Diabetes in pregnancy among Sri Lankan women: gestational or pre-gestational?

K G H Jayathilaka[1], S Dahanayake[1], R Abewardhana[2], A K P Ranaweera[3], M R M Rishard[3], C N Wijeyaratne[4]

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Abstract

Introduction: There is an exponential rise in the occurrence of diabetes during pregnancy in South Asia. However data is sparse on the actual pre-gestational diabetes mellitus (PGDM) versus gestational diabetes mellitus (GDM) case-mix. The applicability of the WHO gold standard diagnostic tool – 75g oral glucose tolerance test (OGTT) – and its optimal timing between 24-28 weeks gestation in South Asians is unknown.

Objective: To assess optimal timing for diagnosis, determine the case-mix of PGDM and GDM and their specific risk profiles, insulin needs and pregnancy outcomes among Sri Lankans.

Method: Prospective data was collected from consecutive women diagnosed with diabetes in pregnancy, at the Professorial Unit, De Soysa Hospital, Colombo from 1st January 2010, - 28th Feb 2011. All were screened by an initial 2 hour post prandial (PPBS) at antenatal booking and risk stratified to determine the optimal timing of OGTT.

Results: (Total n=140) GDM and PGDM occurred in 82% and 18% of patients respectively.

GDM (n=115) Mean age 32.16±5.26; booking POA 13.7±5.8weeks; booking BMI 26±4.9kg/m^2. Risk factor profile – 1(33%); 2(29.3%); ≥3 (29%); 64% were detected before 24 weeks. Those >30 years were 67% among early diagnosis versus. 36% among those diagnosed between 24-28 weeks (p=0.02). Previous miscarriages were 36% among early diagnosed versus. 18% among those diagnosed late (p=0.145). Pregnancy induced hypertension occurred in 7.8% with similar occurrence in both sub-groups.

Pregnancy outcome was similar in the two subgroups (100% live births, mean birth weight 3.127±0.50kg, macrosomia 21%; LSCS 43%, pre-term 6.9%; neonatal hypoglycaemia and jaundice 11%; congenital malformation=1(0.9%).

Pre-GDM (n=25) Mean age 32.92±5.9 (2/3 >30 years); booking POA 12.7±6.1weeks; booking BMI 23.49±3.52kg/m^2, significantly less than GDM group (p=0.03). Risk factor profile – 1(28%); 2(28%); ≥3 (32%). Previous miscarriage had occurred in 24% with more still births than in GDM group (p=0.002). Previous GDM was significantly more (p=0.03). Pregnancy induced hypertension occurred in 8%.

Pregnancy outcome: 100% live births. Mean birth weight 3.014±0.56kg; macrosomia 20%; LSCS 44%; pre-term 16%; neonatal jaundice and hypoglycaemia 20% (significantly more than GDM group, p=0.02); congenital malformation =1(4%).

Conclusion: Unequivocal PGDM occurs among 18% of pregnant diabetics, among older multiparous women with previous GDM and still births. GDM was diagnosed before the internationally recommended 24 weeks in 64%, although their insulin requirement was significantly less than those diagnosed after 24 weeks.

Recommendations: 1) The current timing in pregnancy for screening by OGTT in Sri Lanka requires review. 2) A comprehensive pre-conception screening programme, particularly for older women with previous GDM and/or previous pregnancy loss, is required.

[1]Research Coordinator, Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Colombo, [2]Diabetes Educator Nursing Officer, [3]Registrar in Obstetrics and Gynaecology, De Soysa Hospital for Women, Colombo, [4]Professor in Reproductive Medicine, Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Colombo, Sri Lanka and Honorary Consultant Physician, De Soysa Hospital for Women, Colombo, Sri Lanka.

Introduction

There is an exponential rise in the prevalence of diabetes throughout the world, with South Asia being its focal point. Its incidence has increased in South Asia by 111% in the past 15 years, when compared to other continents such as North America, Australia and Europe which have less than a 50% rise (1). Hence, Sri Lankans are clearly a high risk population. Gestational diabetes mellitus (GDM) is emerging as a common medical complication of pregnancy (2), with a parallel increase to the pandemic of type 2 diabetes mellitus. Currently GDM affects approximately 7% of all pregnancies and up to 14% of pregnancies in high-risk populations while pregestational diabetes mellitus (PGDM) is estimated to affect about 1.3% (3). The incidence of GDM in South India is reported to be 16.55%, while our own incidence in the community was 10.3 % (4, 5).

