Original Article

Diabetes in pregnancy: diagnosis, management, outcome and complications

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Abstract

Introduction: Numerous perinatal complications of diabetes in pregnancy have been recognised. Maternal post-partum complications can be equally devastating.

Method: In this study, a cohort of known type 1 and type 2 pregnant diabetics and newly diagnosed Gestational Diabetes Mellitus (GDM) patients were analysed. Data collected was analysed in terms of method of diagnosis, gestational age at diagnosis for GDM, relevant medical or obstetric history, subsequent management and follow up.

Results: Out of 79 viable pregnancies, 69.6% of patients were diagnosed with GDM, 13.9% with type 2 DM and 16.5% with type 1 DM. Mean gestational age for the GDM cohort was 37.9 (±1.6) weeks, 35.5 (±3.7) weeks in Type 2 and 37.1 (±0.7) weeks in the Type 1 cohort (p=0.010). 20.3% of all cohort and specifically 23.6% of GDM pregnancies had a fetus which was large for gestational age. 30% of GDM patients, 25.5% of Type 2 DM patients and 84.6% of Type 1 DM patients, had their blood glucose controlled by an insulin infusion pump peri-partum. Mean HbA1C in the third trimester was 6.0%, 6.3% and 7.1% in GDM, Type 2 and Type 1 diabetics respectively (p=0.004). A negative correlation was seen between HbA1C levels in third trimester and delivery gestational age (p<0.001).

Conclusion: Our findings emphasize the need for close follow up of these patients. Implementing a structured and holistic multidisciplinary team may have an impact on outcome, focusing on maternal education, in particular in GDM patients and their risk of developing type 2 DM in the future.

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Introduction

Diabetes mellitus (DM) is the most common medical condition complicating a pregnancy, affecting 16% of all life births[1]. Diabetes is the epidemic of the 21st century, with recorded increase in the incidence globally. Possibly, one may attribute this to an increased tendency for a sedentary lifestyle and a shift towards a western diet. The unmodifiable genetic predisposition is a major determinant which is quite relevant to the Maltese population. The prevalence of gestational diabetes in Malta was 15.5% in 2010 based on WHO criteria,[2] rising up to 16.5% when using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria.[3-4] A rise in obesity and delayed childbearing age have led to an increase incidence of gestational diabetes mellitus (GDM) and earlier onset of type 2 diabetes mellitus . The potential devastating effects of diabetes can affect both the mother and fetus with

the management and outcomes differing according to the aetiology of the condition.

This retrospective study conducted at Mater Dei Hospital in Malta, has analysed how pregnant mothers who had diabetes during pregnancy (GDM, type 1 & type 2 DM) are diagnosed and managed, further focusing on follow-up and subsequent maternal and fetal outcome.

Methods and Materials

A retrospective study consisting of a cohort of type 1, type 2 and newly diagnosed GDM patients, over a 5-year period. These patients consisted of all consecutive patients who presented to a single firm with any of the mentioned conditions in the study period. Our study comprised of 79 pregnancies, of which 69.6% were diagnosed with GDM, 16.5% were Type 1 DM patients and 13.9% Type 2 DM patients. The IADPSG criteria (Figure 1) was used for diagnosing GDM, based on an oral glucose tolerance test (OGTT) according to risk factors at booking and a fasting blood glucose level above 5.1 mmol/l. Risk factors for GDM include a high body mass index (BMI), strong first-degree family history of type 2 DM, severe polycystic ovarian syndrome (PCOS), previous unexplained stillbirth or macrosomia and macrosomia or polyhydramnios during the index pregnancy. However, two GDM cases were diagnosed during the third trimester of pregnancy secondary to clinical parameters such as polyhydramnios or increased fetal abdominal circumference.

The data collected included the method of diagnosis, gestational age at diagnosis, variations in HbA1c levels throughout pregnancy, management, gestational age and weight at delivery, any peri-natal maternal or fetal complications and long term follow up of the mother. Macrosomia was classified as birth weight above 4.5kg. Infants with weight above the 90th centile for gestational age were classified as large for gestational age. This was performed by ultrasound fetal measurements plotted on a growth chart. Data was collected on a proforma created using Microsoft Access.

