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Biochemical markers of renal and hepatic function in gestational diabetes mellitus

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Abstract

Aim: To assess the biochemical parameters of renal and hepatic function in women with GDM and compare the results with those of normal pregnant women.

Materials and Methods:

Cases: The study group consisted of 45women with GDM.

Controls: 45 healthy pregnant women without any complications of pregnancy were taken as controls. The parameters of renal function which include serum urea, creatinine, uric acid and liver function which includes serum bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were estimated between 24 to 28 weeks of gestation using a fully automated clinical chemistry analyzer.

Results: Serum creatinine and uric acid levels were found to be significantly elevated in cases. On the contrary, the serum albumin levels were significantly reduced in cases. No significant change was found in serum urea, bilirubin, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase levels between the groups.

Conclusion: The increased serum creatinine and uric acid levels in cases suggest that GDM may jeopardize the renal function and also increase the risk for future kidney disease in these women.

Keywords: Gestational Diabetes Mellitus(GDM), Urea, Creatinine, Uric acid, Albumin

Introduction

Gestational Diabetes Mellitus is a condition that develops in around 2 percent of pregnant women, in their third trimester of pregnancy. These women generally do not have a history of impaired glucose tolerance before the onset of pregnancy. The insulin resistance is the hallmark of glucose intolerance in these women. Hyperglycemia is a well-known feature that occurs in this condition because of the effect of the hormones of pregnancy on the blood glucose level. This hyperglycemic state combined with the reduced insulin secretion is responsible for the inability to cater to the high insulin requirement of pregnancy.[(1)] GDM also has long-term impacts on the child. Intrauterine exposure to the diabetic environment places children born to GDM mothers at an increased risk of obesity, the development of altered glucose tolerance and eventually type 2 diabetes mellitus (T2DM) in later life. It is thought that exposure to the abnormal metabolic environment during gestation leads to dysfunctional in utero programming of the offspring's metabolism. Mechanisms by which this occurs include epigenetic modifications such as DNA methylation of genes involved in metabolism.

The microvascular complications of Diabetes Mellitus like neuropathy, nephropathy and retinopathy have been studied in detail. In a normal pregnancy, the renal blood flow and the glomerular filtration rate increases as the pregnancy progresses. So the Creatinine clearance increases during the first trimester of pregnancy and remains so until the last trimester. Whereas in GDM the estimated glomerular filtration rate (eGFR) is reduced, thereby increasing the serum creatinine and the uric acid levels. The raised creatinine levels is suggestive of impending renal disease in GDM. The increased uric acid levels in GDM might also be due to the insulin resistance[(2)] seen in this condition. GDM, might also increase the glomerular membrane permeability to proteins and even decrease the tubular reabsorption of filtered proteins that may be responsible for the accelerated excretion of proteins, especially albumin. Further, the diminished liver function seen in this condition may be the reason for the altered serum albumin levels seen in GDM. So, we performed this study to find out if the changes in serum urea, creatinine, uric acid albumin, AST, ALT, ALP, bilirubin does occur in women with GDM.

Materials and Methods

Study Population

a. **Cases:** The study sample comprised 45 women with GDM in their third trimester. Pregnant women who had no history of diabetes before pregnancy underwent an oral glucose challenge test (OGCT) with 50 gm of glucose. Women who had plasma glucose values ≥140mg/dl after 1 hour were then made to undergo a 75g oral glucose tolerance test (OGTT) to confirm the diagnosis of GDM according to Carpenter and Coustan[(3)] criteria.
b. **Controls:** Consists of 45 normal pregnant women without any complications of pregnancy, in their third trimester attending the antenatal clinic.

Inclusion Criteria: Pregnant women without any other medical complications of pregnancy.
Exclusion Criteria: Women with a history of diabetes before pregnancy, hypertension, preeclampsia, thyroid disorders, preexisting renal and liver disorders and those on other medications were excluded from the study.
Sample Collection and Processing: Blood from median cubital vein was collected from the cases and controls and Plasma glucose was estimated by the glucose oxidase method, Serum Urea by the GLDH-urease method, Serum Creatinine by Jaffe's method, Serum Uric acid by the Uricase method and Serum Albumin by the Bromo-Cresol Green dye binding method, Alkaline phosphatase by Tris carbonate buffer kinetic method, Bilirubin by the Diazomethod, Aspartate aminotransferase and Alanine aminotransferase by IFCC Kinetic method, using a fully automated clinical chemistry analyzer.

