

# **IMPORTANCE OF PRECONCEPTIONAL CONTROL OF DIABETES IN PREVENTION OF CONGENITAL MALFORMATIONS IN THE INFANTS OF DIABETIC MOTHERS**

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## **Summary**

Effect of preconceptional control of diabetes in preventing congenital malformations in infants of diabetic mothers was studied. Six overt diabetic women (two IDDM and four NIDDM) with previous history of delivering infants with congenital anomalies received intensified antidiabetic therapy in the preconceptional period. Glycosylated HbA1c and fasting blood glucose was brought within normal limits in the preconceptional period and these levels were maintained in the crucial first seven weeks of gestation and later part of the pregnancy as well. All the six women delivered healthy infants without congenital malformations. Follow up at the age of 3 months with skeletal X-rays and echocardiography did not reveal any congenital anomalies. Our observations suggest that strict control of diabetes during preconceptional period and crucial first seven weeks of gestation can prevent the congenital anomalies and reduce the perinatal mortality in the offsprings of diabetic mothers.

## **Introduction**

Pregnancies complicated by overt diabetes have been associated with perinatal mortality rate five to ten times that of the nondiabetic population. (1) Major congenital anomalies emerge as the most important causes of mortality in infants of diabetic mothers, as losses from stillbirths, intrapartum asphyxia and hyaline membrane disease diminish (1,2). Malformations in infants of diabetic mothers occur before the seventh gestational week. (3) Poorly controlled diabetes in early pregnancy is associated with increased risk of major structural anomalies in offspring. Of special note and concern are the relatively large numbers of neural tube and cardiac anomalies. Good metabolic control before conception and in the early weeks of pregnancy may decrease the frequency of major anomalies. (4)

The present study was undertaken to evaluate the effect of preconceptional control of diabetes in prevention of congenital anomalies in offsprings of diabetic mothers with previous history of congenital malformed babies.

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Presented at API Conf. Pune in Award Session, 26-1-1988.

## Material and Methods

Six overt diabetic women (two I D D M and four N I D D M) formed the case material. Five of these had given birth to infants with congenital anomalies three of which were fatal. Two had minor anomalies and survived. Sixth patient had aborted twice in first and second trimester of unexplained causes.

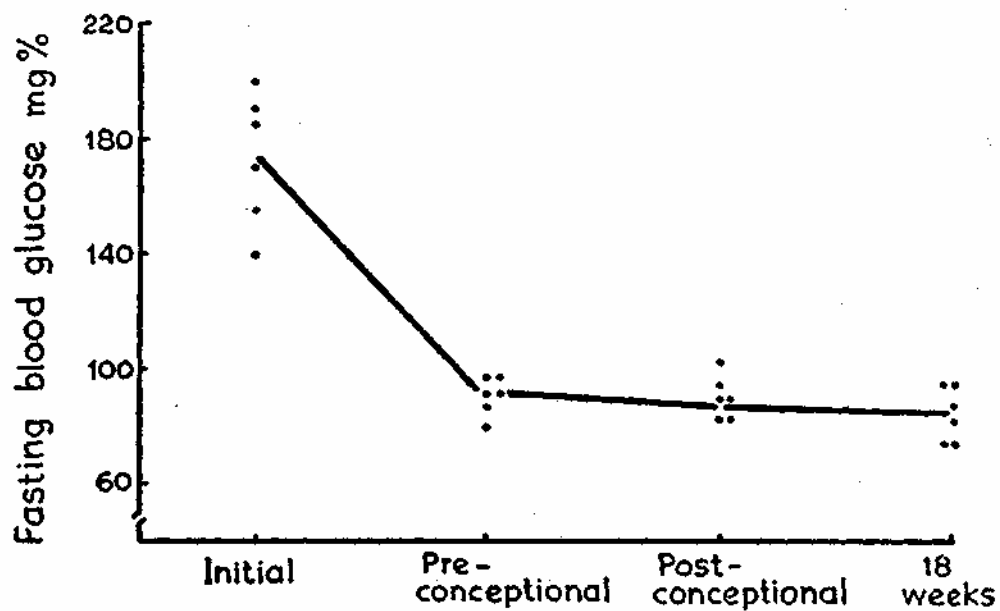
All these patients received counselling before the conception and were explained about the concept of planned parenthood. The status of diabetes was assessed by estimating the glycosylated HbA1 and fasting blood glucose. Glycosylated HbA1 was estimated by the method of Welch and Boucher. (5) Three patients receiving oral hypoglycemic drugs were changed over to insulin. All of them underwent physical examination and were classified as per White classification of pregnancy. (6) Micro and macro angiopathic complications of diabetes were evaluated by fundus examination, twenty four hours urinary albumin excretion and electrocardiogram. These patients were advised to observe contraception till their diabetes was brought under control (glycosylated HbA1 below 9% and fasting blood glucose below 100 mg/dl). After achieving the desired control of diabetes, contraceptive measures were withdrawn. Patients were instructed to keep regular urine glucose monitoring at home. Antidiabetic treatment constituted multiple insulin injections and dietary counselling. Fasting and postprandial blood glucose were done at every three weeks interval and insulin doses were altered to keep fasting blood glucose below 100 mg/dl. Pregnancy test was done after seven days of missing menstrual cycle. After confirmation of pregnancy obstetrical counselling was initiated and glycosylated HbA1 was repeated. At eighteen weeks of gestation pelvic ultrasound examination was done to rule out any major congenital anomaly. At completion of eighteen weeks of gestation, glycosylated HbA1 was repeated. Immediately after the birth these infants underwent physical examination and after three months skeletal X-rays and echocardiography.

