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Clinical and Epidemiological Profile of Diabetes Mellitus in Pregnancy, Isle of Youth, 2008

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ABSTRACT

INTRODUCTION Diabetes in pregnancy threatens both maternal and neonatal health, with risks of lung immaturity, fetal macrosomia, dystocia and impaired maternal kidney function. Before insulin, diabetes resulted in maternal mortality rates of 30–50% and perinatal mortality rates of 50–60%. Global prevalence estimates vary by population, geographical area and diagnostic criteria. Diabetes accounts for some 90% of endocrine complications in pregnancy.

OBJECTIVES Determine diabetes mellitus prevalence in pregnancy and characterize the population of diabetic women who gave birth in the Isle of Youth Special Municipality in 2008.

METHODS A descriptive retrospective study was carried out from January to December 2008. Clinical records were reviewed of 180 diabetic women who gave birth on the Isle of Youth in 2008, their diagnosis based on WHO criteria modified by municipal health authorities. Study variables were: maternal age, nutritional status, glucose tolerance, gestational age at diagnosis, history of diabetes, and pregnancy outcome; as well as risk factors such as diabetes family history, pregnancy weight gain and comorbidities.

RESULTS Overall prevalence (pregestational and gestational diabetes) among these cases was 17.3%; highest in the group aged ≥35 years. Gestational diabetes was more frequent (96.1% of cases) than pre-gestational diabetes. Multiparity (62.1%), a first-degree family history of diabetes mellitus (26.1%), excess weight before pregnancy (50%) and adequate weight gain during pregnancy (54.4%) were the most frequent conditions found. Among gestational diabetics, diabetes was most frequently detected at 20–28 weeks gestation (31.8%). Fetal macrosomia appeared in 4.4% of cases and a high percentage of deliveries were by Cesarean section (30%). There were no low Apgar scores or congenital abnormalities among neonates.

CONCLUSIONS Despite using modified, more inclusive, WHO diagnostic criteria, the clinical and demographic characteristics of the population studied were comparable to those in other studies of diabetes in pregnancy, except for the low frequency of fetal macrosomia and absence of birth defects present in our study.

KEYWORDS diabetes mellitus; pregnancy; risk factors; diabetes, gestational

INTRODUCTION

Diabetes mellitus (DM) in pregnancy is a serious threat to the health of both mother and child, bringing with it risks of lung immaturity, fetal macrosomia, dystocia and impaired maternal renal function. At the beginning of the 20th century, many diabetic women were infertile; the few who managed to conceive faced a poor prognosis. Before insulin, DM resulted in maternal mortality rates of 30–50% and perinatal mortality rates of 50–60%. Both maternal and perinatal prognoses have since improved remarkably with the use of insulin, greater understanding of gestational glucose metabolism, and improved techniques and equipment for neonatal care. Today, maternal deaths from DM are exceptional and DM-related perinatal mortality has decreased to 3–6%.[1–3]

Diabetes in pregnancy involves two large groups: women with pre-existing DM and women with gestational diabetes, the latter first diagnosed during the course of pregnancy.[3] In this paper, the term "diabetes in pregnancy" will be used to refer to both types collectively.

Diabetes is the main endocrine condition affecting pregnancy.[4,5] Estimates of prevalence vary depending on the population analyzed, geographic region and diagnostic criteria. Kieffer (1999) reported a 5.1% prevalence of DM in 372 pregnant women in Canada,[6] while Forsbach (1998) reported 6–8% prevalence in 667 pregnant women in Mexico.[7]

More recently, Alvariñas and Salzberg (2009) reported 5% in Argentina;[8] Rodríguez and Román et al. (2005) reported 6.4% in 1059 pregnant women in Spain;[9] and in Chile, Huidobro (2004) reported 11.2% in 234 patients,[10] while Belmar et al. reported a prevalence of 7.7% (2004).[11]

In Cuba, Terrero et al. (2005) reported that DM in pregnancy increased from10.5% in 1994 to12.2% in 2000.[12] However, some later studies show lower rates: Torres and colleagues (2007) found DM in only 1.63% of 13,603 pregnant women in Cienfuegos province.[13] Studies in various Cuban sites by Lambert (2009), Santana et al. (2010), and Cruz et al. (2008) found prevalences of 4–5%.[14–16]

