

FOETAL LOSS IN PREGNANCIES ASSOCIATED WITH ABNORMAL GLUCOSE TOLERANCE

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SUMMARY

In a group of 1178 pregnant subjects with previous history of foetal loss, abnormal glucose tolerance (AGT) during the index pregnancy demonstrated by 100gm OGTT was present in 719 subjects (60.9%). Gestational Diabetes Mellitus (GDM) constituted only 23.1% of the subjects with AGT, while minor abnormalities of Glucose tolerance (Impaired Gestational Glucose Tolerance (IGGT) and Isolated Abnormalities of Blood Glucose on OGTT (IABG) were more prevalent than true GDM. The foetal loss in previous pregnancies was 77% in subjects with GDM, 76.9% in subjects with IGGT and 83.8% in subjects with IABG. Thus the prevalence of foetal loss among subjects with trivial abnormalities of glucose tolerance, who constitute the bulk of pregnant subjects with abnormal glucose tolerance, is as high as in those subjects with GDM, who constitute just one fourth of those with AGT during pregnancy. Maternal Hyperglycaemia is an established risk factor contributing towards excess foetal wastage, but the study reveals that even minor abnormalities of Glucose tolerance are as much associated with increased foetal loss as GDM. Among subjects with minor abnormalities of glucose tolerance, routine monitoring by meal related blood glucose may be normal. But, continuous ambulatory glycemic monitoring has revealed that the glycemic excursions in such subjects are higher than in subjects with normal response to OGTT. Such higher glycemic excursions possibly contribute towards excess foetal wastage seen in these subjects. With adequate follow up and treatment, the foetal loss in subjects with AGT was 2.7%, a figure comparable to that of the general antenatal population.

INTRODUCTION

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The association of foetal loss in pregnant women with glucose intolerance on one hand and

the improved foetal outcome with institution of adequate insulin therapy in such pregnancies on the other hand have distinctly established maternal hyperglycaemia as an important causative factor for foetal wastage. O'sullivan et al (1973) Cabbe S.G. (1977) While the foetal loss in a known diabetic subject marching through pregnancy or a gestational diabetic is well established, the contribution by subtle abnormalities of glucose tolerance during pregnancy towards foetal loss has not been appreciated. Analysis of pregnant subjects with bad obstetric history has enabled us to formulate an impression that minor degrees of abnormal glucose tolerance like IGGT, and IABG may be of importance towards foetal outcome, as much as established categories of Glucose intolerance. To substantiate this impression, in the present study, the prevalence of various categories of abnormal glucose tolerance, among pregnant subjects with Bad Obstetric History (BOH) was analysed and the percentage foetal loss in all categories of AGT

including GDM, IGGT and IABG was determined and outcome of intervention in such pregnancies was analysed.

MATERIALS AND METHODS

One thousand one hundred and seventy eight pregnant women with BOH attending the antenatal clinic formed the material for the study. BOH was defined as the loss of one or more foetuses or the new born in the perinatal period in their previous pregnancies. The mean age of the subjects was 23 + 4 years and they did not have any associated problems like hypertension or RH incompatibility and VDRL was non-reactive. Each one of them was subjected to a 100g OGTT after Sullivan & Mahan (1964). Based on their response to the OGTT, they were classified as having normal glucose tolerance, Impaired Gestational Glucose Tolerance (IGGT) and Gestational Diabetes Mellitus (GDM) as per the recommendations of the National Diabetes Data

TABLE I
Criteria for Diagnosis of Gestational Diabetes

Two or more of the following values after a 100g. Oral glucose challenge should meet or exceed.

	Venous Plasma	Venous Whole Blood
Fasting	105 mgm%	90 mgm%
1 hour	190 mgm%	170 mgm%
2 hour	165 mgm%	145 mgm%
3 hour	145 mgm%	125 mgm%

Impaired Gestational Glucose Tolerance (IGGT) is defined by a 2- hour plasma glucose level between 120 and 164 mgm% or venous whole blood value between 100 and 144 mgm%.