## Results

The mean age of the patients was 28.16 years. (Table 1) Initial mean fasting blood glucose was 173.33 mg/dl % after intensified antidiabetic therapy it was reduced to 91.66 mg %. In the immediate post conceptional period and at eighteen weeks of gestation the mean values were 89.66 mg/dl and 85.33 mg/dl respectively. (Fig. 1). Initial mean glycosylated HbA1 was 11.2 % and was brought down to 8.26 % in the preconceptional period. In the immediate post conceptional period and at eighteen weeks of gestation the mean a-HbA1 values were 8.06% and 8.21 % respectively. (Fig. 2). The period required to achieve

**Table 1**  
**Clinical data of the patients**

S. No.	Age	Age of onset	Type of Diabetes	White Class	Prexious Anomaly
1.	27	23	NIDDM	B	Meningo-Myelocele
2.	26	24	N1DDM	B	Cleft Lip
3.	35	19	IDDM	C	Anencephaly (8 abortions)
4.	28	18	IDDM	C	Large V.S.D.
5.	25	22	NIDDM	B	Omphalocele
6.	28	23	NIDDM	B	2 abortions



**Fig. 1. Fasting Blood Glucose Values**

desired metabolic control of diabetes ranged between 30 to 90 days mean being 49.66 days. The period required after achieving the desired metabolic control of

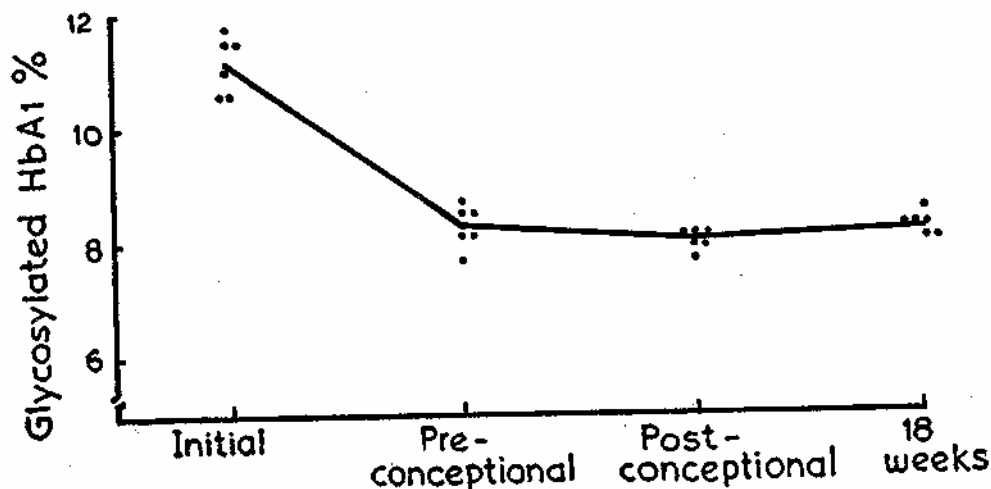


Fig. 5. GHbA1 Values

diabetes and the diagnosis of pregnancy ranged between 60 to 200 days mean being 133.33 days.

