Epidemiology of Diabetes in Pregnancy

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PRACTICE POINTS

- The World Health Organization (WHO) (3) has recommended that hyperglycemia first detected at any time during pregnancy should be classified as either:
 - diabetes mellitus in pregnancy (DIP), or
 - gestational diabetes mellitus (GDM).
- Pre-gestational diabetes is diabetes that had been diagnosed before pregnancy.
- The prevalence of pre-gestational diabetes has been increasing across the world over >40 years and has a prevalence of 1–5%. Approximately 0.3–0.8% of pregnancies are complicated by type 1 diabetes; the rest are type 2 diabetes, and a small fraction have rare forms of diabetes.
- DIP has a prevalence of 0.2–0.4%, mostly type 2 diabetes postpartum.
- WHO (3) criteria for GDM have now changed, involving a much lower fasting criterion (≥5.1 mmol/l), the introduction of a 1 h value after a 75 g oral load (≥10.0 mmol/l), and an increased diagnostic cutoff 2 h post load (≥8.5 mmol/l). These criteria substantially increase the prevalence of GDM, in some populations to over 35%.
- Non-European ethnicity and obesity are the major risk factors for hyperglycemia in pregnancy; others such as a family history of diabetes, previous GDM, polycystic ovarian syndrome, age, and previous stillbirth or macrosomic infant are important.
- Pre-gestational diabetes and DIP contribute significantly to malformations.
- Total hyperglycemia in pregnancy contributes to adverse pregnancy outcomes on a population level, particularly shoulder dystocia.
- GDM is a precursor of up to 34% of type 2 diabetes in women.
- There is an association between maternal hyperglycemia in pregnancy and obesity, diabetes, and metabolic syndrome in the offspring.

Case History

A 32-year-old woman, G3P2, with no significant past medical history and no family history of diabetes, had a random glucose of 7.8 mmol/l at 8 weeks gestation with a normal oral glucose tolerance test (OGTT) (4.3, 7.6, and 7.4 mmol/l) at 11 weeks (1). Her pre-pregnancy BMI was 19.9 kg/m². At 28 weeks, she presented acutely, afebrile but with severe general fatigue. A random plasma glucose was 27.2 mmol/l, blood pressure was 110/84 mmHg, and heart rate 106 beats/min. Ketones were 3+, arterial pH was 7.45, bicarbonate 12.1 mmol/l, and base excess –9.8 mmol/l (i.e., compensated metabolic acidosis). HbA1c was 125 mmol/mol (13.6%). Antiglutamic acid decarboxylase (GAD) antibody was 25.0 (reference range 1–5). She was diagnosed

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as having type 1 diabetes and commenced insulin therapy. The rest of the pregnancy was uneventful, although total weight gain was only 3 kg and birth weight was 3006 g. Questions to be answered in this chapter:

- What proportion of pregnancies are complicated by type 1 diabetes, type 2 diabetes, monogenic diabetes, or other rare forms of diabetes?
- What proportion of pregnancies are complicated by GDM?
- What type of patient develops hyperglycemia first detected in pregnancy?
- What is the public health impact of hyperglycemia in pregnancy?

Prevalence of Total Hyperglycemia in Pregnancy

Diabetes in pregnancy (DIP) and gestational diabetes mellitus (GDM) have been terms used in clinical medicine for over 100 years. In 2010 and 2013, respectively, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) (2) and the World Health Organization (WHO) (3) reclassified hyperglycemia in pregnancy into three groups to incorporate all aspects of the range of raised glucose that can increase pregnancy complications:

| Known pre-gestational diabetes | (Overt) diabetes in pregnancy (DIP) | Gestational diabetes mellitus (GDM) |
|--|---|--|
| Known diabetes | Diagnosed first time in pregnancy and expected to continue postnatally | Diagnosed first time in pregnancy and no permanent diabetes expected postnatally |
| For example: type 1 diabetes, type 2 diabetes, and rare forms of diabetes (e.g., monogenic diabetes) | Usually type 2 diabetes; occasionally, rare forms or type 1 diabetes | I 1 |

The global prevalence of total hyperglycemia in pregnancy has recently been estimated to have been 16.9%, or 21.4 million, live births (women aged 20–49 years) in 2013 (4). The highest prevalence was in Southeast Asia at 25.0%, with 10.4% in North America and the Caribbean Region. Low- and middle-income countries are estimated to be responsible for 90% of cases.

