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ROLE OF ULTRASOUND AND DOPPLER IN PREDICTING PERINATAL OUTCOME IN PATIENTS WITH IMPAIRED GLUCOSE TOLERANCE OR GESTATIONAL DIABETES MELLITUS.

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ABSTRACT

Aim: The aim of our study was to find the role of ultrasound and Doppler indices in predicting perinatal outcome in patients with impaired glucose tolerance (IGT) or gestational diabetes mellitus (GDM). **Methods and Materials:** The prospective study was conducted on 30 Patients with GDM, 30 controls, and 12 patients with IGT over one year period. Doppler and ultrasound were performed at 28-32 weeks of gestation. Perinatal Outcome was recorded. Statistical analysis was performed by chi-square test, Fishers exact test, ANOVA and other appropriate tests. **Results:** Most patients in IGT group had normal UA–PI. All 72 subjects had normal mean uterine artery–PI. MCA-PI between the groups was not significant. More than 60% of women in GDM group had operative delivery as compared to only 26.7% in controls. 10%, 33% and 40% of women required NICU admission in control, IGT and GDM respectively. This difference was statistically significant **Conclusions:** Women with GDM have adverse pregnancy and neonatal outcome though not significantly different from normal patients if well controlled and under strict medical supervision. Our study concludes Doppler (PI) is not useful in predicting perinatal outcome in GDM.

KEYWORDS: Gestational diabetes, Doppler, Perinatal Outcome, impaired glucose tolerance.

INTRODUCTION

Diabetes mellitus is a chronic disease of great significance in modern times.[1] It is a disease induced and increased by modern sedentary lifestyles and increasing prevalence of obesity in the population.

Asians, especially Indians and Pakistanis have highest risk of GDM.[3] There are very few comprehensive studies on GDM in Indian population. Most of the studies on GDM are done by European or American authors where incidence of GDM is much less and so their observations may not be completely applicable for Indian population. Gestational diabetes mellitus causes increase in perinatal mortality and morbidity.[6] The frequency of adverse perinatal and maternal outcome varies with the degree of metabolic/glycemic control.[10] Most important perinatal concern is excessive fetal growth, which result in birth trauma.[7] Unlike in women with overt diabetes, fetal anomalies are not increased in women with GDM.[8] Similarly the likelihood of fetal death with appropriately treated gestational diabetes has been found to be no different than in the general population.[6]

Ultrasound and Doppler study of umbilical artery(UA) flow velocity waveform is one of the established means of fetal surveillance in high risk pregnancies, but its application in diabetic pregnancies have shown conflicting results.[11]

There are not many comprehensive studies about GDM in Indian population which are at high risk due to their race. In our study we aim to find the role of ultrasound and Doppler indices in predicting perinatal outcome in gestational diabetes patients.

MATERIALS AND METHODS

It was a prospective study conducted in the department of Obstetrics and Gynecology of a 150 bedded tertiary care private teaching hospital over a one year period. Patients were recruited from among women attending antenatal clinic of our hospital. The study was conducted on 30 women with GDM, 30 controls, and 12 women with IGT. The study had the approval of the hospital's ethics committee. All the selected patients were explained about the project and written informed consent was taken from them including Prenatal Diagnostic Techniques (PNDT) (appendix) act' 1994, rules 1996-consent forms G & F.

Selection Criteria

Diagnosis of IGT: 50 gram oral glucose challenge test (OGCT) was performed between 24-28 weeks gestation irrespective of the meal status. Women with plasma glucose>140 mg%, but subsequent normal OGTT are taken in IGT group.

Diagnosis of GDM: Oral glucose tolerance test was performed after an overnight fast following a 250 gram/day (approximately) carbohydrate diet for previous three days. A positive test was defined using Carpenter and Coustan criteria of any two of the following plasma glucose values exceeding the following: Fasting <95mg per 100 ml; one hour <180 mg per 100ml; two hours <155 mg per 100ml; three hours< 140 mg per 100ml.

Exclusion Criteria: Multiple pregnancy, Unexplained bleeding before the time of performing ultrasound, Cervical incompetence, Placenta praevia, Women with known pregestational diabetes mellitus (type I or type II), Known case of preclampsia and IUGR before the time of doing ultrasound and Doppler.

