Research

Managing gestational diabetes – a two year study of 200 patients

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Abstract

Introduction: Doubling of the prevalence of Gestational Diabetes Mellitus (GDM) in the last eight years has necessitated a review to evaluate the outcome and complications of these pregnancies in a local perspective, in comparison to the data obtained from the western literature.

Objective: To study the outcomes and complications of 200 antenatal mothers diagnosed with GDM at the Teaching Hospital Kandy, Sri Lanka, and to compare these with results obtained from the western literature.

Method: 200 antenatal mothers with documented risk factors for GDM were screened by a 75 g standard Oral Glucose Tolerance Test (OGTT) and GDM diagnosed using the 2006 WHO Diabetes criteria. They were managed and delivered at the Teaching Hospital, Kandy, outcomes and complications documented and followed-up where feasible up to a period of two years.

Results: Family history as a risk factor was documented in 65% with obesity accounting for only 5%. Only 34% in the series, (31% with a family history of diabetes and 50% with a previous history of GDM) had carried out at least one blood-sugar estimation prior to this conception.

A total of 88% required insulin therapy along with dietary regulation but queried later only 58% vouched for the advised dietary restrain, A normal maternal weight gain, a higher average birth weight of 3206 grams is reported with a congenital abnormality rate of 2.5% and three still births. 78% were delivered surgically and 34% of the babies needed to be admitted to the Special Care Baby Unit (SCBU) and the average SCBU stay being 2 to 3 days.

22% were found to have a new diagnosis of Type 2 Diabetes mellitus six-weeks post-partum with 77% of them having had very high blood sugar profiles in their antenatal GTTs. On long-term follow up, 8% of mothers who were normotolerant or with impaired glucose tolerance post-partum were found to be diabetic just 2 years after delivery.

Conclusion: A glaring deficiency in pre-pregnancy counselling for diabetes with an inadequate public awareness is highlighted.

Introduction

Gestational diabetes mellitus (GDM) is defined as "glucose intolerance of any degree with onset or first recognition during pregnancy". It affects 3 - 14 % of pregnant women and its prevalence has doubled in the last 8 years, a 12% increase per year[1].

It has long been deduced that pregnancy outcomes from GDM, reported frequently in the literature obtained from studies in the developed western world, would not be applicable unerringly to countries in the eastern hemisphere, with its different cultural, social and economic background. This study was conducted on 200 antenatal mothers diagnosed with GDM, from 2007 to 2009, at the Teaching Hospital, Kandy, Sri Lanka, to determine the outcomes of these pregnancies.

Objective

The objective of this study on 200 antenatal mothers with GDM, is to ascertain the complications and clinical outcomes of these pregnancies and compare these with results obtained from the western literature.

Materials and Methods

This study was conducted at the antenatal clinic and wards of the Teaching Hospital, Kandy, which has one of the busiest maternity wards in Sri Lanka, with over 6000 annual deliveries per unit. A detailed history was obtained from each expectant mother attending the antenatal clinic.

Mothers with the following risk factors, eg. maternal age more than 35 years, previous infant weighing more than 3500 g, glycosuria in second urine

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sample, previous unexplained fetal demise, previous pregnancy with GDM, strong immediate family history of Type 2 Diabetes Mellitus (T2DM) or GDM, obesity (>90 kg), fasting glucose value greater than 140 mg/dl (7.8 mmol/L) or random glucose value greater than 200 mg/dl (11.1 mmol/L), were selectively screened for GDM.

This selective screening involved a 75 g standard Oral Glucose Tolerance Test (OGTT) performed in a laboratory with reputed quality control measures. The OGTT was performed in the morning after an overnight fast of between 8 and 14 hours. During the three previous days the subject was on an unrestricted diet and unlimited physical activity. The subject was seated during the test and was given a standard solution containing 75 g of glucose to drink within a 5 minute time frame.

GDM was diagnosed using the 2006 WHO Diabetes criteria of venous blood and plasma glucose levels, as depicted in Table 1[2].

Table 1. 2006 WHO Diabetes Criteria

Condition	*Fasting glucose mmol/l(mg/dl)*	*2 hour glucose mmol/l(mg/dl)*
Normal	<6.1 (<110)	<7.8 (<140)
Diabetes mellitus	≥7.0 (≥126)	≥11.1 (≥200)

The control of the glycaemic levels were obtained with dietary regulation and insulin therapy.

(a) Dietary regulation

The foundation of treatment for all patients was diet adherence with the percentage of carbo-hydrates lower than 40%. Mothers with a fasting plasma glucose < 105 mg/dl were selected for a 'trial of diet therapy', without medication, for a 2- to 4-week period[3]. Failure of dietary regulation for blood glucose control beyond this period required insulin therapy for optimal control. Mothers with a fasting glucose concentrations more than 115 mg/100 mL, were commenced instantaneously on insulin therapy in addition to dietary regulation.

