Review

MANAGEMENT OF DIABETES IN PREGNANCY, LABOR AND POST PARTUM

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ABSTRACT

Diabetes in pregnancy is a significant contributor to neonatal mortality and morbidity. Control of blood glucose from the preconception period significantly reduces the risk. Very tight glycemic control does not confer additional benefits as compared to tight control. Persistent maternal hypoglycemia is nowadays considered unacceptable. The place of standard OGTT in the management of gestational diabetes mellitus (GDM) perhaps needs to be reexamined. Perfectly acceptable results are possible within the constraints of a hospital setting in India. It is important that post partum, the mothers at risk of diabetes are not lost to follow up.

KEY WORDS : Gestational diabetes; OGTT; Glycemic control; GDM management; Maternal hypoglycemia.

INTRODUCTION

The fact that diabetes has an adverse effect on pregnancy was recognised in the early days of diabetology, when in fact the correct advice to a diabetic woman was not to venture into pregnancy at all. It was soon realised that the risk to the mother and the baby could be stratified depending on the degree of control and the duration of diabetes. In 1949 Dr Priscilla White produced a classification of diabetes in pregnancy which is still in use today in a modified form (1). In 1964 O'Sullivan and Mahan did oral GTT's on pregnant subjects to predict their future vulnerability to diabetes (2). The cut off values proposed by them were such that subjects testing positive were more likely to develop diabetes in later life. The criteria of O'Sullivan and Mahan have since been altered to take into account the changing technology of measuring blood glucose and several systems are in use at present (3). Diagnostic criteria in current use are shown in table 1.

Table 1 : Diagnostic Criteria for GDM in Current use.

Author	Glucose		Source	Fasting	1hr	2hr	3hr
				(values in mg/dl)			
O'Sullivan & Mahan (2)	100g	venous blood	90	165	125	145	
NDDG	100g	venous plasma	105	190	165	145	
Carpenter & Coustan (3)	100g	venous plasma	95	180	155	140	
WHO	75g	venous plasma	140			200	

THE PLACE OF OGTT

The import of all published criteria remain the same i.e. to help quantify future maternal risk of diabetes. It is one of the ironies in diabetology that these criteria have gradually come to indicate fetal well being during pregnancy. Work in the 80's clearly showed that values of blood glucose well within the cut off values were still associated with significant fetal morbidity. In other words a mother could 'pass' the O'Sullivan and Mahan criteria and still have a complicated pregnancy and a poor outcome. Tallarigo studied 249 women in their 3rd trimester (4). All had a 2hr OGTT value below 165 mg/dl i.e. they did not have gestational diabetes. The women were divided in 3 groups based on their 2hr glucose value. The women with the lowest values had the best pregnancy outcome (Table 2).

Table 2: Pregnancy Outcome Related to the 2hr Glucose Value on OGTT (4).

	Group A <100mg/dl n=151	Group B 100-119 mg/dl n=58	Group C 120-164 mg/dl n=40
Macrosomia	9.9%	15.5%	27.5%
Congenital anomalies	0.7%	3.5%	5.0%
Toxemia/C. Section	19.9%	25.9%	40%

TIGHTNESS OF CONTROThe level of blood glucose

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that drives neonatal mortality and morbidity to non diabetic levels is still not known. It was however realised in the Diabetes in Early Pregnancy Study published in 1988 (5), that hypoglycemia was not teratogenic in humans. The emphasis since then has been to achieve lower and lower maternal blood glucose values almost without regard to the episodes of severe hypoglycemia in the mother. Typical of this period was a study from Dusseldorf that looked at 85 pregnancies in 77 women with type 1 Diabetes (6). Of these 32 women had 94 episodes of severe hypoglycemia with loss of consciousness (LOC) as shown in Table 3.

Table 3: Management of Episodes of Loss of Consciousness due to Hypoglycemia in Pregnancy (6).

Treated by spouse with glucagon	59
Treated by ER Physician	29
Occured in hospital	6
Required admission	6

The authors found that there was no difference in outcome of pregnancy between the mothers who had LOC and those who did not. They felt it was quite feasible to aim for a pre meal glucose of 58-90 mg/dl and treat LOC as it occured. Severe hypoglycemia rates upto 15 times higher than those reported in DCCT, have been reported from clinics where the policy was to accept values of blood glucose as low as 60 mg/dl (9).

