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Gestational diabetes mellitus: management during and after pregnancy - a systematic literature review

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ABSTRACT

Gestational Diabetes Mellitus (GDM) is one of the most common complications of pregnancy. Women with gestational diabetes have a higher risk of serious health outcomes for mother and baby such as preeclampsia, premature birth and the long term development of type 2 diabetes. This study was conducted to present a review of available research in several countries about GDM management during and after pregnancy.
Several databases including PubMed, ScienceDirect and EBSco were searched for relevant articles published between January 2009 and January 2019.
Of the 1186 initial articles identified, this study analyzed 7 relevant articles that met the inclusion criteria. This study showed that management for GDM includes medical nutrition therapy, exercise, monitoring of blood glucose, and insulin therapy if blood glucose is not achieved with that treatment. Exclusive breast feeding for at least three months has been shown reducing the risk of childhood obesity of children, particularly in those born to obese and mothers with GDM
There is a need to increase awareness of long-term consequences on gestational diabetes, both in patients and in healthcare professionals. Counseling is needed for dietary intervention and physical activity for all postpartum women with a history of GDM to stay healthy or to improve future health.

1. Introduction

Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy (Committee on Practice Bulletins—Obstetrics, 2018). GDM is estimated affecting around 7-10% of all pregnancies (Behboudi-Gandevani et al., 2019) with an estimated GDM prevalence of 6-13% around the world (Zhu and Zhang, 2016). The prevalence of GDM varies from some country, European countries 5.4%, Africa 14% (Mwanri et al., 2015), and Asian countries range 0,7-51% (Nguyen et al., 2018). The difference in prevalence can be caused by ethnic differences, diagnostic criteria, screening strategies, and population characteristics(Lee et al., 2018).

GDM is associated with adverse maternal and fetal outcome. The adverse maternal complications include gestational hypertension, pre-eclampsia, polyhydramnios, cesarean section, and shoulder dystocia (Johns et al., 2018). GDM can cause type 2 diabetes within 10 years of pregnancy

and associated with hearth desease. Furthermore, children born to mothers with GDM have high risks of developing macrosomia, preterm birth, neonatal hypoglycemia, intensive care, and jaundice (Kc et al., 2015a). Not only when they are children, but when adolescents also, they have a risk of being obese or having type 2 diabetes (Johns et al., 2018). Lifestyle changes are the most important component in GDM management (Buchanan et al., 2012). GDM management begins with nutritional therapy, exercise, and glucose monitoring. 70-85% of mothers with GDM can control glycemic targets with lifestyle modification. However, about 15-35% of women with GDM need insulin therapy (Association, 2019a). Women with GDM who cannot achieve their glycemic goals with diet and exercise. They still need insulin to control their GDM (Subiabre et al., 2018). It is important to understand earlier on how GDM is detected and managed appropriately so that maternal and neonatal morbidity can be reduced. This research identifies how GDM is managed during and after pregnancy in several countries. This study is useful in enriching the literature on GDM management best-practice.

2. Method

Our method was a Systematic Literature Review (SLR). SLR is a systematic way of collecting, critically evaluating, integrating, and presenting findings from various research studies regarding research topics or research questions that have been determined (Pati and Lorusso, 2018).

2.1 Research Question

We determined the research questions based on the objective of this study. Question format was helpful to structure a question that facilitated a focused search. This study used PICO framework. The PICO framework is commonly used in evidence-based clinical practice and considered a widely known strategy for framing a foreground research question (Cyrus, n.d.). This format identifies four concepts: Patient problem or Population, Intervention, the Comparison (if there is one), and Outcome(s)**.** PICO framework is provided in Table 1.

