Gestational Diabetes Mellitus: an audit at Tygerberg Academic Hospital

by

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DECLARATION

By submitting this dissertation electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Sibusiso Goodenough Nhlapo **Date: December 2015**

ABSTRACT

Aim: To describe the profile of patients with gestational diabetes mellitus (GDM) at Tygerberg Academic Hospital, managed according to the new Provincial Guidelines.

Methods: There was the performance of a retrospective audit of all pregnant patients with GDM, seen at the Special Care Clinic of Tygerberg Academic Hospital over a period of 12 months. Dictation of the size of the study sample was by the time interval and the number of patients diagnosed with GDM and seen at the clinic during the period of study. Patient data were extracted from the files and loaded into a spreadsheet in a strictly anonymous fashion. Within the patient profile the study sought to identify the mode of diagnosis, interventions required, as well as the courses of the pregnancies for both the women and their foetuses. There was the use of descriptive statistics for analysis, and logistic regression was employed to investigate continuous variables (age and body mass index).

Results: One hundred and forty-seven women had the diagnosis of GDM from August 2010 to July 2011. Fifty-eight percent of women had a positive family history of diabetes; 57% developed glycosuria, and 38% underwent diagnostic testing due to morbid obesity. Previous GDM and previous unexplained IUD were present in 8% of women. The median age of the women in this group was 32 years and 80% were found to be obese. The median gestational age at diagnosis was 28 weeks with a median glycosylated haemoglobin of 6.3%. The upper range of glycosylated haemoglobin (13.3%) and the lower range of gestational age at diagnosis (7 weeks) indicate that cases of undiagnosed, pre-existing diabetes mellitus were also present in this group of women with “gestational diabetes”. Concerning glycemic control during pregnancy 23% responded to lifestyle modification alone, 68% required additional metformin and 9% insulin as a final addition to therapy. It is noteworthy that despite the diagnosis of GDM, 29% of women still required metformin at discharge. Twenty-nine percent of the group delivered before 38 weeks’ gestation with hypertensive complications (14%) and spontaneous pre-term labour (8%) featuring prominently. The median birth weight was 3280 grams. There was a high incidence of peripartum foetal distress (26%) reflected in the caesarean rate of 55%.

Conclusion: A positive family history, obesity and glycosuria are useful to diagnose GDM. Although approximately one-quarter of women achieved glycemic control on lifestyle modification alone; most required metformin but avoided insulin therapy. Despite the goal of elective delivery at 38 weeks' gestation, hypertensive complications and spontaneous pre-term labour resulted in many earlier deliveries. The overall rate of caesarean section was high but during vaginal delivery shoulder dystocia was rare. The policy of screening using history and selective clinical findings, together with the addition of metformin to the management programme (as advocated by the provincial guidelines) appears to be fulfilling its purpose within the specific context of public health care within the Western Cape Province of South Africa.

DEDICATION

This work is a dedication to my parents, family and friends for their constant support and encouragement.

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Chapter 1

Introduction and context

Gestational diabetes mellitus (GDM) is a common and important medical condition of pregnancy. The incidence of GDM has been found to be as high as 8.8% in some regions of South Africa [1]. This incidence of GDM is likely to increase as the South African society becomes more obese [2]. Diabetes in pregnancy has an association with an increased perinatal mortality rate [3]. Gestational diabetes mellitus has an association with some adverse outcomes, which include: foetal macrosomia, birth trauma, primary caesarean delivery, neonatal hypoglycaemia, shoulder dystocia and preeclampsia [4, 5].

Recent robust studies have shown benefit in treating women with milder forms of GDM. Examples of these benefits are a reduction in the incidence of macrosomia, reduction in maternal weight gain and preeclampsia in experimental groups compared to controls [6,7,8]. Despite these benefits, no reduction in perinatal death rates has been demonstrated for the specific sub-group with milder forms of GDM (cases falling below previously accepted cut-off values) [6]. However to expand the benefits of decreased perinatal morbidity more women need to be treated.

Lifestyle modification (diet and exercise) is a long-standing pillar of diabetic management. The oral biguanide agent, metformin is a recent, non-invasive, safe addition to standard practice. Recent studies comparing the benefits and risks of oral agents to insulin for the management of GDM have shown no substantial differences in major outcomes [9, 10].

Chapter 2

Literature review

Gestational diabetes mellitus (GDM) by definition is any degree of glucose intolerance diagnosed for the first time in pregnancy [11, 12, 13]. This definition does not exclude glucose intolerance that may have been present before the pregnancy and whether the intolerance normalises after the pregnancy [13]. Prevalence of GDM is on the rise with many implications for maternal health, pregnancy outcomes and foetal health. It is of importance to identify and diagnose those women at high risk of GDM, monitor their pregnancies closely and treat the glucose levels to try and minimise adverse pregnancy outcomes. Also of importance is to flag them out for the possible long-term development of DM later in their life or for possible recurrence of GDM in subsequent pregnancies.

2.1. Prevalence of gestational diabetes mellitus

In one South African study, the prevalence of GDM was found to be 8.8% among rural pregnant women in Limpopo province [1]. In a Canadian study by Liu and colleagues they found the prevalence of GDM to be higher in First Nations women when compared with Non-First Nations women in Ontario (6.5 vs. 4.2%, $P < 0.001$), with the overall prevalence of diabetes 10.3 vs. 6.0%, $P < 0.001$, respectively. The mean age of women with GDM was younger for First Nations women (28.76 ± 6.98 vs. 32.79 ± 5.39 years, $P < 0.001$) [14]. The incidence of GDM is rising globally due to some factors that include the rising prevalence of obesity and pregnancy complications relating to it. Previously problematic in developed countries, it is now an epidemic in the developing countries as well. In the USA by 2002 one-third of adult women were found to be obese (NHANES) and African-Americans were the most affected (49%) [2]. In Canada there was a 13% rise in obesity among adult women from 1992 (40%) to 2004 (53%) when compared with a 6% rise from 1978 (34%) to 1992 (40%) and in South Africa 38% of adults (age>15years) were obese by 1998 [2]. The incidence of gestational diabetes is said to have increased from 10 to 100 percent in some race/ethnicity groups in the past 20 years and its frequency usually reflects the frequency of type 2 diabetes in the underlying populations [15, 16, 17].