Gestational DM was originally described by O'Sullivan and Mahan, based on statistical criteria including two or more plasma glucose (PG) results greater than two standard deviations over the mean, after an oral challenge of 100 g glucose, measuring PG at fasting, 1-hour, 2-hour and 3-hour post-challenge.[17] After ten years of follow-up by periodic clinical and laboratory examinations, patients thus diagnosed exhibited a noticeably increased risk of developing type II DM in the medium- or long-term.[18] Sullivan's method has been the standard, since it reliably predicts risk among patients identified as gestational diabetics, based on a critical PG of >7.7 mmol/L two hours after an oral glucose challenge (oral glucose tolerance test, OGTT).[17]

Nevertheless, differing diagnostic criteria have been proposed in the last decade, and differences persist among the World Health Organization (WHO), the American Diabetes Association and expert groups, as recognized by the current guidelines of the Latin American Diabetes Association, updated in 2006, defining gestational DM by a fasting PG ≥100 mg/dL (5.6 mmol/L) or OGTT ≥140 mg/dL (7.8 mmol/L).[19] The most universally accepted criteria are those of the WHO,[20] which have the advantage of easy implementation (requiring only two blood samples) and are compatible with diagnostic criteria for "non-pregnant" patients, for whom OGTT of 7.7–11.0 mmol/L is considered altered glucose tolerance, and defines patients at risk for developing the disease.

Diabetes in the general population is diagnosed at OGTT >11.0 mmol/L.[21] In pregnant women, this risk group does not exist as such: OGTT >7.7 mmol/L is diagnosed as gestational diabetes. Cuba's National Diabetes and Pregnancy Group recommends the WHO criteria for clinical diagnosis of gestational DM, assuming that detection will identify pregnant women who present greater risk of morbidity and mortality for themselves and their newborns. However, as recognized by one of Cuba's most respected experts on the subject, Dr Lemay Valdés, research to date has not conclusively identified the critical PG threshold, so screening that strictly follows the WHO criteria could fail to detect some women truly at risk.[22]

According to Isle of Youth Special Municipality health department statistics, the number of major and minor congenital abnormalities in infants of diabetic mothers tripled between the periods 2000–2003 and 2004–2007. As a public health measure to increase the sensitivity of screening and better predict and prevent complications of diabetes in pregnancy, the municipal obstetrics and gynecology group and its health department advisors agreed to modify WHO criteria, reducing the OGTT screening threshold to ≥7.0 mmol/L from >7.7 mmol/L during 2007 and 2008.[22]

Detection of gestational DM has been the subject of longstanding debate over whether to use universal screening or identify patients at risk using specific risk factors.[23] The factors most commonly used are maternal age >30 or >35 years, obesity, prior or present fetal macrosomia, and unexplained third-trimester fetal death. However, some investigators have found that as much as 50% of cases occur in women without these risk factors, and so favor universal screening,[24] as is the practice in Cuba.

Many authors have proposed adding other risk factors to the list: fasting PG >4.4 mmol/L (80 mg/dL), DM in a first-degree relative, polyhydramnios in current pregnancy, children with birth defects, gestational DM in previous pregnancy, morning glycosuria, ventricular septal hypertrophy, and hypertension in pregnancy, among others.[4,6,7,11,13,23,25,26]

On the Isle of Youth, with a total population of 87,000, approximately 27,000 women in fertile age, and an average of 1000 births annually, DM screening is routinely carried out in primary care settings during antenatal doctor visits. As elsewhere in Cuba, women begin prenatal care by 13.6 weeks gestation on average.[27] On the first visit, PG is tested whether or not any DM risk factors are present. PG in women without standard risk factors is tested again at 28–32 weeks; PG in at-risk women is tested again at 24 weeks and OGTT at 28–32 weeks.

