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Correlation of Clinical-Laboratory-Sonography Parameters in Patients of Gestational Diabetes Mellitus with Maternal and Fetal Outcome

¹Dr. Aditi Modi, Senior Resident, Department of Obstetrics & Gynecology Seth G.S. Medical College and KEM Hospital, Mumbai.

²Dr. Niranjan Mayadeo, Head of department, Department of Obstetrics & Gynecology Seth G.S. Medical College and KEM Hospital, Mumbai.

³Dr. Aditi Phulpagar, Additional associate professor Department of Obstetrics & Gynecology Seth G.S. Medical College and KEM Hospital, Mumbai.

Corresponding Author: Dr. Aditi Modi, Senior Resident, Department of Obstetrics & Gynecology Seth G.S. Medical College and KEM Hospital, Mumbai.

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Abstract

Background: Gestational diabetes mellitus (GDM) is among the most frequent metabolic disorders in pregnancy, and it can lead to complications related to health of the mother and offspring. The present study was undertaken to find out correlation between clinicallaboratory-sonography parameters and maternal-fetal outcome in patients with GDM.

Method: Total 90 cases of age more than 19 years who were diagnosed with GDM were included in the study. A detailed history, clinical-laboratory and sonography parameters and total score were noted and correlated with the fetal and maternal outcome.

Results: The maternal glycemic control, first trimester BMI, fetal abdominal circumference percentile on USG and total score based on clinical-laboratory-sonography parameters were significantly associated with maternal and fetal outcome in GDM patients, (p<0.05). Majority (84.4%) of babies had birth weight between 2.5-3.99 kg and 66 (73.3%) babies were AGA. Average gestational age at GDM diagnosis in mothers of live newborn babies was higher compared to mothers of dead newborn babies, (p-value<0.05). Whereas average PLBS and total score in mothers of dead newborns was more than mothers of live newborns, (p-value<0.05). Overall, 66.7% of patients were managed on diet alone, while remaining patients required insulin and/or metformin along with diet.

Conclusion: Poor maternal glycemic control can cause adverse perinatal outcome such as IUFD, stillbirth, prolonged NICU care. Overweight and obesity in pregnancy are associated with co-occurrences of preeclampsia and GDM. Fetal abdominal circumference percentile can be used to predict LGA and subsequent management. Total score may complement to predict perinatal and maternal outcome.

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Keywords: Gestational diabetes mellitus; Correlation; Clinical-laboratory-sonography; Maternal-fetal outcome; Insulin; Metformin

Introduction

Gestational diabetes is defined as carbohydrate intolerance that results in hyperglycemia of variable severity that occurs during the pregnancy [1]. It is a major health problem for pregnant women and their offspring. GDM complicates approximately 7% of all pregnancies worldwide. In India, approximately 4 million pregnancies are complicated by GDM annually [2]. Because of epidemic of obesity, GDM cases are increasing with its complications. It causes a huge economic burden to society. Various prevalence rates have been reported in different parts of India depending on difference in age, socioeconomic status, dietary and lifestyle habits. Highest prevalence was reported on south India (17.8%) [3] followed by Haryana (13.9%) [4], western India (9.5%) [5], Kashmir (7.8%) [6].

As previously mentioned GDM has significant influence on maternal outcomes such as need for instrumental delivery or cesarean section, infection, pelvic soft tissue injury, preeclampsia and fetal outcomes such as macrosomia, hypoglycemia, need for NICU, respiratory distress, malformation etc. Despite the advent of newer guidelines and constantly evolving and improving management strategies for treatment of GDM, it continues to be a major antenatal problem [7]. GDM can result in adverse perinatal outcomes like macrosomia, birth trauma, shoulder dystocia and higher rates of cesarean section. The most important neonatal outcome is excessive fetal growth/macrosomia which can cause maternal and fetal trauma. 15-45% of macro somic newborns are of women with GDM [8]. Increased incidence of LGA (28%), hypoglycemia (20%),

hyperbilirubinemia are associated with GDM. Adequate screening and treatment can improve these [9, 10]. Also, there is risk of developing overt diabetes in women with GDM and in their offspring in future.

Kim M and et al studied that increased NICU admission, macrosomia, shoulder dystocia, ARDS, hypoglycemia was associated with increased BMI of mother and large fetal abdominal circumference on USG. These two parameters were majorly associated with adverse outcome [11]. Most studies have shown that adequate control of blood sugar has been associated with improved maternal and fetal outcome. Some GDM patients respond well to diet modifications while others may require Metformin and/or insulin along with diet modifications [12, 13].