Table 1. PICO Framework

Patient problem or Population	Intervention	Comparison	Outcomes
- Gestational diabetes mellitus - Gestational diabetes - Diabetes in pregnancy - Maternal obesity - Hyperglycemia - Postpartum period	- Management - Intervention - Therapy - Self-management	No treatment	All study related to management of GDM during and after pregnancy

PICO framework is helpful to determine the research question

a. RQ 1: How is intervention of gestational diabetes mellitus?
   RQ 1 aims to identify forms of GDM intervention during pregnancy because women with GDM are identified having high blood sugar levels and gestational weight gain,
b. RQ 2: How is intervention of postpartum for women who have a history of gestational diabetes mellitus?
   RQ 2 focuses on management of postpartum women with a history of GDM. Women with a history GDM have higher risk of GDM in subsequent pregnancies and the development of type II diabetes up to 25 years after giving birth.

2.2 Search strategy design

In order for a comprehensive systematic literature review, it is essential that all terms relevant to the research objective are covered in the search. Moreover, we needed to include relevant synonyms and relevant terms, both GDM intervention during and after pregnancy. The search used three categories of keywords. The first category included the following terms as synonyms for gestational diabetes mellitus: "gestational diabetes, diabetes in pregnancy, and hyperglycemia". The second category focus on management and included the term "intervention, therapy, and self-management". For the third category, time content of GDM, the following search terms were used: "during pregnancy, after pregnancy, and post-partum. Keywords and synonyms were connected to logical connector OR and AND. We used the Boolean 'OR' to enter alternative spellings and synonyms and

used the Boolean 'AND' to link the major terms. The search process began with collecting articles from all database sources used, then selecting articles relevant to the research questions.

We used three electronic databases (PubMed, ScienceDirect and EBSco). Zotero software was used to collect and manage article search results. Study selection was performed by reading the titles, abstracts, or full text of the papers. Selected articles with following criteria: 1) Identification management of GDM during and after pregnancy; 2) Publication in the period 2009-2019 and presented in English; and 3) Original research articles. To systematize the process of inclusion of studies, we opted for Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The selection of articles is presented in a flow diagram in Figure 1