Control: was a woman who was matched for parity and gestation till the time of diagnosis of diabetes (GDM or IGT) was made. They did not have any known medical, surgical or obstetric complication up to the time of doing ultrasound and Doppler. But any complication developing after ultrasound and Doppler was done was taken as part of adverse outcome for that subject.

GE Voluson730 ultrasound and Doppler system was used. It was performed by the same operator in all the three groups after the diagnosis of GDM or IGT was made, between 28 to 32 weeks.

The Study variables in sonograms included the assessment of amniotic fluid index (AFI), Dopplers – uterine artery pulsatility index (UA PI), middle cerebral artery pulsatility index (MCA PI) and mean uterine artery pulsatility index (UTA PI). Pulsed Doppler with color mapping was performed with an Acuson 120 machine using a 3.5 MHz transducer and 125 Hz high pass filter. The transducer was placed on the left and right lower quadrant of the abdominal wall. The external iliac artery was visualized and uterine artery was identified medial to it. Flow velocity waveforms were obtained from each uterine artery near the external iliac artery before division of the uterine artery into branches. From each uterine artery, 3 consecutive waveforms of good quality were obtained. The 3 waveforms were averaged to obtain peak systolic velocity (S) and end diastolic velocity (D). For the measurement of umbilical artery (UA)-PI, the Doppler range-gate was placed over the umbilical artery in a free vertical loop of umbilical cord. For MCA-PI, the Doppler range-gate was placed over the MCA arising from the circle of Willis in a transverse plane of the fetal head. The parameters studied were defined as.

Amniotic fluid index (AFI) - was calculated by adding largest vertical pocket in all four abdominal quadrants. Polyhdramnios= AFI> 24.[46]

Pulsatility Index (PI): $\frac{S-D}{\text{Mean of S and D}}$

Abnormal UA PI as >1.5,[47]

Abnormal MCA PI as<1.5,[47]

Abnormal mean UT Artery PI as >1.45.[47]

A data book was maintained and all the women were followed up in routine antenatal clinic and pregnancy managed according to standard guidelines and any complication developing after the Doppler was done was recorded as adverse outcome. The outcomes were noted till the time of discharge from hospital.

Criteria for adverse outcome were.

SGA: birth weight < 10^{th} centile for their gestational age.[48]

LGA: birth weight > 90^{th} centile for their gestation.[49]

Macrosomia: birth weight > 4 KG.[49]

Prematurity: Period of delivery < 37 weeks.[50]

Postdatism: Period of delivery > 40 weeks.[51]

Metabolic Complications such as Hypoglycemia[52], Neonatal hyperbilirubinemia[53], Low Apgar ≤ 7[54], Respiratory distress syndrome (RDS)[55]

Statistical analysis was performed by chi-square test, Fishers exact test, ANOVA and other appropriate tests. Statistical significance was defined as probability value < 0.05. The performance of the tests in the prediction of subsequent complications was expressed by sensitivity, specificity, positive and negative predictive values, odds ratio and p values.

RESULTS

60% of women with GDM had increased BMI compared to only 16.7% in controls and 41.7% in IGT group. The difference in the BMI between three groups was significant (p value 0.009, chi square test). The Odds ratio of developing GDM during pregnancy for someone who has increased BMI (overweight or obese) was 7.6. The confidence interval for it is very wide ranging from 2.244 to 25.062.

Table 1.

	Controls Median± SD	IGT Median±SD	GDM Median±SD	P value(chi square test)
Age (yrs)	26±2.9	28±3.3	28±4.8	0.004
BMI	22.2±2.2	24.5±3.56	26.41±4.23	0.009
Significant family history of DM	63.3%	50%	66.7%	0.597

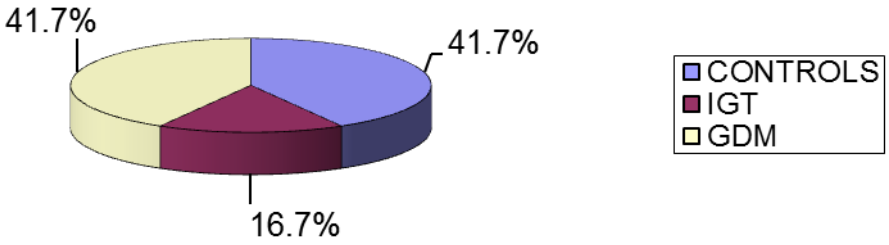

Figure 1.