Hence a combination of various clinical, laboratory and sonographic parameters can be used to diagnose and monitor effectiveness of treatment. However no specific combination has been universally acceptable. There are some parameters like clinical, laboratory, sonography that can be used to assess maternal and fetal outcome in patients with GDM. We have used a similar scoring system described by Valle et al [14] as a guide for management and to assess the outcome. Through this study, we attempt to correlate the various parameters with maternal-fetal outcomes.

Materials And Methods

This observational descriptive study was conducted in the Department of Obstetrics and Gynecology at tertiary care center over a period of around 2 years from August 2018 to July 2020. The study was initiated after approval by the Institutional Ethics Committee. Total 90 cases of age >19 years who were diagnosed with GDM at any gestational age, but in this pregnancy- 1) fasting blood glucose >95 mg/dl; 2) 1 hour postprandial >140 mg/dl

and 3) 2 hour postprandial >120 mg/dl; patients fulfilling criteria 1- but who had documented 1st trimester weight and who present late in pregnancy but who knew their first trimester BMI/ weight were included in the study. Patients with disease other than GDM such as preexisting medical disorders like hypertension (blood pressure >= 140/90 on two separate occasions 4 hours apart), cardiac disease (any asymptomatic/ symptomatic cardiac disease), untreated thyroid disorders (including clinical /subclinical/ hyperthyroidism/ hypothyroidism), renal disease (Reno vascular disease/ glomerulonephritis/ nephritic syndrome/ nephrotic syndrome), liver disease, autoimmune disease, patient on steroid, diabetes mellitus were excluded from the study.

A detailed history, clinical examination and laboratory investigations were done on routine basis for all pregnant women. All the relevant parameters were documented in a structured study proforma. Patients who had been following up antenatally in this institution or those who had been referred for any reason were included. Written informed consent for participation in the study was taken after the patient has delivered and before the patient was discharged. The demographic parameters, the antenatal profile, obstetrics history, USGs, clinical findings, FBS, PLBS, fetal abdominal circumference on USG (measured by transverse section through the upper abdomen, which should demonstrate the following fetal landmarks- fetal stomach, umbilical vein, portal sinus), weeks of gestation (calculated by first trimester scan preferably) when GDM diagnosed for the first time in pregnancy, her height and weight of first trimester, first trimester BMI, maternal and fetal outcome were noted during data collection. Score was given for each value of FBS, PLBS, fetal abdominal circumference percentile, time at which gestational age GDM was detected and first trimester

BMI. The total score was given according to Table 1. Mode of delivery, maternal morbidity and mortality, APGAR score at one and five minute, NICU admission, perinatal morbidity and mortality were noted. All treatment decisions were taken by the unit doctors under whom the patient was admitted. Outcome of the study was measured in terms of association of clinical laboratory and sonography parameters and total score with fetal outcome (alive / death/ spontaneous abortion, fetal Malformation, preterm delivery, polyhydramnios, birth injury, birth weight, APGAR score at 1 minute and 5 minute, NICU admission) and maternal outcome complications, (preeclampsia, antenatal Diabetic Neuropathy, Diabetic retinopathy, Diabetic Nephropathy, Diabetic ketoacidosis, Infection, pelvic soft tissue injury, Shoulder dystocia).

Table 1: Total score

	-2	-1	0	1	2
FBS (mg/dl) at	-	<80	≥80	≥90	≥100
time of diagnosis			<90	<100	
of GDM					
PLBS (mg/dl) at	-	<100	≥100	≥120	≥140
time of diagnosis			<120	<140	
of GDM					
Fetal abdomen	<10	>10 -	≥25 -	≥75 -	≥90
circumference		<25	<75	<90	
percentile- 1 st					
USG after GDM					
diagnosis					
Gestation age at	<28	≥28 -	≥32 -	≥36	-
GDM detected		<32	<36		
first(weeks)					
First trimester	-	<18.5	18.5	>25.9	-
BMI (kg/m2)			_		
			25.9		

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Statistical Analysis

Data were statistically described in terms of mean (\pm SD), frequencies and percentages when appropriate. 1) Unpaired t-test with unequal variance was used to assess-The relationship between clinical, laboratory and sonography parameters with fetal outcome, with pelvic soft tissue injury, pre-eclampsia, NICU admission, fetal malformation and pre-term delivery. 2) Analysis of variance was used to assess- The relationship between clinical, laboratory and sonographic parameters with baby's birth weight categories and mode of delivery. 3) Linear regression was used to assess- The relationship between clinical, laboratory and sonographic parameters with birth weight and APGAR score at one and 5 minutes.