2.2. Screening for and diagnosis of gestational diabetes mellitus

The purpose of screening for any medical condition is to distinguish people who probably have a condition from those who probably do not. This screening is followed by a diagnostic test for those who have screened positive. The health-care system offers screening, and it is important that it causes no harm. Screening programmes need to meet certain criteria as set by the World Health Organisation (WHO) before initiation of screening is. Screening for GDM has therefore been very controversial because it meets some of these criteria, but not all of them [18].

The most important criteria are:

- The condition should be an important health problem.
- All the cost-effective primary prevention interventions should have been implemented as far as practicable.
- There should be a simple, safe, precise and validated screening test.
- The distribution of test values in the target population should be known, and a suitable cut-off level defined and agreed.
- There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.
- There should be an effective treatment or intervention for the patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.
- There should be agreed evidence-based policies covering which individuals to offer treatment and the appropriate treatment to be offered.
- There should be evidence from randomised controlled trials that the screening programme is effective in reducing mortality and morbidity.
- The benefit from screening should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment).
- The opportunity cost of a screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced about expenditure on medical care as a whole [18].

Controversy surrounding screening for gestational diabetes stems from the fact that there is no consensus on universal screening methods or agreed policies. There are also differences in population features of pregnant women globally and lack of evidence based on randomised controlled trials on screening versus no screening of patients. Tere is also a lack of precise and cost-effective screening tests, and differences in health care resources in different countries or regions of the world.

Despite the aforementioned, there is agreement on the fact that GDM is a significant health problem (the diagnosis is associated with adverse pregnancy outcomes and the risk of future diabetes in the mother) [18, 19, 20]. It has also been proven that elevated glucose levels less than diabetic levels and unknown to the woman and her carers can also have adverse pregnancy outcomes (such as large for gestational age (LGA) or macrosomic babies, neonatal hyperinsulinism at birth, neonatal hypoglycaemia, increased adiposity, shoulder dystocia and birth injury, neonatal hyperbilirubinaemia, primary caesarean section and pre-eclampsia). These outcomes were demonstrated in the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study. However, the study did not show that hyperglycaemia less than that of overt diabetes has an increase in perinatal mortality [19, 21].

Early detection of diabetes is important, and screening detects diabetes at an asymptomatic stage. Treatment of hyperglycaemia in pregnancy is effective, and treatment of GDM has been shown to be effective in reducing adverse events [18, 22]. Screening refers not only to plasma or capillary glucose testing but also to identifying risk factors. So in selective screening, the first step involves identifying risk factors such as age and BMI. The selective screening would occur at the booking clinic (or ideally, before conception) with a view to preventing hyperglycaemia in pregnancy. Only those women with risk factors would proceed to the second step using blood glucose tests [18]. Pregnant women who fulfil the criteria for low-risk pregnancy need not undergo screening for GDM. Women with risk factors such as marked obesity, a history of prior GDM, glycosuria or a strong family history of diabetes and previous adverse pregnancy outcomes should undergo glucose testing. If they do not have GDM on the initial screening (negative screening results), they should be retested between 24 and 28 weeks of gestation [20]. Traditionally screening for GDM has been done at 24 – 28 weeks of pregnancy, but some commentators have raised concern about leaving it so late. In the American College of Obstetricians and Gynaecologists (ACOG)

2001 guidelines, it states that insulin resistance increases with pregnancy progression and testing later in pregnancy will have a higher yield of abnormal tests. The later the abnormality is diagnosed; the less time will be available for intervention [11].

Screening will not only help in detecting hyperglycaemia but also early detection of undiagnosed type 2 diabetes. The severity of complications associated with this condition, which include congenital abnormalities and increased perinatal mortality justifies such screening [18]. The issue is about screening and treating at glucose thresholds higher than normal, but lower than diabetic levels. Two studies addressed this issue, namely the Australian Carbohydrate Intolerance Study (ACHOIS) and the Maternal-Foetal Medicine Units Network treatment of mild gestational diabetes (MFMUN-GDM). These studies demonstrated that diagnosis and treatment of GDM are worthwhile, as this does reduce the risk of many adverse pregnancy outcomes of GDM without causing harm [7, 8]. There is broad agreement about treating women with the highest glucose levels, but uncertainty as illustrated by disagreement amongst guidelines and policies, about management of lesser degrees of hyperglycaemia [18]. The ACHOIS and NICHD-MFMU Network trials have shown that intervention at lower levels specified in these trials is worthwhile and cost effective [4,7]. However, there are no randomised clinical trials on screening versus no screening [22].

The harms of screening include the inconvenience of screening and diagnostic follow-up and the anxiety raised by screening tests. The harms may come partly from the impact of the diagnosis rather than the condition, such as the increased rate of caesarian sections [18]. The harms of interventions also need to be considered, including insulin treatment and hypoglycaemia [23]. According to Kjos and Buchanan only 20 – 30% of babies of women with GDM have macrosomia [24]. A Cochrane review found that reducing macrosomia did not necessarily reduce the rates of Caesarean section, forceps delivery or birth trauma [25]. The balance of harms and benefits will depend partly on the prevalence of hyperglycaemia in pregnancy. This is because the number of women who need to be screened to detect one case of hyperglycaemia in pregnancy will fall as the prevalence rises [18].

There is a range of options that have been proposed to screen for GDM. Screening tests do not refer only to blood glucose. Clinical risk factors are easy to record and are identifiable at the booking visit. Identification of the clinical risk factors would be the basis for selection

and only those considered to be high-risk would go on to have their blood glucose measured. Blood glucose levels can be taken at varying times e.g. fasting, random, and post-prandial following an oral or intravenous glucose load or following a standardised meal [18]. The International Association of Diabetes and Pregnancy Study Groups (AIDPSG) consensus panel advocated testing all women with a 75g oral glucose tolerance test (OGTT) at 24 – 28 weeks. Earlier testing only for the women who had been found to have abnormal glucose levels earlier in pregnancy or were known to have diabetes [26]. The UK National Institute for Health and Clinical Excellence (NICE) recommended selective screening based on the American Diabetes Association (ADA) criteria, or on high-risk ethnicity [27]. The basis of this recommendation was on the probability of being diagnosed with GDM on the basis of a 75g OGTT, and so belongs to the dichotomy era [18]. A health technology assessment (HTA) report published in 2002 concluded that selective screening by risk factors would miss about half of the women with GDM [28]. A before and after study from Paris, comparing selective versus universal screening reported that GDM was diagnosed in 8.3% and 12.6% respectively [29].

