

ORIGINAL ARTICLE

EFFECT OF GESTATIONAL DIABETES ON BLOOD SUGAR,
LIVER AND RENAL FUNCTION TESTSRadhia Khan, Zakkia Khan*, Khalid Javed**, Khurshid Ali[†]Department of Biochemistry, Khyber Girls Medical College, *Gynaecology, Khyber Teaching Hospital,
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Objective: Type 2 diabetes adversely affects the liver and kidney function tests. This study was conducted to determine that either the liver and kidney functions are disturbed in the patients having gestational diabetes mellitus (GDM). **Methods:** One hundred and three women with GDM, and 97 healthy pregnant women (HPW) in their third trimester were registered in the Obs/Gyn Unit of Khyber Teaching Hospital, Peshawar in the time period Apr–Sep 2012. Blood sugar level, glycosylated haemoglobin status HbA1c, haemoglobin concentration, platelet count, liver function tests including alanine amino transferase (ALT), alkaline phosphatase (ALP) and bilirubin, renal function tests including urea and creatinine were determined. **Results:** Blood glucose level and HbA1c of GDM was significantly higher ($p < 0.001$) than HPW. Fasting and random blood glucose and HbA1c of GDM and HPW were 110.90 ± 9.10 vs 84.68 ± 7.01 mg/dl, 148.53 ± 7.21 vs 124.42 ± 9.46 mg/dl and 6.49 ± 1.20 vs 4.99 ± 0.55 respectively. Haemoglobin percentage, platelet count, ALT, ALP, serum bilirubin and urea were not significantly different among the two groups. However, mean serum creatinine (0.82 ± 0.32 mg/dl) in GDM was significantly higher ($p < 0.05$) than in HPW (0.74 ± 0.15 mg/dl). **Conclusion:** In gestational diabetes the LFTs may not be disturbed, however serum creatinine value is increased.

Keywords: Gestational diabetes, HbA1c, liver function tests, urea, creatinine

INTRODUCTION

Gestational diabetes mellitus (GDM) is any degree of glucose intolerance with onset or first recognition during pregnancy.¹ GDM patients are usually identified during second or third trimester of pregnancy. Glucose tolerance usually returns to normal range within 6 weeks after pregnancy ends. Most GDM patients do not develop diabetes mellitus later in life; however some will develop impaired glucose tolerance. The prevalence rate of GDM in US is 1–14 percent depending upon the population studied and the rate of incidence is constantly increasing in multiethnic populations.² In Chicago, the cumulative prevalence of type 2 diabetes in women with previous history of GDM increased rapidly in the first two years after delivery, and approximately 50% of GDM patients developed type 2 diabetes within 5 years postpartum.³ The Diabetes Prevention Program demonstrated that subjects who were having previous history of GDM had a 71% increased risk of developing type 2 diabetes, as compared with women without such a history.⁴ Lee *et al* reported that previous GDM history was a greater risk factor than waist circumference or family history of diabetes for developing type 2 diabetes.⁵ In the united Kingdom, South Asian women had a higher risk of developing diabetes, as compared with Caucasian women (48.6% vs. 25.0%), within a mean period of 4.83 years after delivery.⁶ GDM is one of the well-known risk factor for developing type 2 diabetes later in life. Various factors on the basis of which one can predict that either a pregnant woman will become diabetic in future are: early diagnosis of GDM in pregnancy, need for insulin treatment during

pregnancy, high blood glucose level at diagnosis, preterm delivery, macrosomic babies and an abnormal oral glucose tolerance test after two months of delivery.⁷ Crowther *et al* reported composite end point of shoulder dystocia, bone fracture, foetal death and nerve palsy in women with gestational diabetes.⁸ London *et al* had also reported a composite but slightly different endpoint, namely foetal death, neonatal hypoglycaemia, hyperbilirubinemia and birth trauma.

The negative impact of diabetes on the cardiovascular, nervous and retinal systems is well recognized and regular screening for complications with these systems is advised by health care provider's world over. However, awareness about gestational diabetes complications on the liver, an organ that plays a central and crucial role in the regulation of carbohydrate metabolism and maintenance of blood glucose levels is still falling short. The liver has a major role in glucose homeostasis and, in liver diseases; hepatic carbohydrate metabolism is commonly disturbed. Altered portal insulin levels and the insulin/glucagon ratio in gestational diabetes may influence hepatocyte function and predispose them to various hepatic disorders.¹⁰ Although no specific liver disease is known to be associated with gestational diabetes mellitus, however, altered hepatic glucose metabolism may be involved in the pathogenesis of non-insulin-dependent diabetes.¹¹ Disturbances in liver function tests (LFTs) and renal function tests (RFTs) are well recognized in some diabetic patients, especially in acute metabolic decompensation. However, in gestational diabetes the

