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NARRATIVE REVIEW

Gestational Diabetes: A Comprehensive Review

Erum Akhter[1] | **Almas Siddique**[1]

1. Department of Pharmacology, Faculty of Pharmacy, University of Karachi, **Pakistan.**

Corresponding author
Erum Akhter
Department of Pharmacology, Faculty of Pharmacy, University of Karachi, **Pakistan**
Drerumakhter2017@gmail.com

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ABSTRACT

Gestational diabetes mellitus (GDM) is defined as hyperglycemia which occurs for the first time in pregnancy. World widely events of gestational diabetes mellitus (GDM) are growing at a worrying pace especially in South Asian countries .It is linked to unfavorable maternal and newborn outcomes. Understanding the many risk factors, pathophysiological processes and genetic components of GDM will assist us in identifying at-risk women, developing effective preventative strategies, and providing proper disease management. The main issue is the absence of consensus among healthcare practitioners on screening procedures. This comprehensive article synthesizes existing knowledge and current developments in the field of gestational diabetes, with the goal of providing a full understanding of its pathophysiology, risk factors, diagnosis, treatment, and influence on maternal and fetal outcomes as it emphasizes the complex character of gestational diabetes through an exhaustive examination of current research, finding significant risk variables such as age, family history, obesity ,diagnostic tools, including oral glucose tolerance tests, and developments in screening techniques are described in the context of early identification and timely intervention. Strategies to self-monitoring blood glucose concentrations and therapy with food, oral medicines, and insulin injections are discussed. It main aim is to lessen the burden of gestational diabetes and pave the path for better pregnancies and for future generations and continuous devotion to improving mother and child health.

Key Words:
Gestational diabetes mellitus (GDM), Insulin resistance, β-Cell Dysfunction

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Layman Summary
Gestational diabetes globally and especially in South Asian nations is becoming a greater problem. It is discovered in the second or first trimester of pregnancy, is caused by insulin resistance and delayed pancreatic beta cell response to elevated blood sugar levels In order to prevent negative obstetric outcomes and lessen the effects on various organs, screening is required. The oral glucose tolerance test (OGTT) is frequently used. One-step screening is simple and economical, but two-step screening necessitates more testing and patient cooperation. Both approaches offer benefits and drawbacks, such as delayed therapy and improved diagnosis of less severe GDM. Fasting plasma glucose (FPG) and inflammatory biomarkers can be used in the early stages of pregnancy to detect gestational diabetes mellitus (GDM). Asian women are more prone than Australians to get GDM. Obese and older women are twice as likely to acquire gestational diabetes mellitus (GDM), and more likely to experience pregnancy-related issues. GDM, which affects 52% of pregnant women, increases labor problems and decreases glucose metabolism. Cancer, chronic renal disease, polyhydramnios,hypertension, preeclampsia are among the issues that affect mothers. Managing GDM requires lifestyle changes, including physical activity, glucose monitoring, and food therapy. If lifestyle changes are insufficient, glucose-lowering medication is recommended.Vitamin D supplements can help women with GDM manage glycaemia, and probiotics can help reduce pro-inflammatory mediators and gut flora. Future studies in GDM aim to normalize short- and long-term outcomes for women and their offspring.