Summary of some international screening programmes

- *American Diabetes Association (ADA):* Risk assessment for GDM should be at the first prenatal visit. Women at high risk of GDM should undergo an OGTT as soon as feasible. If not found to have GDM at initial screening, they should be retested between 24 and 28 weeks of gestation. Women of average risk should have testing at 24 – 28 weeks. Low-risk status requires no testing. Initial screening using 50g 1-hr oral glucose challenge test (GCT) should precede an OGTT on women exceeding the threshold value on the GCT [30].
- *Canadian Diabetes Association (CDA):* all pregnant women should undergo screening for GDM between 24 and 28 weeks gestation. Women with multiple risk factors should undergo screening in the first trimester [31].
- *International Association of Diabetes and Pregnancy Study Groups (IADPSG):* first phase: first prenatal visit, detection of women with overt diabetes or GDM using fasting plasma glucose, HbA1c or random glucose on all, or only high-risk women. Decision-based on background frequency of abnormal glucose metabolism in the

population or on local circumstances. Second phase: 75g OGTT at 24 – 28 weeks in all women not previously found to have overt diabetes or GDM [26].

- *National Institute for Health and Clinical Excellence (NICE):* women offered screening at booking appointment using any of five risk factors for GDM. Early self-monitoring of blood glucose or a 2-hr 75g OGTT at 16 – 18 weeks to test for GDM if the woman has had GDM previously followed by an OGTT at 28 weeks if the first test is normal. An OGTT should be done to test for GDM at 24 – 28 weeks if the woman has any other risk factor. The NICE guidelines excluded age, because; advanced maternal age should not be used as a risk factor because this would result in pregnant women requiring an OGTT (section 33) [27].

The OGTT has been the standard test for diagnosing GDM, often preceded by a screening test such as clinical risk factors or a 50g GCT. Various OGTTs with different glucose loads (50g, 75g and 100g glucose) and different durations (2-h and 3-h) have been used [18]. The HAPO study has led to the IADPSG consensus recommending standardisation on a glucose load of 75g and glucose testing at fasting, 1-h and 2-h [26]. The OGTT has however been found by Agarwal and Dhatt to have some shortcomings of being expensive and time consuming. It is non-physiologic, unpleasant, not reproducible, unrelated to body weight, and its predictive value may vary with ethnic origins [32].

As an alternative to an OGTT, the fasting plasma glucose (FPG) as a screening test is easy to administer, well tolerated, inexpensive, reliable and reproducible [32, 33, 34]. They note that the value of FPG varies according to the diagnostic criteria used: good with the ADA criteria and poor with the WHO criteria [34]. One problem with FPG is that it misses post-prandial hyperglycaemia, which may be enough to cause overgrowth of some foetuses [23, 35]. Measurement of HbA1c is a current recommendation by an expert committee for diagnosing non-gestational type 2 diabetes because advances in its measurement have made it a more reliable and standardised, test [36]. Measurement of HbA1c at the same time as 75g OGTTs at 24 – 28 weeks in a high-risk population yielded overlapping results in women with and without GDM. Therefore, no level of HbA1c could be used as a cut-off to rule out GDM. Other studies reviewed by Agarwal and colleagues nearly all reported that HbA1c was not useful [37]. Aldasoqui and Gossain suggested that using the serial measurement of HbA1c at four weekly intervals starting around mid-pregnancy might

reduce the numbers of women requiring OGTT [38]. The HAPO study measured HbA1c at the time of the OGTT and found a rise with advancing gestational age [39].

Simplified OGTTs have been suggested as an alternative to a full OGTT, and they could make screening much more convenient. Anderberg, et al., used a 75g load but measuring only the 2-h plasma glucose, (with the cut-off at 9mmol/l for diagnosing GDM) and those in the borderline group of 7.8 – 8.9mmol/l getting a repeat OGTT a week later [40]. Anjalakshi, et al., compared a 75g GCT (non-fasting) with the standard OGTT. They found no difference in their population, implying that it makes no difference whether the women have fasted or not [41]. Ayach, et al., used a 100g OGTT shortened by using a 1-h level of under 7.8mmol/l to rule out GDM and no measurement at 2-h and 3-h [42].

Although screening for HGP does not meet all criteria usually required for implementation of screening programmes, its case has been strengthened in recent years by:

- The rising prevalence due to rising incidence of obesity and women having babies later in life.
- The demonstration by the HAPO study that adverse outcomes occur across a wider range of plasma glucose than previously thought to be the case.
- The results of the ACHOIS and NICHD-MFMUN trials showing that treatment at lower levels of PG is effective.
- The knowledge that metformin and glibenclamide are safe and effective, making treatment easier and cheaper.

Given advances in the evidence base from these and other studies, it is unlikely that there will be a randomised trial of screening versus no screening. Therefore, the uncertainties around the remaining unmet criteria might have to be met by a further analysis of existing data from large studies such as HAPO [18].

2.3. Management of gestational diabetes mellitus

The aim of the management of GDM is to achieve tight glycemic control to prevent adverse pregnancy outcomes. Management entails lifestyle modification (diet and exercise), oral glycemic agents (metformin and glibenclamide) and insulin or a combination of these methods as required. The 5th International Workshop-Conference on GDM made

recommendations relating to glycaemia in GDM pregnancies, and the potential role of foetal growth targets. The recommendation was to maintain capillary blood glucose at < 5.3 mmol/L (fasting state), < 7.8 mmol/L at 1- h and < 6.7 mmol/L at 2-h after starting a meal [51]. Careful analysis of the metformin versus insulin in gestational diabetes study (MiG study) showed a strong association between the level of glycaemia achieved and pregnancy outcomes. The authors of the MiG study commented that lower glycemic targets might be necessary [9].

Lifestyle modification is an important component of the management of GDM, and it entails proper diet to ensure appropriate weight gain in pregnancy and exercise to burn calories as well as limit excess weight gain. Pregnant women with GDM should be evaluated and followed up by a registered dietician to ensure that nutrition promotes euglycaemia, appropriate weight gain and adequate nutritional intake [43, 44, 45, 46]. Exercise or physical activity should be encouraged unless there are specific obstetric contraindications or if the glycemic control is worsened by the activity [47, 48]. To delay efforts at improvement of lifestyle changes until after diagnosis of GDM at 24 – 32 weeks of pregnancy is almost certainly a lost opportunity. Efforts to improve the lifestyle of women at risk of GDM, both pre-pregnancy and from early pregnancy need to be considered. Such an approach has a potential of preventing GDM as well as improving short and long-term outcomes for mothers and babies [19]. Frequent monitoring using self-monitoring of blood glucose is essential to guide treatment, and both fasting and postprandial testing are recommended to guide therapy to reach glycemic targets [49, 50].

