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Original Research Article

HbA1c level in last trimester pregnancy in predicting macrosomia and hypoglycemia in neonate

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ABSTRACT

Background: The usefulness of single value of HbAlc during last trimester in pregnancies complicated by diabetes either pre-existing or gestational diabetes in predicting macrosomia and neonatal hypoglycemia is investigated. 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.
Methods: A Prospective observational study of 96 mothers was done for a period of one year from June 2012 to September 2013 in a tertiary care centre. HbAlc level was estimated as one time blood test in the last trimester of pregnancy. At delivery anthropometric measurements of the baby were recorded and an intra-uterine growth chart was used to check whether the baby is macrosomic or not. Any difficult or non-progression of labor and ceaserian section details are recorded. Macrosomia is birth weight more than 90th percentile for the gestational age. Hypoglycemia occurs when blood sugar level found to be <40 mg/dl at 3 hours of life. Chi square test is used to see the correlation between HbAlC and macrosomia and hypoglycemia.
Results: 20 babies had macrosomia and 22.9% of them had hypoglycemia. HbAlc <5.7 is defined as normal and HbAlc > 5.7% as abnormal. Mothers with abnormal HbAlc levels had a statistically significant correlation (P <0.001) to occurrence of Macrosomia and hypoglycemia in babies.
Conclusions: An abnormal HbAlc in third trimester in pregnancies complicated by diabetes can predict Macrosomia and hypoglycemia in the neonates.

Keywords: HbA1c level, Hypoglycemia, Macrosomia, Pregnancy

INTRODUCTION

The interpretation of HbAlc level in last trimester of pregnancies with pre-existing DM or GDM in predicting Macrosomia and neonatal hypoglycemia is investigated in various studies. There are only a very few studies showing the usefulness of a single estimation of HbA1c level in last trimester in predicting occurrence of the macrosomia or hypoglycemia in newborns.

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.[1] Arumugam et al had shown in his study as HbA1c level in late pregnancy is a good predictor for hypoglycaemia in the newborn.[2] However Brenner W et al said in his study that maternal HbA1c is not a useful test in the prediction of birth weight and is therefore cannot be used to improve the accuracy of sonographic EFW.[3] 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.[4]

Similarly a study by Taylor R concluded that neonatal hypoglycemia correlates with maternal hyperglycemia in

labor, not with HbA1c during pregnancy. Macrosomia does not correlate with HbA1c during pregnancy.[5] It is still in controversy as some studies have shown no relation of hba1c with macrosomia. Rackham O et al says HbA1c estimation provides evidence that hyperglycemia not only causes fetal macrosomia but also an angiopathy affecting the utero-placental blood vessels and consequent fetal hypoxia.[1,6]

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.

In a developing country like India where the expenditures of serial monitoring of HbA1c is often not possible for various reasons like the cost constraints in frequent monitoring of sugar levels during the antenatal period which is a huge burden on the community and lack of periodical follow up of un-booked cases.

This study is done to identify the high risk mothers with onetime 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 thereby preventing the neonatal morbidity.

METHODS

A prospective observational study was done for a period of one year from June 2012 to September 2013 in a tertiary care centre. All pregnant women with either pre-existing or gestational diabetes, attending out-patient department were included in the study. A total of 96 pregnant mothers were included in the study. Mothers having pregnancy induced hypertension, multiple pregnancies, fetal anomalies, pre-term labor, post-term labor and those babies who were small for gestational age were excluded from the study.

The study was approved by institutional ethical committee. Informed consent was obtained from all the pregnant mothers. With existing data and hospital statistics 'n' was computed to be n = 92. The mothers included in the study were either on insulin therapy or oral hypoglycemic agents or on meal plan. All the mothers either with pre-existing diabetes or GDM were tested for their glycaemic status.

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 5.7% was taken as normal and 5.7% and above as abnormal.[7]

At delivery anthropometric measurements of the baby were recorded for all babies and an intra-uterine growth chart was used to check whether the baby is macrosomic or not.[11] Any difficult labor, non-progression of labor and caesarian section details 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.[9] 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.[9]

Chi square test is used to see the correlation between HbAlC and macrosomia and hypoglycemia. P value less than 0.05 is taken as significant. Another study by Paul PK et al published an article where point of care estimation for hypoglycemia was CBG < 40 mg/dl.[12] In present study neonatal hypoglycemia was defined as CBG < 40 mg/dl taken at 3 hours of life.

RESULTS

The correlation between different variables was analysed by Pearson chi square test. The data analysis was computed using the SPSS version-l5 software and P <0.05 was considered statistically significant.

A total of 96 mothers were included in the study with a minimum age of 20 years and maximum of 38 years. The mean age of the mothers included in the study was 29 years (29.34). Majority of them were of gravida 2 (42.7%).

Primi gravid mothers were 31.3%, 18% mothers were of gravida 3 and one of them was gravida 4. Gravid 5 was of 4.2% and another 2.1% were gravida 6. Out of all the maternal subjects 12.5% of them had pre-existing DM and 84 (87.5%) of them were diagnosed as GDM.

Out of all the maternal subjects 12.5% of them had pre-existing DM and 84 (87.5%) of them were diagnosed as GDM. Glycated hemoglobin was evaluated in the third trimester and 5.6% was taken as upper limit of normal.