Prevalence of Known Pre-Gestational Diabetes in Pregnancy

The prevalence of both type 1 and type 2 diabetes among reproductive-aged women has been increasing globally (5). In the USA, the incidence of type 1 and type 2 diabetes among those aged under 20 years is projected to triple and quadruple by 2050, respectively (5). An example of the growth in pre-gestational diabetes between 1999 and 2005 is shown for Southern California in Figure 1.1 (by age group), where age- and ethnicity-adjusted rates increased from 8.1/1000 in 1999 to 18.2/1000 by 2005 (6).

There are significant ethnic differences in prevalence. For example, in 2007–2010 among women aged 20–44 years across the USA, prevalence ranged from 2.7% (1.8–4.1%) among non-Hispanic whites, to 3.7% (2.2–6.2%) among Hispanic women, to 4.6% (3.3–6.4%) among non-Hispanic blacks (7). Prevalence rates are higher in other populations (4).

Prevalence of Type 1 Diabetes in Pregnancy

The prevalence of type 1 diabetes in pregnancy is less than in the nonpregnant population in view of the lower standard fertility ratio (SFR) (fertility rate in comparison with the wider population). The SFR in type 1



Figure 1.1 Pregnancies complicated by pre-gestational diabetes, 1999–2005 (per 1000), by age.

diabetes is 0.80 (95% CI: 0.77–0.82), and is particularly low among women with retinopathy, nephropathy, neuropathy, or cardiovascular complications (0.63, 0.54, 0.50, and 0.34, respectively) (8). The gap in fertility between women with and without type 1 diabetes has closed considerably over time, and it appears to be greatest for women who were diagnosed as a child, rather than as an adult (9).

The prevalence of type 1 diabetes in pregnancy increases with age, as shown in Table 1.1 for Norway (1999–2004) (10) and Ontario, Canada (2005–2006) (11).

Besides women with preexisting type 1 diabetes, a small proportion of women with diabetes first diagnosed during pregnancy are found to have type 1 diabetes (see, e.g., the Case History for this chapter). In New Zealand in 1986–2005, 11/325 (3.4%) of women with new diabetes diagnosed postpartum had type 1 diabetes (12). Other women with GDM have autoimmune markers (islet cell antibody

| Norway 1999–2004 | | Ontario 2005–2006 | | |
|---------------------|-----|----------------------|------|-----|
| Type of diabetes | 1 | Type of diabetes | 1 | 2 |
| Overall | 4.5 | Overall | 7.5 | 4.3 |
| By age | | By age | | |
| ≤20 years | 2.9 | ≤20 years | 2.0 | 0.2 |
| 20-34 | 4.5 | 20-29 | 5.7 | 2.9 |
| 35-39 | 5.0 | 30-34 | 8.3 | 4.9 |
| 40+ | 4.7 | 35+ | 11.5 | 7.3 |

[ICA], GAD antibody [GADA], or tyrosine phosphatase antibody [IA-2A]) without necessarily overt DIP. Overall, the prevalence of such autoimmune markers ranges between 1 and 10%, and it is greatest in populations where the prevalence of type 1 diabetes is higher (13). In a Swedish study, 50% women with antibody positivity had developed type 1 diabetes, compared with none among the GDM control subjects (14).

Prevalence of Type 2 Diabetes in Pregnancy

While fertility rates in type 2 diabetes have not been reported, they would be expected to be low (particularly in view of the associated obesity, polycystic ovarian syndrome [PCOS], and vascular disease) (15). Nevertheless, the rates of type 2 DIP are increasing more rapidly than those of type 1 diabetes in pregnancy (16).

