

Study of serum uric acid and erythrocytic superoxide dismutase levels in gestational diabetes mellitus and normal pregnancy

Amol D Shinde^{1*}, Archana Dhotre², Suresh Ghangle³, Mangesh Tekade⁴, Sucheta Ghule⁵

^{1,3}Assistant Professor, ²Associate Professor, Department of Biochemistry, Government Medical College, Nagpur, Maharashtra, INDIA.

^{3,5}Associate Professor, ⁴Assistant Professor, Department of Biochemistry, Indira Gandhi Government Medical College, Nagpur, Maharashtra, INDIA.

Email: ams3085@gmail.com

Abstract

Level of non-enzymatic antioxidant like serum uric acid and enzymatic antioxidant like superoxide dismutase is found to be deranged in patients of gestational diabetes mellitus. Serum uric acid and superoxide dismutase levels were estimated in sixty patients of gestational diabetes mellitus admitted in obstetrics and gynecology department of G.M.C., Nagpur and sixty normal healthy pregnant controls. The result of the study showed that serum uric acid levels were increased significantly in the gestational diabetes mellitus group compared to the normal pregnant group and serum superoxide dismutase levels were decreased significantly in the gestational diabetes mellitus group compared to the normal pregnant group. Furthermore when levels of serum uric acid and superoxide dismutase were correlated with the fasting and post meal blood glucose in gestational diabetes mellitus patients, significant positive and negative correlation was observed respectively.

Keywords: Gestational diabetes mellitus, Pregnancy, Uric acid and Superoxide dismutase, Cross sectional study.

*Address for Correspondence:

Dr. Amol D. Shinde, Assistant Professor, Department of Biochemistry, Government Medical College, Nagpur, Maharashtra, INDIA.

Email: ams3085@gmail.com

Received Date: 14/08/2016 Revised Date: 06/09/2016 Accepted Date: 29/10/2016

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Volume 6 Issue 4

INTRODUCTION

Gestational diabetes mellitus (GDM) refers to any degree of glucose intolerance with onset or first recognition during present pregnancy. Indian women are more likely to develop GDM compared to Caucasian women¹. A recent meta-analysis showed that pregnant women with GDM have a sevenfold increased risk of developing type 2 diabetes mellitus compared to women who did not have diabetes during their pregnancy². When action is taken through lifestyle modifications or pharmaceutical intervention, studies have revealed that it is possible to

prevent or delay the onset of type 2 diabetes mellitus in high-risk individuals including women with a history of GDM^{3,4}. Addressing GDM thus constitutes a window of opportunity for early intervention and reduction of the future burden of type 2 diabetes. In addition to the increased risk of developing type II diabetes mellitus, there are other reasons for addressing GDM. These include elevated risk of adverse pregnancy outcomes, including maternal- and peri-natal mortality, obstructed labour, spontaneous abortion, congenital abnormalities and macrosomia⁵. GDM is characterized by impaired glucose homeostasis and insulin resistance. The increase in blood glucose levels induce oxidative stress and decrease antioxidant defenses. Uric acid is a non-enzymatic antioxidant is also the chain breaking water soluble extracellular antioxidant. It contributes about two-thirds of all free radical scavenging capacity in plasma⁶. In GDM, Serum uric acid level is found to be increased. So this increase in uric acid level may be a compensatory phenomenon to confer protection against raised free radical activity⁷. In GDM, plasma insulin level is increased. This insulin has physiological action on renal tubules which causes decrease in urinary excretion

of uric acid⁸. Elevated glucose levels seen in GDM are associated with increased production of reactive oxygen species (ROS)⁹. Erythrocytic super-oxidase dismutase (SOD) is an antioxidant enzyme and its level in maternal blood of GDM patients is found to be decreased¹⁰. In India very few studies have been done about the biochemical markers for gestational diabetes mellitus, especially with respect to Inflammation and oxidative stress. So far data available regarding anti-oxidant status in gestational diabetes is insufficient. Hence this study was designed to compare the blood level of uric acid and superoxide dismutase in gestational diabetes mellitus and normal pregnant women.