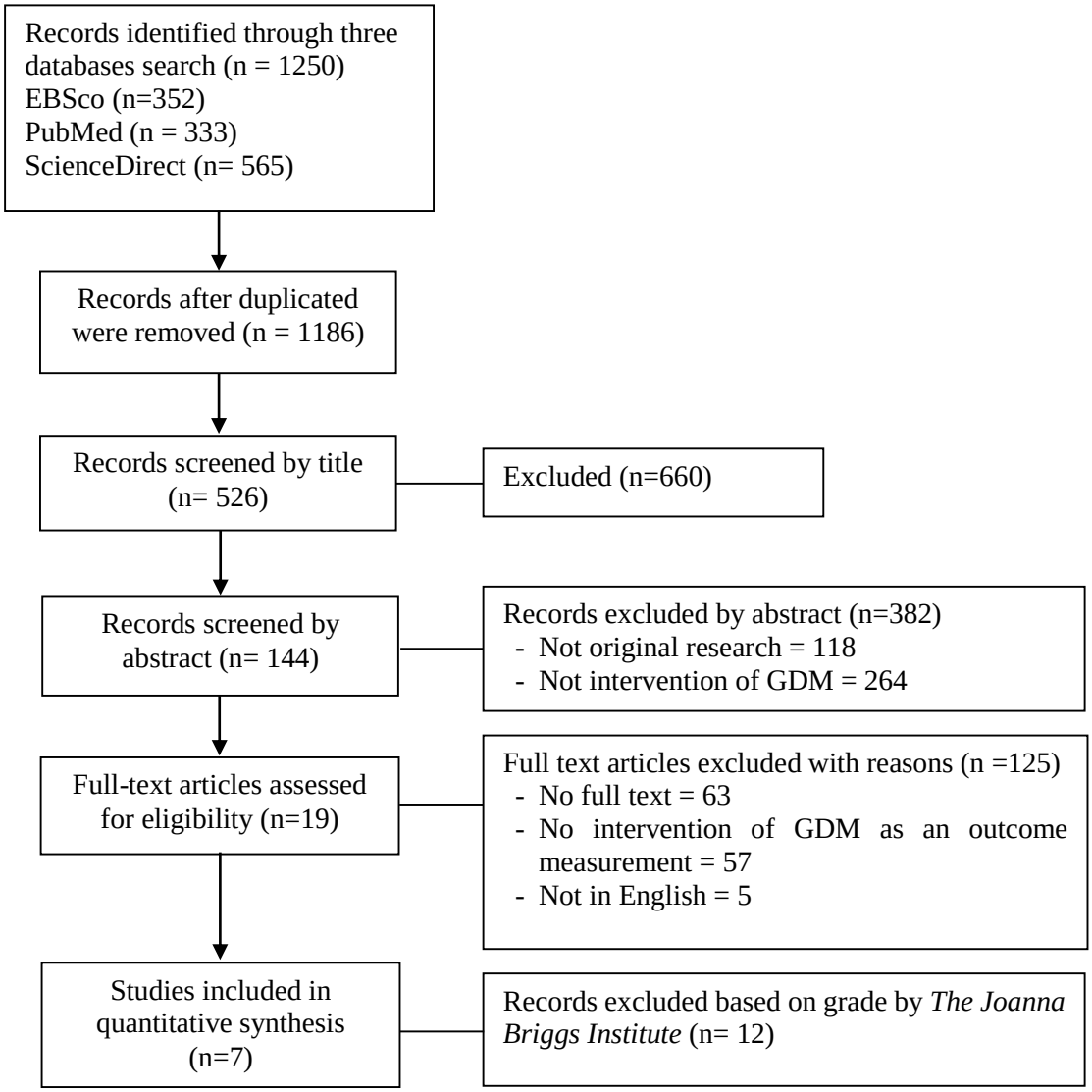

Figure 1. PRISMA-Flow diagram of screening, selection process and inclusion of studies.

To get articles that match the research question, excluded articles are needed. This study found 12 relevant articles, then it was critically assessed using critical appraisal tool from *The Joanna Briggs Institute*. JBI is evidence-based organizations formed to develop methodologies and guidelines on the process of conducting a systematic review (Munn et al., 2014). The final result of PRISMA flow diagram was seven articles. To provide greater insight into the context and nature of the seven articles, an overview was provided in Table 2.

Table 2. Overview of articles

Author	Country	Main objective of study	Study design	Data collection	Sample size	Result
Au et al. (Au et al., 2016)	Australia	To describe neonatal outcomes in full term infants from GDM mothers and hyperglycemic mothers	Cross-sectional study	Data on mothers and newborns are collected from hospital records	There are 609 respondents (mother and baby). Of these, there were 532 women who had normal glucose tolerance and 67 were identified as GDM	Glycemic control can be achieved in the majority of GDM mothers. GDM infants were more likely to be induced (p = 0.013) and born earlier than infants with non-GDM mothers (p <0.001)
Sklempe Kokic et al. (Sklempe Kokic et al., 2018)	Croatia	To investigate the impact of a structured exercise program consisting of aerobic exercise and resistance on glycemic control parameters	A randomized control trial	Participants were randomly assigned to a randomized block using a web-based computerized procedure into two groups: experimental and control	42 women diagnosed with GDM were enrolled in the trial and randomized into two groups: 20 for the experimental group and 22 for the control group	The experimental group had lower postprandial glucose levels at the end of pregnancy (P <0.001). So there is no significant difference between groups in fasting glucose levels at the end of pregnancy. Also, there were no significant differences in the rates of complications during pregnancy and birth
Elvebakk et al. (Elvebakk et al., 2018)	Norwegia	To assess whether women's food and beverage intake with GDM is different from non-GDMT	A longitudinal study	Trials and invitations to participate are sent by mail, together with invitations for ultrasound scanning at 17-19 week gestation	Respondents were participants in the Training in Pregnancy trial, a two-armed, two-centered randomized controlled trial. 855 women fulfill as inclusion criteria	There is a difference food intake in women with GDM and non-GDM. However no relationship was found between food variables and OGTT values. This study explains that there is no reason for differences in diet that can develop GDM
Utz et al. (Utz et al., 2018)	Morocco	To test the hypothesis that GDM screening and initial management at the primary service level will reduce the incidence of macrosomia	A cluster randomized controlled trial	Respondents were collected from pregnant women who attended antenatal services and who were offered offers for GDM screening. Women diagnosed with GDM are given education about nutrition, exercise and further monitoring	Statistical analysis was performed on 210 women who were selected regardless of gestational age at diagnosis and their adherence based on the intention-to-treat principle	GDM screening and care through antenatal services in primary health facilities can have a positive impact on the outcome of the baby, the birth weight of the baby

