right tool? *Redox Rep*.
 231 2004;9(3):145-52.
- 232 11. Casanueva E, Viteri FE. Iron and Oxidative Stress in Pregnancy. *The Journal of*
 233 *Nutrition*. 2003 May 1, 2003;133(5):1700S-8S.
- 234 12. Coughlan MT, Vervaaert PP, Permezel M, Georgiou HM, Rice GE. Altered placental
 235 oxidative stress status in gestational diabetes mellitus. *Placenta*. 2004 Jan;25(1):78-84.
- 236 13. Wender-Ozegowska E, Kozlik J, Biczysko R, Ozegowski S. Changes of oxidative stress
 237 parameters in diabetic pregnancy. *Free Radic Res*. 2004 Aug;38(8):795-803.
- 238 14. Marfella R, Quagliaro L, Nappo F, Ceriello A, Giugliano D. Acute hyperglycemia induces
 239 an oxidative stress in healthy subjects. *J Clin Invest*. 2001;108(4):635-6.
- 240 15. Bruskov VI, Malakhova LV, Masalimov ZK, Chernikov AV. Heat-induced formation of
 241 reactive oxygen species and 8-oxoguanine, a biomarker of damage to DNA. *Nucleic acids*
 242 *research*. 2002 Mar 15;30(6):1354-63.
- 243 16. Lee J, Lee M, Kim JU, Song KI, Choi YS, Cheong SS. Carvedilol reduces plasma 8-
 244 hydroxy-2'-deoxyguanosine in mild to moderate hypertension: a pilot study. *Hypertension*.
 245 2005 May;45(5):986-90.
- 246 17. Qiu C, Hevner K, Abetew D, Enquobahrie DA, Williams MA. Oxidative DNA damage in
 247 early pregnancy and risk of gestational diabetes mellitus: A pilot study. *Clin Biochem*. 2011
 248 Jul;44(10-11):804-8.
- 249 18. Ramkumar KM, Latha M, Ashokkumar N, Pari L, Ananthan R. Modulation of impaired
 250 cholinesterase activity in experimental diabetes: effect of *Gymnema montanum* leaf extract.
 251 *Journal of basic and clinical physiology and pharmacology*. 2005;16(1):17-35.
- 252 19. Loeken MR. Free radicals and birth defects. *Journal of Maternal-Fetal and Neonatal*
 253 *Medicine*. 2004;15(1):6-14.
- 254 20. Blankenberg S, Rupprecht HJ, Bickel C, Torzewski M, Hafner G, Tiret L, et al.
 255 Glutathione peroxidase 1 activity and cardiovascular events in patients with coronary artery
 256 disease. *N Engl J Med*. 2003 Oct 23;349(17):1605-13.
- 257 21. Livingstone C, Davis J. Review: Targeting therapeutics against glutathione depletion in
 258 diabetes and its complications. *Br J Diab Vasc Dis*. 2007 November 1, 2007;7(6):258-65.
- 259 22. Organization WH. Definition and diagnosis of diabetes mellitus and intermediate
 260 hyperglycaemia. 2006.
- 261 23. Draper HH, Squires EJ, Mahmoodi H, Wu J, Agarwal S, Hadley M. A comparative
 262 evaluation of thiobarbituric acid methods for the determination of malondialdehyde in
 263 biological materials. *Free Radic Biol Med*. 1993;15(4):353-63.
- 264 24. Noiri E, Nakao A, Uchida K, Tsukahara H, Ohno M, Fujita T, et al. Oxidative and
 265 nitrosative stress in acute renal ischemia. *Am J Physiol Renal Physiol*. 2001;281(5):F948-57.
- 266 25. Look MP, Rockstroh JK, Rao GS, Kreuzer KA, Barton S, Lemoch H, et al. Serum
 267 selenium, plasma glutathione (GSH) and erythrocyte glutathione peroxidase (GSH-Px)-
 268 levels in asymptomatic versus symptomatic human immunodeficiency virus-1 (HIV-1)-
 269 infection. *Eur J Clin Nutr*. 1997;51(4):266-72.
