



Review Article

Gestational Diabetes Mellitus: Current Insights and Advances in Diagnosis, Management, and Maternal-Foetal Health

A. R. Shabaraya, Sarah Rafiq*

Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore-574143.

ARTICLE INFO

Received: 25 Nov 2023

Accepted: 30 Nov 2023

Published: 04 Nov 2023

Keywords:

Gestational Diabetes, diagnosis, management, maternal complications, foetal complications, postpartum implications

DOI:

10.5281/zenodo.10254087

ABSTRACT

Gestational Diabetes Mellitus (GDM) is a metabolic disorder that develops during pregnancy and poses risks to both maternal and foetal health. GDM requires a multidisciplinary approach involving healthcare providers, dieticians, and educators to ensure optimal outcomes. Understanding the complexities of GDM is essential for providing effective care and improving the health of pregnant individuals and their offspring. This condition underscores the importance of early diagnosis, appropriate management, and vigilant postpartum care. Regular monitoring and close collaboration between the pregnant individual and their healthcare provider are critical for achieving optimal outcomes. This review provides an overview of GDM, including its definition, prevalence, risk factors, and potential complications. It also discusses the importance of screening and diagnosis, the management of GDM, and the long-term implications for both maternal and foetal health. With proper control and care, many women with gestational diabetes go on to have healthful pregnancies and infants. Controlling blood sugar levels thru lifestyle modifications and scientific guide is prime to decreasing associated risks.


INTRODUCTION

Diabetes that develops during pregnancy and typically disappears after giving birth is known as gestational diabetes mellitus, or GDM. High blood sugar levels are one of its hallmarks, which can be harmful to the developing baby as well as the mother. GDM is diagnosed by looking for blood glucose levels that are higher than usual, but not to the same extent as in pre-existing diabetes. Regional differences in the prevalence of GDM

exist around the world and are influenced by factors including as obesity rates, ethnicity, and maternal age. Since GDM is estimated to affect 7% to 14% of pregnancies, it is a significant problem for maternal healthcare. It can have a significant effect on both the mother and the child and affects roughly 7% of expecting moms.¹ Controlling hyperglycaemia throughout pregnancy is essential for the developing foetus as well as the health of the expectant mother.

*Corresponding Author: Sarah Rafiq.

Address: Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore-574143.

Email  : sarahrafiq8@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



Uncontrolled hyperglycaemia during pregnancy is associated with a higher risk of adverse outcomes, including macrosomia (larger birth weight), delivery trauma, preterm birth, and neonatal hypoglycaemia. Inadequate management of gestational diabetes mellitus might increase the mother's risk of developing hypertension, type 2 diabetes, and caesarean delivery.²

Causes of Gestational Diabetes:

GDM occurs when hormonal changes during pregnancy disrupt insulin production and utilization, resulting in elevated blood sugar levels. Several risk factors contribute to the development of GDM, including maternal age, family history of diabetes, obesity, and certain ethnic backgrounds. Understanding these causes is crucial for early detection and effective management.³

The pathogenesis of gestational diabetes appears to be associated with two factors: i) a delayed response of beta cells to glucose levels, or malfunction of the pancreas; and ii) a notable increase in insulin resistance as a result of placental hormone release. Prolactin, corticotropin-releasing hormone, progesterone, growth hormone, and other hormones are also linked to the development of this condition. These hormones also stimulate insulin resistance and hyperglycaemia during pregnancy.⁴

Several factors contribute to the development of gestational diabetes:

a. **Hormonal Changes:** During pregnancy, the placenta produces hormones that help the baby grow and develop. Some of these hormones can interfere with the action of insulin in your body, making it harder for your cells to use glucose for energy. Foetal hormones have a profound effect throughout pregnancy, orchestrating the delicate rhythm of mother and growing foetus. These hormones mainly human chorionic gonadotropin (hCG), human placental lactogen (hPL), oestrogen and progesterone

plays a role in many aspects in the maintenance of pregnancy in the corpus-luteum in order to maintain the supports, which are essential for the nutritional content of the placenta. As pregnancy progresses, placental production of hPL regulates maternal metabolism, providing a continuous supply of nutrients for foetal growth. A powerful stimulator of many physiological changes, oestrogen facilitates the development of the uterus and prepares the mother's body for childbirth. Progesterone maintains the contents of the uterus, prevents premature miscarriage, and creates the right environment for pregnancy. Together, these foetal hormones dance an incredible rhythm, navigating the complex journey of pregnancy, promoting the well-being of both mother and child.

b. **Insulin Resistance:** As pregnancy progresses, your body becomes more resistant to insulin. This means that even though your pancreas is producing insulin, your cells may not respond to it effectively, leading to elevated blood sugar levels. It causes an imbalance in the delicate balance of blood glucose regulating resulting in high blood glucose level. Insulin resistance has its basic causes in genetic predisposition, obesity, sedentary lifestyle, and the hormonal cycle. In response to these stimuli, the pancreas usually increases insulin release to counteract reduced cellular sensitivity. Nevertheless, these compensatory mechanisms may not be sufficient enough to achieve normalization of the elevated blood glucose levels. Insulin resistance can cause type 2 diabetes as well as other metabolic complications, including heart disease. Insulin resistance can be alleviated by having a balanced diet and engaging in physical workouts or even medicine in some

cases to regain the insulin sensitivity before the problem escalates into full-grown metabolic disorders. Insulin resistance is a vital point that should be understood and addressed if the metabolic health of an individual is to be maintained and the development of diabetes-related complications prevented.