The American Diabetes Association (ADA) defines GDM as "glucose intolerance of any degree with the onset or first recognition during pregnancy, and irrespective of whether or not insulin is required or the condition persists after pregnancy" (6). Therefore pregnancy can be perceived as a "stress test" for glucose intolerance and a predictor of future diabetes/pre-diabetes in any given population. Diabetes in pregnancy, both GDM and pre-gestational diabetes mellitus (PGDM), are linked to several maternal and fetal/neonatal complications (7, 8, 9). PGDM carries a greater risk for mother and baby, particularly if poorly controlled prior to a planned pregnancy. There is no reliable data on the actual pre-gestational diabetes mellitus (PGDM) versus gestational diabetes mellitus (GDM) case-mix in Sri Lanka. A formal pre-conception assessment package to screen for diabetes mellitus is yet not in place. Neither is the suitability of the diagnostic tool (the 75g oral glucose tolerance test - OGTT) to be performed in South Asian women at the recommended 24-28 weeks of gestation clearly known.

Objectives

We proceeded to determine the case-mix of PGDM and GDM, specific risk profiles, insulin requirement and pregnancy outcomes and to assess the optimal timing for diagnosis by OGTT in a cohort of pregnant Sri Lankan women with diabetes attending a single tertiary care unit in Colombo, Sri Lanka.

Method

This is a prospective review of 140 diabetic pregnant women attending the antenatal clinic conducted by Professorial Unit of De Soysa Hospital for Women. Consecutive women with abnormal glucose tolerance, who attended the clinic between January 2010 and February 2011, were recruited.

The database was maintained by pre-intern medical graduates, by using a previously validated interviewer-administered questionnaire. The information was gathered during the patients' antenatal clinic visits and hospital admissions, through a one to one in-depth interview and reliability of clinical information determined by cross checking past medical records of each subject. Ethical approval was granted by the Ethics Review Committee of the Faculty of Medicine, University of Colombo to maintain a database.

We defined pre-gestational diabetes mellitus (PGDM) as abnormal glucose tolerance recognized prior to conception, which the patient was aware of at the time of her antenatal booking visit in the first trimester. We included into the GDM group all patients who revealed no previous history of diabetes mellitus but were diagnosed by the attending physician (CNW) based on WHO criteria for diagnosing abnormal glucose tolerance by a 75g oral glucose tolerance test (OGTT).

This was possible because we adopted an in-house protocol that all women with previously unknown diabetes/pre-diabetes undergo a 2 hour postprandial blood glucose (2hr PPBS) test at antenatal booking in the first trimester. When this value exceeds 120 mg/dl, which is the upper limit of target for normoglycaemia in pregnancy complicated by diabetes, we proceed to performing the OGTT as soon as possible in early pregnancy (well before 24 weeks gestation). If the OGTT is abnormal in early pregnancy and particularly before 24 weeks of period of gestation (POG), we categorize them as with 'early diagnosed' GDM. If the OGTT thus performed as soon as the 2hr PPBS shows a result >120 mg/dl proves to be normal, we repeat the OGTT in later pregnancy at the recommended period of gestation (24-28 weeks) and if found to be abnormal categorize them as 'late diagnosed' GDM.

We identified the standard risk factors for GDM in all women to risk stratify the pregnant women. These include the booking visit and first trimester BMI $\geq 25 kg/m^2$ recognized as maternal obesity, maternal age ≥35 years, polycystic ovary syndrome (PCOS), family history of diabetes mellitus in first degree relatives, migrant workers, previous fetal macrosomia (>3.5 kg at term pregnancy), previous fetal loss as still birth or late spontaneous miscarriage, recurrent pregnancy induced hypertension particularly of the gestational non proteinuric variety, medications with steroids or anti psychotics and excessive weight gain in the current pregnancy (10). We also adopted a standard clinical approach that despite a "normal" 2hr PPBS value at antenatal booking in very early pregnancy, in the presence of multiple risk factors (≥2) that there is compelling evidence of a higher risk for diabetes and ensured that the OGTT is performed "as early as possible" in the high risk women rather than awaiting the recommended 24-28 weeks of gestation.

