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Cholesterol Abnormalities are Common in Women with Prior Gestational Diabetes

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Abstract

Objectives: The primary objective was to investigate the prevalence of persisting diabetes and high cholesterol in postpartum women with prior Gestational Diabetes Mellitus (GDM).

Research design and methods: All women with a diagnosis of GDM who delivered from April 2010 to 30 June 2012, at Joondalup Health Campus were included in the study. On the postnatal ward, women were given an appointment to attend a diabetes follow up clinic at 6-12 weeks postpartum. They were provided with a pathology request for a glucose tolerance test, fasting cholesterol, triglycerides, LDL-C and HDL and cardiac risk ratio.

Results: Of 4956 women with no prior known history of diabetes who delivered at the hospital over the audit period, 168 (3.4%) were diagnosed with GDM, of whom 136 attended for postpartum review (85%) at 6-12 weeks. Persisting glucose intolerance and type 2 diabetes were diagnosed in 16% and 6% of the patients. Fasting cholesterol, low-density lipoprotein C and triglyceride levels in excess of Australian recommended standards were identified in 54%, 50% and 13% respectively.

Conclusions: 6% and 54% of women had persisting glucose and cholesterol abnormalities at 6-12 weeks postpartum. Specific follow up to address cardiovascular risk factors is recommended.

Keywords: Gestational diabetes; Cholesterol; Glycaemic control

Introduction

Gestational Diabetes Mellitus (GDM) is a common medical condition that is associated with a substantial increase in risk of maternal and perinatal complications [1-4]. The main maternal complication which has been identified is the persistence of Diabetes Mellitus. Perinatal complications of GDM include macrosomia, birth injuries and long-term adverse effects of health such as impaired glucose tolerance, obesity and impaired intellect [1].

The Australian Institute of Health and Welfare 2005-06 (AIHW) report'Gestational diabetes mellitus in Australia', showed that 4.6% of women aged 14-59 years old who gave birth in hospital, were diagnosed with GDM [2]. This figure reflected that the incidence of GDM increased by over 20% between 2000-2001 and 2005-2006 [2].

High blood cholesterol is also a very common medical condition with 1.3million Australians reported to have this condition in 2004-05, according to self-reports from the Australian Bureau of Statistics' National Health Survey [5-7]. This figure translates to 7% of the population [7]. High cholesterol is a major risk factor of cardiovascular disease (CVD) and some forms of stroke [5]. CVD is the leading cause of death in both Australia and globally. According to the World Health Organisation (WHO), CVD was responsible for 30% of deaths worldwide and the AIHW reported that 3.5 million Australians had the disease in 2007-08 [6]. Despite the strong link between high blood cholesterol and CVD, it is important to note that these two medical conditions may present independently [5].

Common modifiable risk factors between GDM and high blood cholesterol include diet, BMI and exercise [8,9]. Diet is arguably the most influential lifestyle factor and hence dietary education and control is a key component in the intervention and treatment upon GDM and high blood cholesterol [3,4]. Several studies have reported on the effect of GDM treatment has on pregnancy outcomes and the effectiveness of GDM interventions such as dietary advice, blood glucose monitoring and insulin therapy or medications for glycaemic control [1,3,4,8]. These previous studies have provided evidence that GDM interventions reduce serious perinatal morbidity and may also play a role in improving the mother's quality of life [1,3,8,9].

It has been established that the prevalence of development of post-partum type 2 diabetes mellitus increases over time [10-16]. Epidemiological review has shown that the prevalence of type 2 diabetes mellitus in women with previous GDM ranges from 2.6% - 70%, with variations in rates of prevalence due to the duration of follow-up [14,16]. Additionally, studies have indicated that women with previous GDM are more likely to be insulin resistant and develop metabolic syndromes in later years [10,14]. Insulin resistance and metabolic syndrome are both linked to an increased risk of cardiovascular disease and subsequently GDM follow-up studies have discovered that GDM is associated with hypertension, dyslipidaemia and coronary artery disease at post-partum review [16]. Another study provided evidence that women with prior GDM and a family history of type 2 diabetes in

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a first-degree relative, were not only more likely to be at a higher risk of CVD disease but experience CVD disease and events at a younger age [14].