In addition to the increasing age-standardized prevalence and lowering of the age at onset of type 2 diabetes (driven by the obesity epidemic), demographic changes (e.g., ethnicity) may partly explain the changes in prevalence over time in individual locations. For example, in Birmingham, UK, in 1990-1998, the ratio of type 1 to type 2 diabetes was 1:2 in South Asians but 11:1 in Europeans (17). In the north of England in 1996-2008, the prevalence rates of type 1 and type 2 diabetes in pregnancy were 0.3% and 0.1%, respectively (18), but while 97% of women with type 1 diabetes were European, 21% of women with type 2 diabetes were non-European. Table 1.1 also shows the increasing proportion of women in Ontario having type 2 diabetes in pregnancy as age increases (11).

Prevalence of other Forms of Pre-Gestational Diabetes in Pregnancy

There are few reports of the prevalence of monogenetic forms of diabetes or secondary diabetes in pregnancy. Glucokinase mutations are present in up to 5–6% of women with GDM and up to 80% of women with persisting fasting hyperglycemia outside

pregnancy combined with a small glucose increment during the OGTT, and a family history of diabetes (19).

Cystic fibrosis is associated with a doubling in the prevalence of diabetes outside of pregnancy, with a further increase during pregnancy (e.g., from 9.3% at baseline to 20.6% during pregnancy, and 14.4% at follow-up) (20).

PITFALL

A significant proportion of younger women with diabetes in pregnancy have rare forms of diabetes, which often remain undiagnosed.

Prevalence of Hyperglycemia First Detected in Pregnancy

The prevalence of hyperglycemia first detected in pregnancy globally was examined in 1998 by King *et al.* (21). However, such an epidemiologic comparison between studies was difficult to interpret for the reasons shown in Figure 1.2 and discussed more fully in Chapters 4 and 5. Key issues are the diagnostic criteria and screening approaches used. In addition, screening too early (before 24 weeks) could result in fewer cases with hyperglycemia in pregnancy being detected. In some women, the diagnosis of GDM is only made later in pregnancy, and they will have had a normal test on conventional screening between 24 and 28 weeks.

Overweight, obesity, and extreme obesity (BMI 35+) are significant contributors to the development of GDM and DIP. Recently, the respective population attributable fractions (PAFs) in South Carolina, USA, have been calculated to be 9.1%, 11.8%, and 15.5% (i.e., a total of 36.4% of GDM is attributable to excess weight) (22). This did vary marginally between ethnic groups (e.g., 18.1% [16.0–20.2%] American blacks vs. 14.0% [12.8–15.3%] non-Hispanic whites vs. 9.6% [7.3–12.0%] Hispanics of all GDM was attributable to extreme obesity).



Figure 1.2 Difficulties in comparing prevalence data in gestational diabetes mellitus (GDM) with different approaches. OGMM = Oral glucose tolerance test.

Diagnosis of diabetes in Pregnancy and Gestational Diabetes Mellitus

The diagnoses of DIP and GDM are discussed in detail in Chapter 5. Few other areas in medicine have been associated with such confusion and controversy, while the differing criteria for diagnosis have, until recently, made epidemiological comparison problematic. Adoption of the new WHO (IADPSG) criteria in 2013 (2,3) has, for the first time, brought uniformity to this confused field, although they have not been accepted universally. These criteria were based upon epidemiologic data generated by the HAPO study (23) rather than either consensus or risk of future maternal diabetes. HAPO also highlighted the relevance of hyperglycemia to maternal fetal outcome, independent of maternal obesity. A further important observation was the comparable relationship between hyperglycemia and maternal/fetal outcome between all participating ethnic groups. One caveat is that some ethnic groups, such as Polynesians, were not included in HAPO, and evidence from New Zealand suggests that hyperglycemia may increase their birthweight more than among Europeans (24) after adjusting for maternal weight.