Current thinking on the tightness of control is changing. It has been noted that hypoglycemia was teratogenic in rodents. It is felt that in the presence of maternal hypoglycemia with a limited glucose supply, fetal hypoglycemia and hypoinsulinemia can ensue (7). Fetal nutrient deprivation can have short and long term consequences. It has been suggested that the timing of some third trimester losses in the early morning hours may coincide with maternal hypoglycemia (8). In the long term there is intrauterine growth failure. This in turn is associated with higher rates of gestational age-specific neonatal mortality and with long term cognitive defects. Further, there is ample evidence now that small babies are more likely to develop diabetes, hypertension and coronary artery disease in later life. It has long been suggested that pancreatic failure in adult life may be a response to chronic maternal hyperglycemia. It is equally possible that chronic nutrient deprivation leading to fetal growth restriction and reduced islet cell proliferation can lead to the same consequence. Fears about subtle neuropsychological defects in the offspring exposed to chronic hypoglycemia in utero have been expressed by several authors (9). A study from the US showed a relationship between maternal blood glucose and fetal size (Table 4).

Table 4: Association of Maternal Blood Glucose with Fetal Size (10).

Glucose in mg/dl	No.	Fetal growth			Large for
		Preterm	Very Preterm		
		Restriction	Gest. age		Delivery
Preterm Delivery					
<99	574	6.97%	8.01%	10.63%	2.61%
99-130	502	5.98%	11.98%	12.95%	2.99%
>130	81	1.23%	22.22%	14.81%	3.70%

It has been found that in spite of near normal GHb levels, macrosomia rates remain significantly higher compared to non diabetic controls. This has been explained in part by the rebound hyperglycemia that often accompanies maternal hypoglycemia (9). A Cochrane review (11) of two trials comparing tight with very tight control of maternal glycemia found no difference in perinatal outcome. The reviewer's conclusion was that very tight control conferred no clear evidence of benefit but had a substantial adverse effect on lifestyle.

PRECONCEPTION CONTROL

It has been recognised since the 80's that preconception diabetes control was essential to prevent the high rates of congenital malformations. This is because organogenesis begins approximately from the 17th day after conception and is complete by the 42nd day. Thus by the time a woman realises she is pregnant, defects in organogenesis caused by hyperglycemia have already occurred. Data from several studies make this clear (Table 5) (12). The current stress in Western countries is to make pre conception control and counseling widely available.

Table 5: The Effect of Pre Conception Control on Major Congenital Anomalies (12).

	Non diabetic	Pre conception control	Post conception control
Fuhrmann '83	1.4%	0.8%	7.5%
Steel '89	NA	1.8%	10.5%
Kitzmiller '91	NA	1.2%	10.9%
DIEP '88	2.1%	4.9%	9.0%

MONITORING OF TREATMENT

There is evidence to show that checking post prandial glucose is more effective than checking pre prandial glucose. In one study (13), 66 GDM women were divided into 2 groups, one group kept their pre

prandial glucose between 60 to 105 mg/dl and the other group kept their post prandial glucose below 140 mg/dl. The differences in outcome are summarized in Table 6.

Table 6 : The Effect of Pre Prandial Versus Post Prandial Glucose Monitoring (13).

Variable	Pre prandial monitoring (n=33)	Post prandial monitoring (n=33)
C* Section for CPD#	36%	12%
Total C* Section	39%	24%
Large for gest** age	42%	12%
Small for gest** age	0%	3%
Neonatal complications	48%	21%

**C-Caesarian **Gest-Gestational #CPD-Cephalo Pelvic Disporportion*

Current practice in our clinic had to take all these scientific facts into consideration. Our clinic has the following types of patients :

1. General endocrinology patients including those with polycystic ovarian disease (PCOD) contemplating pregnancy or receiving ovulation inducing agents. These patients are warned that hyperglycemia may ensue in early pregnancy and are prescribed testing with a 50 g glucose load every 4 weeks from the 16th week.

2. Known diabetic patients who are contemplating pregnancy. These patients are taken off ACE inhibitors or angiotensin blocking agents and started on insulin if medical nutrition therapy is not sufficient.

3. Pregnant patients with hyperglycemia, referred to the clinic.

ROUTINE SCREENING

All pregnant patients presenting to us are advised a one step 50g glucose load at 24th to 28th week with the cut-off set at 140 mg/dl for venous plasma at 1 hour. It is worth noting a recent study (14) on 235 pregnant women which showed that a 50 g glucose load at 16 weeks could pick up 24 out of the 25 women eventually found to have GDM.

Any pregnant patient with a glucose value over 130 mg/dl at any time, is taken up by our programme. Our target from then on is to prevent glucose values rising over 130 mg/dl at any time and to keep the 2 hr PPBG value = or < 120 mg/dl. Based on the evidence given above, we do not routinely do a GTT as the values obtained therein will not alter the management in any way. In our hospital with over 4000 annual deliveries it is not practical to offer OGTT on a large scale.