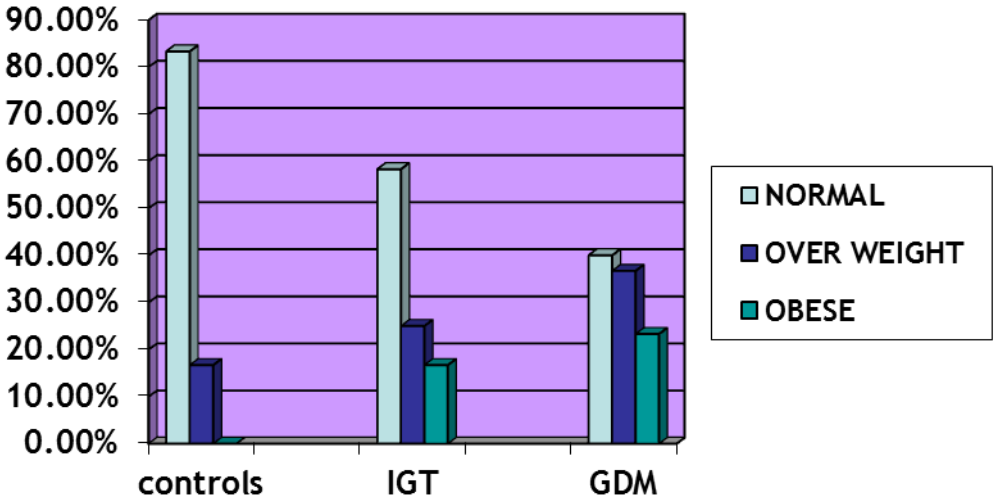

Figure 2.

Table no. 2 shows Median Amniotic Fluid Index (AFI) of all the three groups was within normal range. Only one (3.3%) woman in GDM group had polyhydramnios. Rest had normal AFI. 100% of women in control and IGT group had normal AFI. Median UA-PI of all groups was in normal range. All women, except one subject in IGT group, had normal UA–PI (Not significant, $p<0.05$). The median MCA PI of controls was 1.95±0.40 ranging from 1.0 to 2.66. The median MCA PI of IGT group was 2.00±0.36 ranging from 1.04 to 2.0. The median MCA PI of GDM group was 2.00±0.43 ranging from 0.80 to 2.83. These differences were not statistically significant. One patient (11.1 %) in abnormal MCA-PI group developed PIH and four (44.4%) patients delivered SGA babies. The median of mean uterine artery PI of controls was 0.77±0.24.l. The median of mean uterine artery PI of IGT group was 0.90±0.07. The median of mean uterine artery PI of GDM group was 0.84±0.20.l. All (100%) subjects had normal uterine artery PI. Therefore p value could not be calculated.

Table 2.

	Controls Median, SD	IGT Median, SD	GDM Median, SD	P value (chi square test)
AFI	12.50±2.86	13.00±4.31	15.00±5.86	0.073
UA PI	0.99±0.17	1.02±0.54	1.00±0.19	0.240
MCA PI	1.95±0.40	2.00±0.36	2.00±0.43	0.886
Mean Uterine A PI	0.77±0.24	0.90±0.07	0.84±0.20	0.123

Table no. 3 shows the median and standard deviation of all the perinatal outcome parameters in all the three groups. The median period of gestation at delivery of IGT group and GDM group was respectively 38.00±1.85 and 38.00±1.66. This difference was not statistically significant. Median birth weight of controls, IGT group