While obesity, ethnicity, maternal age, and a family history of diabetes are the major risk factors for GDM/DIP, others also exist (e.g., previous large baby, previous stillbirth, multiple pregnancy, and physical inactivity), and these form the basis of screening strategies (25) (see also Chapter 4). There is also clear evidence of the importance of PCOS as a risk factor for GDM/DIP (26). Another important group of women at increased risk of GDM are those with a previous history of GDM (27), particularly in association with excess weight or with weight gain between pregnancies and where previous GDM was diagnosed early in pregnancy and required treatment with insulin (28).

Prevalence of Diabetes in Pregnancy

Few studies have reported the prevalence of DIP as defined by the new WHO 2013 criteria (3): fasting glucose \geq 7.0 mmol/l, HbA1c \geq 6.5% (47 mmol/mol), random glucose \geq 11.1 mmol/l, and confirmed with another test. A number of

studies have previously reported the prevalence of diabetes immediately after a pregnancy complicated by GDM, such as in New Zealand where 21% of Polynesians and 4% of Europeans had diabetes postpartum (29). However, these studies were before the IADPSG/WHO criteria for DIP and DIP is often not associated with diabetes postpartum. For example, in one Australian cohort study, only 21% had diabetes postpartum (41% returned to normal) (30).

PRACTICE POINT

DIP does not always imply permanent diabetes postpartum.

Of the 133 patients with overt diabetes in pregnancy who attended a follow-up oral glucose tolerance test (OGTT) at 6–8 weeks postpartum, 21% had diabetes, 37.6% had impaired fasting glucose or impaired glucose tolerance, whilst 41.4% returned to normal glucose tolerance.

Few papers to date describe the characteristics of women with DIP. The Japan Diabetes and Pregnancy Study Group reported that compared with women with GDM, women with DIP had higher pre-gestational Body Mass Index (BMI: 24.9 ± 5.7 vs. 26.2 ± 6.1 kg, P < 0.05), earlier gestational age at delivery (38.19 ± 2.1 vs. 37.89 ± 2.5 weeks, P < 0.05), more retinopathy (0% vs. 1.2%, P < 0.05), and more pregnancy-induced hypertension (6.1%vs. 10.1%, P < 0.05) (31). Others have also found women with DIP to have a greater BMI and more adverse pregnancy outcomes (30).

Prevalence of Gestational Diabetes

There are major differences in the prevalence of GDM between ethnic groups, reflecting both the background prevalence of type 2 diabetes and its age at onset (32). All populations apart from those of European descent (and even including some European populations) are now considered at high risk. The prevalence has also generally increased over time (33,34). While this most likely reflects the epidemics of obesity and type 2 diabetes in the nonpregnant state, an additional feature is likely to be the increasing age at which pregnancy occurs, and for some total populations, the immigration of high-risk ethnic groups. Prevalence rates vary within the same ethnic group in different locations, with migrant populations generally having a higher prevalence than those remaining in traditional rural areas, probably relating to lifestyle change (a higher energy diet and less physical activity) and greater adiposity. Such data need careful scrutiny to recognize these factors and to ensure that no change in ascertainment (e.g., screening approaches) or diagnostic criteria have occurred.

Many studies describing prevalence of GDM include different screening approaches that underreport the true prevalence.

The prevalence of GDM using the WHO 2013 criteria is now being increasingly reported from different sites, allowing a more global picture to be obtained beyond the original HAPO sites as shown in Table 1.2. The prevalence is substantially more than using the older criteria, and this is discussed more in Chapter 5.

No data using the WHO 2013 criteria have yet been published from Africa, although women of African descent have been shown to have a high prevalence of GDM in, for example, Oslo (33). The IDF Atlas (4) cites a prevalence of hyperglycemia in pregnancy in Africa at 16.0% (4.6 million affected births in 2013), the region with the greatest number of cases. This prevalence is more than in Europe (15.2%), North America (13.2%), South/Central America (13.2%), or the Western Pacific (11.8%), but less than in the Middle East/North African (22.3%) or South/Eastern Asia (23.1%).

