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RESEARCH ARTICLE

STUDY OF FETAL OUTCOME IN RELATION TO HbA1C VALUES IN 3rd TRIMESTER DIABETIC WOMEN

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ABSTRACT

Background: The usefulness of single value of HbAlc during last trimester in pregnancies complicated by gestational diabetes in predicting perinatal outcome. The aim of the study was to anticipate and manage the difficult labor due to macrosomia and to monitor these high risk newborns closely for hypoglycemia thereby preventing the neonatal morbidity and mortality. **Methods:** A Prospective observational study of 80 mothers was done for a period of three years from 2015 to 2017 in Department of Obstetrics and Gynaecology, Rajah Muthiah Medical college and hospital, Annamalai University Chidambaram. HbAlc level was estimated as one time blood test in the last trimester of pregnancy. At delivery anthropometric measurements of the baby were recorded. Any difficult or non-progression of labor and ceaserian section details, NICU admission,TTN, still birth, babies going for sepsis, congenital defects,other blood parameters like hypoglycaemia, hyperbilirubinemia, polycythemia were recorded. **Results:** HbAlc <6.5% is defined as normal and HbAlc > 6.5% as abnormal. In Present study mothers with abnormal HbAlc levels had two macrosomic babies ,four babies with hypoglycaemia, four babies with TTN, one baby with hyperbilirubinemia, Admission to Neonatal unit was required in 7.5%. **Conclusion:** Maternal morbidity**,** perinatal morbidity and mortality are increased in women with gestational diabetes mellitus**.** An abnormal HbAlc in third trimester in pregnancies complicated by diabetes can predict these adverse perinatal outcome, since glycemic control in third trimester determines the perinatal outcome.

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INTRODUCTION

Gestational diabetes mellitus appears as glucose intolerance, which begins or is first detected during pregnancy.(1,2) Diabetogenic effect of pregnancy is thought to play a role in the development of gestational diabetes mellitus where Human Placental Lactogenic hormone (HPL) secreted from placenta results in insulin desensitization leading to physiological increases in blood glucose levels, particularly during the 2nd and 3rd trimesters.(3) Also increase in the circulating levels of growth hormone, cortisone, estrogen and progesterone is considered to play a contributing role for the insulin resistance.(4,5)

Gestational diabetes mellitus is especially common during the last three months of pregnancy. Gestational diabetes mellitus is associated with an increased risk of complications for both the mother and the baby during pregnancy and birth. It has been further seen that increasing levels of plasma glucose are associated with birth weight above the 90th percentile, and the cornerstone of the management of gestational diabetes mellitus cases is glycemic control. An antepartum control of sugars is found to provide good peripartum control for the reduction of neonatal complications. Studies therefore, indicate that an appropriate management of gestational diabetes mellitus can improve both maternal and perinatal outcomes.

My study encomprises of interpreting HbAlc level in last trimester of pregnancies with GDM in predicting perinatal outcome. In a study by Mikkelsen MR *et al*, women with GDM not obtaining HbA1c within the normal range before delivery had a threefold increased risk of having an LGA infant and a sixfold increased risk of neonatal hypoglycaemia.(6) Arumugam *et al* had shown in his study as HbA1c level in late pregnancy is a good predictor for hypoglycaemia in the newborn.(7) Kline GA *et al*, in his study said that a third trimester HbA1c >6.5% had a stronger association with NICU admission and I.V. glucose requirement.(8)

Similarly a study by Taylor R concluded that neonatal hypoglycemia correlates with maternal hyperglycemia in labor, not with HbA1c during pregnancy.(9) Rackham O *et al* says HbA1c estimation provides evidence that hyperglycemia

not only causes fetal macrosomia but also an angiopathy affectingthe utero-placentalblood vessels and consequent fetal hypoxia.(1,10)

The aim of the study was to find the relationship of HbA1c level in the last trimester to fetal macrosomia and hypoglycemia occurring after birth and other perinatal outcome.

This study is done to identify the high risk mothers with one time blood estimation of HbA1c level in predicting the neonatal complications. The aim of the study was to identify difficult labor due to macrosomia and to monitor these high risk newborns closely for hypoglycemia and other perinatal outcome thereby preventing the neonatal morbidity.

METHODS

A prospective observational study was done for a period of three years from 2015 to 2017 in Department of Obstetrics and Gynaecology, Rajah Muthiah Medical College and Hospital, Annamalai University Chidambaram. Total of 80 patients were enrolled in this study as per inclusion criteria. Written and informed consent was obtained from the patients before participations into the study. Study group comprised of 40 number of cases with GDM, control group comprised of 40 number of normal antenatal women. All antenatal women included in the study was being taken from labour ward, outpatient department, antenatal wards. ***Inclusion Criteria:*** Antenatal women of age group 19 to 36yrs with gestational diabetes mellitus. ***Exclusion Criteria:*** Patients with other medical disorders like hypertension, bronchial asthma, epilepsy, thyroid. 2. Patients with twin pregnancy.