Patients who fail to control their glucose after lifestyle modification need to be put on pharmacological treatment while being encouraged to continue with lifestyle modification as part of the treatment. Rowan, et al., in 2008 studied women with GDM, who were randomly assigned to open treatment with metformin (with supplemental insulin if required) or insulin. Of the women assigned to metformin, 43.6% required supplemental insulin. Metformin (alone or with supplemental insulin) was not associated with increased perinatal complications when compared with insulin only. There was less severe hypoglycaemia in neonates whose mothers received metformin, but more spontaneous preterm deliveries (i.e. < 37weeks gestation) occurred in this group [51, 52]. Other studies have confirmed the safety of metformin, demonstrating less neonatal hypoglycaemia [53].

One study conducted to compare metformin with glyburide, however, did not corroborate the findings of increased prematurity in the metformin group [54]. While metformin appears to be a safe alternative to insulin therapy, it does cross the placenta, plus metformin clearance increases in pregnancy [55]. Results of the follow-up of children from the Metformin in Gestational diabetes trial (Mig-TOFU), expected in several years, will provide more data on the safety of metformin in pregnancy [56]. Metformin appears safe and effective in the treatment of GDM, and it reduces the requirement for supplementary insulin. Women treated with metformin have a significantly lower incidence of macrosomia and large for gestational age (LGA) neonates as well as a reduced rate of caesarian section [57].

Insulin is an effective therapy for maternal glucose control. However it is expensive, must be injected and requires skilled handling [54]. The use of insulin to achieve glycemic targets has been shown to reduce foetal and maternal morbidity [58, 59]. There has been use of a variety of protocols with multiple injections being the most effective [60]. Insulin usually needs to be continuously adjusted to achieve glycemic targets [56]. Women with obesity, high fasting blood glucose and early need for pharmacological treatment may be more suitable for insulin therapy [61].

2.4. Complications of gestational diabetes mellitus

GDM has many implications for both the baby and the mother. These implications are short term, and long term, and prevention or treatment of GDM can help in decreasing their incidence.

Short-term complications of hyperglycaemia in the foetus include LGA/macrosomic babies, neonatal hyperinsulinism at birth (as reflected by elevated cord C-peptide), neonatal hypoglycaemia, excess neonatal adiposity, shoulder dystocia or birth injury, neonatal hyperbilirubinaemia, bone fractures, nerve palsies and death. With the increasing prevalence of diabetes, some women may be diagnosed with GDM when in fact they have unknown pre-existing diabetes in particular type 2 diabetes mellitus (T2D). The outcomes of T2D may be comparable to those of type 1 diabetes mellitus (T1D). These adverse outcomes include increased rates of congenital malformation and perinatal death [62, 63].

There may be a question whether there is long-term evidence showing that the intrauterine environment of GDM can contribute to adult disease? There is evidence in animal studies but human data is more limited [64]. There was an association between maternal diabetes in-utero and age at offspring's diagnosis of T2D in the multi-ethnic SEARCH for diabetes in youth study [65]. Both lines of evidence support the concept that exposure to hyperglycaemia in-utero increases the subsequent risk of diabetes in the offspring. The mild hyperglycaemia of GDM, however, was not considered in these studies [19]. In a Danish study, offspring of women with diet-controlled GDM and women with T1D were followed up, and a prevalence of 21% of T2D/pre-diabetes at 22years was present. Offspring of women with GDM are at a significantly higher risk of overweight (obesity) and T2D. While it is difficult to determine the relative contributions of the intra-uterine environment compared with genes and the post-pregnancy environment on these findings in the children of GDM women, the same trends for the children of T1D women strongly indicate that the hyperglycaemia of the intra-uterine environment is important. This conclusion is reinforced by the finding of an association between maternal glucose control late in pregnancy and the risk of T2D/pre-diabetes in the offspring of the T1D mothers [66, 67].

Women with GDM are very often on a pathway to the development of T2D. In an Australian study of 5470 GDM patients and 783 control subjects, the risk of developing diabetes was 9.6 times greater for patients with GDM. The cumulative risk of T2D for the GDM patients was 25.8% at 15 years post diagnosis [68]. In a systematic review of 28 studies, the cumulative incidence of T2D following GDM ranged from 2.6% to 70%. There were considerable differences across the studies in factors such as duration of follow-up (6 weeks to 28 years), diagnostic criteria used for GDM used and the rate of retention of subjects in follow-up [69]. GDM is also a risk factor for cardiovascular disease (CVD) events. In a large population-based study in Canada, women who had GDM when compared with a matching control group were at a slightly higher risk of CVD events with a hazard ratio of 1.71 (95% CI; 1.08 – 2.69). After adjustment for the development of T2D, this hazard ratio was no longer significant such that a considerable part of post-GDM increased CVD risk was attributable to progression to T2D [70].

2.5. Motivation for the study

The Western Cape Provincial Guideline for Management of Diabetes in Pregnancy (WCPGMDP) has recently recommended the addition of oral medication, metformin in the management of GDM. The diagnostic criteria for GDM have been broadened thus increasing the patient workload to obtain the anticipated benefits indicated in the literature discussed. At Tygerberg Academic Hospital (TBH) pregnant women are screened for GDM using historical risk factors and glycosuria. The diagnosis is not made by using a standardised oral glucose tolerance test, but rather by a glucose profile that comprises a fasting and 2-hour postprandial capillary blood glucose value after a non-standardised glycemic load (breakfast brought by the patient to the clinic). An audit of specific aspects of diagnosis, management and outcomes of the increasing population of women with GDM was deemed a valuable exercise to assist with future planning.

Chapter 3

Research methodology

3.1. Study setting

Tygerberg Academic Hospital is a secondary and tertiary referral centre. Patients requiring secondary and tertiary care from the Metro East region of Cape Town get referrals to this centre for specialist management.

