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Original Research Article

Factors influencing foetal growth in pregnancy complicated by diabetes

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ABSTRACT

Background: Gestational diabetes mellitus represents a metabolically altered fetal environment due to an increased maternal supply of carbohydrates. It leads to fetal hyperinsulinemia and stimulates insulin-sensitive tissue, predominantly of the abdomen, resulting in increased fetal growth and delivering large-for-gestational-age newborns. Implications of fetal hyperinsulinemia reach far beyond delivery. Children of mothers with diabetes in pregnancy are predisposed to develop obesity and glucose intolerance through a non-genetic “fuel-mediated” mechanism. The objective of the present study was to study the “fetal growth pattern at different periods of pregnancy complicated by diabetes” and to identify the factors that influence the fetal growth pattern in pregnancy complicated by diabetes

Methods: 69 pregnant women with diabetes and 34 pregnant women without diabetes were included in the study by random sampling. Maternal parameters such as age, parity, height, weight at registration, and weight gain during pregnancy, BMI at the time of registration of pregnancy and at the time of delivery, detailed diabetic profile and management including meal plan, insulin administration and dosage were recorded. The fetuses were monitored for Biparietal diameter, abdomen circumference, femur length by 2 ultrasound examinations, one at 18-22 weeks and another at 28-32 weeks were performed. Soon after delivery, sex, gestational age, birth weight, length, head circumference and chest circumference of the newborn were recorded and infants were classified as LGA/SGA/AGA.

Results: Maternal age, parity, BMI at the time of delivery and maternal weight gain had significant influence on the birth weight. The abdominal circumference of the fetus detected at 18-20 and 28-32 ultrasound scans had a very significant correlation with neonatal mean birth weight percentile.

Conclusions: Not all babies born to diabetic mothers are macrosomic. SGA babies were not uncommon in pregnancies with diabetes especially in those who did not have significant micro vasculopathy. Maternal nutrition plays a significant key role in determining birth weight of babies even in pregnancies complicated by diabetes.

Keywords: Birth weight, Diabetes, Pregnancy

INTRODUCTION

Diabetes has become a global pandemic because of aging population, sedentary life style, urbanization, and increasing incidence of obesity. Prevalence of diabetes is rising in epidemic proportion in developing countries such as India and China and more women of childbearing age are at increased risk of diabetes during pregnancy. A high prevalence of gestational diabetes mellitus (GDM) of the order of 18% has been reported from India.[1] Women with GDM are at high risk for developing diabetes later in life. Thus, GDM provides a unique opportunity to study the early pathogenesis of diabetes and to develop interventions to prevent the disease. Abnormal metabolic milieu due to hyperglycemia has a profound impact on maternal and fetal outcome. Indians belong to higher risk for developing diabetes due to their ethnicity.[2]

METHODS

A case-control study with 69 pregnant women with diabetes and 34 pregnant women without diabetes attending the Institute of Obstetrics and Gynecology, Chennai, were included in the study over a period from January 2011 to October 2011. Random sampling method was utilized for the selection of cases as well as for controls included for study. Pregnant women who showed documented evidence of glucose intolerance or those who had diabetes prior to pregnancy were included. Mothers with infections at early pregnancy, hypertension, and medical problems like cardiac, autoimmune disorders, presence of identified fetal anomalies by ultrasonography and multiple gestation were excluded from the study.

Maternal parameters that were assessed include age, parity, height, weight at registration, and weight gain during pregnancy measured by recording weight at delivery and BMI at the time of registration of pregnancy and at the time of delivery. A detailed diabetic profile and management including meal plan, the insulin administration and dosage were recorded. The fetuses were monitored for biparietal diameter, abdomen circumference, femur length by 2 ultrasound examinations, one at 18-22 weeks and another at 28-32 weeks were performed. Soon after delivery, sex, gestational age, birth weight, length, head circumference and chest circumference of the newborn were recorded and infants were classified as LGA/SGA/AGA.

Descriptive statistics (frequency tables, mean and standard deviation), graphical analysis, correlation analysis, analysis of variance (ANOVA) were utilized to analyze the results.

RESULTS

The incidence of diabetes in pregnancy has been steadily increasing in the last decade. In our institute, the number of diabetes complicating pregnancy was 208 cases during the period in which this study was conducted. Macrosomia is defined as fetal weight greater than 4 kg or birth weight above the 90th percentile for gestational age. However, in our institute the average birth weight of term babies born to women who had diabetes complicating pregnancy without any other co-morbid features was 3.1 kg. This study was done to identify the factors that determine the fetal growth and their pattern of growth in diabetic pregnancies.

Table 1: Maternal age and foetal growth pattern.