Observations and Results

Total 90 participants were enrolled in the study. The maximum percentage of cases (62.2%) were in the age group of 20-30 years, multigravida (65.6%), delivered between 38-38.6 weeks (25.6%) and 39-39.6 weeks (25.6%) of gestation and maximum percentage of patients (84.4%) had spontaneous onset of labour. Most of the patients (56.4%) were induced in view of postdatism followed by PROM (28.4%). LSCS (47.8%) was the most common mode of delivery followed by vaginal delivery (43.3%), (Table 2).

 Table 2: Demographic and obstetrics characteristics of the patients

Parameters		Number of	Percentage	
		GDM cases	(%)	
Age	in	<20	1	1.1
years		20-30	56	62.2
		30-40	32	35.6
		>40	1	1.1
Parity		Primigravida	31	34.4

	Multigravida	59	65.6
Gestational	<37	4	4.4
age at	37-37.6	16	17.8
delivery in	38-38.6	23	25.6
weeks	39-39.6	23	25.6
	40-40.6	18	20
	>41	6	6.7
Type of	Spontaneous	76	84.4
labour	Induced	14	15.6
Indication	PPROM	1	7.1
for	PROM	4	28.4
Induction of	Postdatism	8	56.8
labour	bour IUFD		7.1
Mode of	Vaginal	39	43.3
Delivery	LSCS	43	47.8
	Instrumental	8	8.9

Out of 90 cases, 43 patients had LSCS (47.8%) for various indications as depicted in figure 1. Most frequent indication for LSCS was fetal distress (25.6%) followed by previous 2 LSCS in labour (18.60%). Antenatal complications were 5.6% of patients had PROM and 4.4% patients had preterm delivery. Patients with PPROM, IUGR, IUFD and malformation of baby were 2.2% each.





Only total score had significant association with preterm

delivery with p-value <0.05. Rest of the parameters were not significantly associated with preterm delivery (pvalue >0.05). The first trimester BMI (p value 0.003) and total score (p value 0.007) were significantly associated with preeclampsia in GDM patients. However, there was no significant association between clinical, laboratory and sonography parameters and pelvic soft tissue injury and mode of delivery (p-value >0.05) as shown in table 3.

Maternal outcome	Pre-term	delivery	p-	Mode of	delivery		p-	Pre-eclar	mpsia	p-
	livery		value				value			value
	No (n	Yes		Normal	LSCS	Instrumental	-	No (n	Yes (n=	
	= 86)	(n=4)		(n= 39)	(n=43)	(n= 8)		= 79)	11)	
Gestational age at	31.46	26.25	0.117	31.71	30.47	33.00	0.063	31.32	30.59	0.462
GDM diagnosis in	(3.03)	(4.79)		(3.01)	(3.58)	(1.41)		(3.32)	(2.95)	
weeks, mean (SD)										
FBS, mean (SD)	98.11	117.0	0.267	101.15	97.51	95.87	0.428	96.96	113.18	0.133
	(13.13)	(27.83)		(18.32)	(11.11)	(2.64)		(8.04)	(32.80)	
PLBS, mean (SD)	135.26	170.00	0.304	133.97	140.86	128.75	0.406	133.20	162.63	0.121
	(26.78)	(56.15)		(26.48)	(32.93)	(13.70)		(20.85)	(57.22)	
First trimester	23.13	24.55	0.577	23.51	23.12	22.09	0.457	22.70	26.8	0.003
BMI in kg/m2,	(2.91)	(4.51)		(3.51)	(2.72)	(2.89)		(2.54)	(3.42)	
mean (SD)										
Fetal abdominal	66.04	78.13	0.334	63.97	70.51	58.12	0.106	66.13	69.77	0.578
circumference	(18.15)	(20.95)		(18.03)	(18.47)	(15.57)		(18.17)	(20.01)	
percentile on USG,										
mean (SD)										
Total score	2.63	4.0	0.034	2.67	2.84	2 (1.19)	0.426	2.48	4.18	0.007
	(1.67)	(0.81)		(1.49)	(1.86)			(1.56)	(1.66)	

Table 3. Relationship	n between clini	cal laboratory	and sonograph	v narameters w	ith maternal	outcome
rable 5. Kelauolisin	p between chin	cal, laboratory	and sonograpi	ly parameters w	iui matemai	outcome

Majority (84.4%) of babies had birth weight between 2.5-3.99 kg and 66 (73.3%) babies were AGA as shown in table 4. Mean of total score (4.09) and fetal abdominal circumference percentile (83.59) for LGA was more than SGA and AGA.