An OGTT is also indicated for women with PG >4.4 mmol/L on any antenatal visit. If abnormally high glucose values are found, compatible with gestational diabetes diagnosis, the patient is sent to the Héroes del Baire Hospital (the only secondary institution in the Municipality) for assessment of metabolic status on diagnosis; from then on, her metabolic status is monitored at 24, 34, and 36 weeks, as prescribed in the Cuban Manual of Obstetrics and Perinatology Diagnosis and Treatment.[28]

Despite high DM prevalence (>15%) in pregnant women on the Isle over the last five-year period (2003–2008),[27] there are no previous clinical-epidemiological studies of these patients describing variables—risk factors such as gestational age, PG values at diagnosis, metabolic monitoring, and effect of DM on the health and viability of the neonate—that would enable design of more effective diagnostic and treatment strategies. The objectives of the present study are to determine the prevalence of DM in pregnancy on the Isle and provide a clinical-epidemiological description of women with DM who gave birth in the Municipality during 2008.

METHODS

A descriptive retrospective study was designed to characterize pregnant women with DM who gave birth at the Héroes del Baire General Teaching Hospital, Isle of Youth, between January 1 and December 31, 2008. The study was approved by the Hospital's Scientific Research Ethics Committee.

Of the 186 pregnant diabetics who gave birth on the Isle of Youth in 2008, complete clinical histories were available on diagnosis and course of pregnancy for 180, culled from records of the three community polyclinics and the Obstetrics Department of the Héroes del Baire General Teaching Hospital, where all births took place. The study population consisted of cases diagnosed both before and during pregnancy.

According to histories consulted, all gestational diabetics were diagnosed in local primary care facilities following municipal health authorities' criteria, modified from those of the WHO,[20] diagnosing DM if any one of these criteria is met:

- two fasting PG ≥6.1 mmol/L
- one random PG ≥11.0 mmol/L
- 2-hr 75g OGTT ≥7.0 mmol/L

Lists of pregnant women with DM diagnosis were matched with the Hospital's birth registry to obtain global information about births and neonates: total number of births in 2008 and maternal age.

Table 1 lists maternal clinical and demographic variables included in the study.

Also recorded for neonates were presence or absence of congenital abnormalities, 5-minute Apgar score, and weight percentile according to Enzo-Dueñas tables in the Manual of Obstetrics and Perinatology:[28] <10, 10–25, 26–50, 51–75, 76–90, 91–97, >97 (this last defining fetal macrosomia).

A database was created in Microsoft Excel and summary measures calculated: absolute and percent frequencies, means and standard deviations for quantitative variables. Results were presented in tables and figures using the same software.

RESULTS

There were 1003 live births in the Municipality during the study period; DM presented in186 pregnant women (17.3%). Incomplete records for six left a series of 180 cases for inclusion in our study.

The highest prevalence of DM was in women ≥35 years old, at 29.7% of total births to women in that age group (41/138 births), followed by those 30–34 years old, at 23.7% (36/152 births). Both the 25–29 and 20–24 age groups showed 14.8% (36/243 births and 47/319 births, respectively), although the younger of these

Table 1: Maternal clinical and demographic variables

Variable	Parameters	
Age at diagnosis (years)		<20 20–24 25–29 30–34 ≥35
Parity		0 1 2 ≥3
Nutritional status at beginning of pregnancy Body Mass Index, BMI (kg/m^2)	Underweight Normal weight Overweight Obese	<19.0 19.0–25.9 26.0–29.9 ≥30.0
Family history of diabetes mellitus	Yes (any first degree relative) No	
Gestational weight gain (kg)	low adequate excessive	<8 8–12 >12
Comorbidities, gestational or pre-existing	Urinary tract infection Hypertension* Anemia (hemoglobin <110 g/L OR hematocrit <0.33) Oligoamnios Placenta previa	
Gestational age at diagnosis (weeks)		<20.0 20.0–28.0 28.1–32.0 ≥32.1
Glucose tolerance (oral glucose tolerance test, OGTT: plasma glucose 2 hours after 75 g oral glucose, mmol/L)		7.0–8.0 8.1–9.0 9.1–10.0 >10.0
Glycemic profile at diagnosis (mmol/L)	Satisfactory: fasting blood sugar 3.8–5.2, post-prandial 3.8–6.3 Unsatisfactory: fasting blood sugar >5.2, post-prandial >6.3	

NOTE: All reference values from the Manual on Obstetrics and Perinatology in Cuba.[28]

* Any of the following criteria: two blood pressure measurements ≥140/90 mmHg; one blood pressure measurement ≥160/100; one average of systolic and diastolic pressure >105 mmHg; increase over baseline in systolic blood pressure of 30 mmHg, diastolic 15 mmHg or average of 20 mmHg.

two groups contributed most DM cases, since there were more pregnancies in that group. The age group <20 years had the lowest prevalence, at 13.2% (20/151 births) (Figure 1).