The Fifth Annual International Conference on Gestational Diabetes Mellitus in 2007 reviewed that a substantial number of women with GDM have overlapping characteristics with patients who have a metabolic disease [12]. Evidence was provided showing that patients with GDM may present with short-term endothelial dysfunction and hence transient hypertension in late pregnancy [12]. Furthermore, patients with long-term endothelial dysfunction are at an increased risk of chronic hypertension and CVD [10,12]. Studies suggested that chronic insulin resistance might produce chronic inflammation that may increase the likelihood of future hypertension and ischaemic vascular disease [11,12].

It is evident that there is an association between GDM and CVD [12,14,16]. However the specific relationship between GDM and prevalence of high blood cholesterol requires clarification and follow-up studies need to be conducted to establish the risks and mechanisms for the development of CVD in women previously diagnosed with GDM [12].

Our hypothesis was that the prevalence of high cholesterol in women with a recent diagnosis of GDM would be higher than that observed in the general Australian adult population. The aim of the study was therefore to determine the prevalence of persisting glucose intolerance, type 2 diabetes and elevated cholesterol in a population of postnatal women who had GDM. Our secondary aims were to explore the proportion of women with triglyceride and low-density lipoprotein-C (LDL-C) abnormalities, in this population.

Methods

A retrospective study was undertaken of all patients referred to postnatal gestational diabetes follow up (Appendix) clinic from 1 July 2010 to 30 June 2012. The study subjects delivered at a large secondary hospital in the northern suburbs of Perth, Western Australia, Australia.

All patients with a diagnosis of gestational diabetes delivered at the hospital were referred to the clinical service between 6 and 12 weeks postpartum. Women were diagnosed with GDM if they had a fasting BSL>5.5 mmol/L or 2 hour BSL>8.0 mmol/L in accordance with the Australian standards at that time [2,17]. On the postnatal ward women were given an appointment to attend the diabetes follow up clinic at 6-12 weeks postpartum. They were provided with a pathology request for a glucose tolerance test, fasting cholesterol, triglycerides, LDL-C and HDL and cardiac risk ratio.

The study involved the audit of routine demographic materials and all routine test results from the postnatal review clinic and collection of prenatal information on pre-existing diabetes and cholesterol status if known. For each participant a survey form was completed that detailed: relevant patient history, type of GDM intervention received and relevant postpartum blood results. Postpartum weight and time since delivery were also audited.

Postpartum glucose intolerance was diagnosed if the glucose tolerance test had either fasting blood sugar level of 6.1-7.0 mmol/L or 2-hour of 7.8-11.1 mmol/L [17]. Type 2 diabetes was diagnosed if fasting blood sugar level was >7.0 mmol/L or 2-hour>11.1 mmol/L [17]. Elevated triglycerides was diagnosed if fasting triglycerides was >1.7 mmol/L and elevated low-density lipoprotein C (LDL-C) was diagnosed if >4.0 mmol/L [17].

As it was departmental policy that all women diagnosed with Gestational Diabetes Mellitus were offered a follow-up clinic review at 6-12 weeks postpartum, and this was a retrospective audit of clinic outcomes, the Hospital Ethics Committee deemed that this study met the NHMRC Criteria of a quality assurance and audit study and no formal application for ethical approval was required.

Data were entered into a data base and analysed using Minitab (University of Melbourne, 2011). Data were presented as number and percentage for discreet variables and as mean and standard deviation for continuous variables that had a normal distribution.

Results

Women with a pre-existing (that is pre index pregnancy) diagnosis of diabetes were excluded. A total of 4956 women with no prior known history of diabetes delivered at the hospital over the audit period. Of these, 168 women were diagnosed with GDM (3.4%). Of the 168 women with GDM, two came from rural areas and were not able to attend for follow up. Of the remaining 166 women, eight did not receive a follow up appointment due to oversight on the postnatal ward. Of the 158 women who were given an appointment, a total of 136 attended for follow-up care (86%) at a mean time of 11.2 (sd 0.5) weeks following delivery.