Age in years	No Of Cases		Mean USG-1 in Percentiles			Mean USG-2 in Percentiles			Birth Weight Centiles (SD)	'p' value	Length Centiles	HC Centiles	CC Centiles
	N	%	BPD	AC	FL	BPD	AC	FL					
Foetal growth pattern in pregnancies with diabetes													
<25	29	42%	52.14	41.72	58.62	48.21	41.72	60.59	35.76 (23.88)	<0.05	34.28	35.59	75.62
25-29	23	33%	62.00	57.48	68.09	50.96	57.48	66.26	50.96 (33.90)		51.65	44.78	83.15
>30	17	25%	71.82	63.24	71.35	57.65	63.24	65.53	54.53 (25.09)		46.76	52.59	85.74
Total	69	100%	60.28	52.28	64.91	51.45	52.28	63.70	45.45		43.14	42.84	80.62
Foetal growth pattern in pregnancies without diabetes													
< 25	16	47%	54.69	54.56	59.69	51.56	48.69	59.63	46.63	>0.05	37.19	36.25	74.22
25-29	12	35%	53.83	52.42	56.58	45.83	55.75	58.17	45.75		47.33	35.33	69.25
>30	6	18%	55.17	37.67	51.50	46.17	31.17	51.67	29.83		29.17	18.17	58.50
Total	34	100%	54.69	54.56	59.69	51.56	48.69	59.63	43.35		39.35	32.74	69.69

Of the 69 cases of pregnancies with diabetes and 34 control cases, we found that the mean birth weight percentile in diabetes complicating pregnancy was at higher level (45.45) than the mean birth weight percentile in normal pregnancies (43.35).

In diabetic pregnancies as the maternal age increased, the neonates' birth weight percentile also increased and was found to be statistically significant. The baby length percentile increased from 34.28 to 51.65 and then decreased to 46.76. The head circumference centile also increased from 35.59 to 34.78 and then to 52.59. The chest circumference centile increased from 75.62 to 83.15 and then to 85.74 (Table 1).

In diabetic pregnancy as the maternal parity increases from primi to para 2 and then to para3 and more, the neonatal birth weight percentile first increases from 37.14 to 55.87 and then decreases to 43.5. The length centile increases from 35.55 to 52.63 and then decreases to 36.5. The head circumference centile increases from 35.88 to 51.93 and decreases to 35.75. The chest circumference percentile increases from 75.77 to 86.2 and then decreases to 77.58 (Table 2).

Table 2: Maternal parity and foetal growth pattern.

Parity	No. of Cases		Mean USG-1 in percentiles			Mean USG-2 in percentiles			Birth weight centiles (SD)	'p' value	Length centiles	HC centiles	CC centiles
Foetal growth pattern in pregnancies with diabetes													
	N	%	BPD	AC	FL	BPD	AC	FL					
Primi	37	39%	57.04	51.78	57.67	50.63	49.11	56.59	34.74 (23.09)		35.55	35.88	75.77
Para 2	30	43%	63.47	53.3	71.3	53.03	61.9	71.07	55.87 (28.57)	<0.05	52.63	51.93	86.2
Para 3 and more	12	17%	59.58	50.83	65.25	49.33	50.25	61.25	43.5 (33.29)		36.5	35.75	77.58
Foetal growth pattern in pregnancies without diabetes													
Primi	7	21	53.29	45.29	52.29	43.86	38.71	57.29	38.29		45.71	27.57	63.57
Para-2	18	24	49.5	51.25	61.5	44.63	47	54.63	41.38	> 0.05	38.13	31.38	71.63
Para-3 and more	19	56	57	52.68	57.11	52	52	59.16	46.05		37.53	35.21	71.13

Table 3: BMI at delivery and foetal growth pattern.

BMI	No. of cases		Mean USG-1 in percentiles			Mean USG-2 in percentiles			Birth weight centiles (SD)	'p' value	Length centiles	HC centiles	CC centiles
Foetal growth pattern in pregnancies with diabetes													
	N	%	BPD	AC	FL	BPD	AC	FL					
18-23	12	17%	45.83	52.5	59.92	48.33	48.08	55.92	30.5 (25.27)		44.42	32.42	75
23-25	10	14%	42.5	46.6	59.6	39.8	45.1	52.8	34.2 (26.51)	<0.05	24.2	30.3	71.45
>25	47	68%	56	65.17	67.32	59.74	53.66	68	51.66 (28.37)		46.85	48.17	84.01
Total	69	100%	52.28	60.28	64.91	54.87	51.45	63.7	45.45		43.14	42.84	80.62
Foetal growth pattern in pregnancies without diabetes													
18-23	8	24%	40	56.25	54.63	36.75	50.75	57	29.88		30.63	21.75	61.63
23-25	9	26%	51.89	51.44	61.89	53.56	48.11	58.67	46.22	>0.05	44.78	36.22	71.89
>25	17	50%	55.35	55.24	55.82	50.53	47.82	57.53	48.18		40.59	36.06	72.32
Total	34	100%	50.82	54.47	57.15	48.09	48.59	57.71	43.35		39.35	32.74	69.69

In diabetic pregnancy as the maternal BMI at the time of delivery increases from 18-23 to 23-25 and then >25 the neonatal birth weight percentile increases from 30.5 to 34.2 and then to 51.6.