Nonparametric assessments were used. Assessments between categorical variables were analysed using χ^2 test and Fisher's exact test. Associations between independent samples were analysed using the Mann-Whitney U or Kruskal-Wallis as appropriate. Correlation analyses were carried out using Spearman correlation. Statistical assessments were carried out using IBM SPSS® Statistics for Windows, Version 22.0, (IBM Corp. Armonk, NY, USA). A two-sided $P < 0.05$ was considered statistically significant.

Results

From a total of 79 pregnancies, 55 patients were diagnosed with GDM (69.6%), 13 patients had pre-existing type 1 DM (16.5%) and 11 patients had type 2DM (13.9%). The vast majority of GDM patients (50.9%) were started on oral hypoglycaemic agents specifically Metformin, while 32.7% required insulin mostly human insulin (Actrapid®) pre-prandially. About 63.6% of Type 2 DM patients were on insulin mostly combination regimes involving intermediate and short acting human insulins (Insulatard® and Actrapid®), 36.4% on both insulin and oral hypoglycaemic agents and 18.2% on oral hypoglycaemic agents only (Metformin). All our Type 1 patients were on insulin, the majority of which were on insulin analogues (insulin glargine and insulin aspart). The median gestational age at which a GDM diagnosis was made was 29 weeks (IQR: 28-32).

The mean fasting blood glucose in the GDM cohort was 6.31mmol/l (SD+/- 1.79), the mean blood glucose during the first hour of OGTT was 12.06 mmol/l (SD+/- 2.77) and the mean second hour blood glucose was 10.73 mmol/l (SD+/- 2.95).

The shortest mean gestational age of 35.5 weeks was in the Type 2 DM cohort compared to 37.1 and 37.9 weeks in the Type 1DM and GDM groups respectively (P=0.010). Type 1 DM mothers had generally a younger age (Mean +/- SD: 27.0 +/- 4.3 years) compared to GDM mothers (Mean +/- SD: 31.5 +/-6.8 years) and Type 2 DM mothers (Mean +/- SD: 32.4 +/-4.4 years) (P=0.031).

The mean gestational weight in the GDM group was 3.5kg (+/-0.7 Kg) and the mean neonatal weight in the type 1and type 2 cohort was 3.2kg (P=0.041). In 20.3% of patients, an antenatal scan showed a large for gestational age fetus, 23.6% of which were GDM pregnancies.

The median HbA1c in the pre-conception period was 7.8 (IQR: 7.25-9.35 %) and 7.6 (IQR: 6.65-8.18 %) in the Type 1 and Type 2 group respectively. In the Type 1DM cohort this went down to 7.4 in the first trimester and 7.2 and 7.1 in the second and third trimesters respectively. In the Type 2DM group, the HbA1c declined gradually from 7 to 6.8 and 6.3 in the first, second and third

trimesters respectively.

A statistically significant negative correlation (*P*=<0.001) was found between gestational age and HbA1c levels.

During the intra-partum period 30% of GDM and 25.5% of Type 2 DM patients required an insulin infusion pump. However, as expected, up to 84.6% of Type 1DM patients required an insulin infusion pump. No metabolic complications were reported during the intra-partum period. Apart from macrosomia, respiratory distress was common in babies of diabetic women, with a number of infants requiring neonatal intensive care admission for glucose monitoring. Two infants suffered a hypoglycaemia induced seizure at birth. Other neonatal complications reported include two intra-uterine deaths in the GDM group and a number of organ anomalies in 3 fetuses in the Type 1 and 2 group.

Six weeks post-partum, 52% of GDM patients attended for an OGTT, 21.8% of which had Type 2DM and 5.5% impaired glucose tolerance.

Discussion

Malta, an island in the Mediterranean Sea, has one of the highest rates of diabetes in Europe.[5] The estimated prevalence of diabetes in adults was 13.9% in 2015, according to the International Federation of Diabetes Atlas. Moreover, the prevalence of gestational diabetes is on the rise. A study conducted by Aganovic et al, in 1983 has shown that the prevalence of gestational diabetes was 11.5%, compared to a prevalence of 16.5% in 2010, according to IADPSG criteria.[6-7]