MATERIALS AND METHODS

The present study was conducted in the department of Biochemistry of Government Medical College, Nagpur for duration of one and half years.

Diagnosis: Diagnosis of GDM was based on the recommendations of Fourth International Workshop-Conference on Gestational Diabetes which adopts the Carpenter-Coustan criteria¹¹.

Timing of measurement	Plasma Glucose(mg/dl) Carpenter and Coustan Criteria(1982)
Fasting	95
One hour	180
Two hour	155
Three hour	140

Gestational diabetes is diagnosed when any two values are met or exceeded.

Study Design

Hospital based cross sectional study with comparison groups.

Study Population

Sixty gestational diabetes mellitus patients and sixty healthy pregnant women.

Inclusion Criteria

Gestational diabetic pregnant women above 20 weeks of gestation, nullipara were taken as cases, normal pregnant women above 20 weeks of gestation were taken as controls.

Exclusion Criteria

Multiple gestations, Long term medical/surgical conditions that may affect glucose metabolism such as post pancreatectomy, acromegaly and hyperthyroidism. Long term intake of medications that may affect glucose metabolism such as steroids, β-adrenergic agonists and antipsychotic drugs. Previous history of hypertension, diabetes mellitus, dyslipidemia. Women having addiction of alcohol, nicotine. Acute febrile illness, presence of infection, chronic illness like malignancy, inflammatory disorders, recent (less than three months) history of major trauma, surgery or burns.

Collection of blood sample

About 8ml of blood from each patient was collected after an overnight fast (after 12 hours) by venipuncture, 4ml of it is collected in clean plain bulb and remaining in the EDTA and fluoride bulb. Blood was allowed to clot. Serum was then separated by centrifugation.

Sr. No.	Parameter	Method
1	Blood sugar	Glucose Oxidase and Peroxidase- End point (Enzymatic method) ¹²
2	Serum uric acid	Uricase method (Enzymatic method) ¹³
3	Erythrocytic Superoxide dismutase	Enzymatic method ¹⁴

Statistical analysis

All the values were expressed as mean ± SD. p value<0.05 was considered as statistically significant, that<0.001 was considered as highly significant. Pearson’s correlation coefficient (r) was calculated to assess the correlation between biochemical parameters and the blood glucose. Data was analyzed using STATA version 10.0 software.

RESULT

Demographic and anthropometric data

Mean age and gestational age between the gestational diabetic cases and healthy pregnant controls were not significantly different. While body mass index between cases and controls was significantly different.

Table 1:

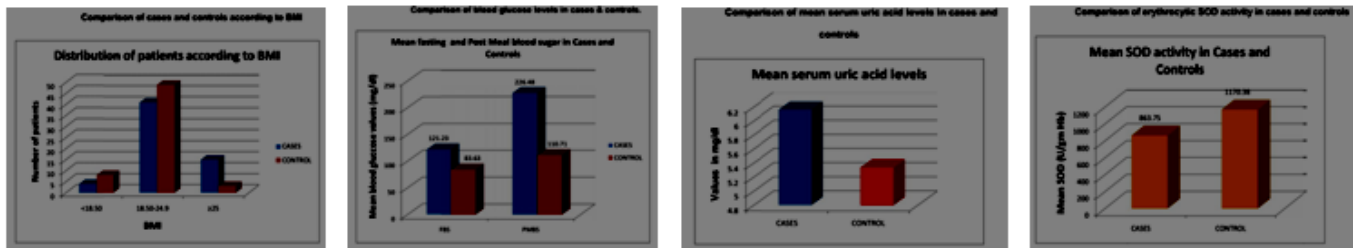
Parameter	Cases (n=60)	Controls (n=60)	p-value	Significance
Age (years)	23.78 ± 2.76	23.21 ± 3.00	0.28	Non-Significant
Gestational Age (weeks)	31.88 ± 2.87	32.86 ± 2.84	0.06	Non-Significant
BMI (kg/m2)	26.06 ± 3.43	22.95 ± 2.12	<0.001	Highly Significant

Biochemical parameters

Serum uric acid level was increased statistically highly significantly in gestational diabetic patients as compared to healthy pregnant controls. Erythrocytic superoxide dismutase level was decreased statistically highly significantly in gestational diabetic patients as compared to healthy pregnant controls.