Results

Statistical analysis was done using 't' test.

Table 1: Renal Function - Comparison of Key Parameters

Parameters of renal function	Cases (n = 45)		Controls (n= 45)		Difference between means	(t) value	Significance P value
	Mean	SD	Mean	SD			
Urea	20.5	2.3	20.3	2.7	0.2	0.2	>0.05
Uric acid	3.7	0.5	2.9	0.3	0.8	8.9	<0.001
Creatinine	1.2	0.3	0.9	0.1	0.3	8.0	<0.001

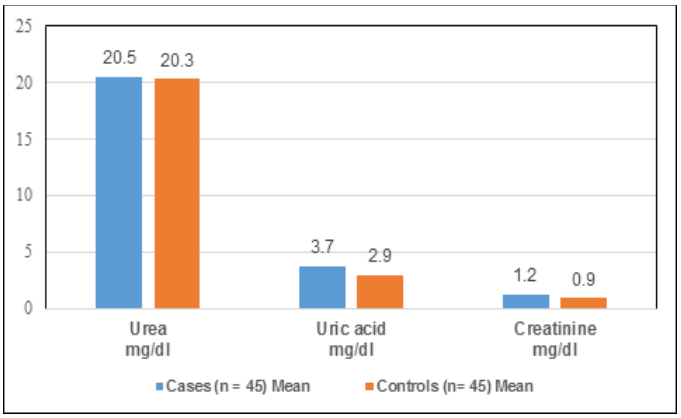

Fig. 1: Renal Function - Comparison of Key Parameters

The GDM patients had high mean uric acid values (3.7+ 0.5) compared to controls (2.9+0.3). The GDM group also had high mean creatinine values (1.2+0.3) compared to controls (0.9+0.1). So, a significant increase in the serum creatinine and uric acid levels was seen in the GDM patients as compared to the controls, while no significant difference was seen in the mean urea values between the groups.

Table 2: Liver Function - Comparison of Key Parameters

Parameters of liver function	Cases (n = 45)		Controls (n= 45)		Difference between means	(t) value	Significance P value
	Mean	SD	Mean	SD			
Albumin	3.2	0.5	5.6	0.6	2.4	20.6	<0.001
AST	28.2	7.7	28.8	7.1	0.6	0.4	>0.05
ALT	30.4	6.9	28.8	8.3	1.6	0.9	>0.05
ALP	74	24.1	66.7	20.8	7.3	1.5	>0.05
Bilirubin	0.9	0.2	0.8	0.2	0.1	1.1	>0.05

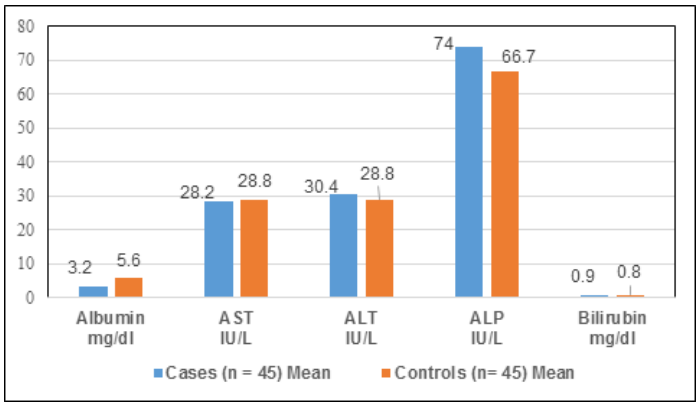

Fig. 2: Liver Function - Comparison of Key Parameters

Among the parameters of liver function, the mean value of Serum Albumin was significantly reduced in the GDM group (3.2+0.5) compared to controls(5.6+0.6). No significant difference was found in the case of AST, ALT, ALP and Serum Bilirubin between the groups.