3.2. Aim

The aim of this study was to create a profile of current patients with GDM, managed according to the new provincial guidelines for the management of diabetes in pregnancy at TBH [71].

3.3. Objectives

- The first objective was to determine the mode of identification of GDM (history, urine test, blood glucose – fasting or 2-hour value).
- The second objective was to determine the number of patients requiring metformin and or insulin in addition to lifestyle modification (diet and exercise) for management of GDM.
- The third objective was to determine the mode of delivery (elective or spontaneous) for patients with GDM.
- The fourth objective was to determine specific perinatal outcomes for GDM pregnancies.
- The fifth objective was to describe the broad profile of patients with GDM at TBH.
- The sixth objective was to describe maternal complications in GDM pregnancies at TBH.

3.4. Study design

A retrospective audit of all pregnant patients with GDM, seen at the Special Care Clinic of Tygerberg Academic Hospital over a period of 12 months was performed. Patient data (see data capture sheet) were extracted from the files by the investigator with the assistance of Dr D Mason (10 of 147 files), and loaded onto a MS Excel database in a strictly anonymous fashion.

3.5. Study population

The study population comprised all pregnant women with GDM, seen at the Special Care Clinic of Tygerberg Academic Hospital during the period from August 2010 to July 2011. The dictation of the size of the study sample was by the time interval and the number of patients diagnosed with GDM and seen at the clinic during the period of study.

3.6. Record review

Files of all diabetic patients seen at the special care clinic during the study period were retrieved using the clinic attendance register. All retrieved files were reviewed to distinguish those of patients with pre-GDM from those with GDM. All files of patients with GDM were then reviewed to collect data as per the data collection tool. All data collected from the files were recorded in the data collection tool and later entered into an excel spreadsheet for statistical analysis.

3.7. Statistical analysis

STATA version 13 (StataCorp LP. 2013) was used to analyse the data [72]. Where indicated descriptive statistics alone were used to describe the data. Frequencies (counts and percentages) and measures of location (mean and median) and spread (standard deviations, range and percentiles) were used depending on the distribution of the data. 95% confidence intervals were presented for measures of location as well as for the relative frequencies (proportions).

In subsequent analyses, the patient profile as well management methods were compared to the delivery outcome. Where indicated the following tests were used:

- Mann-Whitney test for categorical variables.
- For categorical variables with more than two categories, the Kruskal-Wallis ANOVA.
- Logistic regression analysis for continuous variables.

A p-value of $p < 0.05$ represents statistical significance in hypothesis testing and 95% confidence intervals were used to describe the estimation of unknown parameters.

3.8. Ethical considerations

The study protocol was submitted to the University of Stellenbosch Academic Ethics Committee for approval (SU study number N11/01/012). After obtaining approval from the University's Ethics Committee, permission to review patient records was obtained from Tygerberg Academic Hospital's Research Ethics Committee via the Medical Superintendent. Informed consent was waivered since the study would be a retrospective audit-type record review. Data from patient files were extracted in a strictly anonymous fashion with no patient identifying data extracted.

Chapter 4

Results

Presented in this chapter are the results of the study in tables. Of the 265 records reviewed from the Special Care Diabetes Clinic, 147 (55.47%) records had a diagnosis of GDM and those 147 pregnant women with GDM accounted for 151 deliveries.

Table 1 shows the characteristics of the study population at booking. The age of pregnant mothers ranged from 18 years to 46 years with an average of 32 years. The majority of patients were of Coloured origin (57.1%) followed by Blacks (38.1%), and only 4.8% were Caucasian.

Table 1: Characteristics of the patients at booking

Characteristic	Distribution
Age (years)*	32 (18-46)
Race n (%)	
Black n (%)	56 (38.1)
Coloured n (%)	84 (57.1)
White n (%)	7 (4.8)
BMI (kg/m^2)*	36.6 (18.4-60)
BMI categories n (%)	
<30 n (%)	30 (20.4)
30 – 39.9 n (%)	60 (40.8)
≥40 n (%)	57 (38.8)
Parity*	2 (0-6)

*median (range), BMI = body mass index

Table 2 outlines the statistics of the risk factor profile of the patients in the study. Those patients who had glycosuria in the index pregnancy were of a significant proportion (56.5%.) The number of glycosuria episodes in the antenatal visits at the clinic had a median of 1 and a range of 0-10.

Table 2: Risk factors of the patients at booking and after that

Risk factor	Distribution n (%)
Previous GDM	12 (8.2)
Previous Big Baby ≥ 4.5kg	10 (6.8)
Glycosuria	83 (56.5)
Number of glycosuria episodes at ANC*	1 (0-10)
Unexplained Previous IUD	11 (7.5)
BMI at booking > 40kg/m^2	56 (38.1)
Maternal age > 40 years	9 (6.1)
Family history of diabetes (primary relative)	85 (57.8)
Family origin high prevalence of diabetes (Asiatic)	1 (0.7)
Acanthosis nigricans	2 (1.4)
Polycystic ovarian syndrome	3 (2.0)

*ANC = antenatal care expressed as median (range); GDM = gestational diabetes mellitus; IUD = intrauterine death; BMI = body mass index (calculated as weight in kilograms divided by the square of height in meters)

Another significant proportion of patients were those with a positive family history of diabetes mellitus (57.8%). Importantly certain patients had a combination of risk factors for GDM. Table 3 shows the blood profile of patients and gestational age at diagnosis of GDM.

Table 3: Serum creatinine, HbA1c and gestational age at diagnosis

Serum creatinine*	49 (20-88)
HbA1c*	6.3 (4.8-13.5)
Gestational age (weeks)*	28.2 (7.6-39.6)
<24.0 weeks n (%)	41 (27.9)
24.0-28.0 weeks n (%)	27 (18.4)
>28.0 weeks n (%)	79 (53.7)

*median (range)

The patients' files evaluation for documented episodes of hypo- and hyperglycaemia both as out-patients (home monitoring) or in-patients was performed. Home monitoring using a

glucometer was only performed on patients receiving insulin. Table 4 shows the number of hospital admissions as well as documented episodes of hypo- and hyperglycemia after the diagnosis of GDM.