Rayanagoudar et al. (Rayanagoudar et al., 2015)	United Kingdom	To assess the knowledge and health professionals in postpartum care in women with a history of GDM	Questionnaire-based survey	The questionnaire used aims to assess postpartum screening practices, service provision, future risks, and strategies to prevent diabetes in women with a history of GDM.	The study surveyed 106 health professionals including fields, general practitioners, obstetricians and diabetes experts	Most midwives (81%) and obstetricians (52%) underestimate the responsibility of screening immediately after giving birth to mothers with a history of GDM. they are referred to as elements of diabetes risk in the future.
Wang et al. 2015 (Wang et al., 2015a)	China	To evaluate whether exercise interventions can be applied to pregnant women with GDM to control excess weight gain during pregnancy and to handle GDM-related outcomes .	A large retrospective study	The questionnaire was designed to obtain information on all pregnant women and collect their medical records after giving birth.	14,168 single pregnant women without diabetes from 15 hospitals	19.4% of pregnant women were diagnosed with GDM, 74.9% of them received sports intervention during pregnancy with a starting time of 25 week of pregnancy. They had the lowest increase in BMI during late and mid-pregnancy compared to women with GDM without sports intervention. However, women with GDM with exercise interventions with diet have the lowest macrosomia rates.
Persson Winkvist & Mogren (Persson et al., 2015)	Sweden	To investigate the associations between lifestyle and health outcomes.	Retrospective study	Random samples were identified from the Medical Birth Register and questionnaires sent by post to eligible women about four years after pregnancy	882 were identified from the Medical Birth Register and 444 women (50.8%) agreed to participate,	Counseling is needed by postpartum women with a history of GDM to educate about dietary interventions and physical activity in order to continue to improve health in the future. Counseling should be carried out by registered nutritionists and experienced nutritionists in GDM management

3. Results and Discussion

The seven articles were originated from developed and developing countries. Four articles from Europe and one article each from Asia, Africa and Australia, perhaps reflected a greater governmental and researcher attention to deal with GDM issues. Among the seven studies investigated in this systematic review, five studies focused on GDM management for pregnant women (Sklempe Kokic et al., 2018); (Elvebakk et al., 2018); (Utz et al., 2018); (Wang et al., 2015a); (Persson et al., 2015), one showed neonatal outcome of GDM (Au et al., 2016), and another one showed postpartum care of women with GDM (Rayanagoudar et al., 2015).

3.1 Management of GDM

The initial treatment of GDM involves diet modification, glucose monitoring, and moderate exercise. These findings highlight that medical nutritional therapy is the basis of GDM treatment (Persson et al., 2015) and is defined as the process of planning eating patterns, adapting the eating patterns and assessing the success of dietary interventions (Schübert et al., 2019). Persson Winkvist and Mogren (Persson et al., 2015) found that food plans should provide adequate calorie intake to improve fetal and maternal health, to acquire glycemic goals, and to increase weight according to gestational age. American Diabetes Association (ADA) recommended that the daily meal plan for GDM includes three small to moderate-sized meals and two-four snacks (Association, 2018). One of which should be at bedtime to prevent the development of ketosis overnight. Meals is defined as three main eating occasions "breakfast, lunch and dinner". Some women consume snacks as recommendations from healthcare professionals, their own preferences due to hunger/appetite or out of habit (Schübert et al., 2019).

