Original Article

Study of serum CRP and malondialdehyde levels in gestational diabetes mellitus and normal pregnancy

Amol D Shinde[1*], Archana Dhotre[2], Suresh Ghangle[3], Mangesh Tekade[4], Sucheta Ghule[5]

[1,3]Assistant Professor, [2]Associate Professor, Department of Biochemistry, Government Medical College, Nagpur, Maharashtra, INDIA.
[3,5]Associate Professor, [4]Assistant Professor, Department of Biochemistry, Indira Gandhi Government Medical College, Nagpur, Maharashtra, INDIA.
Email: ams3085@gmail.com

Abstract

Introduction: Markers of inflammation and oxidative stress like C Reactive Protein and Malondialdehyde may provide information about risk of developing Type II DM, cardiovascular disease and hypertension in future in patients of Gestational diabetes mellitus. Serum C Reactive Protein and serum MDA level 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 C Reactive Protein and Malondialdehyde levels were increased significantly in the gestational diabetes mellitus group compared to the normal pregnant group. Furthermore when levels of serum C Reactive Protein and Malondialdehyde were correlated with the fasting and post meal blood glucose in gestational diabetes mellitus patients, significant positive correlation was observed.
Keywords: Gestational diabetes mellitus, Pregnancy, C Reactive Protein, Malondialdehyde, 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
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INTRODUCTION

Gestational diabetes mellitus (GDM) refers to any degree of glucose intolerance with onset or first recognition during pregnancy. Indian women are more likely to develop GDM compared to Caucasian women[1]. A recent meta-analysis reported that pregnant women with GDM have a sevenfold increased risk of developing type 2 diabetes mellitus compared to women who did not have diabetes mellitus during their pregnancy[2]. When action is taken through lifestyle modifications or pharmaceutical intervention, studies have shown 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 defences. Possible source of oxidative stress and damage to protein in diabetes include free radicals which are generated by auto oxidation of unsaturated lipids in plasma and membrane proteins[6]. C-reactive protein (CRP) is a normal plasma protein. In patients of Gestational Diabetes Mellitus (GDM), the rise of serum CRP level can predict the risk of type II diabetes later in life[7]. The oxidative stress in GDM lead to lipid peroxidation. The level of lipid peroxidation can be estimated by measuring serum MDA (Malondialdehyde) level. MDA is formed by fatty acids which have three or more double bonds[8]. 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 pro-oxidant status in gestational diabetes is insufficient. Hence this study was designed to compare the blood level of CRP (C-reactive protein) and MDA

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(Malondialdehyde) 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[9].

Table 1

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. Hospital based cross sectional study with comparison groups. 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.

Table 2

Sr. No.	Parameter	Method
1	Blood sugar	Glucose Oxidase and Peroxidase- End point (Enzymatic method)[10]
2	C Reactive Protein	Immuno-turbidimetric method[11]
3	Serum malondialdehyde	Kei- Satoh method[12]

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

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 3:

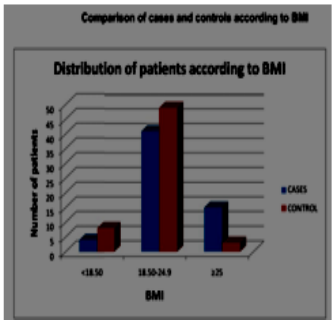
Parameter	Cases (n=60)	Controls (n=60)	p-value	Significance
Age (years)	23.78 ± 2.76	23.21 ± 3.00	0.28	Non-Significant
Gestational Age (weeks)	31.88 ± 2.87	32.86 ± 2.84	0.06	Non-Significant
BMI (kg/m2)	26.06 ± 3.43	22.95 ± 2.12	<0.001	Highly Significant

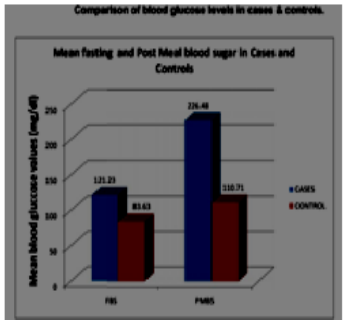
Biochemical parameters

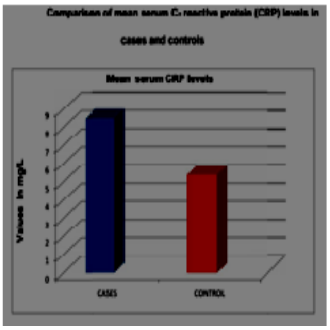
C Reactive Protein and serum MDA level were increased statistically highly significantly in gestational diabetic patients as compared to healthy pregnant controls.