HbAlc level was estimated as one time blood test in the last trimester. Blood sample for HbAlc was taken in tubes containing EDTA. HbAlc levels were measured by the fully automated haemoglobin testing system which uses reversed phase cation exchange high performance liquid chromatography (HPLC) method. HbAlc was expressed as a percentage of total haemoglobin. HbAlc level below 6.5% was taken as normal and 6.5% and above as abnormal.(11)

At delivery anthropometric measurements of the baby were recorded for all babies.(12) Any difficult labor, non-progression of labor and caesarian section details NICU admission, TTN, still birth, babies going for sepsis, congenital defects, other blood parameters like hypoglycaemia, hyperbilirubinemia, polycythemia were recorded. Macrosomia is defined as birth weight more than 90th percentile for the gestational age.

Glucose levels of the neonates were checked for hypoglycemia as per National Neonatology forum protocol.(13) Glucose estimation is done by glucose oxidase (calorimetric) method. Neonatal hypoglycemia is defined as blood glucose levels less than 40 mg/dl at 3 hours of life based on National Neonatology Forum (NNF) guideline.(13)

RESULTS

A total of 80 mothers were included in the study with a minimum age of 18 years and maximum of 39 years. The mean age of the mothers included in the study was 29 years (Table-1)

Majority of them in both study group and control group were primi gravida. Primi gravid mothers were 57.5% in control group and 50% in study group. Gravid 2 was of 17.5% in control group and 22.5% in study group another 25% were gravid 3 and above in control group and 27.5% in the study group. (Table-1)

Table 1 Distribution of Maternal Factors

Variables	Sub-Variables	Control Group		Study Group	
		N	%	N	%
Age (in years)	18-24 yrs	14	35.0	5	12.5
	25-29 yrs	19	47.5	26	65.0
	30-34 yrs	6	15.0	5	12.5
	35-39 yrs	1	2.5	4	10.0
Obstetric index	Primi	23	57.5	20	50.0
	Gravida (G2)	7	17.5	9	22.5
	G3 & above	10	25.0	11	27.5
Gestational age	<37	3	7.5	6	15.0
	37-40	30	75.0	33	82.5
	>40	7	17.5	1	2.5
Body Mass Index	Mild (19-24)	27	67.5	22	55.0
	Moderate (25-29)	13	32.5	16	40.0
	Obesity (30-39)	0	0.0	2	5.0

In this study control group had 75% of cases in the gestational age 37 to 40 weeks, whereas study group had 82.5 %.The control group had 7% of cases with gestational age more than 40 weeks were as study group was not allowed for postdatism. (Table-1)

Glycated hemoglobin was evaluated in the third trimester and 6.5% was taken as upper limit of normal and above as abnormal. Normal values (<6.5%) were found in 18.8% of the mothers and 81.2% had abnormal values.

Table 2 Analysis between HbAlc and Birth Weight

Birth weight	Study HbAlC		Total	P value
	<6.5	>6.5		
<2.5	3	0	3	0.742
2.51-2.999	16	4	20	
3.0-3.499	8	3	11	
3.5-4.0	3	1	4	
>4.0	1	1	2	
Total	31	9	40	

In the study group minimum birth weight recorded was 2522 grams and maximum weight was 4490 grams. The lowest gestational age at birth was 259 days (37 weeks) and highest was 280 days (40 weeks). Control group had 4 babies of birth weight more than 3.5 kg were as study group had 4 babies between 3.5 to 4 kg and 2 babies more than 4 kg. (Table-2)

Table 3 Analysis between HbAlc and mode of delivery

MOD	Control HbAlc		Study HbAlc		P value
	<6.5	>6.5	<6.5	>6.5	
Normal	10	0	4	0	0.256
LSCS	30	0	27	9	

10 babies were delivered by normal vaginal delivery in control group, 4 babies in study group. 30 cases were taken up for caesarean section in control group, 27 cases in study group. 2 cases of macrosomia was seen in babies delivered by LSCS in study group. (Table-3)

Table 4 Analysis between HbAlc and NICU care

NICU	Control HbAlc		Study HbAlc		P value
	<6.5	>6.5	<6.5	>6.5	
Observation	36	0	30	7	0.057
Admission	4	0	1	2	

Control group had 36 babies under NICU observation, 4 babies in admission. where as study group had 37 babies in NICU observation, 3 under admission. These babies were checked for

hypoglycemia as per National Neonatology forum protocol.(13)