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1 | INTRODUCTION

Background

Gestational diabetes is an endocrine condition which commonly affects pregnant women [1]. It effect up to 25% women during pregnancy. Gestational diabetes was initially identified in a pregnant woman by German researchers in 1824 while in the year of 1926 during 5th or 6th month of pregnancy lambie identified the disease's. John O'Sullivan's publications were released in 1961 and 1964 [2]. This study is grounded in the outcomes of an oral glucose tolerance test (OGTT) administered to a random sample of pregnant women. A 100-gram OGTT was employed to establish diagnostic criteria. Using updated analytical techniques, glucose levels were later estimated from whole blood data provided in the study to approximate probable blood glucose levels. In 1978, the American College of Obstetricians and Gynecologists (ACOG) recommended interpreting OGTT results based on O'Sullivan's criteria, as well as the standards established by Mahan, Mestman, and their colleagues, to screen pregnant women with a history of diabetes risk factors for gestational diabetes mellitus (GDM). Subsequently, in 1979, the National Diabetes Data Group (NDDG) introduced guidelines for categorizing diabetes and glucose intolerance, including GDM. These guidelines specifically targeted women whose glucose tolerance was impaired during pregnancy. Women diagnosed with GDM were identified as being at high risk for developing type 2 diabetes mellitus. Despite these advancements, significant debate persisted over the necessity and strategies for the detection and management of GDM, extending well into contemporary discussions [3]. GDM is associated with prenatal complications, maternal future risk of hyperglycemia and heart disease, as well as childhood obesity [4]. Unfavorable outcomes during pregnancy, such as pre-eclampsia, caesarean births by women and neonatal hypoglycemia are related with a higher chance of GDM [5]. Multiple health outcomes have been related to psychosocial factors, such as depression, traumatic childhood events and social support. Recent studies have connected maternal depression to GDM and shown that it increases the likelihood of a variety of adverse pregnancy outcomes [6]. Although the rate of GDM has been rising significantly in many countries, including China, it is difficult to estimate and compare the prevalence of GDM globally because there is a wide range throughout the examination methods also diagnostic standards that are employed to detect GDM in females [4]. Compared to white European women, South Asian Women of South Asia (heritage is from the Indian subcontinent) have a double more chance to develop GDM [7]. This review article on GDM may be useful for giving an overview and assessment of the current state of knowledge on the illness, including its prevalence, risk factors, diagnostic criteria, available treatments, and long-term outcomes. This information may be helpful for researchers who want to further our understanding of GDM and for medical professionals who work with pregnant patients. It can help increase public awareness and comprehension of GDM, which might improve the condition's detection, diagnosis, and treatment.

1.Definition of Gestational Diabetes

It is explained physiologically by the degree of glucose sensitivity that pregnant women exhibit [8]. Gestational diabetes is classified by the American Diabetes Association (ADA) as Diabetes that is first discovered in the 2nd or 1st trimester of pregnancy and does not have a definite history of diabetes, either type 1 or 2 [9]. Significant metabolic changes occur during pregnancy, which have an impact on insulin sensitivity and action that cause increase in effect for the latter pregnancy stages because of resistance to insulin and associated hyperglycemia. If a woman has GDM and had it since her most recent pregnancy, as well as a history of T2DM and PCOS, she is more likely to experience the disease's development [2]. It has been proposed that the two primary causes of gestational diabetes are the significant insulin resistance brought on by the placenta's hormone release and the insufficient or delayed reaction of the pancreatic beta cells to elevated blood sugar levels. GDM can be separated into two groups: A1GDM and A2GDM. Dietary-controlled gestational diabetes mellitus, or A1GDM, is a condition that can be treated with food alone and doesn't need medication. On the other hand, A2GDM refers to gestational diabetes that is treated with medication to maintain adequate glucose control [10].

2. Screening and Diagnosis methods

A screening test for gestational diabetes should be able to distinguish between those who already have the condition and those who have a increase risk of acquiring gestational diabetes mellitus (GDM). These two key processes may result to the management process are screening and diagnosis. Screening is essential to prevent negative obstetric results that minimizing the GDM's over time impact on numerous systems organ. Based on recent study an analysis of FPG, fasting insulin, androstenedione, and sex hormone binding globulin (SHBG) levels may aid in predicting the onset of GDM before conception in first-degree family members who have type 2 diabetes. Despite the fact that these characteristics might cause prediction of GDM, although this test is not advisable for all women before start of pregnancy [11]. In US it is advisable to pregnant women to test in their mid trimester (gestation between 24 and 28 week) on the basis of American College of Obstetricians and Gynecologists (ACOG). Even though there isn't an international, standardized for the screening test to be used, the oral glucose tolerance test (OGTT) is used frequently [12]. Regardless of fasting, it applies to pregnant women between 24 and 28 weeks gestation. They are known for GDM diagnosis if their 1 h plasma glucose concentrations are higher than established cut-off levels, which are typically 7.2 mmol/L or 7.8 mmol/L.(13) A 2-step procedure (Test for screening followed by diagnostic procedure) or a 1-step process (diagnostic procedure given to all patients) are both used to screen for gestational diabetes in asymptomatic people [14].

i.One-Step Screening:

The landmark Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study comprise of 23,316 women who are pregnant undergo a 75-g, 2-hour oral glucose tolerance test (OGTT) in pregnancy between 24- and 28 weeks of gestation [9].

i.Two-Step Screening:

In view of the 18% prevalence of GDM, the NIH rejected the one-step strategy in 2013 due to a greater strain on the American healthcare system [15]. Through screening female that are positive (1-hour glucose more than 130-140) are subjected to 50-gram, 1-hour non-fasting examination before undergoing a 100-gram, 3-hour OGTT is a conclusive diagnosis [9].