Diabetes in pregnancy has well been recognized as the commonest medical condition complicating a pregnancy. The effects of diabetes mellitus on the mother and her fetus can be described as diverse, complex and occasionally resulting in permanent end-organ damage. Albeit, in the vast majority of cases, complications can be avoided and prevented if the mother is followed-up closely and managed within a multi-disciplinary team. Maternal obstetric complications include a higher risk of pre-eclampsia, pregnancy-induced hypertension, higher risk of operative vaginal delivery and caesarean section wound infection.[7] The well-known medical complications associated with diabetes and micro-vascular disease tend to get worse during pregnancy. Diabetic nephropathy has a worse prognosis during pregnancy when compared to equivalent stages of chronic kidney disease outside pregnancy.[8] Pregnant Type 1 and 2 DM patients, should be screened for diabetic nephropathy throughout pregnancy, with albumin-creatinine ratio being a more accurate test.[9] Around 30 to 40% of diabetic patients suffer from chronic hypertension, however, during pregnancy 60 to 70% of diabetic patients develop hypertension thus exacerbating any pre-existing nephropathy. [10,8] The changes associated with diabetic retinopathy progress in around 50-70% of cases.[11] Screening should be done in the pre-conception period and in every trimester of pregnancy coupled with good blood pressure and glycaemic control.[12] On a positive note, despite the programmed routine screening in our cohort of type 1 and 2 patients, no cases of progressive nephropathy or retinopathy complications were reported. Fetal complications include, an increased risk of first trimester miscarriage, congenital anomalies, macrosomia, stillbirth, shoulder dystocia, neo-natal hypoglycaemia and respiratory distress syndrome.[13-14]

The IADPSG criteria were used for a diagnosis of gestational diabetes, in line with recent recommendations from the HAPO study.[15] Gestational diabetes can be defined as 'any degree of glucose intolerance with onset or first recognition during pregnancy'.[16-17] Our results show that the mean gestational age at delivery was highest in the GDM cohort compared to the Type 1 and Type 2 group. One can possibly explain these results by the fact that obstetric patients with pre-gestational diabetes are considered to be high risk patients and hence the obstetricians will have a lower threshold to deliver the fetus prior to the estimated date of delivery. Moreover, the lowest gestational age was recorded in the Type 2 DM group of patients. We also report that patients with Type 2 DM tend to be older and with a higher BMI, these results are in agreement with other authors.[18]

A strong positive correlation exists between percentage fetal body fat, fetal insulin levels and maternal glycaemia.[15] On average, patients with GDM had a fetus of a higher gestational weight, while mean gestational weight in Type1 and 2 DM patients was similar. This could possibly be explained by a relatively later diagnosis, monitoring and initiation of treatment in the GDM cohort as compared to patients with pre-existing diabetes mellitus.

The HbA1c during the pre-conception period in the pre-diabetic patients was sub-optimal in both groups. The median HbA1c level in both groups improved during the first trimester possibly due to the decreased insulin requirements in the first trimester. Nielsen et al have reported a decrease in HbA1c level, from 6.3% pre-pregnancy, to 5.6% in the third trimester in normal pregnant patients.[19] Moreover, the life span of erythrocytes during pregnancy shortens secondary to increased erythropoietin secretion.[20] Therefore, irrespective of glycaemic control, HbA1c will drop during the first and third trimester, and lowering the threshold by 0.4% in diabetic pregnancies will translate into better glycaemic monitoring during pregnancy.[21] The mean HbA1c levels remained highest in the Type 1DM group, throughout pregnancy. Adequate glycaemic control in Type 1DM during pregnancy is challenging mainly due to the risk of hypogylacemia coupled by peaks and troughs in insulin requirements which are not necessarily met by the insulin dosage regimen.

Women with GDM have a higher risk of developing Type 2DM, despite the fact that in most cases euglycaemia is achieved immediately after delivery.[21] All the GDM patients in our cohort were invited for a repeat OGTT 6 weeks after delivery. A low turnout of 52% was reported and 21.8% were diagnosed with Type 2DM. In a systemic review of 20 studies, patients with gestational diabetes have a 7-fold increased risk of developing Type 2DM when compared to patients with a euglyacemic pregnancy.[22]

Our study has shown a significant correlation between the different types of diabetes and pregnancy outcomes, emphasizing a known fact that pre-existing diabetes mellitus both Type 1 and 2, greatly determines obstetric outcomes. Our study has also confirmed the idea that women are at a higher risk of developing diabetes mellitus after a pregnancy affected by gestational diabetes. This underpins the importance of prevention of diabetes, and the emphasis on follow up once the condition has been diagnosed.

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