- c. **Genetics:** A family history of diabetes can increase your risk of developing gestational diabetes. If you have a parent or sibling with diabetes, you may be more susceptible to it. Although GDM mainly arises from insulin resistance during pregnancy, a person can also inherit some genes that make him or her prone to the condition. Apparently, research has shown that such women have an inherited tendency to develop insulin resistance during pregnancy. As a result, they are likely to experience diabetes in pregnancy (GDM). It has been observed that some genetic variants that are related to insulin sensitivity, glucose metabolism, and pancreatic function are associated with increased risk of GDM. Notwithstanding, genetics do not alone explain why GDM happens. There are other essential elements in the environment such as diet and lifestyle that contribute significantly to explaining the condition. High-risk individuals are determined by the interaction between genetic susceptibility and external circumstances. Prevention and treatment of gestational diabetes mellitus is achieved by individualized approach. Finally, although genetics predispose a woman to GDM, effective care and management approaches incorporating both genetic and environment aspects are critical in managing the disease.
- d. **Previous Gestational Diabetes:** If you had gestational diabetes during a previous pregnancy, you are more likely to develop it again in subsequent pregnancies. Gestational

diabetes mellitus is one condition that may be linked to previous GDM and which has the potential to recur in subsequent pregnancies. There is an increased risk of recurrence of GDM among women who have had it during a prior gestation. These women are vulnerable to recurrent challenges in glucose metabolism during subsequent pregnancies because the body's response to the pregnancy-related hormonal changes and insulin resistance can be altered by this process. However, not only is the risk limited to genetics, but also includes some lifestyle changes, such as obesity between the two pregnancies and persistent hyperinsulinemia postpartum. Women who had GDM in previous pregnancies are closely monitored by healthcare providers who initiate early interventions with screening and management strategies aimed at preventing complications. This is a proactive approach to controlling blood sugar levels by modifying lifestyles, conducting routine checks, and providing required medical therapy. Health care providers should recognize the consequences of GDM on previous pregnancies and strive towards better maternal and neonatal outcomes during the new GDM pregnancy.

- e. **Polycystic Ovary Syndrome (PCOS):** Women with PCOS are at an increased risk of developing gestational diabetes. PCOS is a condition characterized by hormonal imbalances and insulin resistance. Women with polycystic ovary syndrome (PCOS) have about twice the risk of having GDM than the general population, suggesting that PCOS may serve as a significant risk factor for the development of GDM during pregnancy. Insulin resistance is one of the hallmarks of PCOS and it increases women's susceptibility to high glucose levels. Glucose



intolerance that may be associated with pre-existing insulin resistance in this condition can be exacerbated further because of the hormonal changes associated with PCOS during pregnancy. These hormonal disturbances, mainly hyperandrogenaemia and hyperinsulinemia, cause glucose intolerance in women with PCOS thus putting them at risk for GDM. Moreover, PCOS is also associated with obesity and high BMI, making the risk of GDM even higher. Pregnant women with PCOS are closely monitored with early screening for GDM and subsequent intervention measures such as dietary modifications, exercise programs, and if necessary, medications to manage blood glucose levels and prevent complications of GDM. The relationship between PCOS and GDM and how it helps in taking appropriate actions for optimum maternal and foetal health during pregnancy in case women have PCOS.

Not only is the precise cause of gestational diabetes not always known, but many women who develop the condition do not have any of these risk factors. To maintain the health of the unborn child and the expectant mother, routine prenatal exams, which include glucose testing, can aid in the diagnosis and treatment of gestational diabetes. Adhering to a healthcare provider's recommendations for proper treatment usually entails dietary modifications, exercise, and occasionally medication (such as insulin or oral medicines).²

Risks Associated with Gestational Diabetes:

Gestational diabetes poses risks to both the mother and the baby. For the mother, it increases the likelihood of developing type 2 diabetes later in life and raises the risk of preeclampsia, caesarean delivery, and postpartum depression. The baby is also at risk of macrosomia (large birth weight), birth injuries, hypoglycaemia, and a higher

likelihood of developing obesity and type 2 diabetes in the future.⁵

For the mother, gestational diabetes increases the risk of developing high blood pressure (preeclampsia) and caesarean delivery. It also raises the chances of developing type 2 diabetes later in life. Additionally, women with gestational diabetes are at a higher risk of developing gestational hypertension, which can lead to complications during pregnancy.⁶

For the baby, gestational diabetes increases the risk of excessive birth weight (macrosomia), which can lead to difficulties during delivery and an increased likelihood of caesarean section. Babies born to mothers with gestational diabetes are also at a higher risk of low blood sugar levels (hypoglycaemia) immediately after birth. They may also develop breathing problems and have a higher risk of developing type 2 diabetes later in life.⁷

Proper management of gestational diabetes, including regular monitoring of blood glucose levels and prenatal check-ups, is crucial for tracking progress and adjusting treatment plans. Lifestyle modifications such as healthy eating, regular physical activity, and weight management can also help reduce the risks associated with gestational diabetes.

Screening and Diagnosis:

Screening for gestational diabetes is typically performed between weeks 24 and 28 of pregnancy. The most common diagnostic method is the oral glucose tolerance test (OGTT), where blood glucose levels are measured before and after consuming a glucose solution. Early detection through proper screening is essential for timely intervention and management.⁸

- a. **One-Step vs. Two-Step Screening:** Explore the differences between the one-step and two-step approaches in GDM screening, discussing the diagnostic tests involved (e.g., glucose challenge test, oral glucose tolerance

test) and their timing during pregnancy. The one-step approach offers immediate diagnosis, reducing the need for a subsequent visit or additional testing for confirmation. However, it can lead to slightly higher rates of GDM diagnosis compared to the two-step method. On the other hand, the two-step approach offers a preliminary screening to identify those who may need further testing, potentially reducing unnecessary diagnostic procedures. It has historically been associated with lower rates of GDM diagnosis but can also miss cases that would be detected by the one-step method.

b. Universal vs. Risk-Based Screening:

Analyse the pros and cons of universal screening for all pregnant women versus risk-based screening based on maternal characteristics, family history, or previous pregnancy history. The two methods of identifying GDM include universal and risk-based screening. Universal screening tests all pregnant women with or without some risk factors during their 24-to-28-week period. This approach helps identify undiagnosed cases of GDM with the objective of early intervention. Such an intervention leads to improved maternal and foetal health outcomes. Such is a proactive approach that does not depend on certain risk factors, and has a wider net in searching for such potential cases. In contrast, risk-based screening targets only those women deemed at higher risk for GDM due to factors such as obesity, a family history of diabetes, advanced maternal age, or previous history of GDM. This approach involves selectively screening individuals based on identified risk factors, potentially missing cases in women without apparent risk factors.

c. Oral Glucose Tolerance Test (OGTT):