The risk of hyperglycemia in pregnancy is associated with lower socioeconomic status on a population basis. In an Australian study, women living in the three lowest socioeconomic quartiles had higher adjusted odds
 Table 1.2
 Prevalence of GDM using WHO 2013/IADPSG criteria in complete populations and in the HAPO study for comparison.

| Location | Year | Prevalence: WHO (2013) (%) | Other criteria used | Prevalence: other criteria |
|-----------------------------------|------|-------------------------------|------------------------|-------------------------------|
| Europe | | | | |
| Belgium (35) | 2014 | 23 | NDDG | 8 |
| Norway-Western European (36) | 2012 | 24 | WHO (1999) | 11 |
| Norway-ethnic minorities (36) | 2012 | 37 | WHO (1999) | 15 |
| Spain (37) | 2010 | 35.5 | NDDG | 10.6 |
| UK-Belfast-HAPO (2) | 2010 | 17.05 | WHO (1999) | 1.5% |
| UK-Manchester-HAPO (38) | 2010 | 24.28 | | |
| Ireland (39) | 2011 | 12.4 | WHO (1999) | 9.4 |
| Hungary (40) | 2011 | 16.6 | WHO (1999) | 8.7 |
| Middle East | | | | |
| Petah-Tiqva, Israel-HAPO (38) | 2010 | 10.06 | | |
| Beersheba, Israel-HAPO (38) | 2010 | 9.25 | | |
| UAE (41) | 2010 | 37.7% | ADA | 12.9% |
| North America | | | | |
| Barbados-HAPO (38) | 2010 | 11.9 | | |
| Canada (42) | 2014 | 10.3 | CDA (2008) | 7.3 |
| Canada-Toronto-HAPO (38) | 2010 | 15.53 | | |
| California-USA-HAPO (38) | 2012 | 25.5 | | |
| Ohio-USA-HAPO (38) | 2012 | 25.0 | | |
| Chicago-USA-HAPO (38) | 2012 | 17.3 | | |
| Rhode Is-USA-HAPO (38) | 2012 | 15.5 | | |
| Central/South America | | | | |
| Mexico (43) | 2011 | 30.1 | NDDG | 10.3 |
| Asia | | | | |
| India (44) | 2012 | 14.6 | DIPSI | 13.4 |
| Hong Kong-HAPO (38) | 2010 | 14.39 | | |
| Singapore-HAPO (38) | 2010 | 25.13 | | |
| Thailand-HAPO (38) | 2010 | 22.97 | | |
| Japan (45) | 2011 | 6.6 | JSOG | 2.4 |
| China (46) | 2014 | 18.9 | NDDG | 8.4 |
| Vietnam (47) | 2012 | 20.36 | ADA | 6.07 |
| Pacific | | | | |
| Newcastle-Australia- HAPO (38) | 2012 | 15.3 | | |
| Brisbane-Australia-HAPO (38) | 2012 | 12.4 | | |
| Wollongong-Australia (48) | 2011 | 13.0 | ADIPS | 9.6 |

ratios (ORs) for GDM compared with women in the highest quartile, who had an OR of 1 versus 1.54 (1.50-1.59), 1.74 (1.69-1.8), and 1.65 (1.60-1.70) for decreasing socioeconomic status quartiles (49).

Another key finding from the HAPO study has been the different patterns of hyperglycemia in different ethnic groups, with 55% of women diagnosed on the fasting glucose, 33% on the 1 h, and 12% on the 2 h. This has major implications for decisions over whether to drop the fasting, 1 h, or 2 h time point during the OGTT. The proportion diagnosed on the fasting ranged from 74% in Barbados to 26% in Hong Kong and 24% in Thailand (38). This naturally shifted the diagnostic "time point," such that in Thailand and Barbados, 64% and 9% were diagnosed at the 1 h time point and in Hong Kong 29% were diagnosed at the 2 h time. The greater likelihood of diagnosis on the 2 h glucose among Asians was predictable from studies outside of pregnancy (50).