Table 1 Advantages and Disadvantages of One-Step Screening and Two-Step Screening.

Screening	Advantages	Disadvantages
One-Step	Easy to operate, good patient adherence, Cost-effective for high-risk patients; simple diagnostic, higher sensitivity detection of lesser GDM, which would result in fewer problems such as pre-eclampsia, which would be relevant to women of any gestational age, newborn hypoglycemia, neonatal mortality, and NICU hospitalization.	Insufficient reproducibility, Women must be in fasting.
Two-Step	Less false positive findings avoids OGTT in almost 75% of females	Lower level of patient compliance requires individuals to visit the doctor twice for testing Inadequate diagnosis Compared to the single-step, 100 g OGTT, this test has an 84% specificity and a 75% sensitivity. Delay in starting therapy even for those who tested positive

3. Diagnose of eGDM using Fasting Plasma Glucose

The IADPSG 2010 guidelines recommended using fasting plasma glucose (FPG) in early pregnancy to identify preexisting diabetes or GDM. They suggested classifying FPG levels between 92–126 mg/dL (5.1–7.0 mmol/L) as GDM but later revoked this due to insufficient evidence. Large retrospective studies in China reported that FPG

levels decrease until 16–19 weeks of gestation and then stabilize, highlighting variability in early pregnancy [16].

a. Glycated hemoglobin A1c (HbA1c):

Glycated hemoglobin (HbA1c) forms when glucose binds to hemoglobin's N-terminal valine. Reflecting average glucose over 8–12 weeks, HbA1c is influenced by the 120-day lifespan of erythrocytes. For pregnant women, it is more convenient than the 100g OGTT as it doesn't require fasting. HbA1c offers better stability, reproducibility, and lower biological variance than glucose tests and can be done anytime. While not yet recommended, it may help diagnose GDM [17].

b.Inflammatory biomarkers:

Inflammatory indicators are likely implicated in the development of GDM and might be employed as predictive markers since the inflammatory response is amplified in GDM. In fact, a number of studies have demonstrated that inflammatory indicators potentially predict GDM as soon as the first trimester of pregnancy [18].

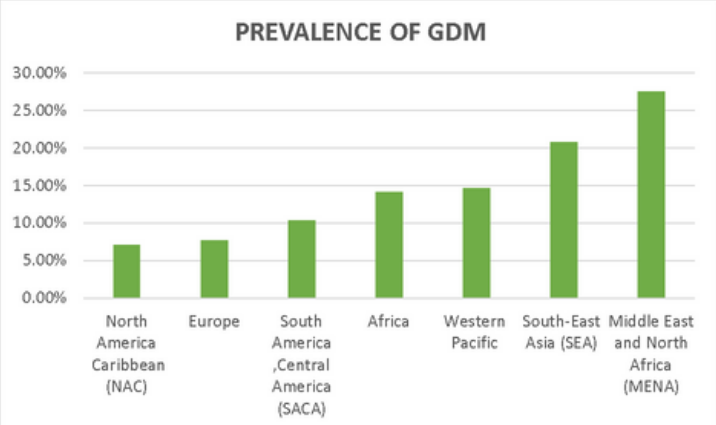
Table 2 Types of Inflammatory biomarkers