and GDM group was respectively 2.99 ± 0.43 Kg (2.36 Kg to 4.2 Kg), 2.79±0.53 (1.87 Kg to 3.72 Kg) and 3.13±0.54 (1.87 Kg to 4.4 Kg). 3.3 % of babies of women with GDM were macrosomic, same as controls. None of the babies in IGT group had macrosomia. This difference was not significant. 3.3% and 10% of babies in control and GDM group respectively were LGA. The difference was not significant (p value 0.409). More than 60% of women in GDM group had operative delivery (caesarean or assisted vaginal) as compared to only 26.7% in controls (figure 3). The CS rate after excluding CS for previous LSCS was 6.7%, 25% and 46.7% in controls, IGT and GDM groups respectively. The difference in caesarean rate was significant between the two groups (p< .007). 12 out of 30 GDM women required NICU admission, compared to three patients in control group. The difference was significant (p value=.026). IUGR/SGA was the commonest reason for NICU admission. Two babies were admitted in view of premature delivery due to APH. One admission of each of meconium aspiration, macrosomia, observation for prolonged leaking per vaginum, and transient tachypnea of new born was present.

Table 3.

	Controls N=30(100%) Median±SD	IGT N=12(100%) Median±SD	GDM N=30(100%) Median±SD	P value (chi square test)
PoG[Wks]at delivery	38.50±1.24	38.00±1.85	38.00±1.66	0.251
Birth weight.,(Kg)	2.99±0.43	2.79±0.53	3.13±0.54	0.409
Birth wt , centiles	30.00±25.33	13.00±25.44	43.50±26.08	0.268
Apgar	9.00±0.76	9.00±0.87	9.00±0.58	0.934
NICU, days	0.00±4.55	0.00±1.95	0.00±2.33	0.993
LSCS rate (%)	18.7%	58.3%	56.7%	.007

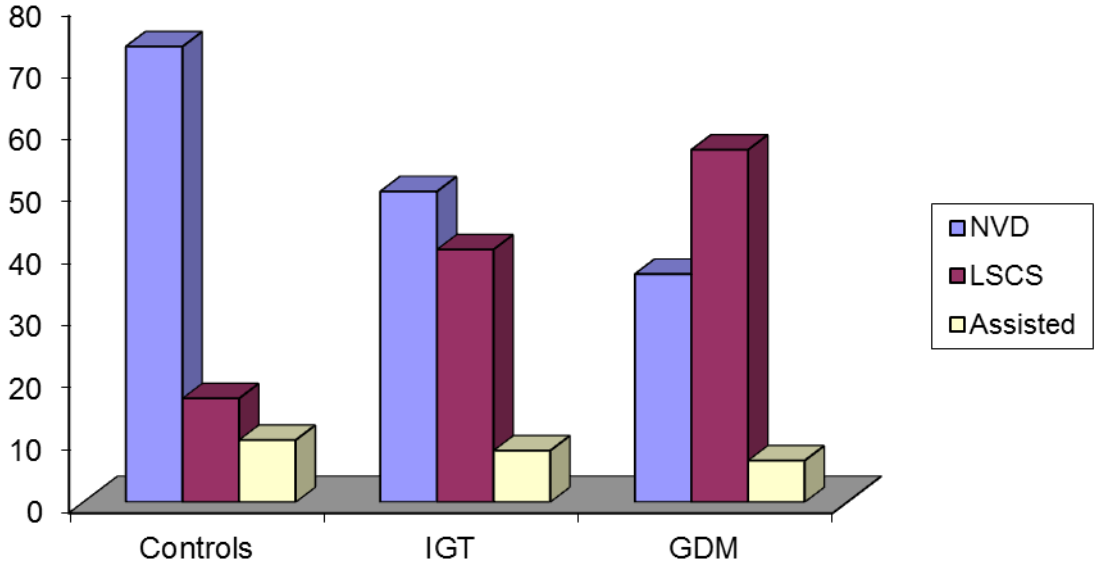

Figure 3.

Table 4 shows that median Apgar was same in all groups. Two babies in GDM group had Apgar score less than 7, one baby in the control and none in IGT group had Apgar less than 7, the difference was insignificant. 1(3.3%) neonates in GDM group developed RDS. Six (20%) of babies in the GDM group developed hyperbilirubinemia, compared to four (13.4%) in controls. four (13.4%) neonates in GDM group developed metabolic complications like hypoglycemia.

Table 4.

