



# Pharmaceutical Advancement in Treating Gestational Diabetes Mellitus: A Review

**Aman Kumar Singh and Amarish Kumar Sharma**

**Department of Bioscience and Bioengineering, Lovely Professional University, Jalandhar, India-144001.**

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\*Corresponding Author Email: [amugoldy12@gmail.com](mailto:amugoldy12@gmail.com)

## Abstract

Gestational diabetes mellitus (GDM) is a serious health issue that has become a worldwide concern. GDM and its prevalence that to a great extent affects the mother and the offspring to be born. Various researches are conducted to control or cure GDM by various researchers from last decades, but still is lagging behind in terms of curability indicating the need of advanced treatment therapy. Hence, the present review represents the pharmaceutical advancement in treating gestational diabetes mellitus (GDM). The review focuses on the various aspects including the symptom and risk factor associated with GDM. The medication and treatment therapy are discussed indicating the importance of research and requirement of newer medication technology.

## Keywords

Gestational diabetes mellitus, Medication, Insulin, Treatment.

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## 1. INTRODUCTION:

Diabetes mellitus is an illness that needs medical care for the long run and self-education of patients to ensure that it does not lead to acute complications which can include diabetic ketoacidosis and long-term complications like cardiovascular disease, chronic kidney disease, and cognitive impairment. The care which is needed to control diabetes requires awareness as it is a complex process and needs multifactorial risk reduction strategies [1].

Gestational diabetes mellitus (GDM) is a widespread medical complication of pregnancy that has serious health implications for both mother and child. [1,2]. The consequence of pregnancy, in terms of the mother as well as baby, worse with GDM.[3] It has also been seen from many studies[4,5], in the literature that Suboptimal glycemic control in women with GDM is associated with adverse maternal & neonatal outcomes. Therefore Blood sugar levels can be an indicator of maternal and

perinatal morbidity and mortality in GDM cases[6]. It is apparent from the literature that women with a history of GDM are prone to both adverse maternal, perinatal, and neonatal outcomes, and there is a high risk of future diabetes predominantly Type II in mothers as well as their children, and hence there are two generations at risk. Record says that 7% of pregnancies are affected by GDM and this percentage can be much higher among the outnumbered population who are prone to diabetes. Patients with GDM are susceptible to excessive weight gain, preeclampsia, and cesarean sections. Infants with GDM are receptive to macrosomia, birth trauma, and shoulder dystocia. Post-delivery infants have a higher risk of developing hypoglycemia, hypocalcemia, hyperbilirubinemia, respiratory distress syndrome, polycythemia, and subsequent obesity and type 2 diabetes [5,6].

The root cause of type 2 diabetes which is prevailing globally, has genetic factors and acquired factors

such as obesity caused by a high-fat diet, stress, and aging impairing insulin action which leads to the start of diabetes. In Japan, there is a shift in records indicating delayed marriage and childbirth. It has been expected that the number of women with decreased carbohydrate tolerance who develop gestational diabetes mellitus during pregnancy will increase with a high number. It is a comprehended fact that the incidence of GDM rises by approximately 8 times for pregnant women aged 35 y and over compared to women aged 25 y or under. Initially, GDM was interpreted as decreased carbohydrate tolerance that cultivates or is first observed during pregnancy, but in 2010 the definition was changed as follows. GDM is a carbohydrate intolerance that is not diabetes that has developed or been discovered for the first time during pregnancy. The GDM definition hence does not include overt diabetes in pregnancy. Accordingly, hyperglycaemic disorders that are eliminated from the thought to have been disregarded until the pregnancy are eliminated from the definition of GDM and are instead diagnosed as “overt diabetes in pregnancy” [7,8]

Hence, the present review focuses on the various aspects including the symptom and risk factor associated with GDM. The medication and treatment therapy are discussed indicating the importance of research and requirement of newer medication technology.