The length percentile decreases from 44.42 to 24.2 and then increases to 46.85. The head circumference centile decreases from 32.42 to 30.3 and then increases to 48.7. The chest circumference percentile first decreases from 75 to 71.45 and then increases to 84.01 (Table 3).

In diabetic pregnancy as the maternal weight gain increases from <8 to 8-10 and then >10 kg the neonatal birth weight percentile increases from 30.79 to 48.96 and then to 69.46. The length percentile increases from 34.46 to 47.14 and then to 53.23.

The head circumference centile increases from 35.36 to 45.93 and then to 52.31. The chest circumference percentile first decreases from 78.04 to 80.88 and then increases to 85.65 (Table 4).

Table 4: Maternal weight gain and foetal growth pattern.

Weight gain	No. of Cases		Mean USG-1 in percentiles			Mean USG-2 in percentiles			Birth weight centiles (SD)	'p' value	Length centiles	HC centiles	CC centiles
	N	%	BPD	AC	FL	BPD	AC	FL					
Fetal growth pattern in pregnancies with diabetes													
<8	28	41%	61	46.71	64.93	51.07	45.04	60.96	30.79 (22.39)	<0.05	34.46	35.36	78.04
8-10	28	41%	58.96	54.43	61.86	51.61	59.04	61.86	48.96 (29.22)		47.14	45.93	80.88
>10	13	13%	61.54	59.62	71.46	51.92	67.08	73.54	69.46 (21.76)		53.23	52.31	85.65
Fetal growth pattern in pregnancies without diabetes													
<8	11	32%	56.09	35.09	57.45	45.09	26.18	58.36	22.64	>0.05	24.55	19.55	59.55
8-10	15	44%	55.4	56.93	57.93	49.2	61.13	59	55.4		49.2	40.07	75.87
>10	8	24%	50.5	61	55.25	52.25	53.75	54.38	49.25		41.25	37.13	72.06

Table 5: Correlation analysis of different variables on birth weight.

Variables	Birth weight
US-AC (28-32)	0.821492277
US-AC (18-22)	0.73176747
US-FL (28-32)	0.583087365
US-FL (18-22)	0.534692679
US-BPD (28-32)	0.510999092
Pregnancy weight gain	0.507282751
US-BPD (18-22)	0.467418719
BMI	0.379731079

Among the parameters, which gave an indication of the fetal growth pattern, it was the abdominal circumference of the fetus detected at 18-20 and 28-32 ultrasound scans, which had a very significant correlation with neonatal mean birth weight percentile (Figure 1).

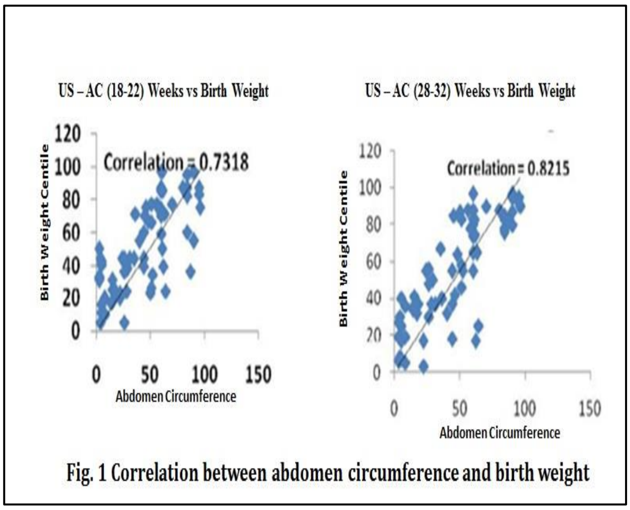

Figure 1: Correlation between abdomen circumference and birth weight.

The fetus showed an asymmetrical growth pattern with decrease in the mean biparietal diameter, which was not observed in the mean abdominal circumference and mean femur length percentiles (Table 5).