Table 5 Analysis between HbAlc and APGAR score

APGAR score (mean)	Control HbAlc		Study HbAlc		P value
	<6.5	>6.5	<6.5	>6.5	
1 min	5.92	0	5.9677	5.1111	0.029
5 min	7.62	0	7.7742	7.2222	0.080

Mean APGAR score in control group was 5.9 at 1 minute and 7.6 at 5 minutes. The study group had mean APGAR of 5.1 at 1 minute and 7.2 at 5 minutes. (Table 5)

Table 6 Analysis between HbAlc and perinatal morbidity

	Control HbAlc		Study HbAlc	
	<6.5	>6.5	<6.5	>6.5
Neonatal hypoglycemia	0	0	0	4
Transient tachypnoea of new born	2	0	1	3
Macrosomia	0	0	0	2
Neonatal hyperbilirubinemia	0	0	0	1
Still birth	0	0	0	0
Intracranial hemorrhage	0	0	0	0
Erb's palsy	0	0	0	0
Polycythemia	0	0	0	- 0
Meningomylocele	0	0	0	1
Meconium stained liquor	3	0	2	4

In present study 4 babies of our subjects developed hypoglycemia. All 4 babies who had hypoglycemia had mothers with abnormal HbA1c more than 6.5%.

In our study Transient Tachypnoea of new born was seen in 4 babies.1 baby had Hyperbilirubinemia, Sepsis in 2 babies, macrosomia in 2 babies. Congenital anomaly (meningomyelocele) in 1 baby. (Table 6)

DISCUSSION

Proper screening, diagnosis and management of diabetes in pregnancy can reduce both maternal and neonatal morbidity. Diabetes and pregnancy may mutually affect each other over a range of interaction from conception to delivery.

The highest incidence of GDM was found in the age group 25-29 years. There were more number (50%) of GDM cases in primi gravida in study group Moderate obesity were 40% in study group and 32.5% in control group. There were two obese patients in study group.

In this study rate of caesarean section in uncontrolled HbAlc group was 9% which is lower than the study done by Shikdar K *et al* (14), Ivy R *et al* (15). Mode of delivery was of no significance in the outcome of this study. HAPO study does suggest that abnormal glycaemic control resulted in primary cesarean section. No significant association was found that abnormal HbAlc resulted in cesarean section probably because of quantum of patients studied as HAPO was done on very large number of patients. (16)

The incidence of macrosomia was significantly high in uncontrolled HbAlc group which is equivalent to study done by Beard R *et al*.(17)

Mean APGAR score in control group was 5.9 at 1 minute and 7.6 at 5 minutes. The study group had mean APGAR of 5.1 at 1 minute and 7.2 at 5 minutes. The p value was statistically significant at $p < 0.02$, 0.08 respectively at 1 min and 5 minutes. In present study 4 babies of our subjects developed hypoglycemia. All 4 babies who had hypoglycemia had mothers with abnormal HbA1c more than 6.5%. Arumugam *et al* had shown in his study as HbA1c level in late pregnancy is a good predictor for hypoglycaemia in the newborn.(7) The study has also shown a significant correlation of HbA1C with neonatal hypoglycemia.

Study by Deborn L Conway shows an incidence of 2-5% (18). Hold M *et al* gestational diabetes mellitus is linked to several maternal, fetal, neonatal complications. (19) In our study Transient Tachypnoea of new born was seen in 4 babies.1 baby had Hyperbilirubinemia, Sepsis in 2 babies, macrosomia in 2 babies. Congenital anomaly (meningomyelocele) in 1 baby.

Holland brews reported incidence of congenital anomaly to be about 1-2% in gestational diabetes mellitus.(20) In well controlled patients perinatal loss was zero. Perinatal mortality occurred more in uncontrolled or poorly controlled diabetes. Still births are usually due to poor controlled, untreated cases or when there is previous history of IUD or presence of PIH

CONCLUSION

HbAlc has to be monitored from first trimester and should be matched with intrauterine growth charts, a single value of HbAlc in third trimester has shown to be a good predictor of neonatal hypoglycaemia and macrosomia. As we have many un-registered antenatal cases coming to our hospital in the last trimester without any regular monitoring of HbA1c level and as a measure of cost effectiveness in a developing country like India, the single one time estimation of HbA1c level in last trimester will be helpful in predicting fetal macrosomia and this can help the obstetrician to anticipate a difficult labour. More over as it was found out in this study atleast one value of HbAlc in the last trimester can predict fetal hypoglycaemia and help pediatricians in monitoring the baby for hypoglycaemia.

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