Pelvic ultrasound examination was done at eighteen weeks of gestation was normal in all these cases. About thirty six weeks, the six infants were delivered three by cesaerian section and three by vaginal route. Physical examination of the infants did not reveal congenital malformations. At three months, skeletal X-rays and echocardiography was done. None of the infants showed evidence of congenital anomalies.

## Discussion

Perinatal mortality is five to ten times higher in pregnancies complicated by overt diabetes. Major congenital anomalies emerge as the most important causes of mortality in infants of diabetic mothers (1,2). It has been known that fetal malformations occur before seven weeks of gestation when most diabetic pregnant women have not yet come to medical attention. Raised glycosylated HbA1c levels during first trimester have been found to be associated with increased incidence of major congenital malformations (3,4). In the present study five of the six patients had previously given birth to infants with congenital malformations, three of which were fatal. Hence it was planned to control diabetes in these women during the crucial period of organogenesis. Preconceptional counselling was initiated and the diabetes was controlled by intensified antidiabetic therapy. These patients agreed to the concept of planned parenthood because of their previous experiences of delivering malformed babies. This

is otherwise a difficult proposition as these women do not come under medical supervision in the pre and immediate postconceptional period.

None of the patients had well controlled diabetes in the preconceptional period during their previous pregnancies. In fact all of them had come under medical supervision only after the pregnancy was well established by which time the phase of organogenesis was already over. Two of these patients had reported to their physicians as late as twenty first week of gestation.

Three non insulin dependent diabetic women who were receiving oral hypoglycemic drugs were changed over to purified monocomponent insulin. All the six patients received minimum two injections of mixture of soluble isophane insulin. All of them were instructed to do regular urine glucose monitoring at home in addition to frequent laboratory checkup. One patient did home blood glucose monitoring.

Good metabolic control was achieved in all the patients in preconceptional period and was maintained in periconceptional period as well. Glycosylated HbA1 and fasting blood glucose values were normalised in these patients well before conception. Only after achieving the desired metabolic control of diabetes were they allowed to withdraw contraceptive measures. At eighteen weeks of gestation pelvic ultrasound examination was done to rule out any major congenital malformations. Chorionic biopsy and estimation of alpha-fetoproteins were done only in one patient (case No. 3) as these facilities are not freely available.

All these women delivered healthy infants. At three months of age skeletal X-rays and echocardiography was done which did not reveal any congenital malformations. Skeletal X-rays were specifically done to exclude any neural tube defects as such defects are commonly seen in infants of diabetic mothers<sup>7</sup>.

A number of etiologic factors have been proposed to explain the increased rate of congenital anomalies in infants of diabetic mothers. These factors include genetic influences, teratogenic agents, maternal vascular disease and metabolic effects of maternal diabetes.<sup>8</sup> Baker, Egler et al.<sup>9</sup> have shown significant decrease in lumbosacral defects in streptozotocin induced diabetic rats when diabetes was meticulously controlled.

In our study four patients belonged to White class 'B' and two patients to class 'C' indicating shorter duration of diabetes (less than twenty years). None of our patients had evidence of any micro or macro angiopathy. This may be because of relatively shorter duration of diabetes in our cases. Four fold increase

in the incidence of congenital malformations seen in the infants of diabetic mothers is presumably related to some aspect of the maternal milieu that is disturbed in uncontrolled diabetes.

Admittedly the present series is small but it is specific. The gratifying results it has produced carries the message that strict control of diabetes during preconceptional period and the vital first seven weeks of gestation can prevent the congenital anomalies and reduce perinatal mortality in the offsprings of diabetic mothers

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