Discuss the OGTT as the gold standard for

GDM diagnosis, comparing various diagnostic thresholds and protocols recommended by different guidelines. The Oral Glucose Tolerance Test (OGTT) is a crucial diagnostic tool used to detect gestational diabetes mellitus (GDM) in pregnant individuals. Typically performed between 24 to 28 weeks of gestation, the test evaluates the body's ability to process sugar. It begins by fasting for several hours, followed by consuming a concentrated glucose solution. Blood samples are taken before consuming the solution and at regular intervals afterward to measure blood sugar levels. Elevated glucose levels during this test may indicate a difficulty in regulating blood sugar, pointing towards gestational diabetes. While the test can be discomfoting due to fasting and the sweet glucose drink, it plays a vital role in identifying GDM, enabling healthcare providers to initiate timely interventions and support to manage blood sugar levels during pregnancy, ensuring the well-being of both the mother and the baby.

d. Continuous Glucose Monitoring (CGM):

Investigate the use of CGM in GDM screening, its accuracy, and the feasibility of its integration into routine prenatal care. Continuous Glucose Monitoring (CGM) has emerged as a useful era in managing Gestational Diabetes Mellitus (GDM) in the course of being pregnant. This modern device involves sporting a small sensor at the skin that continuously measures glucose stages inside the interstitial fluid. It offers actual-time information on blood sugar trends, providing a more comprehensive expertise of the way different factors, like food consumption and physical interest, effect glucose stages during the day. For pregnant individuals with GDM, CGM no longer best aids in closely monitoring blood sugar

however additionally facilitates healthcare companies customise remedy plans, enabling well timed adjustments in weight loss plan, exercising, and medicine, if essential. This technology plays a pivotal position in empowering individuals with GDM to actively participate in managing their circumstance, selling better being pregnant results and lowering the risks associated with improved blood sugar stages for both the mother and the child.

- e. **Screening in Early Pregnancy:** Discuss the feasibility and benefits of screening for GDM in the first trimester and its potential impact on maternal and foetal outcomes. Screening for Gestational Diabetes Mellitus (GDM) in early being pregnant holds full-size significance in ensuring the properly-being of each the mother and the developing foetus. Typically carried out between 24 to twenty-eight weeks gestation, the screening involves assessing glucose tiers to hit upon any abnormality in sugar metabolism. However, in some instances, particularly if there are danger factors present together with weight problems, a records of GDM, or a circle of relatives records of diabetes, screening might arise in advance inside the being pregnant. Early identification of GDM allows healthcare carriers to put in force interventions directly, which include dietary adjustments, workout workouts, or, if wished, medicine to manage blood sugar levels. By initiating timely measures, risks associated with uncontrolled glucose tiers can be mitigated, reducing the probability of complications at some point of pregnancy, inclusive of macrosomia (large birth weight), preeclampsia, and beginning-associated troubles. Early screening plays a critical position in proactively managing GDM,

making sure a more fit being pregnant journey for both the mom and the child.

Management of Gestational Diabetes:

The primary goal of managing GDM is to maintain normal blood sugar levels to minimize complications for both the mother and the baby. This is achieved through lifestyle modifications, including a healthy diet, regular physical activity, and blood sugar monitoring. In some cases, medication or insulin therapy may be required to control blood sugar levels effectively. The first steps in managing gestational diabetes are nonpharmacologic measures such as dietary changes, physical activity, and glucose monitoring. A licenced dietitian should provide nutritional counselling and create a customised plan based on the patient's BMI, according to the American Dietetic Association. The doctor can make suggestions based on the three main nutritional concepts—calorie allocation, calorie distribution, and carbohydrate intake—in situations where nutritionists are unable to help. 30 minutes of moderate-intensity aerobic activity at least five days a week, or a minimum of 150 minutes per week, is the recommended amount of exercise for those with GDM. Pharmacologic treatment should be started if the patient's glycaemic control is inadequate even with optimal adherence to diet and exercise. Insulin is the ADA's primary choice for treating GDM. When optimal glucose levels cannot be achieved with diet and exercise, insulin therapy has been regarded the standard treatment for gestational diabetes.⁹

Classification of Antihyperglycemic Agents for GDM:

Pharmaceutical therapies such as antihyperglycemic drugs are used to control increased blood glucose levels in gestational diabetes. These agents can be divided into various types, each of which has specific mechanisms of action and administration considerations.



2.1 Insulin Therapy

Insulin remains a cornerstone of gestational diabetes management due to its ability to effectively lower blood glucose levels. It is classified into several types based on its onset, peak, and duration of action¹⁰

- **Rapid-Acting Insulin:** Provides quick onset and short duration of action, often used to control postprandial glucose spikes.
- **Short-Acting Insulin (Regular Insulin):** Has a slightly slower onset but longer duration of action compared to rapid-acting insulin.
- **Intermediate-Acting Insulin:** Offers a more sustained effect, often used to control fasting blood glucose levels.
- **Long-Acting Insulin (Basal Insulin):** Provides a continuous release of insulin to maintain stable glucose levels between meals and overnight.

2.2 Oral Antidiabetic Agents

While insulin is a primary therapy, some oral antidiabetic agents are sometimes used in gestational diabetes management. These agents include:

- **Metformin:** An insulin sensitizer that reduces hepatic glucose production and improves peripheral insulin sensitivity.
- **Glyburide:** A sulfonylurea that stimulates insulin secretion from pancreatic beta cells.
- **Acarbose:** An alpha-glucosidase inhibitor that slows carbohydrate digestion and absorption, reducing postprandial glucose spikes.

2.3 Recent Therapies

Recent advances in pharmacology have introduced newer antihyperglycemic agents that are being explored for use in gestational diabetes:

- **GLP-1 Receptor Agonists:** Mimic the action of incretin hormones, enhancing insulin secretion, reducing glucagon release, and delaying gastric emptying.

- **DPP-4 Inhibitors:** Prevent the degradation of incretin hormones, resulting in improved insulin secretion and reduced glucagon levels.

In many cases, insulin is considered the first-line treatment for gestational diabetes because it can effectively control blood glucose levels and has a long-established safety record during pregnancy. Oral antidiabetic agents like glyburide and metformin may be considered in specific situations when insulin is not practical or when there are concerns about insulin use.¹¹

Ultimately, the management of gestational diabetes should be individualized, and treatment decisions should be made in collaboration with healthcare providers who can carefully evaluate the patient's medical history and specific needs to ensure the best possible outcomes for both the mother and the baby.