DM pre-dated pregnancy in only 7 women; 173 women (96.1%) had no history of DM before pregnancy. More than one quarter of cases (26.1%) had at least one first-degree relative with DM.

Nulliparous women constituted only 13.3% of DM cases (24); while over one third had two previous deliveries; and the groups with ≥3 previous deliveries or one previous delivery each constituted about one-quarter of all cases.

Half of cases were overweight or obese at onset of pregnancy while 45.6% had normal weight (Figure 2). More than half experienced adequate weight gain during pregnancy; while 27.2% had insufficient weight gain and 18.3% excessive gain.

Figure 1: Diabetes mellitus prevalence in pregnancy by age group (n=180)

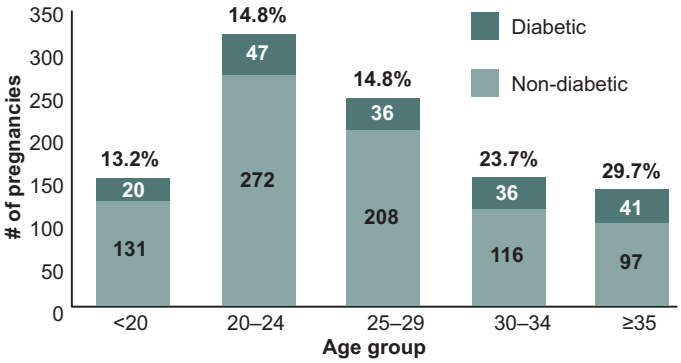


Figure 2: Pregnant diabetics by nutritional status at first antenatal visit (n=180)

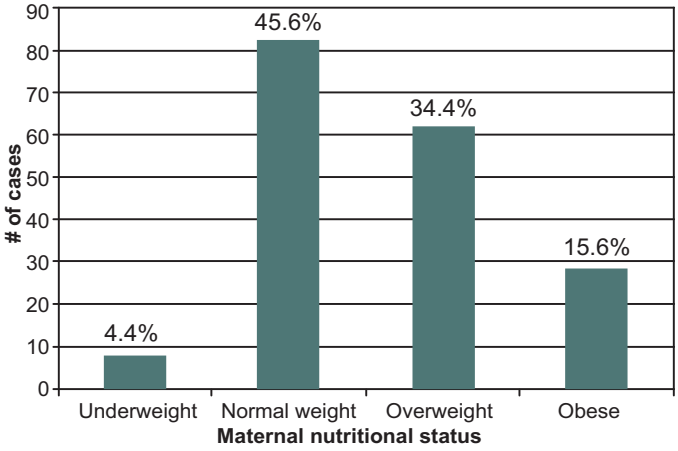
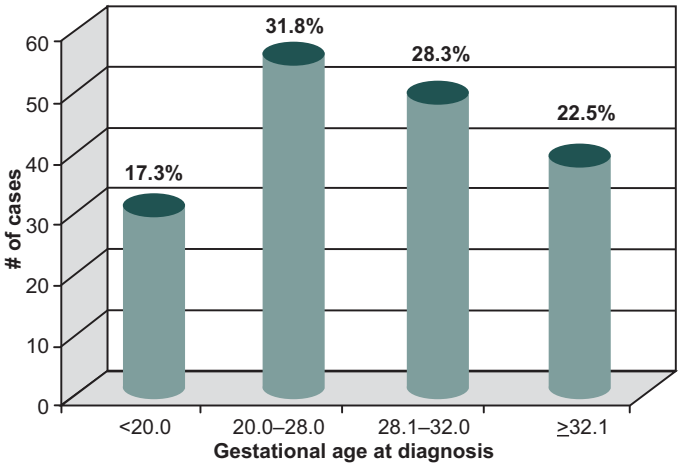


Figure 3: Gestational diabetics by gestational age at diagnosis (n=173)



Among 173 gestational diabetics, DM criteria appeared in 31.8% at 20.0–28.0 weeks; 28.3% at 28.1–32.0 weeks; 22.5% after 32.1 weeks; and just 17.3% in the first half of pregnancy (Figure 3).