Public Health Impact of Hyperglycemia in Pregnancy

The public health impact of hyperglycemia in pregnancy relates to the numbers affected as described here, impact on quality of life, additional resource utilization, and potentially intergenerational transmission. The additional resources required for mitigating the harm from hyperglycemia in pregnancy and potential savings from intervention are shown in Table 1.3.

Table 1.3 Interventions for hyperglycemia in pregnancy and potential savings from intervention.

| | Interventions | Potential savings |
|---|--|--|
| Type 1 and type 2 diabetes | i | |
| Preconception | Optimization of metabolic control, folate therapy, medication optimization | Malformations Fetal loss sequelae |
| Antenatal management | Optimization of metabolic control including blood pressure control | Neonatal, maternal birth complications |
| | Optimization of obstetric management | Offspring risk of diabetes, obesity |
| Retinal management | Retinal screening, laser if needed | Vitreous surgery, cesarean section |
| Other complication management | Renal replacement therapy, hospitalization for cardiac event, autonomic neuropathy | |
| Gestational diabetes mellit | tus (GDM) and diabetes in pregnancy (DIP) | |
| Diagnosis of GDM | Screening and diagnosis program | |
| Antenatal management | Optimization of metabolic control, including blood pressure control | Neonatal, maternal birth complications |
| | Optimization of obstetric management | Offspring risk of diabetes, obesity |
| Retinal management | Retinal screening if likely undiagnosed type 2 diabetes, laser if needed | cesarean section (rare) |
| Postnatal screening and intervention | Screening | Prevention of permanent diabetes |
| | Primary prevention (lifestyle, drugs) | Prevention of undiagnosed type 2 diabetes in pregnancy |

Public Health Impact of Pregnancy Among Women with Known Preexisting Diabetes

Pre-gestational diabetes is a major risk factor for congenital malformations, particularly congenital heart defects (51). Type 1 and type 2 diabetes probably have a comparable teratogenic effect (52). Relative to type 1 diabetes, type 2 diabetes in pregnancy has been associated with higher perinatal mortality (OR: 1.50; CI: 1.15–1.96) and fewer cesarean sections (OR: 0.80; 95% CI: 0.59– 0.94), but similar rates of stillbirth, neonatal mortality, miscarriage, preterm birth, small and large for gestational age infants, neonatal hypoglycemia, jaundice, and respiratory distress (53).

In the USA, the PAF of congenital heart defects among those with pre-gestational diabetes was estimated to be 8% (7), although the PAF rises to approximately one-quarter for atrioventricular septal defects (Table 1.4) (7). Besides death in 2–3%, others require surgery and long-term risks of reoperation, arrhythmia, endocarditis, heart failure, and pulmonary hypertension.

Population impact depends on the implementation of pre-pregnancy care, which is associated with a risk ratio (RR) of 0.25 (95% CI: 0.16–0.37) and number needed to treat (NNT) of 19 (95% CI: 14–24), for congenital malformations and a RR of 0.34 (95% CI: 0.15–0.75) and NNT of 46 (95% CI: 28–115) for perinatal mortality (54).

Public Health Impact From GDM/DIP

Although the costs of GDM/DIP have been difficult to estimate with the variation in criteria across the world, the increasing adoption of the WHO 2013 criteria has made health economic analyses more achievable. Previous estimates of the population impact of GDM/DIP suggested that 2.8% of perinatal mortality, 2.5% of malformations, 5.9% of cesarean sections, 9.9% of babies \geq 4.5 kg, and 23.5% of cases of shoulder dystocia occurred in women with diabetes in pregnancy of some sort (55). However, these estimates were prior to the new criteria and new screening approaches, and hence many women with potentially preventable adverse outcomes were considered "normal" without the opportunity of GDM/DIP treatment.