All those with abnormal OGTT were initially managed by intensive dietary modifications with blood glucose monitoring, with institution of insulin therapy as deemed appropriate by the glycaemic profile. Blood sugar control was assessed by serial blood sugar series over 24 hours. Adjustment of the dose of insulin was made by the attending physician to achieve target blood glucose values of pre-meal 70-90 mg/dl and 2hr PPBS <120mg/dl as early as possible and aimed at being achieved throughout pregnancy by fortnightly review. All those on insulin therapy and with additional risks were admitted at 38 weeks gestation to plan the mode and timing of delivery, while those on dietary modification alone were assessed individually to deliver before 40 weeks. Demographic data, past obstetrics history, current pregnancy factors and associated complications, risk factors for GDM, serial fetal assessment by ultrasound scan, biochemical testing, insulin dose required, mode and timing of delivery, birth weight, pregnancy outcome in respect of maternal, and perinatal complications were carefully recorded and re-checked.

Statistical analysis

Data analysis was performed using SPSS13® software. Mean value and standard deviation was estimated for each continuous variable, such as maternal age, booking BMI, POA of booking visit, birth weight; while proportions by percentages were estimated for categorical variables such as sub groups of early and late diagnosed GDM, dietary modification alone and insulin treated groups, the presence and number of risk factors, mode and timing of delivery, maternal, fetal and neonatal complications.

Chi square value was used to compare frequency and/or proportions while Student's t test was used to compare continuous variables. $P< 0.05$ was considered as the level of significance.

Results

Among a total of 140 women studied during this period, GDM occurred in 115 (82%) with PGDM in 25 (18%).

Table 1. Comparison demographic data, risk factors, pregnancy outcome and neonatal complications of gestational versus pre-gestational diabetes subgroups

Characteristic	*GDM N=115*	*PGDM N=25*	*P value*
Age (years)	32.16±5.26	32.92±5.9	NS
Booking POA weeks	13.7±5.8s	12.7±6.1	NS
BMI (kg/m^2)	26±4.9	23.49±3.5	0.034
Parity	2.44±1.2	3.08±1.4	0.023
Risk Factor			
BMI>25kg/m^2	55 (47%)	5 (20%)	0.037
Age>30 yrs	71 (61.7%)	19 (76%)	NS
Previous birth wt >3.5kg	15 (13.0%)	4 (16%)	NS
Previous IUD	4 (3.5%)	5 (20%)	0.002
Previous miscarriage	31 (26.3%)	6 (24%)	NS
Family T2DM	50 (43.5%)	15 (60%)	NS
Previous GDM	23 (20%)	10 (40%)	0.033
PCOS	6 (5.2%)	1 (4%)	NS
Pregnancy outcome			
Live births	100%	100%	-
Operative delivery	43%	44%	NS
Preterm delivery	6.9%	16%	NS
Neonatal complications	14.7%	40%	0.012
Maternal sepsis	2.6%	16%	0.005
PIH detected	7.8%	8%	NS
Birth weight (kg)	3.127±0.50	3.014±0.56	NS
Macrosomia	21%	20%	NS
Congenital anomalies	0.9%	4%	
Neonatal complications			
Jaundice	8	6	0.01
Hypoglycaemia	7	3	0.295
Low birth weight	1	1	
Prematurity	-	1	
Birth asphyxia	1	-	

(NS = not significant, BMI = body mass index, T2Dm = type 2 diabetes mellitus, IUD = intrauterine death, PCOS = polycystic ovary syndrome, GDM = gestational diabetes, PIH = pregnancy induced hypertension)

Table 2. Pregnancy outcomes in early and late diagnosis groups among those with gestational diabetes (GDM)

