Original Article

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

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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.

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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 women[1]. 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 pregnancy[2]. 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 macrosomia[5]. 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 plasma[6]. 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 activity[7]. In GDM, plasma insulin level is increased. This insulin has physiological action on renal tubules which causes decrease in urinary excretion

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of uric acid[8]. 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 decreased[10]. 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 criteria[11].

Timing of measuremnnt	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:

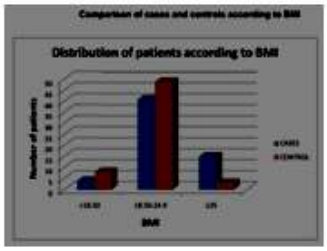
Parameter	Cases (n=60)	Controls (n=60)	p-value	Significance
Age (years)	23.78 ± 2.76	23.21 ± 3.00	0.28	Non-Significant
Gestational Age (weeks)	31.88 ± 2.87	32.86 ± 2.84	0.06	Non-Significant
BMI (kg/m2)	26.06 ± 3.43	22.95 ± 2.12	<0.001	Highly Significant

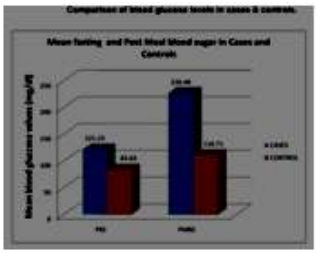
Biochemical parameters

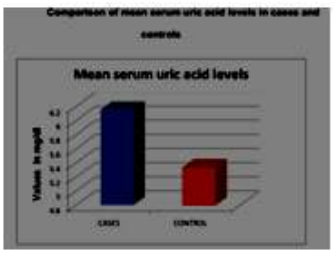
Serum uric acid level was increased statistically highly significantly in gestational diabetic patients as compared to healthy pregnant controls. Erythrocytic superoxide dismutase level was decreased statistically highly significantly in gestational diabetic patients as compared to healthy pregnant controls.

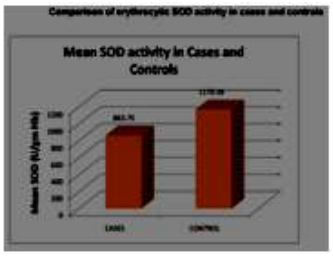
Table 2:

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 GDM[7] 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 syndrome[18]. The higher insulin level reduces urinary excretion of uric acid leading to higher serum uric acid in GDM[16]. 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 super-oxide 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 species[9]. 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 controls[26] 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 responses[15]. 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.

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