## 2. SYMPTOMS OF GESTATIONAL DIABETES MELLITUS:

There are no definite symptoms regarding gestational diabetes mellitus, but the first report about GDM was demonstrated by O'Sullivan et al [9,10]. O'Sullivan and his research group in 1964 executed their study on 752 pregnant women. In their study they screened the women for GDM employing 3-h 100 g OGTT. Then, whole venous

blood glucose was analysed through using Somogyi Nelson measurements. Through process they developed a criterion to predict the emergence of GDM in 29% women in due course of 7-8 years based on their whole blood glucose values [10].

## 3. RISK OF GESTATIONAL DIABETES MELLITUS:

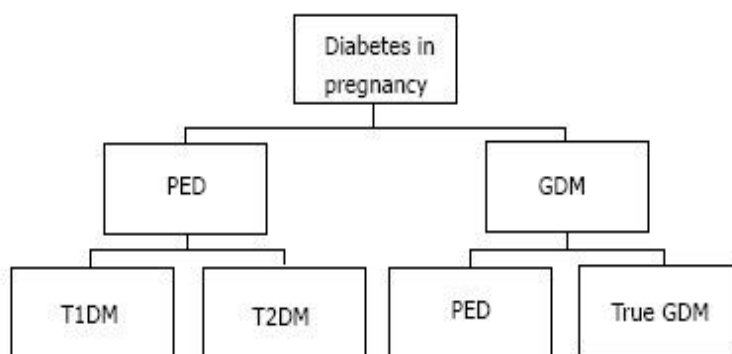
GDM is associated with various risk factors. Various risk factors are discussed below:

### 3.1 Nutritional risk factors

Overwhelming studies suggest that nutritional factor widely affects GDM. Researchers have conducted studies and suggested that “prudent dietary pattern” that includes an increase consumption of leafy vegetables, fruit, fish and poultry whereas, “Western pattern” includes an increase consumption of processed meat, refined grain, French fries, sweets, red meat and pizza. Analysing food consumption and dietary patterns and their associated risk of GDM development, suggest significant relative risk of GDM development increasing the intake of Western diet and decreasing intake of prudent diet [11]. Apart from that various diet that enhance the risk of GDM involves low cereal fiber diet and high content of glycaemic load [12,13]. Micronutrients also to great extent affects GDM.

### 3.2 Typical risk factors

Various risk factors have been considered which may induce development of GDM. The risk factors that increase the risk of GDM are often like diabetes in pregnancy such as T1DM: Type 1 diabetes mellitus; PED: Pre-existing diabetes; T2DM: Type 2 diabetes mellitus [14, 15, 16]. Mirghani Dirar A et al. 2017 mentioned that the risk factors associated with diabetes involves increased of maternal age, family history with diabetes and obesity. Other risk factors that were reported regarding GDM includes essential gestational hypertension and multiple time pregnancies [17].



**Figure 1: Various diabetes reported in pregnancy. GDM: Gestational diabetes mellitus; PED: Pre-existing diabetes; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus (Source: Mirghani Dirar and Doupis, 2017)**

#### **4. PHARMACEUTICAL ADVANCEMENT IN TREATING GESTATIONAL DIABETES MELLITUS:**

##### **4.1 Treatment**

The treatment of GDM in terms of pregnancy complications was conducted in 2005 by the Australian group of researchers regarding carbohydrate Intolerance study in Pregnant Women. That study involves randomized selection of 1000 women of various age group with GDM in gestation period to going through dietary advice, monitoring of blood glucose and insulin therapy. The study demonstrates that treatment of GDM reduced the perinatal complications frequency.”[18]

##### **4.2 Insulin treatment**

Those women fail to maintain glycemic control during period of 1–2 weeks goes through insulin therapy. Insulin therapy includes medication of GDM according to all international guidelines. Often insulin is regarded as safe in pregnancy as it virtually do not cross the placental barrier and does not show any teratogenic effects. Generally, use of insulin are insulin and neutral protamine Hagedorn insulin, that are homogeneous with human insulin and regarded as safe in pregnancy. The major demerits of regular insulin (RI) is that its activity profile do not match of physiological insulin. The onset action of RI starts within 30 and 60 min after injection, with maximum action after 2–3 h with an effective working period up to 8–10 h. A main demerits of NPH insulin is that both its peak effect and duration of action are intermediate. The onset of NPH starts 2–4 h after injection, and shows maximum action between 4 and 10 h, with effective working duration within 12–18 h. Insulin usages has been approved by various agencies such as US Food and Drug Administration (FDA) for implication during pregnancy as its use has shown no adverse effects [19,20]