Characteristic	*Early diagnosed GDM*	*Late diagnosed GDM*	*P value*
Birth weight	3.25±0.07kg/m^2	2.91±0.11kg/m^2	0.012
Shoulder length	37.3 ± 2.7cm	36.4 ± 2.8cm	NS
Preterm delivery	15%	9%	NS
LSCS – Elective	30.7%	27.3%	NS
Emergency	10%	9%	
Neonatal, complications	23%	18%	NS
Maternal complications	5.1%	4.5%	NS
Congenital abnormality	1	-	

Their demographic characteristics, risk factor profiles, pregnancy outcomes are depicted in Table 1. Both groups of women are of similar age and period of gestation at antenatal booking in the first trimester. However the PGDM group had a significantly lower BMI and higher parity. The GDM group when further sub divided into two groups depending on the period of gestation (POG) of diagnosis, as before 24 weeks categorized as 'early' diagnosis and after the recommended 24 weeks as 'late' diagnosis, show that those diagnosed early comprised 64% of the group. Both these subgroups had a similar parity of 2, while women older than 30 years was significantly more (67%) among those diagnosed 'early' (p=0.02). Both groups had similar BMI at antenatal booking 26.10±3.7 versus. 24.97±6.07 kg/m^2 (p>0.05) (Table 2).

Significant risk factors identified included maternal age >35 years, past history of miscarriage or still births, previous birth weight >3.5kg, family history of diabetes mellitus in first degree relative(s), past history of GDM or PIH, previous features of PCOS and current medication with steroids or antipsychotics. Although at least one risk factor was evident in 62% diagnosed 'late' versus 34% in those diagnosed 'early', the presence of 2 or more risk factors was significantly greater in those found to have 'early' GDM (p=0.04) (2 risk factors 37% vs. 22% and ≥3 risk factors in 29% vs. 17%). Comparison of individual risk factors revealed that a previous history of GDM was significantly more in the 'early' GDM group (p=0.03). The only baby born with a congenital abnormality was to a para 2 woman aged 35 years, with a BMI of 32.8 kg/m^2, who had her ante-natal booking at 18 weeks and categorized as early GDM. She was a diagnosed patient with PCOS and had previous history of GDM. Despite dietary modification and achieving good glycaemic control she gave birth to a term, live baby, weighing 3.654 kg, with phocomelia by caesarean delivery.

Discussion

This tertiary clinic based urban cohort of pregnant diabetics reveals for the first time in Sri Lanka that the ratio of pre-gestational to gestational diabetes is approximately 1:4, which is a remarkably high ratio for women in their early 30s. In view of the mean period of gestation at ante-natal booking of the pre-gestational diabetics being at the completion of the period of organogenesis, and the four-fold greater occurrence of congenital fetal malformations in them, this clinic based data further highlights the deficiencies in the current health care delivery system for diabetes care in women of reproductive age. As suggested by others (11), this study highlights the need for a simple low-cost pre-conception package to be made available for all diabetic women of reproductive age attending primary care and tertiary care services and the need to adopt a comprehensive family planning counselling service in the diabetes care for women.

Although there is a limitation in the selection of this clinic based sample, which is more liable to selection bias, it reveals the actual patient characteristics of a busy urban setting clinical service that also brings into question the applicability of the recommended timing of the OGTT for diagnosing diabetes in pregnancy. There is a high probability that those with 'early' GDM we identified were more likely to have had previously undetected pre-gestational abnormal glucose tolerance. The community survey conducted in 2003/4 in a semi-urban Colombo based sample revealed that GDM occurred in 10% of the community (5). In the light of our current findings of the early detection of GDM in this hospital based sample, we need to seriously question the current screening strategy for GDM in the community maternity and child health (MCH) service. Although the ADA recommends any woman with an "average risk" be screened at 24-28 weeks of POA (12), the current data confirms that 66% of the

women diagnosed with GDM before 24 weeks had at least two standard risk factors. This argues for the need for universal screening of Sri Lankan pregnant women irrespective of the number of risk factors, and those without proper pre-conception assessment to be screened in the first trimester. The need to screen early for GDM by the OGTT must be dependent on the presence of a high risk status, absence of pre-conception assessment whilst also taking into account the clear ethnic risk for diabetes in our community (13, 14, and 15). A larger scale case control study is recommended to identify the optimal timing for screening (16). Based on our findings, it can be extrapolated that there is an increase in the prevalence of preexisting diabetes in our population, particularly among younger women early in their reproductive years. These issues require appropriate consideration when planning re-organization of the current health service delivery.

