Glycosylated Haemoglobin as a marker of Neonatal morbidity and mortality

L. Sailo, V. L. Bhargava, M. G. Karmarkar, A. K. Deorari, G. Kinra

ABSTRACT

Hemoglobin A_{1c} (HbA_{lc}) was measured in 48 diabetic pregnancies (GDM = 43, NIDDM = 1, IDDM = 4.) at least once in each trimester. HbAlc was high in early pregnancy in the presence of major foetal malformation in two patients. Foetal macrosomia was associated with high HbA_{lc} (> 8.5%) in the third trimester of pregnancy. High mean maternal HbA_{lc} in the second and third trimester was associated with neonatal hypoglycemia. Poor metabolic control of maternal diabetes during the first trimester is associated with foetal malformations and during the second and third trimester with metabolic derangement in the neonatal period. HbA_{lc} is of value in identifying pregnant diabetics at special risk.

INTRODUCTION

Diabetes mellitus is a syndrome characterised by disordered metabolism of carbohydrates, proteins and lipids resulting from absolute or relative lack or decreased efficacy of insulin in the body. The incidence of diabetes in pregnancy is approximately 1 in 1000 of the overall number of pregnancies for a given population (1).

Over the past decades, changes in the management of diabetic pregnancy have been directed towards a continued reduction in morbidity and mortality of infants of diabetic mothers. Nevertheless, perinatal mortality continues at rates of 3-5%, considerably above 1-2% noted in general population (2). Incidences of neonatal hypoglycemia hyperbilirubinemia, respiratory distress syndrome, macrosomia and congenital malformation are still frequent in infants of diabetic mothers (3,4,5).

With the achievement of better glycemic control, the above complications can be reduced considerably.

A simple and inexpensive indicator of diabetic controls is necessary for the assessment of good diabetic control. While daily monitoring of blood glucose levels is simple and inexpensive, it is a very tedious method of glucose regulation. Home glucose monitoring is not an ideal method because it forces the physicians to completely rely on the patients compliance; hence it is not feasible in patients who are neither educated nor motivated.

Glycosylated hemoglobin reflects the glycemic control over the preceeding 7-8 weeks (6). Raised glycosylated hemoglobin levels are associated with increased incidences of congenital malformation (7) and macrosomia (8). Thus glycosylated hemoglobin is useful in monitoring the glycemic control and in prediction of perinatal outcome.

This study reports an association between metabolic control of maternal diabetes as measured by blood haemoglobin A_{1c} (HbA_{1c}) with fetal malformations and perinatal outcome.

MATERIAL AND METHODS

The study consisted of 48 pregnant women, either known diabetics or detected to have gestational diabetes. Only those patients attending antenatal clinics at AIIMS were included for the study. The criteria of O'Sullivan and Mahan (9) for diagnosis of impaired glucose tolerance test in pregnancy was used.

Known diabetic patients were continued on regular insulin, dose being adjusted according to the blood sugar level so as to maintain a good control. All gestational diabetics were first put on diet control alone. Those who did not get good control on diet alone were put on regular insulin till delivery. HbA_{1c} estimation was done once in each trimester. The levels were correlated with perinatal morbidity and mortality.

RESULTS

Glycosylated HbAIc estimation was done once every trimester in 48 patients, (GDM = 43, IDDM = 4, NIDDM = 1). The mean age was 29.8 years. There were 6 primigravidas and 42 multigravidas. A bad obstetric history in the form of previous intrauterine death and two or more abortions was present in 16 of these women.

A glycosylated HbA_{1c} value $\geq$ 8.5% was taken as high or abnormal. These values were correlated with neonatal outcome. (See Table 1, 2 and 3).

From: Dept. of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi-110 029.

There was no perinatal death. Two major congenital malformations in babies were associated with high maternal HbA_{1c} in early pregnancy (10.2% and 11.5%, respectively).

Table 1
1 st TRIMESTER HbA_{1C}
(Mean HbA1C=7.85%)

	HbA_{1C}<8.5% (N=4)	HbA_{1C}≥8.5% (N=2)
	(Mean HbA_{1C} 6.35%)	(Mean HbA_{1C} 10.85%)
L F D	1	1
S F D	1	0
*Cong. Malformation (Major)	0	2

* Same baby in all the trimester.

In the second trimester, out of nine babies with high maternal HbA_{lc} (mean 10.266%), 5 were large-for-date (LFD) (mean birth wt: 4.015kgs.), and out of four babies in the third trimester with high maternal HbAlc (mean 12.85%), 2 were LFD (mean birth wt: 4.73 kgs).

Table 2
2nd Trimester HbA_{1C}
(Mean HbA1C = 6.76%)

	HbA_{1C}<8.5% (N=19)	HbA_{1C}≥8.5% (N=9)
	(Mean HbA1C 6.39%)	(Mean HbA1C 9.75%)
L F D	2 (10.5%)	5(55.5%)
S F D	1	0
*Cong. Malformation (Major)	0	2
Hypoglycemia	7(36.8%)	8(88.8%)
Symptomatic	1	3
Asymptomatic	6	5
*RDS	0	1
Polycythemia	1	2
Hypocalcemia	1	0
Path. Jaundice	0	1

* Same baby in all the trimesters.