DISCUSSION

In this study, we evaluated the fetal growth pattern and the factors that determine the fetal growth in 69 cases of diabetes complicating pregnancy and 34 control cases. We found that the mean birth weight centile of neonates born to diabetes complicating pregnancy was 45.5 percentile, which is 1.5 SD more than control cases (P value 0.2355). Most of the people who avail our institute's medical facilities belong to lower middle and lower socio-economic status; there could be factors apart from maternal glycemic levels, which could have influenced fetal growth pattern and their birth weight. The age of the women at the time of conception had a role in determining the neonates' birth weight. Mothers who were <25 years of age delivered babies with a mean birth weight centile of 35.73. As age advanced, the mean birth weight centile showed higher values (P<.05). As the parity of the women increased from primi to para 2 and more, the mean birth weight centile increased (P<.05).

The maternal pre-pregnancy BMI and the pregnancy BMI had a definite positive influence on the neonates' birth weight. Study by Schaefer-Graf et al found that abdominal circumference at third trimester and postprandial glucose values were related to BMI at birth and that if the parental BMI was more, then the BMI of the neonate at birth was also above the average.[3] In the present study, as the BMI at the time of registration increased from <18 to >25 the mean birth weight percentile of the neonate also increased. Similarly, when the BMI at the time of delivery increased from 18-23 to >25 the mean birth weight percentile also increased (P<0.05). Lao TT et al also suggested that some of the complications attributed to gestational diabetes mellitus were probably related to maternal weight excess/obesity.[4]

The weight gain of the women during pregnancy had an impact on the neonatal birth weight percentile. When weight gain was less than 8 kg the mean birth weight percentile was 30.75 which increased to 48.96 (when weight gain was 8-10 kg) and to 69.46 when the weight gain was more than 10 kg suggesting a significant factor in determining the fetal growth pattern with a P value of <.05. Similarly Sacks DA et al concluded in their study that both maternal glycemia and maternal weight gain are modifiable factors associated with increased birth weight in women who have diabetes.[5]

Raychaudhuri K et al concluded that if strict blood glucose control was maintained during first and second trimesters, it reduces the incidence of LGA infants.[6] In the present study the women who were on dietary management for diabetes had a mean birth weight percentile of 45.89 compared to 45.28 noted in women who were managed with insulin with P >0.05.

Nevertheless, the insulin requirement during diabetes had an influence in the birth weight percentile; it was 42.7 when the insulin requirement was less than 10 units and it increased to 51.88 when the insulin requirement increased to more than 20 units. Schaefer-Graf UM et al found that in the late second and early third trimester, maternal BMI and LGA in a previous pregnancy, had the strongest influence on fetal growth, while later in the third trimester coincident with the period of maximum growth described in diabetic pregnancies, maternal glycaemia was the significant factor.[7]

Mulder EJ et al, suggested acceleration of abdominal circumference, commencing before or after 25 weeks' gestation, was associated with the birth of a heavy or large-for-dates baby in 94 and 56% of cases.[8] In the present study, ultrasound was done at 18-22 weeks and another at 28-32 weeks. The fetal abdominal circumference recorded at 18-22 weeks had a correlation value with neonatal birth weight of $r = 0.73$ which increased to $r = 0.82$ (fetal abdominal circumference recorded at 28-32 weeks), showing a strong correlation between fetal abdomen circumference and birth weight. The fetal biparietal diameter during the same period showed a correlation of $r = 0.46$ and $r = 0.51$ with neonatal birth weight.

The mean biparietal diameter recorded at 28-32 weeks decreased from its previous value recorded at 18-22 weeks, but such a decrease was not observed in the mean abdominal circumference percentiles and mean femur length percentiles, thus suggesting an asymmetrical growth pattern.

Nasrat H, et al also suggested a disproportionate pattern of growth in fetuses of diabetic mothers, with increased tendency for deposition of subcutaneous fat.[9] Studies have shown that macrosomia occurred in approximately 88% of fetuses in whom the abdominal circumference and estimated fetal weight both exceed the 90th percentile. The biparietal diameter and head circumference appear to be less predictive of macrosomia.

CONCLUSION

As the age of the pregnant women with diabetes increased, the mean birth weight percentile also increased. The mean birth weight percentile also increased as the parity of the pregnant women with diabetes increases.

Maternal weight gain during pregnancy had a significant effect on the mean birth weight percentile with increasing maternal weight gain there was a raise in neonatal birth weight percentile. The pregnancy BMI (after the weight gain during pregnancy) and the pre-pregnancy BMI were definite factors in determining the neonatal birth weight, with the former having a much significant role. The mean birth weight percentile of the neonate increased as the maternal insulin requirement increased.

Not all babies born to diabetic mothers are macrosomic. SGA babies were not uncommon in pregnancies with diabetes especially in those who did not have significant microvasculopathy. Maternal nutrition plays a significant key role in determining birth weight of babies even in pregnancies complicated by diabetes.

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