TABLE II
Prevalence of AGT in pregnant women with BOH - n = 1178

Type of AGT	No. of subjects	Percentage
GDM	166	14.1
IGGT	483	40.9
IABG	70	5.9
Normal	45.9	39.1

Group (NDDG) (1979) (See Table I). We had identified a fourth class of "isolated abnormality" of blood glucose (IABG) to place such of those pregnant women who had only one of 0,1,2 or 3 hour OGTT value elevated. All the subjects were followed up until delivery and the outcome of their pregnancies was recorded.

RESULTS

1. Prevalence of AGT in pregnant women with BOH

Of the 1178 pregnant women with BOH subjected to OGTT, GDM, IGT and IABG were seen in 14.1%, 40.9% and 5.9% respectively (Table II & Fig.1). In other words, about 61% of the study population had some form of AGT during the present pregnancy.

2. Relative prevalence of the various categories of AGT in pregnant women with BOH

When the relative prevalence of the various categories of AGT alone in the study group was analysed, it was found that GDM constituted less than one-fourth of women with AGT, while the minor abnormalities of IGGT and IABG on the OGTT put together formed a major proportion of 76.9% (Table III)

3. Correlation of foetal wastage in previous pregnancies with the type of AGT during the present pregnancy

Correlation of foetal wastage in previous pregnancies with the type of AGT during the present pregnancy, revealed that it was 77% in women with GDM, 76.9% in those with IGGT and 83.8% in those with IABG on OGTT (Table IV & Fig.2). In other words, it is inferred that BOH is associated as much with minor abnormalities of glucose tolerance as it is with GDM.

4. Correlation of universal foetal loss in previous pregnancies with the type of AGT during the present pregnancy

Pregnant women who do not have even a single living child from their previous pregnan-

cies have been designated as those with universal foetal loss. Naturally, the index pregnancy is precious for them. Correlation of universal foetal loss in previous pregnancy with the type of AGT during the present pregnancy showed that it was 56% in women with GDM, 61.3% in those with IGGT and 60% in women with IABG on OGTT (Table V & Fig.3). Once again, strikingly universal foetal loss is associated as much with minor blood glucose abnormalities as with GDM.

5. The outcome of index pregnancies in women with AGT and BOH in previous pregnancies

The outcome of the index pregnancies in the study group was analysed to determine the effect of glycaemic control on foetal outcome. The subjects were treated with insulin achieving an optimal glycaemic control of mean pregnancy plasma glucose level of less than 120 mgm% and were followed up till delivery and the outcome recorded. Among the 147 subjects followed up till delivery, good outcome was obtained in 143 (97.3%). Thus it was found that among subjects with AGT who had adequate follow up and glycaemic control, the foetal loss was 2.7%, a figure comparable to that observed in the general antenatal population.

DISCUSSION

The effect of maternal hyperglycemia on the development of the foetus and the outcome of pregnancy essentially depends upon the time of its manifestation. O'Sullivan (1966) Hyperglycemia present during the time of organogenesis as in pregnant women with established diabetes prior to pregnancy leads to congenital malformations. Categories of abnormal glucose tolerance developing or recognised during the later part of pregnancy are often associated with macrosomia, sudden intra uterine death of the foetus, respiratory distress syndrome, neonatal hyperbilirubinaemia etc.

In the present study involving 1178 pregnant women with BOH, about three fifths (61%) exhibited some form of glucose intolerance

TABLE III

Prevalence of various categories of AGT in pregnant women with BOH - n = 719

Type of AGT	No. of subjects	Percentage
GDM	166	23.1
IGGT	483	67.2
IABG	70	9.7

TABLE IV

Correlation of foetal wastage in previous pregnancies with the type of AGT during the present pregnancy

Type of AGT	No. of Previous Pregnancies	No. of Wasted Pregnancies	% of Wasted Pregnancies
GDM	424	328	77.0
IGGT	1279	983	76.9
IABG	142	119	83.8