prevalence of abnormal LFTs and RFTs results are controversial. Liver function tests like alanine amino transferase (ALT), alkaline phosphatase (ALP) and serum bilirubin show the extent to which hepatocytes are damaged. Renal function tests like urea and creatinine are the parameters to diagnose functioning of the kidney. In gestational diabetes, high sugar in the blood can lead to serious health problems, including heart disease and damage to the nerves and kidneys. The present study was conducted to report the effect of gestational diabetes on liver and renal function tests by measuring the levels of LFTs and RFTs in both GDM and HPW.

MATERIAL AND METHODS

This comparative study was carried at the supervision of the Institute of Chemical Sciences, University of Peshawar in the time period of April–Sep 2012. Gestational diabetic women (GDM) and healthy pregnant women (HPW) for comparison were registered in Obs/Gyn Unit of Khyber Teaching Hospital (KTH), Peshawar, Pakistan. Information was collected from the registered women on an approved questionnaire. Blood sugar level, liver function tests and renal function tests were determined in the main Biochemistry Laboratory of KTH. The selection criteria for GDM and HPW were: admitted patient of Obs/Gyn Unit of KTH, gestational age of 28 weeks or more, not having previous history of medical illness like hypertension, cardiac and renal diseases, and being on any medical treatment that affects lipid profile, hormones concentration, liver and renal function tests.

One hundred and ten gestational diabetic women and 100 healthy pregnant women were registered for the study. Informed consents were obtained. Ethical approval for the study was obtained from Institutional Ethical Medical Board at Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar. Seven GDM patients and 3 HPW were dropped out from the study and the remaining 103 GDM patients and 97 HPW completed the study.

Fasting blood samples were taken from both GDM and HPW. Five ml fasting blood was taken, 1 ml blood was transferred to an EDTA vacutainer for measuring haemoglobin concentration and platelet count. The remaining 4 ml blood samples were centrifuged at 4,000 rpm for 5 minutes for serum separation. Separated serums were transferred to proper labelled eppendorf tubes and stored at -20 °C for liver and kidney function tests. For determination of random blood sugar and HbA1c additional 2 ml blood in fed state were taken from both GDM and HPW.

Both fasting and random glucose was determined by the enzymatic colorimetric method of Trinder.¹² Auto analyzer (Express plus, Ciba Corning USA), and Elitech kit was used. HbA1c was determined

by the method of Korolev.¹³ Full blood count including haemoglobin concentration and platelet count was measured by using three dimension, fully automated Haematology Analyzer Humacount Plus.¹⁴ ALT was determined by Roche kit without pyridoxal phosphate activation.¹⁵ ALP was determined by using an optimised substrate concentration and 2-amino-2 methyl-1 propanol as buffer plus magnesium and zinc cations.¹⁶ Bilirubin was determined by the procedure of Wahlefeld *et al.*¹⁷ Urea was determined by enzymatic procedure of Schubert who used the coupled urease/glutamate dehydrogenase (GLDH) enzyme system.¹⁸ Creatinine was determined by the method of Bartles.¹⁹

RESULTS

The mean fasting blood sugar, random blood sugar, glycosylated haemoglobin (HbA1c), haemoglobin concentration and platelet count of GDM and HPW are given in Table-1. The mean fasting blood glucose level, random blood glucose level and mean HbA1c values of GDM women were significantly higher than HPW ($p < 0.001$). Haemoglobin percentage and platelet count were not significantly different among the two groups.

Table-1: Blood Sugar, Haemoglobin and Platelet Count of GDM and HPW

Blood Parameter	GDM	HPW	p
Fasting Blood Sugar (mg/dl)	110.90±9.10	84.68±7.01	<0.001
Random Blood Sugar (mg/dL)	148.53±7.21	124.42±9.46	<0.001
HbA1c	6.49±1.20	4.99±0.55	<0.001
Haemoglobin (%)	10.89±1.12	11.01±1.03	0.55
Platelet Count (thousand/ml)	226.31±38.20	228.14±37.61	0.49

Alanine amino transferase (ALT), alkaline phosphatase (ALP) and serum bilirubin values were not significantly different in GDM and HPW groups. The mean ALT, ALP and serum bilirubin levels are given in Table-2. The mean ALT, ALP and serum bilirubin level in GDM group were 30.21±12.47 U/L, 190.55±22.20 U/l and 0.67±0.41 mg/dl respectively. In the healthy pregnant women the mean ALT, ALP and serum bilirubin values were 29.64±7.96 U/l, 189.95±21.28 U/l and 0.58±0.17 mg/dl respectively (Table-2).