(b) Insulin therapy

Insulin therapy was administered by pen injectors using mixed insulin 30/70 – combination of regular (one-third) and intermediate (two-thirds) acting insulins. The patients were instructed on their use by medical personnel. Patient's acceptance was excellent with trouble-free self-administration even amongst the poorly educated. On an average 2/3 of the total daily dose was given in the morning and 1/3 in the evening. Regular check-up was by the fasting and 2-hour post lunch, plasma sugar estimations. The use of glucometers were discouraged.

The criteria used for targeted levels of glycemic control were according to recommendations of the Fifth International Workshop Conference on Gestational Diabetes[4] and were as follows:

- Fasting plasma glucose 90-99 mg/dL (5.0-5.5 mmol/L) and
- One-hour postprandial plasma glucose less than 140 mg/dL (7.8 mmol/L) or
- Two-hour postprandial plasma glucose less than 120-127 mg/dL (6.7-7.1 mmol/L)

(c) Ultrasound examination for fetal morphology

A detailed assessment of the fetal morphology was offered to all, whenever feasible at 18 to 20 weeks.

(d) Delivery

Due to the liberal protocol of the unit for caesarean section for delivery of insulin-dependant diabetics, 78% of them were delivered surgically, most after 38 completed weeks of gestation. The rest with a good Bishops score were induced between 38 to 39 weeks and delivered vaginally under enhanced supervision

(e) Post-natal advice

The mothers were counselled on a combination of breastfeeding, lifestyle changes with increased physical activity, weight loss and a healthy diet, which could significantly reduce the maternal risk for T2DM .

(f) Post-partum follow up

A glucose tolerance test was performed 6 weeks post-partum to determine whether it was GDM or a new diagnosis of Type 2 Diabetes.

(g) Long term follow up

Mothers who had delivered earlier in the series were followed, where feasible, for a period of two years with OGTT.

Results

A section of the trial of patients requiring insulin for optimal blood glucose control, with the OGTT results and insulin dosages are tabulated in Table 2.

Table 2

NAME	Age	ADDRESS	Pregnancy	LRMP	EDD	GTT RESULTS mg/dl					Insulin	
						FBS	1/2 HR	1 HR	1 1/2 HR	2 HR	7.0 AM	7:00 PM
Mrs. W.M.N.	29	Sangaraja Pura	P_1C_0	23/10/2007	30/07/2008	160.8 mg/dl	221.1 mg/dl	304mg/dl	289.8 mg/dl	294mg/dl	12	8
Mrs. R.W.G.	27	Katugastota	P_1C_0	6/11/2007	13/08/2008	180mg/dl	233mg/dl	204mg/dl	275mg/dl	206mg/dl	8	4
Mrs. C. L. R	31	Manikhinna	P_1C_0	28/01/2008	4/11/2008	135 mg/dl		315 mg/dl		235 mg/dl	10	5
Mrs. V. S	28	Kandy	P_1C_0	9/3/2008	16/12/2008	199 mg/dl	238 mg/dl	257 mg/dl	270 mg/dl	286mg/dl	8	6
Mrs. L.A.M.	29	Gurudeniya	P_1C_0	27/02/2008	5/12/2008	160mg/dl	200mg/dl	250mg/dl	255mg/dl	290mg/dl	24	20
Mrs. N.M.K.G.	37	Rikillagaskada	P_3C_2	10/3/2008	17/12/2008	114mg/dl		252.4 mg/dl		250mg/dl	10	5
Mrs. R. E	33	Navinna	P2C1	16/6/2009	23/3/2010	158 mg/dl	225.6 mg/dl	266.4 mg/dl	260.8 mg/dl	246.9 mg/dl	10	5
Mrs. A.R.	30	Rajawella	P_4C_2	1/6/2008	8/3/2009	189.9 mg/dl	180.4 mg/dl	209.3 mg/dl	217.4 mg/dl	212.6 mg/dl	4	2
Mrs. S. K	29	Uduwalla	P2C1	30/12/2008	6/10/2009	234 mg/dl	356mg/dl	362 mg/dl	358 mg/dl	286 mg/dl	10	5

The clinically significant results obtained from this study is listed below:

(1) **Risk factors for GDM**

65% of the mothers documented diabetes in an immediate family member. Obesity, the next most common risk factor stipulated in the literature was found in only 5% of mothers with a weight of over 90 Kg.

(2) **Public Awareness of the major risk factor**

The percentage of mothers who had carried out at least one blood-sugar estimation prior to conception was 34 %. Only 31% of the antenatal mothers, with a family history of T2DM, the principal risk-factor, had checked their blood sugar profile prior to conception.