It is noteworthy, that despite no significant difference in the individual risk factors, a past history of GDM was significantly higher among those with early diagnosed GDM. This supports our hypothesis of the high probability for a larger proportion of women in the early diagnosed group of GDM to have had previously undetected chronic diabetes / pre-diabetes as many groups including us have shown that nearly 40-60% of those with previous GDM progress into chronic diabetes and the metabolic syndrome, as early as 3 years post partum (7, 17, 18, 19). It is also interesting that those with clear PGDM in this study had a significantly lower BMI. The absence of data collection of the waist circumference in the 1st trimester affects a clear conclusion or interpreting this finding.

As concluded previously universal screening is the most sensitive strategy in identifying nearly all women with GDM. Because of their high risk of type 2 diabetes later in their life, the opportunity to provide counselling on early lifestyle modification will be missed by not having an effective follow up programme for women with previous GDM. No doubt the accurate and timely diagnosis of GDM will also impact in the short term on pregnancy outcome. The responsibility of long-term follow up for these young women at metabolic risk no doubt falls on our primary care services. This is well supported by the fact that 40% of PGDM women had a past history of GDM. Hence, we recommend that until more reliable evidence is available all women with probable PGDM due to early diagnosis of GDM be encouraged long term follow up to achieve metabolic risk modification and regular screening for metabolic disease (20). This strategy would be in keeping with early initiation of primary prevention of diabetes and its associated medical problems. Furthermore, this will also ensure improved pre-conception assessment and better metabolic status for their future pregnancies.

Our data also confirms that the risk of neonatal as well as maternal complications being significantly more in the pre-gestational diabetic woman; while those with early diagnosis of GDM appear to follow a similar trend. Moreover the significantly greater birth weight in the group with 'early' GDM than those diagnosed at the recommended period of gestation supports our hypothesis that the early diagnosed group possibly falls within a more severe category of pre-pregnant metabolic disease. Albeit a small tertiary hospital based sample, this data provides valuable information to encourage a more detailed assessment of previous pregnancy outcomes and in particular birth weight exceeding 3.5 kg (95th centile of mean birth weight for Sri Lanka), intrauterine deaths and mid trimester miscarriages in young women to help risk stratify them into regular screening programmes for Sri Lanka. The fact that both PGDM and GDM groups had similar occurrence of pregnancy induced hypertension also supports the need for a multiple risk factor approach to the problem of chronic non-communicable disease being adopted in our community health programme, which must also include such young high-risk women.

To summarize, the case mix of diabetes in pregnancy in an urban based tertiary clinic in Sri Lanka confirms a gestational to pre-gestational ratio of 1: 4 among women in their early 30s. Their mean period of gestation at antenatal booking was well after the period of organogenesis. Two thirds of the women with GDM were diagnosed before the recommended period of gestation of 24 weeks, where early screening was necessary due to the presence of 2 or more risk factors in addition to their high ethnic risk. Previous GDM was significantly more in those diagnosed early, who also had a significantly higher birth weight in their current pregnancy. Although the majority of women with early GDM required dietary intervention alone with a smaller proportion requiring insulin than those diagnosed after 24 weeks, the birth weight being higher in the early GDM group requires further study. Women with unequivocal pre-gestational diabetes had more severe neonatal complications in the form of hypoglycaemia and jaundice, more congenital anomalies and a greater incidence of maternal sepsis.

Conclusion

We conclude that pre-gestational diabetes occurs at least in a fifth of urban based women in Sri Lanka and is associated with higher maternal age, multiparity, previous gestational diabetes and intrauterine deaths with maternal BMI not being an important risk factor. Based on the current data we recommend a more comprehensive pre-conception screening programme for the older women with previous GDM and/or previous pregnancy losses and a robust programme to ensure long term follow up of women with gestational diabetes after delivery, with a view to prevent progression to frank type 2 diabetes mellitus and metabolic disease. The MCH programme also requires exploring the optimum timing for screening for diabetes in pregnancy by OGTT in the current context.

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