USUAL CLINIC PRACTICE

All patients are started on folate supplement, if possible pre pregnancy. All patients are encouraged to do home blood glucose monitoring, especially those with pre existing diabetes. The dieticians closely follow the patients and check on the body weight. Usually a 3 meal 4 snack diet of appropriate calorie content is prescribed. All patients are seen at two week intervals and some weekly. The patients doing SMBG are encouraged to check as often as possible and report any value below 90 mg/dl and over 130 mg/dl. In patients not doing SMBG, fasting and post supper values are often difficult to obtain from a laboratory and they are managed with the post breakfast and post lunch values alone. It is known that the post dinner value is the highest of the 3 post meal values and adjustments are accordingly made. We usually do not do pre meal glucose checks except in patients with pre existing diabetes.

CHOICE OF INSULIN

Human insulin is invariably used. Short acting insulin is given before breakfast, lunch and dinner. In patients where the fasting value is over 100 mg/dl, intermediate acting insulin is added before the evening meal. Some patients can even be managed on 2 doses of short acting insulin, i.e. without a lunch time dose. Insulin analogues have an acceptable safety profile but it is not yet our practice to use them.

OTHER AGENTS

Metformin and the glitazones have been widely used as ovulation inducing agents and do not seem to have untoward effects at least in early pregnancy. They should be withdrawn once pregnancy is confirmed. Continued usage during pregnancy is not advisable except perhaps in a clinical trial. Acarbose could possibly be used too as it is not absorbed. The use of sulphonylureas has aroused interest after a recent study (15). Two caveats apply however: one, gliburide was started in GDM patients i.e. well after organogenesis was complete and hence its effects in early pregnancy were not evaluated. Two, gliburide was continued almost upto the time of delivery or Cesarean section (at which time maternal glucose levels would be expected to fall rapidly). Yet no data on maternal hypoglycemia or its outcome were supplied. Results of 100 consecutive pregnancies in our clinic is shown in Table 7.

Table 7: Results in our Clinic of 100 Consecutive Diabetic Pregnancies

Cleft lip/palate	1
Macrosomia (weight over 90th percentile)	4
Hypoglycemia	1
Jaundice	5
Convulsions	1
Septicemia	3

Fetal and neonatal loss	4
Healthy normal babies	81

The Cesarean Section rate was 70% and all the babies spent the first 12 hours in the NICU.

MANAGEMENT DURING LABOR

The target here is to maintain blood glucose at the level seen in non diabetic women i.e. between 70 and 90 mg/dl. Insulin is required till the first stage of labor. Once the 2nd stage actively starts insulin requirements fall to zero and glucose infusion is needed at a more or less constant rate of 2.5 mg/kg/min which translates to 150 ml per hour of 5% dextrose for a 50 kg woman. Hourly blood glucose monitoring with adjustment of the infusion rate is necessary.

MANAGEMENT DURING CESAREAN SECTION

The usual insulin is given the previous night. On the day of surgery insulin and glucose infusions are given to keep the blood glucose under 140 mg/dl. Once the cord is clamped, insulin is immediately discontinued and a glucose infusion started.

MANAGEMENT POST PARTUM

Over 95% of GDM patients require no further insulin. A glucose tolerance test with a 75g glucose load should be performed at 6 weeks post partum, though in our clinic it is rarely possible. We generally do a 2 hr post meal test at the time of discharge and ensure that all patients with abnormal values are followed up. A study on 788 GDM patients assessed 3-6 months after delivery (16) is shown in Table 8.

Table 8 : Fate of 788 Woman After a GDM Pregnancy (16).

Normal	74.6%
Impaired fasting glucose	5.8%
Impaired glucose tolerance	10.4%
Both IFG and IGT	3.7%
Diabetes	5.4%

In this study factors associated with a tendency to diabetes were pre pregnancy obesity, recurrence of GDM, gestational age at diagnosis of GDM, number of abnormal values in the OGTT, C-peptide/glucose score in pregnancy, insulin requirements during pregnancy, GHb levels and macrosomia.

SUMMARY

Diabetes in pregnancy is a significant contributor to neonatal mortality and morbidity. Control of blood glucose from the preconception period significantly reduces the risk. Very tight control does not confer additional benefits as compared to tight control. Persistent maternal hypoglycemia is nowadays considered unacceptable. The place of a standard OGTT in the management of GDM perhaps needs to be re-examined. Perfectly acceptable results are possible within the constraints of a hospital setting in India. It is important that post partum, the mothers at risk of diabetes are not lost to follow up.

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