Table 4: Number of hospital admissions, hypo- and hyperglycemic episodes

Event	Distribution
Number of admissions post diagnosis*	1 (1-4)
One admission# [delivery only] n (%)	81 (55.1)
Two admissions# n (%)	44 (29.9)
Three admissions# (%)	19 (12.9)
Four admissions# (%)	3 (2.1)
Episodes of hypoglycaemia*	0 (0-5)
Episodes of hyperglycaemia*	0 (0-16)
Home monitored$ n (%)	13 (8.8)

*median (range) # includes delivery admission $ self- monitoring at home using a glucometer

Of the total number of GDM patients in the study, 8.8% performed self-monitoring at home because of the addition of insulin to their treatment regimen.

In the high-risk antenatal clinic at Tygerberg Academic Hospital, all patients at risk for intrauterine growth restriction undergo a screening measurement of the umbilical artery Doppler at 24 weeks of pregnancy. Pregnant patients with diabetes including GDM, T2D and T1D undergo an ultrasound growth scan to look for macrosomia. The growth scan involves measurement of the abdominal circumference (AC), mass of the baby and the amniotic fluid index (AFI). This examination usually includes a repeat umbilical artery Doppler measurement. In Table 5 the results of the screening umbilical artery Doppler measurement at 24 weeks' gestation and the same examination, together with the growth scan both performed at 34 weeks' gestation are given. In 59 women (39%) an ultrasound growth scan was not performed at 34 weeks' gestation.

Table 5: Umbilical artery (UA) Doppler and key ultrasound findings

Parameter	Distribution
UA Doppler at 24 weeks	
Normal# n (%)	71 (47.0)
75-95th percentile n (%)	10 (6.6)
Not done n (%)	70 (46.4)
Ultrasound at 34 weeks (growth scan)	
Mass (grams)*	2409 (1610-3315)
Abdominal Circumference	
Normal n (%)	70 (46.4)
>97th percentile n (%)	22 (14.6)
Amniotic Fluid Index	
Normal n (%)	90 (59.6)
Polyhydramnios n (%)	2 (1.3)
UA Doppler at 34 weeks	
Normal n (%)	89 (58.9)
75-95th percentile n (%)	6 (4.0)
Not done n (%)	56 (37.1)

*median (range), #resistance index < 75th percentile

Table 6 outlines the management options used for GDM in this study. There was documentation of compliance with dietary and exercise advice in the patient records. Of the 147 women in the study 34 (23%) were managed with lifestyle (diet and exercise) alone. One hundred (68%) required metformin in addition to lifestyle modifications and 13 (9%) required the additional intervention of insulin.

Table 6: Lifestyle and medical management of patients during pregnancy

Intervention	Distribution
Diet n (%)	144 (98.0)
Exercise n (%)	93 (63.3)
Managed by diet and exercise alone n (%)	34 (23.1)
Metformin	
500mg BD n (%)	32 (28.3)
500mg TDS n (%)	21 (18.6)
850mg TDS n (%)	60 (53.1)
Managed by lifestyle and metformin n (%)	134 (91.2)
Insulin	
Humulin N®* n (%)	13 (8.8)
Humulin R® (breakfast) n (%)	2 (1.4)
Humulin R ® (lunch) n (%)	3 (2.0)
Humulin R® (supper) n (%)	1 (0.7)

BD = twice daily, TDS = three times daily, *all patients receiving insulin were at least on Humulin N

Table 7 shows the details of the deliveries. In 29.2% of cases, delivery occurred at < 38 weeks' gestation. Iatrogenic reasons for earlier delivery included preeclampsia in 10.9% of cases.

Table 7: Delivery details

Outcome	Distribution
Gestation at delivery	
<38 weeks n (%)	43 (29.2)
≥38 <39 weeks n (%)	82 (55.8)
>39 weeks n (%)	22 (15.0)
Mode of delivery	
Spontaneous n (%)	40 (27.2)
Elective n (%)	107 (72.8)
Route of delivery	
Vaginal n (%)	66 (44.9)
Caesarean n (%)	81 (55.1)
Birth weight (grams)*	3280 (1230-5101)

*median (range)

Table 8 shows adverse outcomes of GDM affecting the mother, her baby or both. Table 9 shows details of the two perinatal losses.

Table 8: Complications during pregnancy

Complications	Distribution n (%)
Maternal complications	
Mothers experiencing any complication*	36 (24.5)
Pre-eclampsia	16 (10.9)
Late onset gestational hypertension	1 (0.7)
Acute severe hypertension	3 (2.0)
Preterm labour (spontaneous)	11 (7.5)
Antepartum Haemorrhage	1 (0.7)
Perineal Second-degree tear	1 (0.7)
Postpartum hypertension	1 (0.7)
Perinatal complications	
Babies experiencing any complication*	58 (38.4)
Breech presentation	3 (2.0)
Big baby/macrosomia	4 (2.6)
Monochorionic diamniotic twins	1 (0.7)
Pre-term pre-labour rupture of membranes	3 (2.0)
Foetal distress / pathological CTG (antenatal/intra-partum)	39 (25.8)
Cephalo-pelvic disproportion	4 (2.6)
Cord prolapse	1 (0.7)
Shoulder dystocia	1 (0.7)
Apgar scores < 7	4 (2.7)
Neonatal hypoglycaemia	14/67 (20.9)
Perinatal loss	2 (1.3)
Other complications	
Any historical risk factors and labour observations*	**34 (23.1)**
Previous C/S x 2	4 (2.7)
Previous C/S x 1 declined trial of labour after C/S	4 (2.7)
Previous C/S x 1 + breech presentation	1 (0.7)
Previous C/S x 1 + macrosomia	1 (0.7)
Previous C/S x 1 + failed IOL	1 (0.7)
Previous third-degree perineal tear	1 (0.7)
Failed induction of labour	9 (6.1)
Poor progress during labour	13 (8.8)

*Patients may have more than one complication. Foetal distress or pathological CTG as taken from patient records. CTG = cardiotocography, C/S = caesarean section, IOL = induction of labour

Table 9 shows the characteristics of the perinatal losses that occurred during the study period. One patient experienced a spontaneous miscarriage at 15 weeks' gestation. Despite a positive family history and a BMI of 30 kg/m^2, she had no previous diagnosis of diabetes mellitus, and although classified as GDM she is likely to have had pre-GDM.