(3) **Women with previous gestational diabetes mellitus (pGDM)**

28% of the mothers in the present series gave a previous history of GDM which has been alleviated post partum. It is also noted that only 50% of them had checked their blood sugar profile prior to this conception.

(4) **Birth weight**

The average birth weight of babies in this study was 3206 grams and 30% of them had a birth weight higher than 3500 grams.

(5) **Congenital anomalies**

A congenital abnormality rate of 2.5% is reported, with cardiac anomalies and an imperforate anus. One baby died 30 days later due to multiple fatal anomalies.

(6) **Still births**

There were three still births in the series. Two were unexplained and the other due to undetected reversal of the umbilical blood flow.

(7) **PBU care**

34% of the babies needed to be admitted to the Special Care Baby Unit (SCBU) for observation and sometimes for respiratory difficulty. Excluding the extremes, the average SCBU stay was 2 to 3 days.

(8) **Maternal weight-gain during pregnancy**

The maternal weight gain during this pregnancy

was in par with the non-diabetic population with 5% of mothers gaining more than 20 Kg and 10% gaining more than 15 Kg.

(9) **Post-partum follow up**

22% of women were found to have a new diagnosis of type 2 diabetes mellitus, post-partum. They were referred to the physician for follow up therapy.

(10) **Medication during breast-feeding**

All of the 22% of mothers who were found to have a new diagnosis of type 2 diabetes mellitus, post-partum, was either still on insulin or oral anti-diabetic agents while breast feeding.

(11) **Long term follow-up**

Long-term follow-up showed that 8% of mothers who were normotolerant or with impaired glucose tolerance post-partum were found to be diabetic just 2 years after delivery. Two case reports are documented below:

I. K. R. from Katugastota
33 years, P2, birth weight 3400 g

75 g Glucose Tolerance Test results mg/dl	Fasting	½ hr	1 hr	1 ½ hr	2 hr
Pregnancy	132	190	242	228	208
6 weeks post-partum 30 July 2008	115	170	134	120	117
2 years and 2 months later 17 July 2010	130	200	276	235	210

K. G. Y. from Molagoda
39 years, P2, birth weight 3140 g

75 g Glucose Tolerance Test results mg/dl	Fasting	½ hr	1 hr	1 ½ hr	2 hr
Pregnancy	122	193	240	230	211
7 weeks post-partum	100	130	135	129	110
20 months later 7 July 2010	141	204	228	216	204

(12) **Post partum diabetes with high pregnancy GTT levels**

It was observed that 77% of mothers who developed T2DM later had very high blood sugar profiles in their antenatal GTTs with fasting levels over 150 mg%, one-hour and two-hour levels over 350 mg%. They were established type 2 diabetics, diagnosed for the first time during this pregnancy.

(13) **Fallacy of diligent dietary control**

Although nearly all mothers in this study reported diligent adherence to dietary advice, intensely questioned six months later, only 58% vouched for the advised dietary restrain.

(14) **Childhood obesity**

During the short follow-up period in this study, 86% of the mothers reported a normal weight gain for their children and 14% less than normal.

Discussion

Diabetes, which is spreading rapidly around the globe in a 'pandemic', has a varying incidence, affecting 8.6% of Europeans to 14% for the Hispanics. The prevalence in Sri Lanka stands at 11.5%[5]. A glaring deficiency in pre-pregnancy counselling is noted with the detail that only 34% of mothers in this study had taken at least one blood-sugar estimation prior to conception. The finding of 65% of the mothers documenting diabetes in an immediate family member is significant and we authenticate it as the major risk factor for GDM in this series. This is in concurrence with other series of published data[6,7,8]. However, it was noted that the public awareness of this disability is inadequate, with only 31% of them checking their blood sugar profile prior to this conception.

Obesity, the next frequent risk factor stipulated in the literature[8], was found only in 5% of mothers who weighed over 90 Kg. Literature survey shows that the risk in the second pregnancy for GDM was 41.3% among women with previous GDM vs. 4.2% in women without previous GDM (OR, 13.2; 95% confidence interval [CI], 12.0 - 14.6)[9]. Although 28% of the mothers in the present series gave a previous history of GDM, it is disappointedly noted that only 50% of them had checked their blood sugar profiles prior to this conception.

A significant majority of 88% of mothers in the present study needed insulin therapy for optimal blood sugar control as against a figure between 30-50% quoted in the western literature[3]. Dietary control is 'better said than done' in the South Asian perspective where social conviction demands 'eating for two' as

the sole criteria accountable for the growth and well-being of the baby. Questioned six months later, only 58% vouched for adherence to the given dietary advice! We have selected a threshold fasting plasma glucose of ≥105 mg/dl to initiate insulin therapy[10] in addition to dietary regulation. However, as there is a threefold higher rate of large for gestational age infants in diet-treated patients when the fasting plasma glucose >95 mg/dl, some consider it reasonable and appropriate to recommend assigning these patients to additional pharmacological therapy[11].