Two-hour OGTT in gestational diabetics was as follows: 39.9% at 7.0–8.0 mmol/L, followed by 30.1% at 8.1–9.0 mmol/L and 20.2% at

9.1–10.0 mmol/L (Table 2). More than half of cases studied (52.2%) showed a normal glycemic profile one week after diagnosis.

Hypertension was the most frequent comorbidity, occurring in one third of cases, followed by urinary tract infection (27.2%) and anemia (23.3%). The least frequent comorbidities were oligoamnios (18.3%) and placenta previa (5%) (Table 3).

Table 2: Oral glucose tolerance test results in gestational diabetics (n=173)

Glycemic value* (mmol/L)	n	%
7.0–8.0	69	39.9
8.1–9.0	52	30.1
9.1–10.0	35	20.2
>10.0	17	9.8
TOTAL	173	100.0

** Blood glucose two hours after 75 g oral glucose load.*

Table 3: Comorbidities in pregnant diabetics (n=180)

Condition	n	%
High blood pressure	60	33.3
Urinary tract infection	49	27.2
Anemia	42	23.3
Oligoamnios	33	18.3
Placenta previa	9	5.0

Labor started spontaneously in 38.3% of cases and had to be induced in 61.7%. Cesarean section was required in 30% of cases; the remaining women delivered vaginally.

One quarter of neonates were in the 25–50 weight percentile range; 20.6% in the 50–75 range, and 15.6% in the 75–90 range. Fetal macrosomia was present in 4.4% of neonates, with 6.7% in the 90–97 percentile range. Only one of the eight neonates with macrosomia was born to a mother with pre-existing DM, the other seven to gestational diabetics. All neonates had satisfactory Apgar scores and none presented with congenital abnormalities.

DISCUSSION

Diabetes mellitus in pregnancy is the endocrine condition most associated with pregnancy and has severe consequences for perinatal morbidity and mortality. The prevalence observed in this study is high compared to much of the published literature,[11,29–33] and the low rate of fetal macrosomia is also atypical. The pathogenesis of DM is complex and multifactorial, involving association of conditions and factors that increase risk in pregnancy.

Multiple studies support the idea that DM appears more frequently in pregnancy after age 30 because of age-related metabolic changes; it is rare before age 20. The confluence of conditions more commonly seen at older ages—such as pregnancy-induced hypertension, increased body mass, and dyslipidemias—increases DM risk, as supported by Etchegoyen et al. (2001) in their report on a series of 400 pregnant women in Argentina;[29] Belmar et al. in Chile;[11] Cárdenas and Arroyo (2004) in Peru;[30] and Rodríguez et al. (2005) in Spain.[9]

Similar results have been reported in Cuba, also consistent with this study's findings: Rimbao and colleagues (2007) found that almost half of 134 cases with DM in pregnancy were >30 years old.[26] Valdés et al. (2008) reported that two thirds of pregnant diabetics admitted to a Havana City maternity hospital were over 30.[31]

As in the rest of Cuba and the Americas, most women on the Isle of Youth have their children in the third decade of life.[11,29,30] Thus, it is not surprising that absolute numbers of DM in this age group are greater in our study. However, this reflects the larger share of total pregnancies represented by this age group (563 of 1003), not greater risk. In our study, pregnant women aged ≥30 years in fact show highest DM prevalence: 23.7% for those aged 30–34, and 29.7% for those ≥35, a result consistent with the literature.

Pregestational DM is considered to have a worse prognosis than gestational diabetes, in terms of metabolic changes and perinatal outcomes, so it is fortunate that it represents less than 5% of DM in pregnancy globally, as reported by Huidobro and by Arteaga et al. in Chile,[8,33] and Lawrence in the USA.[32] In the present study, 3.9% of DM cases were pregestational, consistent with the majority of reports.