Table 9: Perinatal losses

	Loss 1	Loss 2
Maternal age (years)	23	29
Gravidity and Parity	G2P1	G2P1
Antenatal Risk factors	Glycosuria BMI > 40 Family history of DM	Uncertainty as to what risk factor led to diagnosis
GA at diagnosis of GDM	30w5d	29w3d
Management	Diet Exercise Metformin 500mg BD	Diet Exercise Metformin 850mg TDS
Umbilical artery Doppler (RI)	Normal at 24 weeks	Normal at 24 weeks 75-95th centile at 34 weeks
Admissions	1	2
GA at delivery	32w5d	37w2d
Route of delivery	C/S	C/S
Birth weight (grams)	1770	1710
Complications	Unexplained IUFD followed by a failed IOL	Unexplained IUFD twin B with signs of foetal distress in the other twin

BMI = body mass index (kg/m^2), DM = diabetes mellitus, GDM = gestational diabetes mellitus, GA = gestational age, BD = twice daily, TDS = three times daily, RI = resistance index, C/S = caesarean section, IUFD = intrauterine foetal death, IOL = induction of labour.

Table 10 shows the proportions of patients and the types of medications they had prescribed on discharge.

Table 10: Medications prescribed for patients on discharge

Medication type	n (%)
Metformin	44 (29.1)
Anti-hypertensive medications	37 (25.2)
Other medications*	92 (62.6)

* Includes antibiotics, analgesics and iron supplements

The following maternal characteristics (variables) underwent testing for association with a 5-minute Apgar score < 7 using linear regression analysis (for continuous variables) and the Kruskal-Wallis test (for categorical variables): age, parity, race, BMI. None of these characteristics showed any univariate statistical significance. A second set of variables associated with pregnancy outcomes underwent testing for association with a 5-minute Apgar score < 7 in the same fashion. This second set comprised: elective delivery, Caesarean delivery, preeclampsia, shoulder dystocia and neonatal hypoglycaemia, none of which showed any univariate statistical significance.

Chapter 5

Discussion

During this year-long audit of patients with GDM, the following salient facts were noted. Fifty-eight percent of women had a positive family history of diabetes; 57% developed glycosuria, and 38% underwent diagnostic testing due to morbid obesity. Previous GDM and previous unexplained IUD were present in 8% of women. The median age of the women in this group was 32 years and 80% were found to be obese. The median gestational age at diagnosis was 28 weeks with a median glycosylated haemoglobin of 6.3%. The upper range of glycosylated haemoglobin (13.3%) and the lower range of gestational age at diagnosis (7 weeks) indicate that cases of undiagnosed (pre-existing) diabetes mellitus were also present in this group of women with "gestational diabetes". Concerning glycemic control during pregnancy 23% responded to lifestyle modification alone, 68% required additional metformin and 9% insulin as a final addition to therapy. It is noteworthy that despite the diagnosis of GDM, 29% of women still required metformin at discharge. Twenty-nine percent of the group delivered before 38 weeks' gestation with hypertensive complications (14%) and spontaneous pre-term labour (8%) featuring prominently. The median birth weight was 3280 grams. There was a high incidence of peripartum foetal distress (26%) reflected in the caesarean rate of 55%.

The dangers of GDM are well established and the interventions to minimise the morbidity and mortality due to GDM are well known. Areas of importance in trying to achieve reduction of GDM morbidity and mortality are recognition of women at risk of GDM and understanding the burden of disease due to GDM. After that, institute good management of GDM and long-term lifestyle modification for women who develop GDM and their offspring.

5.1. Recognition of risk of gestational diabetes mellitus

The risk factors for the development of GDM are generally well understood i.e. previous GDM, unexplained intrauterine death in a previous pregnancy, previous macrosomic baby (>4.5kg), family history of diabetes (first-degree relative with diabetes), family origin with a high prevalence of diabetes (Asiatic), a body mass index of more than 40kg/m^2 at booking,

glycosuria, maternal age older than 40 years, acanthosis nigricans and polycystic ovarian syndrome [71]. Women may have one of these risk factors or a combination of them and in the latter case the risk of GDM becomes even higher. In this study the most frequent risk factors were: family history of diabetes (58%), glycosuria (57%) and BMI at booking greater than, 40kg/m^2 (38%). The other risk factors contributed smaller proportions to the overall risk profile of patients. Combinations of risk factors also existed increasing the individual risk of GDM for those particular patients. Although this study is unable to deduce what percentage of patients might be missed by selective screening it is clear that the large majority would be identified through single or combinations of risk factors.

Recognising pre-existent risks for the development of GDM is not the only issue to consider, but identification of patients with GDM and no pre-existent risks in the index pregnancy is also important to prevent possible complications of the disease. In this study, this was performed by screening those patients with risk factors using urine testing for glycosuria at each antenatal visit and a glucose profile as indicated in the provincial management guidelines. Patients with glycosuria (≥1+ of glucose on diagnostic strips) were tested as soon as feasibly possible with a glucose profile. Those patients with risk factors but no glycosuria were tested at 26 – 28 weeks of gestation [71]. Most patients in the study were diagnosed with GDM at gestational ages beyond 28 weeks (54%) while 28% were diagnosed before 24 weeks. Therefore, only 18% of patients were diagnosed during the traditional period of 24 – 28 weeks' gestation. This incidence suggests that a large proportion of patients with GDM would be missed if testing were restricted to the traditional 24 – 28-week period only. The influence of the other accepted risk factors can be clearly seen. The findings in this study are in keeping with the 2001 statement in the ACOG guidelines which, emphasize that insulin resistance increases with pregnancy progression and that testing later in pregnancy has a higher yield of abnormal results [11].

5.2. The burden of disease

Gestational diabetes is known to have a significant burden of disease for the mother and baby not only during pregnancy and perinatal period but also over the long term. Certain pregnant women diagnosed with GDM might be suffering from undiagnosed, largely asymptomatic T2D. One would expect this to be a particular problem amongst women with

poor control over their diet. Obese women are also at higher risk of preeclampsia with its complications, which has a high association with GDM [19, 21]. Women with diabetes are also more likely to deliver by primary caesarean section further increasing maternal morbidity [19, 21]. The babies of these mothers may be macrosomic / LGA, have neonatal hyperinsulinism and hypoglycaemia at birth and may have shoulder dystocia and birth injury due to increased adiposity [19, 21]. Increased perinatal mortality has even been described [19, 21].