It's crucial to remember that the use of antihyperglycemic medications in gestational diabetes should be supported by thorough evaluation, individualised treatment strategies, and a thorough knowledge of the advantages and disadvantages of each class. The choice of therapy frequently depends on variables such patient preferences, maternal glucose management, and potential effects on foetal outcomes.

3. Efficacy of Antihyperglycemic Agents

3.1 Insulin Therapy

Clinical Research: Several clinical research studies have repeatedly shown that insulin therapy is effective in treating gestational diabetes. These studies have demonstrated that insulin successfully reduces blood sugar levels and aids in maintaining glycaemic control throughout pregnancy.

Maternal Glycaemic Outcomes: Insulin therapy has been linked to better maternal glycaemic outcomes. Better overall glycaemic management is achieved by efficiently lowering fasting and postprandial blood glucose levels. This lessens the chance of complications like macrosomia and

caesarean births that are brought on by uncontrolled hyperglycaemia.

Foetal Outcomes: Some studies have suggested that metformin may be associated with a lower risk of macrosomia and excessive foetal growth compared to other treatments. However, more research is needed to establish its safety and long-term effects on the foetus.

3.2 Oral Antidiabetic Agents

Metformin

Clinical Studies: Research on the use of metformin in gestational diabetes has produced mixed results. While some studies have reported its effectiveness in controlling blood glucose levels, others have raised concerns about its impact on foetal outcomes.

Maternal Glycaemic Outcomes: Metformin has been shown to reduce fasting blood glucose levels and improve insulin sensitivity in some women with gestational diabetes. However, its efficacy may vary among individuals.

Foetal Outcomes: Some studies have suggested that metformin may be associated with a lower risk of macrosomia and excessive foetal growth compared to other treatments. However, more research is needed to establish its safety and long-term effects on the foetus.

When administered carefully, insulin therapy is still a proven and successful treatment for gestational diabetes, regularly showing improved maternal glycaemic outcomes and positive foetal outcomes. Although they are options, oral antidiabetic medications like glyburide and metformin should be carefully assessed for each patient's safety and effectiveness. New treatments such as DPP-4 inhibitors and GLP-1 receptor agonists appear promising, but more research is needed to understand their function in the treatment of gestational diabetes. A thorough evaluation of the mother's and the foetus's health should be the basis for selecting an antihyperglycemic medication, and the

management of glycaemic control should be closely monitored during the entire pregnancy.¹²

Maternal and Foetal Complications

GDM is associated with an increased risk of various complications for both the mother and the foetus. When poorly managed or left untreated, it can lead to various maternal and foetal complications. Timely diagnosis, effective management, and close monitoring are crucial to reducing the risks associated with GDM.⁷ Here are some of the potential maternal and foetal complications associated with GDM:

Maternal Complications:

1. **Preeclampsia:** Women with GDM are at an increased risk of developing preeclampsia, a condition characterized by high blood pressure, protein in the urine, and sometimes organ dysfunction. Preeclampsia can be dangerous for both the mother and the foetus. This condition is characterized by high blood pressure and signs of damage to other organ systems, usually occurring after 20 weeks of pregnancy. When coupled with GDM, the risks for each the mom and the toddler might also escalate. Women recognized with GDM are at a higher danger of growing preeclampsia in comparison to those without GDM. Preeclampsia can lead to numerous headaches, consisting of preterm delivery, restricted fetal boom, or even existence-threatening situations for both the mom and the infant. Vigilant monitoring and coordinated care among healthcare companies are crucial for people with GDM, as they may be extra at risk of preeclampsia. Managing blood sugar stages, routine prenatal take a look at-ups, and well timed interventions can appreciably reduce the chance and severity of complications associated with each GDM and preeclampsia, ensuring a safer and more healthy being pregnant final results.¹³

2. **Gestational Hypertension:** GDM can contribute to the development of gestational hypertension, which is characterized by high blood pressure during pregnancy. This condition increases the risk of preeclampsia. Gestational hypertension typically arises after 20 weeks of pregnancy and can result in headaches along with preeclampsia, preterm start, and constrained fetal growth. When coupled with GDM, the risks of unfavorable effects enlarge, necessitating careful monitoring and control. Women with GDM have a better probability of developing gestational high blood pressure, underscoring the significance of complete prenatal care. Timely interventions, consisting of near monitoring of blood stress, handling blood sugar tiers thru way of life modifications or medications, and normal prenatal test-ups, are critical in minimizing the dangers associated with gestational hypertension and GDM. Collaborative efforts between healthcare vendors and vigilant tracking are vital to mitigate capability headaches, ensuring a more secure pregnancy adventure for both the mom and the child.¹⁴
3. **Increased Risk of Type 2 Diabetes:** Women with GDM are at a significantly higher risk of developing type 2 diabetes later in life. Regular follow-up and screening for diabetes post-pregnancy are important. Women who've had GDM have a drastically improved threat of developing Type 2 Diabetes as compared to individuals who have not skilled GDM. This connection highlights the importance of postpartum comply with-up and ongoing tracking of blood sugar tiers after being pregnant. Lifestyle changes, which includes keeping a healthy food regimen, regular exercise, and weight control, play a pivotal function in reducing the threat of growing Type 2 Diabetes following GDM. Moreover, ordinary screenings for diabetes after childbirth are critical to come across and manage any early signs and symptoms or signs, making an allowance for well timed interventions and the implementation of preventive measures. By acknowledging the heightened chance and taking proactive steps, those who had GDM can successfully manage and doubtlessly decrease their risk of developing Type 2 Diabetes, promoting higher long-time period fitness outcomes.¹⁵
4. **Increased Risk of Future Cardiovascular Disease:** GDM is associated with an elevated risk of future cardiovascular disease in the mother, including heart disease and stroke. Experiencing Gestational Diabetes Mellitus (GDM) during being pregnant poses a enormous difficulty past childbirth, as it elevates the chance of destiny cardiovascular sickness (CVD) for the mom. Women who have had GDM have a heightened susceptibility to developing cardiovascular troubles later in existence, inclusive of hypertension, coronary heart disorder, and stroke. The underlying mechanisms linking GDM to multiplied cardiovascular risk contain insulin resistance, infection, and metabolic imbalances at some point of being pregnant. These elements, if left unaddressed, can make contributions to lengthy-term headaches affecting cardiovascular fitness. Recognizing this heightened risk, postpartum care becomes essential. Implementing lifestyle adjustments including preserving a healthful eating regimen, normal exercise, and weight control can notably mitigate this hazard. Additionally, ongoing tracking of blood strain, levels of cholesterol, and blood sugar put up-being pregnant, in conjunction with habitual medical check-ups, are imperative in handling and reducing the threat of destiny cardiovascular sicknesses in people

with a history of GDM. Early intervention and proactive measures can appreciably lower the hazard, fostering higher cardiovascular health outcomes in the long run.¹⁶