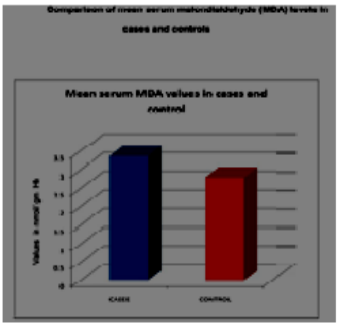
Table 4:

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
CRP(mg/L)	8.46 ± 0.50	5.36 ± 0.19	< 0.0001	Highly significant
MDA (nmol/ gm Hb)	3.34 ± 0.39	2.78 ± 0.12	< 0.0001	Highly significant









Correlation

When serum C - reactive protein and malondialdehyde levels were correlated independently with fasting blood glucose and post-meal blood glucose, a significant positive correlation was obtained.

Table 5:

Parameter	Fasting blood glucose	Post meal blood glucose
C Reactive protein	r = 0.6234; p= <0.0001	r = 0.6242; p= <0.0001
Malondialdehyde	r = 0.9360; **p= <0.0001**	r = 0.9272; **p= <0.0001**

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 C-reactive protein and malondialdehyde 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.

In our study we found that serum CRP was significantly higher in cases of gestational diabetes mellitus as compared to controls (p<0.001). Our study was in accordance with the findings of Xiahong Li *et al* (2007)[13], Liu T. *et al* (2012)[14] and Simin Rota *et al* (2005)[15]. In their study they found that serum CRP level was higher in the women with gestational diabetes mellitus as compared to normal pregnant women. Qiu C *et al* (2004)[16] and Myles Wolf *et al* (2003)[7] also found that CRP was higher in patients of gestational diabetes mellitus compared to normal pregnant women. In the patients of GDM, there is increased expression of genes for chronic stress and inflammatory pathways. This leads to increase in production of CRP[17]. In GDM, TNF-α another inflammatory marker was found to be strongest predictor of insulin resistance in pregnancy[18]. This TNF-α is responsible for production and release of CRP from the liver[19]. GDM show features of insulin resistance and it has been proved by many studies that CRP level is increased in insulin resistance syndrome[20]. Also the underlying pathogenic mechanism for GDM is similar to that of T2DM and it has shown that there is higher CRP level in patients of T2DM[21].

As stated earlier there is increase in oxidative stress in GDM which causes lipid peroxidation. Hence, MDA, a marker of lipid per-oxidation helps to measure the overall oxidative stress. In our study we found that MDA level was significantly higher in cases of gestational diabetes mellitus as compared to controls (p<0. 001). Our study was in accordance with the findings of Lalita Chaudhary *et al* (2002)[6] and Mohd Suhail *et al* (2012)[22] with respect to MDA level. In their study, they found that MDA level is significantly higher in the women with gestational diabetes mellitus as compared to normal pregnant women. Surapaneni K M *et al* (2007)[23],. Kamath U *et al* (1998)[24] and Adetunji O *et al* (2013)[25] demonstrated that serum MDA level was significantly higher in GDM compared normal pregnant women. The reasons quoted for the elevation of MDA in GDM: - In normal pregnancy, there is an increase of lipid peroxidation products in serum with advancing gestation, which is balanced by an adequate antioxidative response[6]. In GDM, the increased blood glucose levels causes auto-oxidation of unsaturated lipids in plasma and membrane proteins which is responsible for generation of free radicals. So this cycle of tissue damage and cell death, leading to increased free radical production and compromised free radical scavenger system continues which further exaggerates the oxidative stress. This ultimately leads to increase in erythrocyte MDA level in GDM. Also the abnormalities in the regulation of peroxide might result in establishment of disease like diabetes as well as its long-term complications[6].

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. A new research reports that C-reactive protein (CRP) as an inflammatory factor is

associated strictly with the physiology and pathology of pregnancy, and the rise of serum CRP level can provide related theoretical basis for them[16]. Pregnancy is itself is a condition associated with increase in oxidative stress, but this is balanced by adequate anti-oxidant responses[26]. The anti-oxidant defense system is also depleted in gestational diabetes. This creates an imbalance in the pro-oxidant status and antioxidant status leading to an increased generation of end products of lipid peroxidation like malondialdehyde. There are not many bio-markers for detecting occurrence of gestational diabetes and related complications, especially in the early stages. Markers of inflammation and oxidative stress 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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