TABLE V

Correlation of universal foetal loss in previous pregnancies with the type of AGT during the present pregnancy

Type of AGT	No. of subjects	No. of subjects with universal foetal loss	Percentage
GDM	166	93	56
IGGT	483	296	61.3
IABG	70	42	60

TABLE VI

Outcome of index pregnancies in women with AGT and BOH in previous pregnancies

Number of subjects followed up	...	147
Number of subjects with good outcome	...	143 (97.3%)
Number of subjects with foetal loss	...	4 (2.7%)

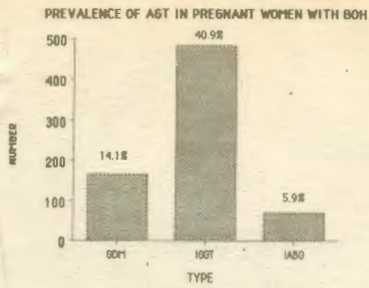


FIG. 1

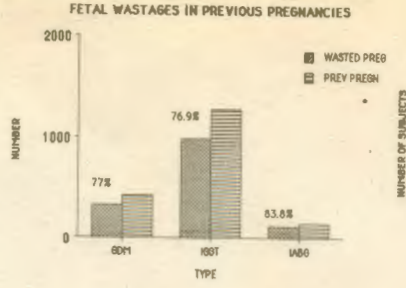


FIG. 2

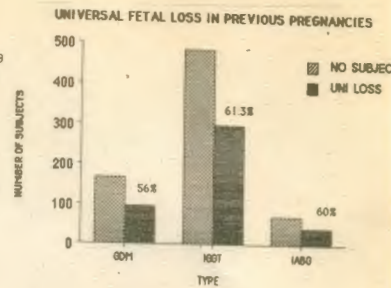


FIG. 3

during the index pregnancy. Foetal loss in previous pregnancies was associated as much with IGGT (76.9%) and IABG on OGTT (83.8%) during the present pregnancy as it was with GDM (72.2%). Likewise, universal foetal loss in previous pregnancies was as prevalent in women with IGGT (61.3%) and IABG on OGTT (57.1%) as in those with GDM(56%).

While the metabolic alterations in pregnant women with GDM can be said to account for poor outcome of such pregnancies Langer O.,(1988) the similar percentage of foetal loss in pregnant women with IGGT and IABG has been observed by us in the last few years is intriguing. The literature is scant with reference to association of such minor degrees of glucose intolerance with foetal outcome. Lindsay et al (1989) have recently documented the relationship of abnormal glucose tolerance test value and pregnancy complications. Conventionally monitoring the glycaemic status of pregnant subjects with abnormal glucose tolerance is achieved by fasting, post prandial or random blood sugar estimations. By continuous ambulatory blood sugar monitoring, Langer et al (1987) have established that glycaemic excursions at certain periods of the day are greater in subjects with IABG or IGGT, than subjects with normal glucose tolerance. Such higher ranges of transient glycaemic excursions contribute to a higher mean blood sugar level, which may be associated with poor foetal outcome. Such an observation underscores the need for close surveillance of pregnant women with even minor degree of glucose intolerance and institution of insulin therapy in them. Studies of Insulin levels in normal pregnant and Gestational diabetic subjects have established that the insulin response is impaired in Gestational diabetic subjects and probably to a lesser degree

in subjects with milder forms of AGT like IGGT and IABG. It is conceivable that such relative insulinopenia compared to normal subjects might contribute to the deleterious outcome of such pregnancies. The fact that intervention measures like introduction of a small dose of insulin improving the foetal outcome in such situation lends support to such a concept. Such a rationale of insulin therapy in pregnant subjects with trivial and often unrecognised categories of AGT is probably similar to the concept of prophylactic insulin recommended by Coustan D.R(1988) and insulin supplementation to diet by O'Sullivan (1975). It has, therefore, been our practice to recommend insulin to pregnant women with BOH who exhibit even minor degrees of glucose intolerance during the index pregnancies, a policy which has paid good dividends.

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