Cytokines	JNK activation phosphorylates IRS-1 serine residues, disrupting insulin signaling via the tyrosine kinase pathway. Adipokines impact insulin resistance in obesity and may similarly affect GDM by regulating insulin production and glucose metabolism, partly through inflammatory mediators.
Adiponectin	Adiponectin is abundant early in healthy pregnancies but low levels predict GDM, insulin resistance, and adverse outcomes. Retnakaran et al. found adiponectin links more strongly to GDM than weight gain.
Tumor-Necrosis Factor-α (TNF-α)	TNF-, an inflammatory cytokine produced by placental cells, has been linked to insulin resistance during pregnancy. Nevertheless, several studies have found a connection between elevated TNF- levels during the first trimester and the development of GDM later in pregnancy.
Leptin	Higher leptin levels early in pregnancy are linked to later GDM diagnoses, though studies also show an inverse independent relationship with GDM risk.(22). Leptin, a 16 kDa "satiety hormone," suppresses hunger and boosts metabolism. Its protein and mRNA levels are notably higher in the placentae of pre-eclamptic women, with severe cases showing an increased adiponectin-leptin ratio compared to moderate ones.
Interleukin-6T	IL-6, a cytokine affecting glucose metabolism, is produced by immune, adipose, and endothelial cells, as well as the placenta during pregnancy. It influences pancreatic beta cells, increasing insulin release. IL-6 levels are 2–3 times higher in obesity, inflammation, GDM, and type 2 diabetes, correlating with higher blood sugar, BMI, and reduced insulin sensitivity. Yi et al. found elevated IL-6 and high-sensitivity CRP levels in GDM, contributing to its progression through distinct mechanisms. A study by Morisset et al. using 75g OGTT (20 GDM, 27 controls) showed significantly higher IL-6 levels in GDM, assessed via ELISA during screening and two months postpartum.
Adipocyte Fatty Acid-Binding Protein:	The pathogenesis and progression of gestational diabetes (GDM) are significantly influenced by adipose tissue. AFABP is a potential indicator which is higher in women with GDM compared to those who do not have it, regardless of the women's level of insulin sensitivity.

4. Prevalence and incidence in gestational diabetes

According to the International Association of Diabetes in Pregnancy Study Group's Criteria the global standardized prevalence of GDM 2021 was 14.0% overall, with regional variations [4].

Figure 1: Global standardized Prevalence of Gestational Diabetes



In this graph according to IADPSG criteria shows MENA and SEA have the greatest standardized prevalence of GDM, followed by Western Pacific and Africa.

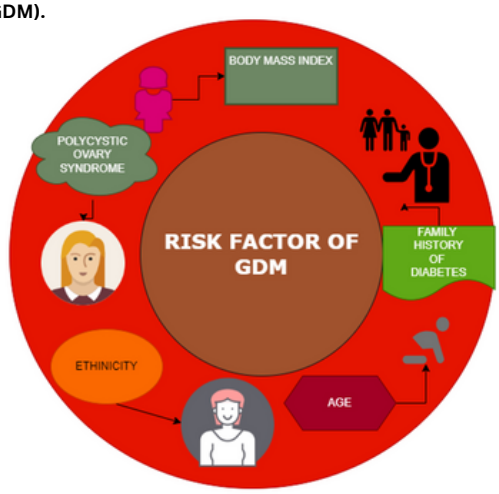
According to Feng-Lin Suhev et al. (2021), research yearly GDM prevalence expand 1.8-fold over the 12-year between 2004 to 2015 in Taiwan, having strong consistently growing pattern [26]. Incidence of GDM was significantly correlated with first-trimester hyperglycemia and hypertriglyceridemia in Saudi pregnant women [27].

Asian women are more likely than Australian women to develop GDM (11.5% vs. 3.7%), according to an Australian research (Women in Asia have more chance of having GDM than Australian women) .In the South Asian area, the prevalence of GDM is notably high. From 13.2% to over 40 percent of cases have been recorded in Bangladesh. In In Pakistan, the cross-sectional survey was carried out between 2013 and 2016 about frequency of GDM using DIPSI criteria that shows frequency of GDM was found 11.8% [28].

5. Risk factors for acquiring gestational diabetes

In Relation to women in the 20–24 age range, older women (>30 years) have a higher risk of pregnancy-related complications. They are also twice that have a medical history of Diabetes , PCOS, or multiparty when it comes to GDM [29].

Figure 2 Significant risk factors for the development of gestational diabetes mellitus (GDM).



i.Body mass index:

It evaluates general obesity and computed by dividing one's weight in kilogrammes by one's height in metres squared [30]. There was a meta-analysis by Chu et al. showed that obese women with a BMI of 25.0–30.0 kg/m2 had a twofold higher risk of getting GDM, a fourfold higher risk for those with a BMI of 30.0–35.0 kg/m2, and an eightfold higher risk for those with a BMI of > 35 kg/m2 [31]. Pregnancy-related overweight or obesity, gestational weight gain (GWG), and excessive GWG all increase the risk of poor foetal development and postnatal outcomes [32].

ii.PCOS (Polycystic ovary syndrome):