The first trimester BMI, fetal abdominal circumference percentile on USG and total score were statistically associated with the baby's birth weight as well as birth weight categories (p-value <0.05) while FBS, PLBS and gestational age at GDM diagnosis were not significantly associated with baby's birth weight and birth weight categories (p-value >0.05).

However, there was no significant association between clinical-laboratory-sonography parameters and APGAR score at 1 and 5 minutes (p-value >0.05) and fetal malformation (p-value >0.05). The only fetal abdominal circumference percentile was significantly associated with the NICU admission with p-value 0.001. Other

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parameters were not found to be significantly associated Table 4: Fetal Parameters with the NICU admission (p-value >0.05).

Fetal Parameters	Number of cases	Percentage (%)	
Baby's birth weight	<2.5 kg	7	7.8
	2.5-3.99 kg	76	84.4
	>4 kg	7	7.8
Baby's birth weight categories	SGA	1	1.1
	AGA	66	73.3
	LGA	23	25.5

Average gestational age at GDM diagnosis and average FBS in mothers of live newborn babies was higher compared to mothers of dead newborn babies, (p-value <0.05). Whereas average PLBS and total score in mothers of dead newborns was more than mothers of live

newborns, (p-value <0.05). There was no significant association of first trimester BMI and fetal abdominal circumference percentile in USG with fetal outcome (p-value >0.05) as shown in table 5.

Table 5: Association of clinical, laboratory and sonography parameters with fetal outcomes

Clinical, laboratory and sonography parameters	Fetal outcome Mean (SD)		t-test value	p-value
	Dead $(n = 2)$	Live (n= 88)		
Gestational age at GDM diagnosis in weeks	30 (0.0)	31.26 (3.31)	-3.57	< 0.001
FBS	90 (0.0)	99.15 (14.45)	-5.94	< 0.001
PLBS	149 (1.41)	136.52 (29.31)	3.81	< 0.001
First trimester BMI in kg/m2	22.99 (1.25)	23.20 (3.00)	-0.231	0.849
Fetal abdominal circumference percentile on USG	85 (14.14)	66.16 (18.25)	1.85	0.301
Total score	4.0 (0.0)	2.66 (1.66)	7.55	< 0.001

Overall, 66.7% of patients were managed on diet alone, while remaining patients required insulin and/or metformin along with diet as depicted in figure 2.



Figure 2: Treatment group and percentage of GDM cases

Discussion

Gestational diabetes mellitus is a major health problem for pregnant women and their offspring. A data from Clausen TD et al study showed that GDM has not only effect on pregnancy and its outcome but also future health and quality of life [15]. Because of these GDM requires comprehensive management in terms of earliest diagnosis, treatment and long term follow up. In the present study maximum GDM women were multiparous (65.6%) and below 30 years of age (62.6%) which is comparable with the study done by Al-Rowaily MA et al [16]. ACOG recommends delivering the GDM patients who are well controlled on medication after 39 weeks and well controlled on diet till 40 weeks 6 days. Timing of delivery for uncontrolled GDM patient is after 37 weeks. In present study approximately 50% delivered between 38 to 40 weeks of gestation, 18% patient delivered at 40 weeks and 6.7% patients delivered after 41 weeks. In patients of GDM and diabetes mellitus, main goal for induction of labour at term is to prevent stillbirth or macrosomia and associated complications. But it needs to be balanced with risk of increased cesarean section rates and increased neonatal morbidity. In current study, 84.4% patients had spontaneous onset of labour while 15.6% patients were induced for labour for various indications (postdatism, PPROM, PROM, IUFD). 43.3% women delivered vaginally while 47.8% women delivered by caesarian section. 8.9% women had vaginal instrumental delivery. But nearly 40% caesarean section was done due to indications related to previous caesarean section (previous 2 LSCS, patient was not willing for vaginal birth trial and caesarean scar tenderness). 25.6% caesarean section was done for fetal distress. There was no significant association of clinical, laboratory and sonography parameters with the mode of delivery.