Demographic data

The demographic features of the study subjects compared to the background population at the hospital are summarised in table 1. The average age of the study subjects was 32 years, with an average booking BMI of 29 and postnatal review BMI of 30.2. This makes them slightly older than the background group of women delivering in Australia where the mean age is 30 years. Most women did not have a family history of diabetes mellitus and approximately half were nulliparous. Approximately one third (37%) were nulliparous in the index pregnancy and the remainder were parous. This is in contrast to background parity in Australia where 75% are nulliparous and only 25% are parous [2,17].

Treatment in index pregnancy

The majority of women (71%) required only diet treatment for their GDM. A further 10% of women were prescribed diet and metformin therapy and 16%received treatment with diet and insulin. Only 3% were administered triple therapy of diet, insulin and metformin.

Birth outcomes

In our study, the average gestational age at delivery was 37.8 weeks gestation and the average birth weight was 3339 g. The unit had a policy of offering induction at 40 weeks to all uncomplicated diabetic patients and this reflects the lower gestational age compared to the Australian population, which is 38.8 weeks gestation [2]. Despite the difference in gestation, birth weight was similar to that of the Australian population (3374 g) [2]. The most common method of delivery was spontaneous vaginal delivery (43%). A further 34% of women underwent caesarean section, of which 21% were elective and 13% non-elective. The spontaneous vaginal delivery rate was lower and than that reported for the Australian population which is 57% [2] (Table 1).

Postnatal issues

Table 2 summarises the rate of complications in the study subjects recorded at GDM postnatal follow up clinic at 6-12 weeks postpartum. Persisting glucose intolerance was detected in 16% and Type 2 diabetes

mellitus was identified in 6% of the study subjects. High cholesterol was identified in 54% and 50% had high LDL-C levels. Additionally, 13% of the women were reported to have high triglyceride levels. Of note, only 2 women (1.4%) had fasting cholesterol <4, which is the Australian National Heart Foundation target (Table 2).

Discussion

This is the first Australian study to formally audit rates of cholesterol abnormalities in a postpartum population of women with GDM. The rate of abnormality was significant.

Our results revealed that women who had prior GDM had a much higher prevalence rate (54.5%) of high cholesterol levels at 6–12 weeks post-partum follow up, compared to the Australian adult population. The National Health Survey of 2004-05 showed that approximately 7% of the Australian female population aged 18 to 65 years had high blood cholesterol [7]. Investigation into post-partum lipid profiles also showed that half of the women in our study cohort had high LDL-C levels and 13% had high triglyceride levels. Only 2 women (1.4%) had a fasting cholesterol <4, which is the National Heart Foundation target [7].

These findings are suggestive of an overall elevated risk of cardiovascular disease in women with a history of GDM.

Additionally, we observed that 16% of women had persisting glucose intolerance, a prediabetic state where intervention may prevent the subsequent development of type 2 diabetes mellitus. A further 6% already fulfilled the criteria for type 2 diabetes mellitus. These results are consistent with previous follow up studies [14,17].

Variable	Study subjects	Australian data [17,18]
Age (in years) Mean (std dev)	31.63 (6.17)	30.0
Gravidity N (%) 1 2 3 or more Missing data	47 (36.72%) 34 (26.56%) 47 (36.72%) 8	
Parity N (%) 1 2 3 or more Missing data	67 (52.34%) 32 (25%) 29 (22.66%)	166 987 (75.1%) 33 395 (15.0%) 21 788 (9.8%) 125 (0.1%)
Treatment N (%) Diet only Dietand Metformin Diet and Insulin Diet, Metformin and Insulin	96 (71.11%) 14 (10.37%) 21 (15.56%) 5 (2.96%)	
Family history of diabetes N (%) No Yes	84 (61.76%) 52 (38.24%)	
Gestational age Mean (std dev)	37.8 (2.29)	38.8
Birth weight Mean (std dev)	3339 (670.8)	3374
Delivery method N (%) Vaginal delivery Forceps/Vacuum delivery Caesarean section	58 (42.65%) 32 (23.53%) 46 (33.83%)	167 202 (56.8%) 34 429 (11.7%) 92 687 (31.5%)
Booking weight Mean (std dev)	76.97 (20.57)	
Booking height Mean (std dev)	161.65 (11.50)	
BMI Mean (std dev)	28.73 (5.57)	

Table 1: Demographic and delivery characteristics of the study subjects compared to the Australian population [17].