Table 2:

Parameter	Cases (n=60)	Controls (n=60)	p-value	Significance
Fasting Blood glucose	121.23 ± 20.44	83.63 ± 5.81	<0.001	Highly significant
Post meal blood glucose	226.48 ± 14.00	110.71 ± 7.74	<0.001	Highly significant
Uric acid (mg %)	6.15 ± 0.46	5.33 ± 0.16	< 0.001	Highly significant
Erythrocytic SOD (U/gmHb)	863.75 ± 32.04	1170.38 ± 25.55	<0.0001	Highly significant



Correlation

When serum uric acid and erythrocytic superoxide dismutase levels were correlated independently with fasting blood glucose and post-meal blood glucose, a significant positive correlation and significant negative correlation was obtained.

Table 3:

Parameter	Fasting blood glucose	Post meal blood glucose
Serum uric acid	$r = 0.5590$; $p < 0.0001$	$r = 0.6766$; $p < 0.0001(0)$
Erythrocytic superoxide dismutase	$r = -0.8923$; $p < 0.0001(0)$	$r = -0.9253$; $p < 0.0001(0)$

Where r - Karl Pearson correlation Co-efficient (-1 to +1). $p < 0.05$ = statistically significant; $p < 0.001$ = highly significant.

DISCUSSION

The present study was undertaken to compare the serum uric acid and erythrocytic superoxide dismutase level in patients of gestational diabetes and normal pregnant women. The study group and the control group were comparable with each other in respect to demographic parameters and anthropometric parameters. In the present study mean BMI was significantly more in GDM group compared to controls.

Uric acid and gestational diabetes mellitus

In our study, we tried to find out whether the levels of serum uric acid, a physiological antioxidant was increased in patients of gestational diabetes mellitus as compared to controls or normal pregnant women. We found that serum uric acid was significantly higher in cases of gestational diabetes mellitus as compared to controls ($p < 0.0001$). Our study was consistent with the findings of Sujata Maitra *et al* (2012)¹⁵, Nagalkshmi C. S. *et al* (2012)¹⁶ and Simmi Kharb (2007)¹⁷ with respect to serum uric acid. In their study they showed higher serum uric acid level in the women with gestational diabetes mellitus as compared to normal pregnant women. Laughon *et al* (2009)¹⁸, Talya Wolak *et al* (2012)¹⁹ and Zhou J *et al* (2013)²⁰ demonstrated that the first trimester hyperuricemia is associated with an increased risk of developing GDM. The elevation in serum uric acid level may be a protective response which is capable of opposing harmful effects of free radical and oxidative stress seen in GDM⁷ as uric acid possesses antioxidant

properties, and contributes about 60% of free radical scavenging activity in human serum. Elevated serum uric acid can predict the development of diabetes and hence can be considered as an early sign of peripheral insulin resistance syndrome¹⁸. The higher insulin level reduces urinary excretion of uric acid leading to higher serum uric acid in GDM¹⁶. The high insulin is also responsible for activation of the sympathetic nervous system which reduces the urinary excretion of uric acid. So both the mechanisms cause elevation in serum uric acid.