	CONTROLS N=30(100%)	IGT N=12(100%)	GDM N=30(100%)
Apgar<7	1	0	2
Hypogylcemia	0	0	4
Hyperbilirubinemia	4	0	6
RDS	0	0	1

SGA	6	4	4
LGA	1	0	3
macrosomia	1	0	1

In our study seven women (23.3 %) required insulin therapy. The median age of this group was 38 years and the median BMI was 35. Family history of diabetes was present in only one woman. Their mean gestation of delivery was 37 weeks. Median birth weight was 3.4 Kg. Two women (28.5 %) developed IUGR whereas three (42.8%) developed preclampsia. Five (71.4%) had caesarean delivery. Three had elective LSCS for previous LSCS and another two underwent emergency LSCS for abnormal fetal heart rate. Median Apgar was 9. Median NICU stay was 2 days. Three neonates (42.8 %) required NICU admission for transient tachypnea of new born, meconium aspiration and intrauterine growth retardation. Only one fetus developed macrosomia. One each had FGR, RDS, and hyperbilirubinemia.

The amniotic fluid index, uterine and umbilical arteries PI were normal in almost 100% of cases, so there predictive value could not be calculated. The accuracy of middle cerebral artery in predicting perinatal outcome is shown in the table no.5. MCA PI had good negative predictive value for FGR (91.7%) and macrosomia (95.8%). It was not useful in predicting the possibility of operative delivery, hyperbilirubinemia or metabolic complications. Its sensitivity and PPV for RDS and metabolic complications was 0%.

Table 5.

	Sensitivity	**Specificity**	**Positive predictive value(PPV)**	**Negative predictive value(NPV)**	**Accuracy**
Operative delivery	10.5%	63.6%	33.3%	29.2%	30%
NICU admission	16.7%	77.8%	33.3%	58.3%	53.4%
Hyperbilirubinemia	16.7%	79.2%	16.7%	79.2%	63.3%
Metabolic complications	0%	76.9%	0%	83.3%	66%
RDS	0%	79.3%	0%	95.8%	76.7%
Macrosomia	50%	82%	16.7%	95.8%	80%
FGR	60%	88%	50%	91.7%	83%

DISCUSSION

Michael D Berkus[55] et al conducted a study in 1993 on 678 women with gestational diabetes. They used National Diabetes Data Group criteria. The mean age of all the groups in this study was comparable to our study. The mean pre-pregnancy weight was 79.3 Kg. 40% of these had BMI greater than 27. In contrast the mean pre-pregnancy weight in our study was 63 Kg and 50% women had BMI more than 27. These differences in BMI and weight can be attributed to racial difference between the subjects in two studies. Michael D Berkus reported that 28.7% of GDM were treated with insulin and 30% of them were poorly controlled. On the other hand in our study 23% subjects were treated by insulin and 20% were poorly controlled. These small differences can be explained by small number of patients in our study. Another study was conducted by Giorgio Mello[29] et al in 1997 on 172 women with impaired glucose tolerance. Their mean age was 31 yrs. 15% of the subjects in their study were obese as compared to 16.7% in our study. They reported significant family history of diabetes in 40% of patients as compared to 50% in our study. Incidence of macrosomia and IUGR was 13.4% and 0.6% respectively. These results are very different from our observations where 33% had IUGR and none had macrosomia. Caesarean rate was 40.66% in our study whereas it was 16.3% in their study. This difference can be attributed to higher percentage of secondary LSCS and higher caesarean rate for IUGR and related complications, in our study.

John L. Kitzmiller[56] et al conducted a detailed analysis of diabetic pregnancies and perinatal morbidity in 1978.The comparisons of their results on GDM patients is given in table no. 6. From this study it is obvious that gestational diabetes in India do not have quite same perinatal outcome as in the study performed by Kitzmiller[56] et al in Boston. The differences in results can be attributed to difference in physical characteristics between Indian and western women. Since Indian women are generally shorter than their western counterparts their babies have lower average birth weights and therefore lesser incidence of macrosomia, and LGA babies. 16.7% of GDM women in our study developed PIH during their antenatal period, which could have affected the maternal and fetal outcome adversely.13.3% of GDM women in our study had spontaneous or induced preterm delivery due to either spontaneous preterm labour, APH, worsening PIH, preterm premature leaking per vaginum, or development of FGR with deranged Dopplers. These are also the reasons for very high caesarean rate in our study as compared to Kitzmiller[56] et al'.