Moreover, The American College of Obstetricians and Gynecologists (ACOG) (Committee on Practice Bulletins—Obstetrics, 2018) has identified that medical nutrition therapy for women with GDM must pay attention to calorie distribution of carbohydrate restriction. The ACOG guidelines recommend a calorie distribution of 33-40% carbohydrates, 20% protein, and 40% fat. Complex carbohydrate intake is better than simple carbohydrate intake because complex carbohydrates are less likely to cause postprandial hyperglycemia (Committee on Practice Bulletins—Obstetrics, 2018). Previous study (Esposito et al., 2010) has shown that consuming fruits and vegetables in large quantities and reducing starchy foods, red meat, and sugary drinks may delay or prevent the development of type 2 diabetes. All women with GDM must receive food counseling at the time of diagnosis, which is provided by a registered or experienced nutritionist in GDM management (Tong et al., 2018).

Similar to medical nutrition therapy, Sklempe Kokic et al (Sklempe Kokic et al., 2018) reported that physical activity is a key component in initial GDM management. Physical activity improves insulin sensitivity and reduces fasting and postprandial glucose concentrations in patients with GDM (Hayashi et al., 2018). This study underlines that exercise interventions performed early in pregnancy can reduce the risk of excessive Gestational Weight Gain (GWG) in the first and early second trimester and can possibly reduce the incidence of GDM (Elvebakk et al., 2018); (Wang et al., 2015b). ADA and ACOG recommends a moderate exercise program consisting of 30 minutes almost every day of the week for women with GDM who do not have medical contraindications for physical activity ("ACOG Committee Opinion No. 650," 2015). Blumer *et al* found that moderate exercise include brisk walking, recumbent bicycling, or 10 minutes of seated arm exercises after each meal (Blumer et al., 2013). Furthermore, the result of this study also found that combining aerobic and resistance exercises has beneficial effects on glycemic control. Moreover, it is a safe therapeutic strategy for pregnant women with gestational diabetes mellitus (Sklempe Kokic et al., 2018). Shepherd et. al explained that each of the dietary and exercise interventions aimed for prevention of type 2 diabetes. But recently there has been a shift that combines the two interventions to get an effective lifestyle intervention (Shepherd et al., 2017).

Women with GDM are advised to control their blood glucose immediately after the diagnosis of GDM in order to minimize adverse pregnancy outcomes. Women are instructed to monitor blood glucose 4 times a day, fasting glucose (upon awakening), and one or 2 hour post-meals (after the first bite of a meal) (Alfadhli, 2015). Other study has suggested that blood glucose monitoring between four and seven times per day (including fasting and post-prandial measurements) can contribute to improving maternal and perinatal outcomes (Brown et al., 2017). ADA recommended the target glycemic goal for women with GDM is to keep the fasting glucose <95 mg/dL (5.3 mmol/L), and either one-hour post-meal <140 mg/dL (7.8 mmol/L) or two-hour postprandial <120 mg/dL (6.7

mmol/L) (Association, 2019b). Pharmacological intervention is recommended when the target glucose level cannot be consistently achieved through nutrition and exercise therapy. In Europe and South Africa, glyburide and metformin have been used in pregnancy for years without reporting side effects on the fetus (Alfadhli, 2015). In contrast with ADA, ADA states that insulin is the first intervention for GDM, whereas metformin and glyburide should not be used as the first intervention in women with GDM because they both cross the placenta into the fetus. Type of insulin, time of insulin injection, and frequency need to be adjusted to the needs of patients based on blood sugar levels. Insulin therapy is considered safe and effective in maintaining glycemic control and is still considered the first pharmacotherapy therapy used by healthcare professionals to intervene in GDM mothers (Committee on Obstetric Practice, 2015).