SOD and GDM

To measure the antioxidant status in GDM, along with uric acid we have also measured the activity of superoxide dismutase in blood. In our study we tried to find out whether the activity of erythrocytic SOD was decreased in patients of gestational diabetes mellitus as compared to normal pregnant women. It was found that activity of SOD was significantly decreased in cases of gestational diabetes mellitus as compared to controls ($p < 0.001$). Our study was consistent with the findings of Prasenjit Dey *et al* (2007)¹⁰ and Oussama Grissa *et al* (2007)²¹ with respect to erythrocytic SOD activity. Prasenjit Dey *et al* (2007)¹⁰ carried out a preliminary study consisting of 18 pregnant women who having GDM and 18 healthy pregnant women as controls. They observed that the erythrocytic SOD level was significantly decreased in women with gestational diabetes mellitus as compared to normal pregnant women ($p < 0.05$). Oussama Grissa *et al* (2007)²¹ and Djordjevic A *et al* (2004)²² also found that

SOD activity is decreased in GDM patients as compared to normal pregnant women. Simmy Kharb (2010)²³, Biri *et al* (2006)²⁴ and Evelyne Peuchant *et al* (2004)²⁵ also showed that the activity of antioxidant enzymes like SOD is decreased in women with gestational diabetes mellitus as compared to normal pregnant women. Elevated glucose levels are associated with increased production of reactive oxygen species⁹. Thus the antioxidant enzyme SOD may be consumed by these increased reactive oxygen species as the SOD detoxifies the superoxide radicals. It has been noticed that there is decreased SOD activity in type 2 diabetes compared with controls²⁶ and as the pathophysiology of GDM is same as that of T2DM, so it may also be applicable in GDM. The decrease in SOD activity may be due to decreased production or inactivation of SOD enzyme by reactive oxygen species.

CONCLUSION

It has been convincingly demonstrated that GDM occurs as a result of a combination of insulin resistance and decreased insulin secretion. It is a hypothesis that GDM may be a systemic inflammation mediated by cytokine, similar to immune disease. Pregnancy itself is a condition associated with increase in oxidative stress, but this is balanced by adequate anti-oxidant responses¹⁵. The anti-oxidant defense system is also depleted in gestational diabetes. There are not many bio-markers for detecting occurrence of gestational diabetes and related complications, especially in the early stages. Markers of antioxidant status like uric acid and superoxide dismutase may provide additional information about risk of developing cardiovascular disease and hypertension in future and this may provide new attractive targets for drug development. Thus further exhaustive studies are required for better understanding of gestational diabetes mellitus.

REFERENCES

1. Dornhost A, Paterson CM, Nicholls, JS *et al*. High prevalence of GDM in women from ethnic minority groups. *Diabetic Med*.1992; 9:820-2.
2. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet*. 2009 May 23; 373(9677):1773-9.
3. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, *et al*. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002 Feb 7; 346(6):393-403.
4. Knowler WC, Fowler SE, Hamman RF, Christophi CA, Hoffman HJ, Brenneman AT, *et al*. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet*. 2009 Nov 14; 374(9702):1677-86.
5. World Diabetes Foundation, Global Alliance for