Table-2: Liver Function Tests of GDM and HPW (Mean±SD)

Liver Function Tests	GDM	HPW	p
ALT (U/L)	30.21±12.47	29.64±7.96	0.71
ALP (U/L)	190.55±22.20	189.95±21.28	0.84
Serum Bilirubin (mg/dl)	0.67±0.41	0.58±0.17	0.64

The mean serum urea and serum creatinine values of GDM and HPW are given in Table-3. The mean serum urea of GDM was 23.70±8.54 mg/dl and of the HPW was 21.97±6.16 mg/dl. Statistically these values were not different from each other. The mean serum creatinine in GDM women was 0.82±0.32 mg/dl, which was significantly higher than 0.74±0.15 mg/dl in healthy pregnant women.

Table-3: Renal Function Tests of GDM and HPW

Renal Function Tests	GDM	HPW	p
Serum Urea (mg/dl)	23.70±8.54	21.97±6.16	0.104
Serum Creatinine (mg/dl)	0.82±0.32	0.74±0.15	0.02

DISCUSSION

The major objective of the study was to report the effect of gestational diabetes on blood sugar level, haemoglobin concentration, platelet count, liver and kidney function tests. Both fasting and random blood sugar and HbA1c of GDM women were significantly higher as compared to healthy pregnant women. It is very much important that pregnant women with gestational diabetes must control their glucose level in the normal range to avoid complications during pregnancy and delivery.

HbA1c provides the extent to which the blood glucose has been controlled in the previous 8–12 weeks. So, by determining this parameter, one can prevent further worsening of the disease by providing better treatment at appropriate time. Significantly elevated levels of glycosylated haemoglobin in gestational diabetes were also reported by researchers in several studies supporting our findings.²⁰ This study showed that GDM was doing nothing with thrombocytopenia but pregnancy itself may results in low platelet count.

Studies about platelet counts during normal pregnancy differed in their conclusion, with some reporting no effect of pregnancy on platelet count and other illustrating a mild reduction during late pregnancy.²¹ In this study, no significant changes were observed in the concentration of haemoglobin and platelet count of the GDM women and HPW. Similarly no significant difference was observed in concentration of ALT, ALP and total bilirubin levels of GDM and HPW. The highest elevation in ALT occurs during severe hepatitis; toxin induced hepatic necrosis and circulatory shocks. Though the enzyme level may reflect the extent of hepatocellular necrosis, but it may not correlate with eventual outcome. In fact declining of ALT has no direct relation with gestational diabetes but it may indicate either good prognosis or recovery of hepatic failure. The little but non significant increase in ALP values is mainly due to extra hepatic and intra hepatic biliary obstruction. The overall difference in ALP levels was not significant between GDM and control groups. The normal values of ALP are 45–115 U/L which rises steadily throughout pregnancy reaching to the peak value of 125–250 U/L in the last trimester.²² ALP values also vary with age and are relatively higher in child hood and puberty, lower in middle age and higher in old age. Alkaline phosphatase levels are likely to be very high in alcoholic hepatitis and biliary cirrhosis.²³

Hyperbilirubinemia is the raised amount of bilirubin in blood and results from over production and

impaired uptake of conjugated and un-conjugated bilirubin from hepatocytes to bile duct. The normal value of serum bilirubin in pregnancy is 0.1–1 mg/dl. In few pregnant women serum bilirubin rises up to 6 mg/dl due to intra hepatic cholestasis; however, gestational diabetes is having no direct correlation with bilirubin.²⁴

Many conditions can affect the ability of the kidneys to carry out their important functions. Some conditions can lead to rapid and some to gradual decline in the kidney functions. A number of clinical laboratory tests that measure the levels of substances normally regulated by the kidneys can help to determine the cause and extent of kidney functions. It has been reported that patients with gestational diabetes had significantly higher levels of creatinine than normal pregnant women.²⁵

CONCLUSION

GDM leads to type 2 diabetes and if not controlled and treated in time may adversely affect renal functions especially the creainine value and to some extent liver functions namely ALT, ALP and serum bilirubin. It is important to control and treat gestational diabetes in time by screening the at risk population so as to reduce the maternal and neonatal complications.

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