In the index study, all women were managed as outpatients. Most of them (55%) achieved glycemic control without any admission other than that required for delivery. Episodes of hypoglycaemia were very few (median = 0), which is an expectation in patients with mild levels of dysglycemia (GDM) treated with lifestyle modification and metformin. The complication of hypoglycaemia is more associated with insulin treatment. Comparing the findings of this study with the HAPO study, patients in the index study had a more than two-fold increase in the incidence of complications such as pre-eclampsia (11% vs. 5%) and total caesarean delivery (55% vs. 24%) [5]. In the post-partum period, there was a higher incidence of neonatal hypoglycaemia in the index study compared to the HAPO study (21% vs. 2%). Unfortunately, a large proportion of babies (56%) did not have glucose testing at birth although this was probably performed in the neonatal wards. The rate of preterm delivery was more than four times higher (29.2% vs. 6.9%) and that of shoulder dystocia was half of that reported in the HAPO study (0.7% vs. 1.3%) [5]. Of the four babies that had macrosomia, only one had a shoulder dystocia. All of these findings indicate the importance of timely diagnosis and proper management of GDM both during the antenatal and intrapartum periods. The perinatal loss in this study was comparable to losses in other studies (1% vs. 1% & 1%) [54].

Long-term complications that may contribute to the burden of disease due to GDM for the mother are: progression to T2D and risk of cardiovascular disease. For the baby the complications are development of overweight (obesity), pre-diabetes and T2D later in life [65, 66, 67, 70]. In this study, the prevalence of obesity was very high with 80% of the patients classified as obese and 38% as morbidly obese. Comparing the weights of women in this study with those in the HAPO study, the median and mean weights of the patient populations differed (37 vs. 28 kg/m^2) [5].

5.3. Management of gestational diabetes mellitus

Good management of GDM is key to preventing complications to both the mother and her baby. Management of GDM involves primary prevention as well as secondary prevention. Primary prevention entails prevention of GDM by paying attention to all the modifiable factors in the pre-conception period, during the pregnancy and in the post-partum period. Women with risk factors need pre-conception assessment for counselling and lifestyle modification measures (advice on weight loss, diet and exercise). Pre-conception glycemic control is of relevance for patients who have previously experienced GDM. During the pregnancy, lifestyle modification continues to be an essential part of GDM management. During the post-partum period there are long term benefits to lifestyle modification such as maintenance of weight loss and reduction in risk of development of T2D as well as possible reduction in recurrence of GDM in subsequent pregnancies [19].

Secondary prevention entails early detection of those patients with GDM (screening and diagnosis) and providing treatment (lifestyle modification, oral hypoglycemic agents, insulin or a combination of these as necessary). Once GDM is diagnosed, patients are followed up more regularly to reduce or at least to detect complications early to minimise their impact. The patients in this study were managed using principles of secondary prevention since most of them got referral to the Special Care Diabetic Clinic from lower levels of care. Lifestyle modification forms the basis of patient management in GDM. As expected during pregnancy most patients, (98%) with the diet although fewer (63%) did so with exercise.

Nearly one quarter (23%) of the patients in the index study managed to achieve euglycaemia using lifestyle modification (diet & exercise). Most patients (77%) required metformin in addition to lifestyle modification as part of their treatment for GDM and 13 (9%) of patients required the addition of insulin to their treatment. In the well-known “MiG” trial the incidence of women with GDM who required the addition of insulin (to metformin) in order to achieve euglycaemia was much higher than the incidence of additional insulin in this study (46% vs.9%) [9].

Almost one-third of patients in the index study were discharged on diabetic medications because their glucose levels were not controlling adequately at the time of discharge. However, none of the patients was discharged on insulin; only metformin was prescribed.

The use of Metformin is safe during lactation [71]. One-quarter of patients on discharge were on anti-hypertensive medications for blood pressure control post-delivery and almost two-thirds of patients got other medications on discharge, including antibiotics, analgesics and iron supplements post-delivery.

5.4. Strengths of the study

The study sheds light on the specific patient profile, the diagnosis and management, perinatal outcomes and maternal complications due to GDM at Tygerberg Academic Hospital. It has highlighted the results of the management approach and identified gaps in the management of patients; e.g. limited use of growth scans at 34 weeks gestation to detect foetal macrosomia and insufficient measurement of serum glucose of babies to detect neonatal hypoglycaemia. Addressing these gaps will help to improve the quality of care provided.

The retrospective audit fashion of the method of this study helped in assessing the quality of record keeping for patients managed at the Special Care Diabetic Clinic at TBH.

It further contributes to the extant knowledge base that is already extensive but extending its borders as milder levels of dysglycemia are regarded as abnormal during pregnancy.

Information from the study can be of potential use in redefining lines of referral from lower levels of health care to TBH, which is a tertiary Academic Hospital. The danger exists that with the expansion of the diagnostic criteria, referral hospitals can be inundated by patient numbers thereby hampering the provision of quality care. Decanting patients with GDM requiring management with lifestyle modification or low doses of metformin would help in ensuring that patients requiring more intensive treatment get adequate management at an appropriate level of care.

5.5. Limitations of the study

The referral-based nature of the study population was a limitation to its representativity. This imitation would of necessity include selection bias towards sicker patients. A population-based study would remove such a bias.

Incomplete records were a source of concern. Missing data does not always mean that e.g. a post-natal serum glucose test was not performed on a baby, it may have been done and found to be normal but was simply not recorded.

The size of the study population could have been enlarged by including data from other years.

5.6. Suggestions for further research

This study could be expanded to include all levels of healthcare in the Cape Town Metro East region to assess the prevalence of GDM in the general population of this region.

A comparison between different health care centres from the same region or the two Cape Town Metro regions could be done to assess GDM.

5.7. Conclusion

The presence of a positive family history, obesity and glycosuria during pregnancy are key elements facilitating the diagnosis of GDM, which most often occurs at the start of the third trimester of pregnancy. Although it is encouraging to note that one-quarter of women with GDM respond to lifestyle modification alone, the recent addition of the oral agent metformin enables the managing clinician to reserve more invasive insulin therapy to < 10% of cases. The goal of elective delivery at 38 weeks' gestation is often hampered by complications requiring earlier delivery such as pre-eclampsia. These complications add to the already high caesarean rate that was 55% in the index study. It is important to separate undiagnosed type 2 diabetes mellitus from true gestational diabetes mellitus as the dangers and outcomes differ. Although an increase in the number of patients with true GDM is to be expected, good maternal and perinatal outcomes can be anticipated when women receive proper management.

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