- Women's Health. Diabetes, Women, and Development: meeting summary, expert recommendations for policy action, conclusions, and follow-up actions. *International Journal of Gynecology and Obstetrics*. 2009; 104(1):46-50.
6. Young IS, Woodside JV. Antioxidants in health and disease. *J Clin Pathol*. 2001; 54:176-186.
 7. Waring WS, Webb DJ, Maxwell SR. Uric acid as a risk factor for cardiovascular disease. *Q J Med*. 2000; 93:707-13.
 8. Martínez-Abundis E, González-Ortiz M, Grover-Páez F, Vera-Hernández A. Excretion of uric acid, sodium, and potassium in preeclampsia patients and its behavior in acute hyperglycemia-hyperinsulinemia. 1999Dec. *Ginecol Obstet Mex*; 67:590-4.28
 9. Baynes JW, Dominiczak MH. *Medical Biochemistry*. 2nd edition. Elsevier Mosby. 2005: 497-501.
 10. Dey P, Gupta P, Acharya NK, Rao SN, Ray S, Chakrabarty S *et al*. Antioxidants and lipid peroxidation in gestational diabetes- A preliminary study. *Indian J Physiol Pharmacol*. 2008; 52(2):149-56.
 11. ADA. Standards of medical care in diabetes-2006. *Diabetes Care*. 2006; 29(suppl 1):S4-S42.
 12. Glucose reagent set (Kit insert). Jalgaon (India): Nirmal Laboratories; 2009.
 13. Uric acid reagent set (Kit insert). Mumbai (India): Accurex Biomedical Pvt. Ltd.
 14. SOD reagent set (kit insert). Crumlin (United Kingdom): RANDOX Laboratories Ltd.
 15. Maitra S, Anitha M, Praveen S, Suresh SK, Vishwanath HL. A Study of Oxidative Stress In Gestational Diabetes Mellitus: An Observational Study at A Tertiary Centre. *Asian J Med Res*. 2012 Feb; 1(1):17-21.
 16. Nagalaksmi CS, Devaki RN, Akila P, Suma KB, Prashant V, Suma MN *et al*. Exploration of the Clinico-Biochemical Parameters to Explain the Altered Renal Mechanisms in Gestational Diabetes Mellitus. *J Clin Diagn Res*. 2012; 6(3):369-71.
 17. Kharb S. Uric Acid And Ascorbic Acid Levels In Pregnancy With Preeclampsia And Diabetes. *Webmed Central Biochemistry*. 2010; 1(10):WMC00718.
 18. Laughon SK, Catovr J, Provins T, Roberts JM, Gandley RE. Elevated first trimester uric acid concentrations are associated with the development of gestational diabetes. *Am J Obstet Gynecol*. 2009 Oct; 201(4):402e1-e5.
 19. Wolak T, Sergienko R, Wiznitzer A, Paran E, and Sheiner E. High Uric Acid Level During the First 20 Weeks of Pregnancy is Associated with Higher Risk for Gestational Diabetes Mellitus and Mild Preeclampsia2012. *Hypertens Pregnancy*. 2012;31(3):307-15.
 20. Zhou J, Zhao X, Wang Z, Hu Y. Combinations of lipids and uric acid in mid-second trimester can be used to predict adverse pregnancy outcomes. *J Matern Fetal Neonatal Med*. 2012 Dec; 25(12):2633-8.97
 21. Grissa O, Atebo JM, Yessoufou A, Tabka Z, Miled A, Jerbi M *et al*. Antioxidant status and circulating lipids are altered in human gestational diabetes and macrosomia. *Translational Res*. 2007; 150:164-71.
 22. Djordjevic A, Spasic S, Jovanovic-Galovic A, Djordjevic R, Grubor-Lajsic G. Oxidative stress in diabetic pregnancy: SOD, CAT and GSH-Px activity and lipid

- peroxidation products. *J Matern Fetal Neonatal Med.* 2004 Dec; 16(6):367-72.
23. Kharb S. Activity of Extracellular Superoxide Dismutase in Gestational Diabetes. *Res J Obstet Gynecol.* 2010; 3(1):1-4.
 24. Biri A, Onan A, Devrim E, Babacan F, Kavutcu M, Durak I. Oxidant status in maternal and cord plasma and placental tissue in gestational diabetes. 2006 Feb. *Placenta*; 27(2-3):327-32.
 25. Peuchant E, Brun JL, Rigalleau V, Dubourg L, Thomas MJ, Daniel JY *et al.* Oxidative and antioxidative status in pregnant women with either gestational or type 1 diabetes. *Clin Biochem.* 2004 Apr; 37(4):293-8.
 26. Pathak R, Pathak A. Study of lifestyle habits on risk of type 2 diabetes. 2012 jul-dec. *Int J Appl Basic Med Res*; 2(2):92-96.

Source of Support: None Declared
Conflict of Interest: None Declared