Naturally, the extent of ascertainment, and therefore achievability of the benefits from treating GDM/DIP, are dependent on the approaches used for its identification (e.g., universal screening vs. risk factorbased screening). Other important determinants are not only the degree to which treatment is implemented, but the extent to which treatment goals are reached. For example, in one study, 24.8% of the women achieving 0% of fasting test results >5.3 mmol/l experienced an adverse pregnancy outcome, compared with 57.9% of women whose fasting glucose was >5.3 mmol/l on over 30% of occasions (56).

| Congenital heart defect | Summary odds ratio (95% CI) | Population attributable fraction, % (95% Cl) |
|-------------------------------------|--------------------------------|---|
| All congenital heart defects | 3.8 (3.0-4.9) | 8.3 (6.6–11.8) |
| Atrioventricular defects | 10.6 (4.7-20.9) | 23.4 (10.6-40.0) |
| Co-arctation of the aorta | 3.7 (1.7-7.4) | 7.9 (2.1–17.6) |
| Hypoplastic left heart syndrome | 3.7 (1.5-8.9) | 8.0 (1.6-20.4) |
| Tetralogy of Fallot | 6.5 (3.3–11.8) | 14.8 (6.6–26.3) |
| Transposition of the great arteries | 4.8 (2.7-8.3) | 10.9 (5.1–19.8) |

Table 1.4 Population attributable fraction of congenital heart disease from pregestational diabetes (7).

Source: Simeone et al. (2015) (7). Reproduced with permission of Elsevier.

Health economic analyses often omit benefits from improvements in quality of life (QoL) and potential to prevent diabetes in mother and offspring. In the ACHOIS study (based on the older WHO 1999 criteria), there was a significant improvement in QoL with GDM diagnosis and treatment and in health economic modeling; this was associated with significant gains on a population basis (57). The first attempt at modeling the intergenerational intragenerational and effects of GDM on type 2 diabetes, from the Saskatchewan database, has suggested that among the high-risk First Nations population, prior GDM may be responsible for 19% to 30% of type 2 diabetes. However, GDM was responsible for only approximately 6% of cases among other persons (58).

Also excluded to date in health economic analyses has been the importance of diagnosing pre-gestational diabetes after a pregnancy complicated by GDM and any subsequent pregnancies. There is evidence of a greater risk of permanent diabetes in mothers with increasing numbers of pregnancies complicated by GDM (59). Identification of GDM also provides an opportunity to manage this risk through timely use of reliable contraception.

Even with these caveats, a number of modeling studies have examined the cost of GDM and the costs-benefits of treatment. Reports

Multiple-Choice Questions

One or more answers are correct.

- 1 The WHO 2013 criteria for gestational diabetes are based upon:
 - A long-term risk of diabetes in the mother.
 - B long-term risk of obesity in the offspring.
 - C 100% greater risk of a pregnancy complication versus "normal" women.
 - D 75% greater risk of a pregnancy complication versus "normal" women.
 - E 50% greater risk of a pregnancy complication versus "normal" women.

from a number of countries have shown a high cost of GDM (e.g., the USA in 2011 dollars, \$831,622,028 per 100,000 women) and cost-effectiveness of treatment (e.g., the USA, Israel, and India (60,61)).

Health economic analyses should include estimates of the benefits of identifying and intervening among women at risk of progressing to type 2 diabetes.

FUTURE NEEDS

- More studies using the WHO criteria for GDM and DIP with universal screening Studies in many more populations on the interplay and independent effects of obesity and GDM Studies looking at the criteria required for GDM in early pregnancy More studies looking at monogenic diabetes and other rare forms of diabetes More studies from Africa More studies looking at population impact of intergenerational effects of maternal diabetes, including GDM More studies looking at the epidemiology of diabetes in pregnancy More studies looking at the health economic impact of total hyperglycemia in
- pregnancy in different economies
- 2 The risk of GDM is greater if:
 - A a woman has normal weight.
 - B a woman has polycystic ovarian syndrome.
 - C a woman has had a stillbirth in the past.
 - D a woman has had a major antepartum hemorrhage in the past.
 - E a woman has been inactive both before and during pregnancy.

Correct answer: B, C, E.

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