Neonatal hypoglycemia was seen in seven out of 19 babies with a mean maternal HbAlc of 6.39% as compared to eight out of 9 babies with a mean HbAlc of 9.75% in the second trimester.

Table 3
3nd Trimester HbA_{1C}
(Mean HbA1C = 6.47%)

	HbA_{1C}<8.5% (N=44)	HbA_{1C}≥8.5% (N=4)
	(Mean HbA_{1C} 6.04%)	(Mean HbA_{1C} 11.2%)
L F D	6 (13.6%)	2(50%)
S F D	1	0
*Cong. Malformation (Major)	0	2
Hypoglycemia	16(36.36%)	4(100%)
Symptomatic	2	1
Asymptomatic	9	3
*RDS	0	1
Polycythemia	3	1
Hypocalcemia	1	0
Path. Jaundice	0	1

* Same baby in all the trimesters.

In the third trimester, hypoglycemia was seen in sixteen babies out of 44, with a mean maternal HbA1c of 6.04% as compared to hypoglycemia in all those 4 babies with a mean HbA1c of 11.2%.

There was one baby with respiratory distress syndrome (RDS) and pathological jaundice with a mean HbAlc of 11.2%. The cause of RDS was patent ductus arteriosus and atrial septal defect.

Four babies had polycythemia. High HbAlc was seen only in one baby.

Hypocalcemia was seen in an infant of IDDM. The same baby had intractable hypoglycemia. The mean maternal HbAlc was 6.04%.

DISCUSSION

The cause of the high number of foetal malformations in diabetic pregnancies is unknown. A lower incidence of malformations has recently been reported in the offspring of diabetic patients treated at diabetic clinics before pregnancy than in the offspring of diabetic patients seen elsewhere (10). In this study the two patients who gave birth to a malformed foetus had high HbAlc values in early pregnancy, suggesting that sustained hyperglycemia in poorly controlled pregnant diabetics is associated with fetal malformations. Hypoglycemia is likely to

be associated with high HbAlc in the second and third trimester. In the present study, 4 babies (100%) with high maternal HbAlc in the third trimester were found to have hypoglycemia. It is not possible to comment upon their correlation, since the number is too small.

High maternal HbAlc in the third trimester was likely to be associated with fetal macrosomia. However the correlation was rather low, probably because several other factors such as placental function, heredity and the degree of vascular complications in the diabetic mothers influence fetal growth.

RDS was seen in one infant with high maternal HbAlc. However the main cause of RDS in this infant was patent ductus arteriosus and atrial septal defect.

Polycythemia was seen in 4 babies. Only one of these babies had high maternal HbAlc suggesting possible factors other than poorly controlled diabetes.

Pathological Jaundice was seen in one baby with a high maternal HbAlc of 11.2%.

CONCLUSION

Poor metabolic control in the first trimester is associated with major foetal malformations and during the second and third trimester with metabolic derangement in the neonatal period. HbAlc is of value in identifying pregnant diabetics at special risk.

REFERENCES

1. Hadden DR. Screening for Abnormalities of Carbohydrate Metabolism in Pregnancy 1966-1977: The Belfast Experience. Diabetes Care 1980; 3: 440
2. Felig P and Coustan D. Diabetes Mellitus In: Medical complications during pregnancy 2nd Ed. Burrow GN, Ferris TF, Eds; W.B. Saunders Company, 1982, P36.
3. Gabbe SG, Mestman JH, Freeman RK, Goebelsmann UT, Lowensohn RI, Cetrulo D and Quillingan EJ. Management and outcome of pregnancy in diabetes mellitus classes B to R. Am. J. Obst Gynecol. 1977; 129: 723.
4. Kitzmiller JL, Cloherty JP, Younger MD, Tobatabaii A, Rothchild SB, Sosenko I et al. Diabetic pregnancy and Perinatal outcome Am. J. Obst Gynecol 1978; 131: 560.
5. Teramo K, Kuusisto AN, and Raivio KO. Perinatal outcome of insulin dependent diabetic pregnancies. Ann Clin Res 1979; 11: 146.
6. Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M and Cerami A. Correlation of glucose regulation and HbA_{lc} in diabetics. New Eng. J. Med. 1970; 95: 417.
7. Ylinen KK, Ravivo K, Terano. HbA_{lc} predicts perinatal outcome in infants of diabetic mothers. Br. J. Obst Gynecol 1981; 88: 10.
8. Yue DK, Morris K, Mclennan S and Turtle JR. Glycosylation of plasma protein and relation to glycosylated hemoglobin in diabetes mellitus. Diabetes 1980; 29: 296.
9. O'Sullivan JB, Mahan CM, Charles D and Dandrow RV. Screening Criteria for high risk gestational diabetic patients. Am. J. Obst Gynecol 1973; 116: 895.
10. Pederson J, Molsted Pederson L. The possible role of diabetes care outside pregnancy. In: Pregnancy, metabolism, diabetes and the foetus. Ciba Found Symp. Excerpta Medica, Amsterdam, 1979; 63: p. 265.