5. **Caesarean Section:** Poorly managed GDM may result in macrosomia (large birth weight), making a caesarean section more likely due to concerns about delivering a large baby vaginally. Gestational Diabetes Mellitus (GDM) can effect the mode of transport, growing the probability of a Caesarean phase (C-phase). While not all pregnancies tormented by GDM lead to C-sections, sure elements associated with GDM, along with macrosomia (larger-than-common child), may additionally necessitate this mode of shipping. In instances wherein the child is greater than ordinary because of increased glucose levels within the womb, vaginal delivery would possibly pose risks, prompting healthcare carriers to opt for a C-phase to make sure the protection of each the mother and the infant. Additionally, if complications arise during labor, which includes difficulties in tracking the toddler's reaction to labour or issues approximately the toddler's length, a C-segment might be endorsed. However, the choice concerning the mode of delivery is individualized and based on various factors, consisting of the general health of the mother and baby. Healthcare vendors paintings carefully with people with GDM to plot the most secure shipping plan, aiming for the nice possible final results for each the mother and the new child.¹⁷

Foetal Complications:

1. **Macrosomia:** High blood glucose levels in the mother can lead to excessive foetal growth (macrosomia), which increases the risk of birth injuries during delivery. Elevated blood sugar levels in the mother can lead to increased foetal insulin production, resulting

in the accumulation of extra fat and larger-than-average size in the baby. This condition heightens the risk of complications during childbirth, as a larger baby might encounter difficulties passing through the birth canal, increasing the likelihood of birth injuries and the need for a Caesarean section. Additionally, macrosomia poses risks to the baby, including shoulder dystocia (difficulty delivering the shoulders after the head), increased likelihood of hypoglycaemia after birth, and a higher chance of obesity and Type 2 Diabetes later in life. Careful monitoring of blood sugar levels, along with appropriate management of GDM through diet, exercise, and sometimes medication, is crucial in minimizing the risk of macrosomia and its associated complications, ensuring a safer delivery and healthier outcomes for both the mother and the baby.¹⁷

2. **Neonatal Hypoglycaemia:** Babies born to mothers with GDM are at risk of experiencing low blood sugar levels (hypoglycaemia) shortly after birth. Neonatal hypoglycaemia can lead to seizures and other complications if not promptly treated. Babies of mothers with GDM might experience a rapid drop in blood sugar levels after birth because they were exposed to higher glucose levels in the womb. This abrupt change can challenge the newborn's ability to regulate their blood sugar independently. Neonatal hypoglycemia can lead to various complications, including seizures, developmental issues, and, in severe cases, neurological damage. Healthcare providers closely monitor at-risk infants, especially those born to mothers with GDM, checking their blood sugar levels regularly after birth. In some cases, early feedings or glucose supplementation might be necessary to maintain stable blood sugar levels. Proper management of GDM during pregnancy,

coupled with vigilant monitoring and prompt interventions after birth, is crucial in preventing and managing neonatal hypoglycemia, ensuring the well-being of the newborn.¹⁸

4. **Respiratory Distress Syndrome (RDS):**

Infants of mothers with GDM may be at an increased risk of developing respiratory distress syndrome, a condition in which the baby's lungs are not fully matured. In some cases, babies born to mothers with GDM might be delivered prematurely due to complications related to high blood sugar levels or other associated conditions. Premature birth can increase the likelihood of RDS as the baby's lungs may not have produced enough surfactant, a substance that helps keep the air sacs in the lungs open, making breathing challenging for the newborn. While not every baby born to a mother with GDM will experience RDS, healthcare providers carefully monitor these infants, especially premature or larger babies, providing necessary support such as surfactant replacement therapy or respiratory assistance to manage RDS and ensure optimal respiratory function for the newborn. Proper management of GDM and close monitoring during pregnancy can mitigate the risks associated with RDS, contributing to better outcomes for the infant.¹⁹

6. **Hyperbilirubinemia (Jaundice):** GDM can increase the risk of neonatal jaundice, a condition characterized by yellowing of the skin and eyes due to elevated bilirubin levels in the baby's blood. This syndrome can be brought on by a number of things, such as accelerated haemoglobin disintegration or problems with the new-born's liver's ability to properly handle bilirubin. Due to factors including increased birth weight or specific metabolic abnormalities linked with GDM,

babies of women with the disease may be more likely to develop hyperbilirubinemia. Jaundice, or yellowing of the skin and eyes of an infant, is one of the symptoms of hyperbilirubinemia. Although moderate jaundice is typical in babies and usually goes away on its own, high bilirubin levels can cause problems if addressed, including kernicterus or brain damage. In order to lower bilirubin levels and avoid consequences, healthcare professionals regularly monitor new-borns at risk for hyperbilirubinemia, measuring bilirubin levels and administering phototherapy or other therapies as needed.²⁰

7. **Stillbirth:** The deadly consequence known as a stillbirth, in which the foetus dies in the womb before 20 weeks of pregnancy, can be made more likely by gestational diabetes mellitus (GDM). GDM increases the incidence of problems that can raise the risk, even if a direct causative association between the condition and stillbirth is still unclear. A foetus's growth and development may be impacted by problems such as reduced blood supply to the foetus resulting from elevated blood sugar levels in gestational diabetes mellitus (GDM). Furthermore, there is a strong correlation between GDM and other risk factors such high blood pressure, obesity, and advanced maternal age, all of which increase the chance of stillbirth. Poorly controlled GDM may increase the risk of stillbirth, although the risk is generally low with proper monitoring and management.²¹