Table 3: Comparison of Maternal age and BMI between the groups

	Cases (n = 45)		Controls (n= 45)		Difference between means	(t) value	Significance P value
	Mean	SD	Mean	SD			
Maternal Age	22.7	2.3	23	2.6	0.3	0.5	>0.05
BMI	22.3	1.5	22.5	2.1	0.2	0.5	>0.05

No significant difference was found in the case of maternal age and BMI between the groups. So the two groups were comparable in terms of age and BMI.

Discussion

This study was done to assess the levels of routinely tested parameters of renal and liver function in GDM. Newer and highly sensitive, though not very specific markers of renal function like the Cystatin C and NGAL (Neutrophil Gelatinase Associated Lipocalin) are being estimated now as indicators of renal function. However, biochemical parameters tested in our study provide a cost effective and reliable assessment of renal function. Though increased serum creatinine levels can be an indicator of the future renal disease in the GDM women, the disadvantage with this marker is that, chronic kidney disease does not show up until the disease reaches an advanced stage and serum creatinine may show very little changes until its clearance falls to very low levels. Our Study also reported higher level of creatinine in patients with GDM as like the study by Tarim et al. Though in their study, the association did not reach a statistical significance,[4,5] the association did reach a level of statistical significance in our Study. Lipid peroxidation is said to play quite an important role in the pathogenesis of GDM. Animal studies implicate that the high levels of oxygen derived free radicals in GDM might have a role in the development of complications associated with the condition and this can be prevented by antioxidants.[6,7] High blood glucose levels by itself can induce oxidative stress and also decreases the antioxidant defence of the body, thereby increasing the free radical formation.

In the present study, significantly elevated levels of serum uric acid were observed in GDM women as compared to the controls ($P \leq 0.05$). The uric acid has antioxidant properties and thus it may be helpful, in neutralizing the adverse effects of free radicals. High serum uric acid levels is a hallmark of all the insulin resistance syndromes.[8] On the contrary, Insulin also has its effect on serum uric acid levels. It acts on the renal tubules and reduces the excretion of uric acid.[9] Moreover, insulin besides decreasing the renal excretion, can also increase the renal reabsorption of uric acid.[10] Though in GDM there is a component of insulin resistance, the effects of insulin on the renal tubules still persists.[9] Thus it can be concluded that the hyperuricemia seen in GDM could be caused by the effects of insulin on the kidneys inspite of the prevailing insulin resistance. In humans, uric acid is the final breakdown product of adenosine, which plays an important role in the pathophysiology of insulin resistance.[11] Adenosine by itself can also cause increased renal uric acid retention.[11] Not many studies done in the past have measured the uric acid levels in GDM or have shown significantly higher serum uric acid levels in these women. However, in our study there was a significant increase in the serum uric acid levels in GDM women compared to controls.

GDM affects the protein metabolism and as serum albumin levels indicate the synthetic function of the liver, a decrease in its levels suggest a derangement of liver function in these women .In addition to the decreased synthesis, there might be an increase in the renal excretion of proteins in GDM. This increased excretion of proteins could be due to the increased permeability of the glomerular basement membrane[12] to proteins as well as decreased renal tubular reabsorption of proteins. On the other hand, microalbuminuria is also an integral aspect of impaired glucose tolerance of the insulin resistance syndromes[13,14] and this could also contribute to the lower albumin levels in these women. Microalbuminuria by itself is an indicator of future renal disease in these women and so regular follow up of these women in GDM for the other markers of kidney disease has been indicated.[15]

Macrosomic or in other words large for gestational age infants are born to these women and the incidence of this condition can be controlled by maintaining euglycemic levels. Future studies involving a larger population and those incorporating new biochemical markers is essential.

Conclusion

Biochemical markers such as serum creatinine, uric acid and albumin can help in assessing the hepatorenal function in women with GDM.As these women have reduced albumin levels in their blood, we may conclude that uric acid may have role in increasing the excretion of albumin in these women. The results of this study suggest that GDM may increase the risk for future kidney disease in these women. Further studies with more sensitive and specific biochemical markers of renal function is necessary.

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