7.8% babies were macro somic and 25.5% babies were LGA, however, there were no cases of shoulder dystocia which is correlated with the previous studies [17, 18]. Current study showed that raised PLBS (149 in IUFD vs 136 in live born, p<0.001)) and GDM diagnosed earlier in pregnancy (mean gestational age 30 weeks in IUFD vs 31.2 weeks in live born, p<0.001) had statistically significant association with IUFD in GDM patients. Both the patients were on Insulin and had poor glycemic control. Both babies were macro somic (birth weight >4000 g). However, we had only 2 cases of IUFD out of 90 patients. Both patients had total score of 4 which has

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statistically significant association (total score 4 in IUFD vs 2.66 in live born, p<0.001). Similar findings are reported in study conducted by Subramanian KK [19]. The positive linear association was found between first trimester BMI (p value 0.006) and birth weight. Increased first trimester BMI was associated with increased birth weight. The fetal abdominal circumference (p value 0.001) also had positive linear

association with birth weight. Increased first trimester

BMI (p value 0.028) and fetal abdominal circumference

(p < 0.001) also significantly associated with Large for

gestational age babies. Similar findings are reported in

other studies [20, 21]. Congenital anomalies most commonly seen in diabetic and GDM patients with their risk ratio are as caudal regression- 252; situs inversus- 84; cardiac anomalies (TGA, VSD, ASD)- 4 and anencephaly- 3 [22]. In current study, 2 out of 90 babies had congenital anomaly. One GDM patient was on insulin for management. Her baby had atrial septal defect. Another baby had ventricular septal defect diagnosed on malformation scan, postdelivery it was confirmed on 2D echocardiography. But no significant statistical association was found between maternal glycemic control and congenital malformation. These results are correlated with the previous studies [23, 24]. 10 out of 90 babies were admitted in NICU. One baby had perinatal asphyxia, one baby was preterm with 1.8 kg birth weight, one baby had respiratory distress and remaining babies were macro somic. The fetal abdominal circumference was significantly associated with the (p-value 0.001). However NICU admission no statistically significant association was found between other laboratory-clinical parameters and NICU admission (p-value > 0.05). These findings are comparable with the study done by Watson D et al [25]. We identified first trimester BMI as a risk factor for preeclampsia in GDM patients (p value 0.003). 11 out of 90 patients (12.1%) developed preeclampsia subsequently in same pregnancy. FBS and PLBS values were higher in GDM patients with preeclampsia than GDM patients without preeclampsia, but it was not statistically significant. Previous studies reported somewhat similar findings [26, 27]. 4 out of 90 patients had preterm delivery. One patient had PPROM at 34 weeks. We did not find any significant association between clinical, laboratory and sonography parameters and preterm delivery. However total score had significant association with the preterm delivery (p value 0.034).

The treatment of GDM includes diet modifications and exercise initially. Nearly 10-20% of GDM patients require pharmacological intervention if target blood sugar level is not achieved through diet and exercise alone [28]. In present study 66.7% patient managed on diet alone, while remaining patients required insulin and/or metformin along with diet. The treatment of GDM reduces serious perinatal morbidity in GDM patients. The relationship between pregnancy BMI, glycemic control, treatment modality and perinatal outcome was investigated by Langer O and colleagues. Obese GDM patient when treated with diet only, had 2-3 times more risk of adverse perinatal outcome [29]. Buchanan TA et al study concluded that fetal ultrasound could guide the insulin therapy in mild GDM patients who are at high risk for macrosomia [30]. Because of these associations, we have assessed total score based on clinical laboratory and sonography parameters in present study. Total score has significant association with fetal outcome (p value <0.001), birth weight and categories (p value <0.001), preterm delivery (p value 0.034) and preeclampsia (p value 0.007). Total score ≥ 4 was significantly associated with adverse perinatal outcome and preeclampsia.

Conclusion

From the results of present study, it can be concluded that maternal glycemic control, the first trimester BMI and fetal abdominal circumference percentile are significantly associated with maternal and fetal outcome in GDM patients. Poor maternal glycemic control can cause adverse perinatal outcome such as IUFD, stillbirth, prolonged NICU care. Pregnancy overweight and obesity in pregnancy are associated with co-occurrences of preeclampsia and GDM. Fetal abdominal circumference percentile can be used to predict LGA and subsequent management. Total score based on clinical-laboratorysonography parameters is also associated with fetal and maternal outcomes. This score may complement to predict perinatal and maternal outcome.

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