Variable	Outcome N=136 (%)
Ongoing diabetes N (%) * No * Glucose intolerance * Type 2 diabetes Missing data	 100 (77.52%) 21 (16.28%) 8 (6.20%) 7
High cholesterol (fasting>5.5 mmol/L) N (%) * No * Yes Missing data Mean cholesterol of population mean (std dev)	 58 (45.67%) 69 (54.33%) 9 6.26 (0.83)
High triglycerides (fasting>1.7 mmol/L) N (%) * No * Yes Missing data Mean triglycerides mean (std dev)	 110 (86.61%) 17 (13.39%) 9 3.06 (0.92)
High low density lipoprotein C (fasting>4.0 mmol/L) N (%) * No * Yes Missing data Mean LDL-C mean (std dev)	 60 (50%) 60 (50%) 16 3.73 (0.66)

Table 2: Rate of complications in study subjects.

Women with prior GDM are known to have a higher prevalence of cardiovascular disease (CVD) and occurrence of CVD events at a younger age [14,16,18-21]. One follow-up study investigated the link between women who had GDM or a family history of type 2 diabetes mellitus and their CVD risk. Results from this study showed that women were at a significantly increased risk of developing CVD at a young age. The authors recommended that cardiovascular interventions should be considered in this group before the advent of disease in order to reduce or prevent risk of CVD [14]. Studies in other populations have identified risk factors for cardiovascular disease such as hypertension, central obesity, and atherosclerosis and type 2 diabetes mellitus to be increased in women with prior GDM [18-21].

The high cholesterol levels may lead to atherosclerosis. One GDM follow-up study reported that women with previous GDM had an increased carotid intima media thickness (IMT) compared to a control group of women who had a normal pregnancy [16]. Carotid IMT is a method of assessment of early atherosclerosis and has been illustrated to be a "predictor of future vascular events" [16].

A number of studies have demonstrated that interventions during and beyond pregnancy may reduce the adverse metabolic impact of diabetes [22-27]. These includes with interventions during pregnancy [22,23].

Overall, our results were supportive of previous studies' findings in that high cholesterol and triglyceride levels were more prevalent in patients with a history of GDM and subsequently their risk of cardiovascular events is higher than that of the general population. Furthermore, our results supported our hypothesis that women with previous GDM would have a significantly higher cholesterol prevalence rate (54.5%) compared to the prevalence amongst the general adult population in Australia (7%) [7].

Recent studies have indicated that a significant proportion of the increased risk of CVD is attributable to the progression of GDM to type 2 diabetes mellitus [24-27]. It has widely reported that GDM greatly increases the prevalence of development of postpartum insulin

resistance and type 2 diabetes mellitus [24-27]. Our results reinforce findings in other studies that cholesterol abnormalities are also prevalent and reflect metabolic dysfunction in this patient population.

Another important predictor of type 2 diabetes mellitus is the time to follow-up of GDM patients; studies have established that the risk of type 2 diabetes mellitus increases with time [13,28-30]. In our study, a higher proportion of women were identified with glucose intolerance than type 2 diabetes mellitus. This means that early identification of glucose intolerance is a window of opportunity for intervention to prevent the development of type 2 diabetes mellitus.

There were some potential limitations to our study. Firstly we had a short follow-up period which consisted of one GDM review for each patient at 6-12 weeks postpartum. This aspect of our study may have had an effect on our results due to existing evidence that prevalence rate of GDM complications increases with time. Secondly, our study did not have access to a women's pre-pregnancy medical history and it is possible some women had pre-existing diabetes and did not disclose this at the antenatal clinic.

In conclusion, our study shows that women with previous GDM havean increased cardio metabolic risk at 6-12 months postpartum. This patient population are a group amenable to intervention to prevent or reduce their future burden of cardiovascular disease. More aggressive postnatal care of women with a prior diagnosis of GDM may identify modifiable risk factors and lower their future risk of chronic disease. A postnatal service can identify modifiable risk factors at a time when women are receptive to messages of lifestyle change as new mothers.

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