##### **4.3 Other oral and injectable treatments**

In management of type 2 diabetes other oral and injectable (non-insulin) agents utilized which have limited or no specific data available when it comes to the safety to the fetus if utilized in pregnancy. Due to its various risk factors this process is not applicable for treating GDM (20,21).

The only two with clinical evidence to support their use in GDM management as either a first-line agent or an alternative to insulin therapy which are glyburide and metformin. The other agents have no human data available. The principles for dosing glyburide and metformin in GDM are quite similar to the management of type 2 diabetes [21]

##### **4.4 Recommendations for the use of oral medications**

Patient-specificity and choice must be considered during selection of patients may be better candidates

for taking insulin, glyburide and metformin. Based on the potentiality and safety evidence with metformin and glyburide, seems applicable to utilize either agent on a case-by-case based on patient-specific factors(22). Both metformin and glyburide are:

(1) Easily available at low cost as generic products to the patient as compare to insulin therapy.

(2) Dosed once to two times a day twice a day based on the dose and formulated concentration selected. During that times, patient-specificity may can to switch from one oral agent to other agent, based on side effects which are intolerable, at the time of switching to insulin. [22,23]

##### **4.5 Proper Diet**

Diet is considered is one of the essential factor for treating any disease, GDM, the first approach for GDM is dietary advice in combination with SMBG. It is observed that dietary advice helps 70%–85% of women with GDM to get optimal glycemic control. There are no particular guidelines for diet or exercise in GDM. There is consensus which is the goal of dietary advice should be to fulfil nutrient intake for neonatal growth and to achieve optimum glycemic control, without inducing weight loss or excessive weight gain. Optimal glycemic control can be easily achieved by following a diet which includes carbohydrate distribution and reduction in rapidly digested sugars, there is a general agreement on limiting excessive carbohydrate intake which states that carbohydrates should be distributed equally throughout the day. It is unknown whether carbohydrate restriction is beneficial in GDM.[23]

#### **5. FUTURE PROSPECTS:**

Recently, there is no proper guidelines that can accurately define the exact treatment to be given to a GDM patient in terms of severity, neither specific guideline regarding diet exist. The only specific factor associated with diet is that it's necessary to limit the carbohydrate intake and lower the glycemic excursions, but still knowledge regarding carbohydrate restriction and its beneficial effects in GDM is lacking behind. Hence, in future development of proper guidelines regarding the diet is necessary (24).

Medication is one the important aspects to treat GDM. Various research studies shows implication of different medicine in treating or controlling GDM. Report suggests that use of insulin in GDM always varies from patient to patient based on different specific issues. In terms of employing oral blood glucose lowering medication, the neonatal hypoglycaemia risk increases indicating deleterious effect of glyburide in GDM. There are reports that suggest the positive results regarding the use

metformin in GDM. But, metformin is also relate to some risk factors that are premature delivery and development of male fertility in long term use of the drugs. Hence, in future apart from nutritional guidelines proper guidelines of medication is needed based on severity of GDM from patient to patient. Moreover, proper analysis of various side-effects and demrits regarding the use of particular medicine or drug is required in future (21-25).

## 6. CONCLUSION:

Various research report and survey suggest that Gestational diabetes mellitus (GDM) is a serious problem which not to eradicate in future. The proper diet and treatments guidelines for controlling of curing GDM are still lacking behind. Although, the researches has been conducted from last few decades, but still there is a scarce of proper information regarding GDM its treatment. Hence, further research needs to carry out to open a new way in medical field regarding the treatment of GDM.

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