This frequency does not differ notably from global DM prevalence in the non-obstetric population, to which it is necessary to add that DM—especially type II— is exceptional <35 years of age, when the largest share of births occurred in our study. Thus, we consider our findings consistent with expectations based on the literature.

DM family history in 26% of our cases concurs with results from several other studies: Fuentes et al. (2005) reported DM family history in one third of pregnant diabetics in Brazil,[34] and Huidobro reported this factor in 30%.[10]

Excess weight's notable contribution to risk of gestational DM is supported by several studies finding that overweight or obesity at start of pregnancy predispose to gestational DM. Huidobro's study in Chile (2004), as well as two Cuban studies—Arias and Chartrand (2008) and Valdés et al. (2008)—found at least half of pregnant diabetics were overweight or obese.[10,31,35] This may be due to increased demands on maternal metabolism during pregnancy from excess weight, resulting in imbalances in hormonal carbohydrate regulation mechanisms, and insulin sensitivity.

The role of nutrition goes beyond maternal weight at the beginning of pregnancy; there is also the factor of weight gain during pregnancy. Several authors maintain that excessive weight gain during pregnancy also creates additional metabolic demands predisposing to DM. Zonana et al. (2010) found excessive weight gain in 37.5% of pregnant diabetics in México.[36] The lower rate of excessive gestational weight gain in the current study (18.0%) may be related to DM education programs in the Municipality's hospital and ambulatory care settings.

Many researchers consider hypertension syndrome the most frequent DM-associated obstetric complication, with frequency up to 40%.[1] Our findings provide additional support: one third of patients were hypertensive (whether pre-existing or pregnancy-induced). High rates of hypertension as a comorbidity of DM in pregnancy were found by Belmar and colleagues; Fuentes et al.; Arias and Chartrand; and Lisson and Pacheco.[11,34,35,37] This

association may be related to the concurrence of several risk factors common to both clinical conditions, such as obesity, dyslipidemias and smoking,[3,11,29,33] although the latter two risk factors were not examined in this study.

Another important issue for pregnant diabetics is fetal macrosomia. Rodríguez et al. in Spain; Valdés in Havana, Cuba; and Terrero et al. in Santiago de Cuba report fetal macrosomia as a relatively frequent finding in neonates of diabetic patients studied. [9,31,38] The low neonatal macrosomia rate found in our study may be due to influences beyond the objectives posed, such as genetic factors or clinical management and metabolic control.

The tendency to higher rates of fetal macrosomia in infants of diabetic mothers contributes to increased rates of Cesarean section due to cephalopelvic disproportion. A study by Cruz et al. in Havana reported Cesarean sections in 96.4% of macrosomia cases. [39] In our study, 70% of pregnant diabetics had vaginal delivery, similar to the 67% found by Rodríguez et al. in Spain [9] and 68.5% by Cormier and colleagues (2010) in pregnant diabetics in the USA (75% in the presence of fetal macrosomia).[40]

The absence of fetal malformations in diabetic mothers in our study is not an isolated finding. A 2009 meta-analysis by Balsells et al. involving >10,000 patients found no significant differences in rates of congenital abnormalities and perinatal mortality between diabetic and non-diabetic women.[41] As in the case of macrosomia, our results may be due to factors not included in this research, such as good metabolic control during pregnancy as suggested by Cruz and colleagues.[16]

This study is limited by use of modified WHO laboratory criteria for DM diagnosis in pregnancy, since this modification makes comparison with other results more difficult, especially with those from studies abroad.

CONCLUSIONS

Despite using modified, more inclusive, WHO diagnostic criteria, the clinical and demographic characteristics of the population studied were comparable to those in other studies of diabetes in pregnancy, except for the low frequency of fetal macrosomia and absence of congenital abnormalities found in our research. This research offers a baseline for future studies on prevalence of DM in pregnancy and diagnostic methodology; as well as for analytic research on characteristics of pregnant diabetics, DM-associated risk factors and their impact on pregnancy course, delivery and perinatal outcomes.

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