- 270 26. Tietze F. Enzymic method for quantitative determination of nanogram amounts of total
 271 and oxidized glutathione: applications to mammalian blood and other tissues. *Anal Biochem*.
 272 1969;27(3):502-22.
- 273 27. Georgiou HM, Lappas M, Georgiou GM, Marita A, Bryant VJ, Hiscock R, et al. Screening
 274 for biomarkers predictive of gestational diabetes mellitus. *Acta Diabetol*. 2008
 275 Sep;45(3):157-65.
- 276 28. Lappas M, Mitton A, Permezel M. In response to oxidative stress, the expression of
 277 inflammatory cytokines and antioxidant enzymes are impaired in placenta, but not adipose
 278 tissue, of women with gestational diabetes. *The Journal of endocrinology*. 2010
 279 Jan;204(1):75-84.

- 280 29. Grissa O, Ategbo JM, Yessoufou A, Tabka Z, Miled A, Jerbi M, et al. Antioxidant status
281 and circulating lipids are altered in human gestational diabetes and macrosomia.
282 Translational research : the journal of laboratory and clinical medicine. 2007 Sep;150(3):164-
283 71.
- 284 30. Zhang C, Williams MA, Frederick IO, King IB, Sorensen TK, Kestin MM, et al. Vitamin C
285 and the risk of gestational diabetes mellitus: a case-control study. The Journal of
286 reproductive medicine. 2004 Apr;49(4):257-66.
- 287 31. Suhail M, Patil S, Khan S, Siddiqui S. Antioxidant Vitamins and Lipoperoxidation in Non-
288 pregnant, Pregnant, and Gestational Diabetic Women: Erythrocytes Osmotic Fragility
289 Profiles. Journal of clinical medicine research. 2010 Dec 11;2(6):266-73.
- 290 32. Lopez-Tinoco C, Roca M, Garcia-Valero A, Murri M, Tinahones FJ, Segundo C, et al.
291 Oxidative stress and antioxidant status in patients with late-onset gestational diabetes
292 mellitus. Acta Diabetol. 2013 Apr;50(2):201-8.
- 293 33. Kharb S. Lipid peroxidation in pregnancy with preeclampsia and diabetes. Gynecologic
294 and obstetric investigation. 2000;50(2):113-6.
- 295 34. Caliskan-Can E, Firat H, Ardic S, Simsek B, Torun M, Yardim-Akaydin S. Increased
296 levels of 8-hydroxydeoxyguanosine and its relationship with lipid peroxidation and
297 antioxidant vitamins in lung cancer. Clin Chem Lab Med. 2008;46(1):107-12.
- 298 35. Al-Aubaidy H, Jelinek H. Oxidative DNA damage; antioxidant response in postprandial
299 hyperglycaemia in type 2 diabetes mellitus. Br J Diabetes Vasc Dis. 2011;11:87-91.
- 300 36. Al-Aubaidy HA, Jelinek HF. 8-Hydroxy-2-deoxy-guanosine identifies oxidative DNA
301 damage in a rural prediabetes cohort. Redox Report. 2010;15(4):155-60.
- 302 37. Miyazaki Y, Kawano H, Yoshida T, Miyamoto S, Hokamaki J, Nagayoshi Y, et al.
303 Pancreatic B-cell function is altered by oxidative stress induced by acute hyperglycaemia.
304 Diabet Med. 2007 Feb;24(2):154-60.
- 305 38. Park JW, Floyd RA. Lipid peroxidation products mediate the formation of 8-
306 hydroxydeoxyguanosine in DNA. Free Radic Biol Med. 1992;12(4):245-50.
- 307 39. Kharb S, Gulati N, Singh V, Singh GP. Superoxide anion formation and glutathione
308 levels in patients with preeclampsia. Gynecologic and obstetric investigation. 2000;49(1):28-
309 30.
- 310 40. Rajdl D, Racek J, Steinerova A, Novotny Z, Stozicky F, Trefil L, et al. Markers of
311 oxidative stress in diabetic mothers and their infants during delivery. Physiological research /
312 Academia Scientiarum Bohemoslovaca. 2005;54(4):429-36.

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