8. **Obesity and Diabetes Risk:** Gestational diabetes mellitus (GDM)-complicated pregnancies can put the foetus at higher risk of obesity and diabetes in the future. Poorly treated GDM can expose a foetus to elevated glucose levels in the womb, which may impact the baby's metabolic programming and disrupt foetal development. This changed

metabolic milieu may make the youngster more susceptible to obesity and Type 2 Diabetes in the future. According to studies, babies delivered to women with GDM may be more likely to accumulate fat, which increases the risk of childhood obesity. Additionally, there is a higher likelihood that these babies will experience insulin resistance, which is a prelude to Type 2 Diabetes. Reducing these risks during pregnancy requires proper management of GDM. Infants born to mothers with GDM may have a higher risk of developing obesity and type 2 diabetes later in life.²²

Postpartum Implications

GDM has long-term implications for both the mother and offspring. Gestational Diabetes Mellitus (GDM) doesn't just have implications during pregnancy; it can also affect both the mother and the child in the postpartum period and beyond. Proper postpartum care and follow-up are crucial to monitor and manage potential long-term consequences.²³ Here are some postpartum implications of GDM:

For the mother:

1. **Increased Risk of Type 2 Diabetes:** Women with a history of GDM are at a significantly higher risk of developing type 2 diabetes in the years following pregnancy. When compared to women without GDM, individuals who have had GDM are significantly more likely to develop Type 2 Diabetes. This link emphasises the significance of continuing blood sugar monitoring during pregnancy and postpartum follow-up. The hormonal alterations and insulin resistance that arise during pregnancy may endure after childbirth, hence increasing the likelihood of Type 2 Diabetes in women with a history of gestational diabetes mellitus. The risk is greatest within the first 5 years after childbirth but persists throughout life.

Postpartum glucose screening is essential to detect the onset of diabetes early.²⁴

2. **Metabolic Syndrome:** GDM increases the risk of metabolic syndrome, which includes components like obesity, high blood pressure, high blood sugar, and abnormal lipid profiles. This cluster of conditions can significantly increase the risk of heart disease.²⁵
3. **Continued Need for Blood Glucose Monitoring:** Some women may need to continue monitoring their blood glucose levels in the postpartum period, especially if they have persistent hyperglycaemia or are at high risk for developing type 2 diabetes.²⁶
4. **Cardiovascular Disease Risk:** GDM is associated with an increased risk of developing cardiovascular disease later in life. Managing cardiovascular risk factors (e.g., blood pressure, cholesterol) and adopting a heart-healthy lifestyle is crucial.¹⁶
5. **Breastfeeding:** Breastfeeding can help improve glucose control in mothers with GDM. Encouraging and supporting breastfeeding can have both short-term and long-term health benefits for the mother.²⁷

For the Child:

1. **Risk of Childhood Obesity and Diabetes:** Children born to mothers with GDM may be at a higher risk of developing obesity and type 2 diabetes later in life. Promoting a healthy lifestyle, including a balanced diet and regular physical activity, is essential to reduce these risks.
2. **Routine Paediatric Check-ups:** Infants born to mothers with GDM should have routine paediatric check-ups to monitor growth, development, and glucose metabolism. Early intervention and monitoring can help detect and manage any potential issues.

For Future Pregnancies:

1. **Increased Risk in Subsequent Pregnancies:** Women who had GDM in one pregnancy are



at an increased risk of developing GDM in future pregnancies. Careful planning, monitoring, and management are important for subsequent pregnancies.²⁸

2. **Preconception Counselling:** Women with a history of GDM should consider preconception counselling to optimize their health and glucose control before becoming pregnant again. This can help reduce the risk of GDM recurrence.²⁹

It is noteworthy that there can be individual variations in the effectiveness of certain antihyperglycemic medications. A pregnant person's unique demands and preferences, as well as the medication's safety profile, are often taken into account while choosing a prescription. The management of gestational diabetes involves not only medicine but also lifestyle changes such as dietary adjustments and consistent physical activity. It is imperative to closely monitor blood glucose levels and schedule follow-up appointments with healthcare specialists to guarantee that the selected treatment plan is effective and blood sugar levels stay within the target range.

Advances in Research

The field of GDM research is continually evolving. Advances in research related to gestational diabetes (GDM) continue to provide valuable insights into its pathophysiology, management, and potential preventive measures. Here are some notable advances in GDM research:

1. **Genetic Predisposition:** Researchers have made significant strides in identifying genetic factors associated with GDM risk. Understanding the genetic basis of GDM can help identify individuals at higher risk and potentially lead to more personalized management and prevention strategies.³⁰
2. **Metabolic Pathways:** Studies have shed light on the metabolic pathways involved in GDM, including insulin resistance, beta-cell

dysfunction, and placental hormones. This deeper understanding may lead to targeted therapies that address the specific mechanisms driving GDM.³¹

3. **Microbiome Influences:** Emerging research explores the role of the gut microbiome in GDM. Alterations in gut bacteria composition may contribute to insulin resistance and glucose intolerance. Manipulating the microbiome through diet or probiotics could potentially have a therapeutic role.³²
4. **Artificial Intelligence (AI):** AI and machine learning are being applied to predict and manage GDM more effectively. Predictive models based on patient data can help identify women at risk, optimize insulin dosing, and improve overall care.³³
5. **Continuous Glucose Monitoring (CGM):** The use of CGM devices in pregnancy has provided real-time data on blood glucose levels, allowing for better glucose control and reducing the risk of complications.³⁴
6. **Telemedicine and Mobile Health Apps:** Telehealth and mobile health apps have gained importance, especially during the COVID-19 pandemic, making it easier for pregnant individuals to monitor and manage GDM remotely and stay connected with healthcare providers.³⁵
7. **Lifestyle Interventions:** Research continues to emphasize the benefits of lifestyle modifications, including diet and exercise, in GDM management. Tailored nutrition plans and exercise regimens are being developed to optimize blood glucose control.³⁶

CONCLUSION

Maternal and foetal health are significantly impacted by gestational diabetes mellitus, which is still a major public health concern. In order to lessen the effects of GDM on maternal and foetal outcomes, better knowledge and treatment of the condition are crucial. Although other risk factors



like obesity, advanced maternal age, and a family history of diabetes all play a role in its development, pregnancy-related hormonal changes are the primary cause.

GDM poses concerns for the unborn child as well as the mother. Complications for the mother could include elevated blood pressure, a caesarean delivery, and a higher chance of type 2 diabetes in the future. The infant may experience issues like macrosomia (high birth weight), postpartum hypoglycaemia, and a higher chance of type 2 diabetes later in life.