3.2 Neonatal outcome

The relation between a woman with GDM and negative outcomes has been widely discussed in several studies. Neonates born to women with GDM were much heavier, were more often born prematurely and were more often delivered by cesarean section than children of woman without diabetes (Domanski et al., 2018). It includes fetal distress, cesarean section and poor Apgar score, large gestational age, neonatal hypoglycemia, and intensive care at the NICU. Other study conducted by Domanski et al. (Domanski et al., 2018) showed that neonatal hypoglycemia is a complication often found in GDM. Research from Kamana (Kc et al., 2015b) explained that hypoglycemia causes more serious complications such as central nervous system and cardiopulmonary disorders disruption. Long-term complications can cause mental retardation, recurrent seizures and developmental delays. In addition, Kamana's research explained that neonates with macrosomia requires high oxygen demand. This can lead to an increase in bilirubin, resulting in neonatal jaundice The results published by Junior et. al (Araujo Júnior et al., 2017) showed that fetal macrosomia is a clinical risk factor for shoulder dystocia and associated with increased risk of cesarean section or trauma in normal births. Children suffering from neonatal hypoglycaemia may develop motor and learning impairments and behavioral difficulties. Au et al. (Au et al., 2016) confirmed that women with GDM who had proper management, neonatal complication were not significantly increased significantly.

3.3 Postpartum care of women with GDM

The postpartum period is the right time to start and improve a healthy lifestyle (Persson et al., 2015). ADA, ACOG, and the World Health Organization (WHO) recommended that women with GDM have to be tested for abnormal glucose tolerance from 6 to 12 weeks postpartum. Also in women with a history of GDM must undergo lifetime screening for the development of glucose intolerance, at least every 3 years. Furthermore, ADA recommends that all women with a history of GDM should be educated about lifestyle modification, while ACOG recommended women with additional risk factors such as obesity to receive diet, exercise, and weight management counseling (Committee on Practice Bulletins—Obstetrics, 2018). In postpartum, exclusive breast feeding for at least three months has been evidenced in reducing the risk of childhood obesity in children, particularly in those born to obese and mothers with GDM (Au et al., 2016) (George et al., 2019),

Persson Winkvist & Mogren (Persson et al., 2015) reported that counseling is needed for dietary intervention and physical activity for all postpartum women with a history of GDM in order to stay healthy or to improve future health. Mutual education about management of GDM provided to all healthcare professionals involved midwives, obstetricians, internists and nutritionist (Persson et al., 2012). Midwives are considered as effective providers of information because midwives have the most frequent contact with women from other health workers, but midwives must collaborative with other healthcare professional. Midwives must consistently screen postpartum women with a history of GDM for using a glucose tolerance either fasting blood sugar or a 2-hour oral glucose test, and motivate this woman to exercise regularly and lose weight if they are overweight or obese (Ko et al., 2013). On the other hand, this review showed that care provider do not continue to follow up early post-partum screening test, some reasons are many obstetricians and general practitioners underestimated, or are uncertain about the increased risk type 2 diabetes for mothers with a history of GDM (Rayanagoudar et al., 2015).

4. Conclusion

GDM management involves diet modification, exercise and glucose monitoring. Pharmacological intervention is recommended when the target glucose level cannot be consistently achieved through nutrition and exercise therapy. ADA states that insulin is the first intervention for GDM, whereas metformin and glyburide should not be used as the first intervention in women with GDM because they both cross the placenta into the fetus. Women with a history of GDM must undergo life-long screening for the development of glucose intolerance, at least every 3 years. Exclusive breastfeeding with a minimum of three months has been shown to reduce the risk of obesity in children, especially those born to GDM, also women with GDM related to a reduced risk of type 2 diabetes and weight gain in the postpartum period. Therefore, increased awareness of the long-term consequences of GDM is needed for both patients and healthcare professionals.

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