Although evidence suggest that glibenclamide and metformin may be a reasonable alternative to insulin for some women with gestational diabetes, especially those who have fasting glucose concentrations less than 110 mg/100 mL[12,13], it was not used in the present series. The cost to the health services of the country is epitomized by the reality that one-third of the babies needed SCBU care even for two to three days. The three still births in the series conveys the need for closer supervision in these complicated pregnancies, with umbilical artery blood flow estimations, after 34 weeks of gestation. A significant congenital abnormality rate of 2.5 % is reported, with cardiac anomalies and an imperforate anus. This is in accordance with population-based registry and database studies showing anomalies for gestational diabetes only 1.2 times higher than in the general population (95% CI 1.1-1.3) as against being 2- to 3-fold higher for established diabetics[14]. Also adjusted analyses show a 3.4-fold increase in anomalies for women with gestational diabetes with fasting hyperglycemia ($P<0.001$), and no difference in risk for women with gestational diabetes with normal fasting glucose when compared with women without diabetes[15] suggesting undetected type 2 diabetes. This is amply amplified in the present series with 22% of mothers found to have a new diagnosis of type 2 diabetes mellitus, post-partum. The average birth weight of babies in this study was 3206 grams which is higher that the average birth weight for Sri Lankan babies of 2854 grams[16] and 30% of them had a birth weight higher than 3500 grams.

It was inspiring to note that of the post-natal advice given to these mothers which could significantly reduce the maternal risk for T2DM , breast-feeding was diligently observed. However, the same could not be observed in lifestyle changes such as increased physical activity and weight loss, which has been documented to reduce the development of type 2 diabetes by 58 percent during a 3-year period[17]. The short follow-up period of this study was inadequate to substantiate the documented relationship between intrauterine exposure to maternal hyperglycaemia with the risk of child-hood obesity[18,19] and features of the metabolic syndrome, such as hypertension, dyslipidaemia and microalbuminuria[20]. 86% of the mothers reported a normal weight gain for their children and 14% less than normal. Women with pGDM have at least a 7.5-times increased risk of developing T2DM in the future compared with those with normoglycemic pregnancy with a 35 to 60 percent chance of developing diabetes in the next 10-20 years[21]. The recommendations protocol of the American Diabetes Association for annual or regular OGTT of women with pGDM[22] who are normotolerant for the 6-week post-partum OGTT is thoughtful, when considering the 8% of mothers who were normotolerant or with impaired glucose tolerance post-partum and found to be diabetic just 2 years after delivery. Bellamy and colleagues in 2009 reported that the relative risk of 4.69 of developing T2DM within 5 years of a pregnancy complicated by gestational diabetes, doubled to 9.34 when examined more than 5 years postpartum[23]. However, the use of oral antidiabetic agents for these normotolerant women for T2DM prevention, known to reduce the risk by 31 percent[21], was not offered in the present study.

Conclusion and recommendations

It is noted that adequate prominence has not been given on the need to check the blood-sugar profile prior to pregnancy. Many studies have emphasized that pre- conception counseling with advice to keep the pre-conception glycosylated hemoglobin (HbA1c) at or below 7% has lead to a decrease in the risk of congenital malformations[24]. More publicity by the health professionals and in the print and electronic media must be made to create public awareness on the importance of a family history of diabetes being the major risk factor for GDM. As it was observed that 77% of mothers who developed T2DM later had very high blood sugar profiles in their antenatal GTTs it is recommended that the obstetricians themselves must be guided to keep contact details of them along with details of mothers requiring higher doses of insulin for optimal blood sugar control, for subsequent periodical recall and testing.

The emphasis must also be for the need for closer supervision of these complicated pregnancies, with umbilical artery blood flow estimations, after 34 weeks of gestation. The frightening statistic of one-fifth of the mothers assembling a new diagnosis of type 2 diabetes mellitus, in the immediate post-partum assessment gives an indication to the perilous spread of diabetes in this country. Insulin therapy involves daily injections, which may lead to suboptimal adherence by many women in poorer countries due to its unavailability, storage difficulties and its cost. Although oral antidiabetic agents endorsed by the Fifth International Workshop on Gestational Diabetes and the North American Diabetes in Pregnancy Study Group[25] for GDM were not used in the present series, it is self-evident that given the choice of insulin injection versus tablets, patients will invariably prefer taking tablets, instead of two to three daily injections.

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