However, these risks can be decreased with appropriate management and lifestyle adjustments. The key to treating GDM is a good diet, frequent exercise, regular blood sugar monitoring, and medication if needed. In order to guarantee the best care and reduce difficulties, it is also critical for expectant mothers with GDM to collaborate closely with medical specialists. These actions can help pregnant women with gestational diabetes manage their health and lower the risks of the condition for both the mother and the unborn child. To protect the health of the mother and the child, it is imperative that GDM management be given first priority.

REFERENCES

1. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The Pathophysiology of Gestational Diabetes Mellitus. *Int J Mol Sci.* 2018 Oct 26;19(11):3342. doi: 10.3390/ijms19113342. PMID: 30373146; PMCID: PMC6274679.
2. Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. *Nat Rev Endocrinol.* 2012 Nov;8(11):639-49. doi: 10.1038/nrendo.2012.96. Epub 2012 Jul 3. PMID: 22751341; PMCID: PMC4404707.
3. Alfadhli EM. Gestational diabetes mellitus. *Saudi Med J.* 2015 Apr;36(4):399-406. doi: 10.15537/smj.2015.4.10307. PMID: 25828275; PMCID: PMC4404472.
4. Salazar-Petres ER, Sferruzzi-Perri AN. Pregnancy-induced changes in β -cell function: what are the key players?. *The Journal of Physiology.* 2022 Mar;600(5):1089-117.
5. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. *Ann Nutr Metab.* 2015;66 Suppl 2:14-20. doi: 10.1159/000371628. Epub 2015 Jun 2. PMID: 26045324.
6. Weissgerber TL, Mudd LM. Preeclampsia and diabetes. *Curr Diab Rep.* 2015 Mar;15(3):9. doi: 10.1007/s11892-015-0579-4. PMID: 25644816; PMCID: PMC4317712.
7. Ornoy A, Becker M, Weinstein-Fudim L, Ergaz Z. Diabetes during Pregnancy: A Maternal Disease Complicating the Course of Pregnancy with Long-Term Deleterious Effects on the Offspring. A Clinical Review. *Int J Mol Sci.* 2021 Mar 15;22(6):2965. doi: 10.3390/ijms22062965. PMID: 33803995; PMCID: PMC7999044.
8. Rani PR, Begum J. Screening and Diagnosis of Gestational Diabetes Mellitus, Where Do We Stand. *J Clin Diagn Res.* 2016 Apr;10(4):QE01-4. doi: 10.7860/JCDR/2016/17588.7689. Epub 2016 Apr 1. PMID: 27190902; PMCID: PMC4866200.
9. Rasmussen L, Poulsen CW, Kampmann U, Smedegaard SB, Ovesen PG, Fuglsang J. Diet and Healthy Lifestyle in the Management of Gestational Diabetes Mellitus. *Nutrients.* 2020 Oct 6;12(10):3050. doi: 10.3390/nu12103050. PMID: 33036170; PMCID: PMC7599681.
10. Choudhury AA, Rajeswari VD. Gestational diabetes mellitus-A metabolic and reproductive disorder. *Biomedicine & Pharmacotherapy.* 2021 Nov 1;143:112183.
11. Priya G, Kalra S. Metformin in the management of diabetes during pregnancy and

- lactation. *Drugs Context*. 2018 Jun 15;7:212523. doi: 10.7573/dic.212523. PMID: 29942340; PMCID: PMC6012930.
12. Kalra B, Gupta Y, Singla R, Kalra S. Use of oral anti-diabetic agents in pregnancy: a pragmatic approach. *N Am J Med Sci*. 2015 Jan;7(1):6-12. doi: 10.4103/1947-2714.150081. PMID: 25709972; PMCID: PMC4325398.
13. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. *Nat Rev Nephrol*. 2019 May;15(5):275-289. doi: 10.1038/s41581-019-0119-6. Erratum in: *Nat Rev Nephrol*. 2019 Jun;15(6):386. PMID: 30792480; PMCID: PMC6472952.
14. Sullivan SD, Umans JG, Ratner R. Hypertension complicating diabetic pregnancies: pathophysiology, management, and controversies. *J Clin Hypertens (Greenwich)*. 2011 Apr;13(4):275-84. doi: 10.1111/j.1751-7176.2011.00440.x. PMID: 21466626; PMCID: PMC8673181.
15. Noctor E, Dunne FP. Type 2 diabetes after gestational diabetes: The influence of changing diagnostic criteria. *World J Diabetes*. 2015 Mar 15;6(2):234-44. doi: 10.4239/wjd.v6.i2.234. PMID: 25789105; PMCID: PMC4360417.
16. Mao Y, Hu W, Xia B, Liu L, Han X, Liu Q. Association Between Gestational Diabetes Mellitus and the Risks of Type-Specific Cardiovascular Diseases. *Front Public Health*. 2022 Jul 5;10:940335. doi: 10.3389/fpubh.2022.940335. PMID: 35865249; PMCID: PMC9294140.
17. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. *Ann Nutr Metab*. 2015;66 Suppl 2:14-20. doi: 10.1159/000371628. Epub 2015 Jun 2. PMID: 26045324.
18. Mitanchez D, Yzydorczyk C, Simeoni U. What neonatal complications should the pediatrician be aware of in case of maternal gestational diabetes? *World J Diabetes*. 2015 Jun 10;6(5):734-43. doi: 10.4239/wjd.v6.i5.734. PMID: 26069722; PMCID: PMC4458502.
19. Yildiz Atar H, Baatz JE, Ryan RM. Molecular Mechanisms of Maternal Diabetes Effects on Fetal and Neonatal Surfactant. *Children (Basel)*. 2021 Apr 6;8(4):281. doi: 10.3390/children8040281. PMID: 33917547; PMCID: PMC8067463.
20. Jiang N, Qian L, Lin G, Zhang Y, Hong S, Sun B, Wang H, Huang M, Wang J, Jiang Q. Maternal blood parameters and risk of neonatal pathological jaundice: a retrospective study. *Sci Rep*. 2023 Feb 14;13(1):2627. doi: 10.1038/s41598-023-28254-3. PMID: 36788268; PMCID: PMC9929053.
21. Rosenstein MG, Cheng YW, Snowden JM, Nicholson JM, Doss AE, Caughey AB. The risk of stillbirth and infant death stratified by gestational age in women with gestational diabetes. *Am J Obstet Gynecol*. 2012 Apr;206(4):309.e1-7. doi: 10.1016/j.ajog.2012.01.014. PMID: 22464068; PMCID: PMC3403365.
22. Page KA, Luo S, Wang X, Chow T, Alves J, Buchanan TA, Xiang AH. Children Exposed to Maternal Obesity or Gestational Diabetes Mellitus During Early Fetal Development Have Hypothalamic Alterations That Predict Future Weight Gain. *Diabetes Care*. 2019 Aug;42(8):1473-1480. doi: 10.2337/dc18-2581. Epub 2019 May 21. PMID: 31332028; PMCID: PMC6647040.
23. Wicklow B, Retnakaran R. Gestational Diabetes Mellitus and Its Implications across the Life Span. *Diabetes Metab J*. 2023 May;47(3):333-344. doi:

- 10.4093/dmj.2022.0348. Epub 2023 Feb 8. PMID: 36750271; PMCID: PMC10244196.
24. Herath H, Herath R, Wickremasinghe R. Gestational diabetes mellitus and risk of type 2 diabetes 10 years after the index pregnancy in Sri Lankan women—A community based retrospective cohort study. *PloS one*. 2017 Jun 23;12(6):e0179647.
25. Dobrowolski P, Prejbisz A, Kuryłowicz A, Baska A, Burchardt P, Chlebus K, Dzida G, Jankowski P, Jaroszewicz J, Jaworski P, Kamiński K, Kapłon-Cieślicka A, Klocek M, Kukla M, Mamcarz A, Mastalerz-Migas A, Narkiewicz K, Ostrowska L, Śliż D, Tarnowski W, Wolf J, Wyleżoł M, Zdrojewski T, Banach M, Januszewicz A, Bogdański P. Metabolic syndrome - a new definition and management guidelines: A joint position paper by the Polish Society of Hypertension, Polish Society for the Treatment of Obesity, Polish Lipid Association, Polish Association for Study of Liver, Polish Society of Family Medicine, Polish Society of Lifestyle Medicine, Division of Prevention and Epidemiology Polish Cardiac Society, "Club 30" Polish Cardiac Society, and Division of Metabolic and Bariatric Surgery Society of Polish Surgeons. *Arch Med Sci*. 2022 Aug 30;18(5):1133-1156. doi: 10.5114/aoms/152921. PMID: 36160355; PMCID: PMC9479724.
26. Kalra P, Anakal M. Peripartum management of diabetes. *Indian J Endocrinol Metab*. 2013 Oct;17(Suppl 1):S72-6. doi: 10.4103/2230-8210.119510. PMID: 24251226; PMCID: PMC3830373.
27. Much D, Beyerlein A, Roßbauer M, Hummel S, Ziegler AG. Beneficial effects of breastfeeding in women with gestational diabetes mellitus. *Mol Metab*. 2014 Jan 21;3(3):284-92. doi: 10.1016/j.molmet.2014.01.002. PMID: 24749058; PMCID: PMC3986583.
28. Nankervis A, Price S, Conn J. Gestational diabetes mellitus: A pragmatic approach to diagnosis and management. *Australian journal of general practice*. 2018 Jul;47(7):445-9.
29. Wei Y, Juan J, Su R, Song G, Chen X, Shan R, Li Y, Cui S, Fan S, Feng L, You Z, Meng H, Cai Y, Zhang C, Yang H. Risk of gestational diabetes recurrence and the development of type 2 diabetes among women with a history of gestational diabetes and risk factors: a study among 18 clinical centers in China. *Chin Med J (Engl)*. 2022 Mar 20;135(6):665-671. doi: 10.1097/CM9.0000000000002036. PMID: 35348312; PMCID: PMC9276490.
30. Ali N, Aldhaheri AS, Alneyadi HH, Alazezi MH, Al Dhaheri SS, Loney T, Ahmed LA. Effect of Gestational Diabetes Mellitus History on Future Pregnancy Behaviors: The Mutaba'ah Study. *Int J Environ Res Public Health*. 2020 Dec 23;18(1):58. doi: 10.3390/ijerph18010058. PMID: 33374764; PMCID: PMC7796159.
31. Petersen MC, Shulman GI. Mechanisms of insulin action and insulin resistance. *Physiological reviews*. 2018 Aug 1.
32. Li WZ, Stirling K, Yang JJ, Zhang L. Gut microbiota and diabetes: From correlation to causality and mechanism. *World J Diabetes*. 2020 Jul 15;11(7):293-308. doi: 10.4239/wjd.v11.i7.293. PMID: 32843932; PMCID: PMC7415231.
33. Zhang Z, Yang L, Han W, Wu Y, Zhang L, Gao C, Jiang K, Liu Y, Wu H. Machine Learning Prediction Models for Gestational Diabetes Mellitus: Meta-analysis. *J Med Internet Res*. 2022 Mar 16;24(3):e26634. doi: 10.2196/26634. PMID: 35294369; PMCID: PMC8968560.
34. Li A, Brackenridge A. The role of continuous glucose monitoring in pregnancy. *Obstet Med*.

- 2022 Mar;15(1):6-10. doi: 10.1177/1753495X211014716. Epub 2021 May 27. PMID: 35444725; PMCID: PMC9014555.
35. Eberle C, Stichling S. Telemedical Approaches to Managing Gestational Diabetes Mellitus During COVID-19: Systematic Review. *JMIR Pediatr Parent*. 2021 Aug 5;4(3):e28630. doi: 10.2196/28630. PMID: 34081604; PMCID: PMC8345174.
36. Zugravu C, Petra A, Pietroşel VA, Mihai BM, Mihai DA, Bohîlţea RE, Tarcea M. Nutritional Interventions and Lifestyle Changing in Gestational Diabetes Mellitus Prevention: A Narrative Review. *Sustainability*. 2023 Jan 6;15(2):1069.

HOW TO CITE: A. R. Shabaraya, Sarah Rafiq Gestational Diabetes Mellitus: Current Insights and Advances in Diagnosis, Management, and Maternal-Foetal Health, *Int. J. in Pharm. Sci.*, 2023, Vol 1, Issue 12, 55-70. <https://doi.org/10.5281/zenodo.10138421>