Any value below 5.7% was considered as normal and 5.7% and above as abnormal. Normal values (<5.7%) were found in 18.8% of the mothers and 81.2% had abnormal values.

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). Lowest blood glucose recorded by Capillary blood glucose was 3mg % and highest was 103 mg%.

Analysis between diabetic status, HbAlc and macrosomia

Twenty five percent mothers with either pre-existing or GDM and abnormal HbAlc > 5.7% had macrosomic babies, which had statistically significant correlation of P<0.05. There were different treatment plans mothers were put on, viz diet (n = 15), drugs (n = 18), insulin (n = 63). There was no significant correlation found between the treatment the mothers were on and the outcome of the study. Twenty percent of the mothers on insulin therapy and abnormal glycemic control had macrosomic babies. Family history of diabetes was seen in 46.9% of the mothers and 14% of them gave birth to a LGA baby.

Table 1: Analysis of HbAlc with macrosomia.

Variable	HbAlc				P value
HbA1c	**Normal (<5.7%)**		**Abnormal (>5.7%)**		
	Macrosomia		**Macrosomia**		
	Yes	**No**	**Yes**	**No**	
Pre-existing diabetes	0	3	5	4	
GDM	0	15	15	54	=0.029
Treatment					
Diet	0	2	2	11	
OHA	0	7	2	9	>0.05
Insulin	0	9	16	38	
Family h/o DM					
Yes	0	11	11	23	>0.05
No	0	7	9	35	
Delivery					
Normal	0	2	7	10	>0.05
LSCS	0	16	13	48	

Table 2: Analysis of HbAlc with macrosomia with hypoglycemia.

Variable	HbAlc				P-value
	Normal (<5.7%)		**Abnormal (>5.7%)**		
	Hypoglycemia	**Hypoglycemia**	**Hypoglycemia**	**Hypoglycemia**	
DM	**Yes**	**No**	**Yes**	**No**	
Pre-existing	0	3	7	2	P<0.001
GDM	0	15	15	54	
Treatment					
Diet	0	2	2	11	
OHA	0	7	2	9	P>0.05
Insulin	0	9	18	36	
Family history of DM					
Yes	0	11	13	21	P>0.05
No	0	7	9	35	
MOD					
NVD	0	2	7	10	P>0.05
LSCS	0	16	15	46	
Sex					
Male	0	10	10	27	P>0.05
Female	0	8	12	29	

Eighty percent of the babies were delivered by LSCS and the rest by normal vaginal delivery. Macrosomia was seen in 13% of the babies delivered by LSCS.

There was no difference in the correlation of macrosomia in relation to sex, 10% of males and 15% of females had macrosomia with abnormal glycemic control in mothers.

Analysis between HbAlc and hypoglycemia

In present study, 22 babies of our subjects developed hypoglycaemia. All the 22 babies (22.9%) who had hypoglycemia had mothers with abnormal HbAlc > 5.7% and statistically significant P value (P = 0.01). The diabetic status in a mother with abnormal glycaemic control was significantly correlated to hypoglycemia in the neonate. The P value was statistically significant at P < 0.001. Mothers with HbAlc > 5.7% and on medication did not show any statistical significance in our study, this could be because of the relatively small sample size (n = 96).

Similarly family history of diabetes even though a very important factor was not significant owing to small sample size of present study. The mode of delivery was found to be not significant in predicting hypoglycemia in a GDM mother with poor glycemic control. Similarly the sex of baby was of no significance in the outcome of this study.

Analysis between hypoglycemia, HbAlc and macrosomia

Mothers with abnormal glycaemic control (HbAlc > 5.7%) have more chances of having a macrosomic baby (LGA) along with hypoglycemia. It was shown in this study that HbAlc > 5.7% in the mother can predict macrosomia and hypoglycemia in the newborn and there is a statistically significant correlation with P value being less than 0.001.

DISCUSSION

Evers IM et al concluded in a study that despite good glycaemic control in a cohort of 289 diabetic women incidence of fetal macrosomia was very high (48.8%), whereas in our study it was 20.8%.[8] This probably could be attributed to the difference in race as western baby's birth weight is significantly higher than Indian. Family history of diabetes was seen in 46.9% of the mothers and 14% of them gave birth to a LGA baby. In present study family history was not significant enough to say that it can predict macrosomia, but according to the HAPO study it is a significant factor and may increase the risk.[10] In this study eighty percent of the babies were delivered by LSCS and the rest by normal vaginal delivery. Macrosomia was seen in 13% of the babies delivered by LSCS. HAPO study does suggest that abnormal glycaemic control resulted in primary caesarean section.[10] No significant association was found that abnormal HbAlC resulted in caesarean section probably because of the quantum of patients studied as HAPO was done on very large numbers of patients.[10]

Arumugam et al had shown in his study as HbA1c level in late pregnancy is a good predictor for hypoglycaemia in the newborn.[2] The study has also shown a significant correlation of HbA1C with neonatal hypoglycemia.

This study has shown that abnormal maternal glycated haemoglobin was statistically significant with fetal macrosomia and neonatal hypoglycaemia. This may be a predictor that those mothers with abnormal HbAlc are more likely to have a difficult delivery due to increased risk of having large babies. Though 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.

CONCLUSION

There is significant association between HbAlc and hypoglycaemia and macrosomia. A large study in a developing country like India with many more subjects in future and taking into account of all variables should justify the study.

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