Table no. 6.

Neonatal complications	Kitzmiller et al(n=13)	Gupta et al (n=30)
PIH	0%	16.7%
Polyhdramnios	0%	3.3%
Prematurity	0%	13.3%
CS	29%	56.7%
Birth weight (mean)	3.5 Kg	3.13Kg
SGA<10th centile	0%	13.3%
LGA>90th centile	15%	10%
Macrosomia>4Kg	15%	3.3%
Pulmonary complication	7.5%	3.3%
Hypoglycemia	15%	13.3%
Hypocalcemia	7.5%	6.7%
Hyperbilirubinemia	0%	20%

These studies did not record Doppler parameters so we compared our results with another study performed by Haddad et al[44] in 1992 on 27 patients with GDM. 6 of these were on insulin. Their mean age was 34.3 yrs, which was less than our cohort. None of the patients in the study had IUGR. Incidence of macrosomia was also similar. 42.8 % of patients on insulin had preclampsia in our study, which was much less in Haddad's study (16.6%). Caesarean rate was high in both the studies 83.3% in Haddad et al[44] and 71.4% in our study. Rate of abnormal fetal heart rate was similar in both studies 33% Vs 28% (our) study. Uterine artery Doppler was normal in more than 90% of patients in their study which is comparable. In the same study 21 patients were on diet control. Their mean age was similar to our cohort, 29 yrs. None of these developed IUGR, whereas 25% developed IUGR in our study. Incidence of PIH was more (25%) in their study as compared to ours. There were 5 stilbirths in their study but none in our study. All the pregnancies with abnormal Doppler were complicated by IUGR or preeclampsia, and their number is comparable in two studies.

Another study was conducted by Pietryga and associates[45] on 117 women with GDM on insulin therapy. Similar to our study Pietryga concluded that Doppler ultrasound of uterine and umbilical arteries do not have clinical value for fetal surveillance unless pregnancy is complicated by preclampsia and IUGR.

Leung et al[16] measured UA-PI and MCA–PI in women with GDM. They concluded that UA-PI and MCA–PI was not useful in predicting outcome in GDM women.
All the studies mentioned above have been performed on western women, who differ markedly from Indian women in their racial and physical characteristics. Very few Indian studies have been done to study gestational diabetes and its adverse outcome. One such study was done by Gajjar et al[58] in 2005 in Baroda to study the intrapartum and perinatal outcome of women with gestational diabetes and mild gestational hyperglycemia. The women in this study had similar socioeconomic and demographic characteristics as in our study. There were 342 normal women, 26 with mild gestational hyperglycemia (MGH) and 10 with gestational diabetes mellitus. The incidence of preclampsia was 60% in diabetic patients, 19.23% in group with MGH and 0.29% in control group. Abruption of placenta was seen in 20% of diabetics, 34.61% of MGH women and 2.92% of normal women. These differences were statistically significant. In this study 10% of women with gestational diabetes had IUGR. The results of Gajjar et al and their comparisons with our study are presented in table no. 7. It is possible that these results have not been found in our study given the small sample size.

Table No. 7.

Outcome in GDM	Gajjar et al	Gupta et al
PIH	6.7%	16.7%
IUGR	10%	13.3%
Prematurity	0%	13.3%
NVD	70%	36.7%
Assisted delivery	11.11%	16%
Caesarean (%)	19.44%	56.7%
Birth weight > 3.5 Kg	8.33%	20%
Neonatal Hypoglycemia	5.5%	13.3%
Neonatal Hypocalcemia	0%	6.7%
Neonatal Hyperbilirubinemia	11.11%	20%

Though sample size in our study is small the results reported are conclusive, but needs validation on a larger sample.

CONCLUSIONS

Women with GDM were older and overweight than others. Women with GDM have Normal Doppler parameters unless the pregnancy is complicated by preclampsia or IUGR. Women with GDM have adverse pregnancy and neonatal outcome though not significantly different from normal patients if well controlled and under strict medical supervision. Our study concludes Doppler (PI) is not useful in predicting perinatal outcome in GDM.

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