It has been shown that women with PCOS are more prone to acquire gestational diabetes mellitus (GDM), a prevalent endocrine and metabolic condition in women .Insulin resistance (IR) may be linked to the underlying mechanism. After pregnancy, PCOS patients' levels of pregnancy hormones such oestrogen, progesterone, and prolactin rise. This raises the degree of IR and enhances the chance of patients developing abnormalities of glucose metabolism [33]. Compared to women without PCOS who are the same age and weight, female having PCOS are at greater chance of IR and glucose intolerance [34]. According to Mikola et al., although overweight was the best predictor of GDM, PCOS enhanced the risk of the condition on its own [35]. Preeclampsia, pregnancy-induced hypertension, and premature birth are all thought to be more likely to occur in women with PCOS and GDM [36].

iii. Age:

Women over the age of 40 had a relative risk of 15.1% for GDM, according to a retrospective study of 138,530 Japanese women. According to Zhang et al., women aged 30-34 years old had the greatest age-specific prevalence of GDM [37]. Early, late, and chromosomal disorders present the greatest chances for miscarriage [38].

iv. Ethnicity:

Women of particular races have long been thought of as having a higher chance of acquiring GDM. Middle Eastern women, Pacific Islander women, and Australian Aboriginal women are among these at-risk ethnic groups . According to Shah e tal ,In the US, incidence of gestational diabetes rose from 2011 to 2019 among women giving birth to their first live child across all racial and ethnic groups and age ranges. Throughout the research period, the absolute rates of gestational diabetes were greatest in Asian and Indian people [39].

i. Family history of Diabetes:

Lee et al. and Moosazadeh et al. conducted systematic studies that revealed inconsistency that cause of GDM chance for "family history of diabetes" is an one factor [40]. According to Retnakaran et al., there is a 2.9-fold higher incidence of GDM with a family background of diabetes than in people without one, which accounts for 38.1% of GDM cases. A recent study found 13.2 times more in persons with a history of GDM through many pregnancies than it is in those who have never had the condition, and it is 25.9 times higher in people who have twice as many prior cases of the condition [41].

6. Pathophysiology of gestational diabetes:

GDM is caused by both reduced Beta-cell function and tissue insulin resistance as GDM frequently originates from Beta -cell dysfunction on a background of chronic insulin resistance during pregnancy [42]. Beta cell hypertrophy and hyperplasia in the pancreas help to increase the amount of insulin secreted in response to glucose, which is necessary to maintain glucose homeostasis. Gestational diabetes develops as a result of these adaptive systems' failure to keep glucose levels in control [9].However, compared to Caucasians, Asians exhibit less of an increase in beta cell function in response to increased insulin resistance [43].

a) β-Cell Dysfunction:

Cell dysfunction when beta cell are unable to detect the presence of glucose in the blood and release adequate insulin as a result [44]. Long-term chronic fuel accumulation is assumed to be the root cause of beta-cell malfunction, which leads to unchecked insulin production in response. As pregnancy proceeds, an elevation in regional and placental hormones promotes insulin resistance. The changes in beta cells can happen at any point in the insulin signalling cascade, including during pro-insulin production, post-translational modifications, and insulin signaling-related gene changes. The principal glucose molecule translocator in cell plasma membranes, GLUT4, cannot move glucose molecules when insulin signalling is altered [29]. Additionally, exposure to long-term hyperglycemia in the foetus causes "glycemic memory" in the foetus, which may lead to epigenetic alterations, such as problems with DNA [45].

b) Insulin resistance :

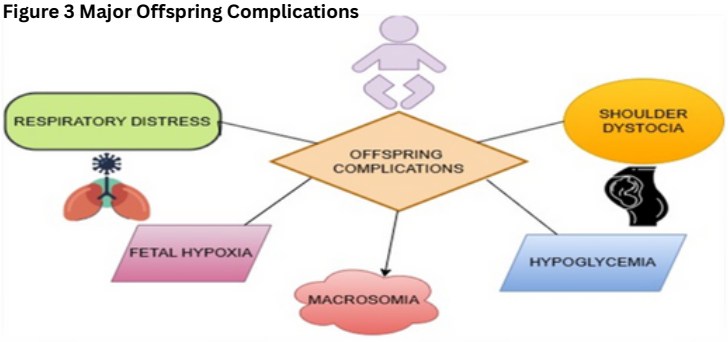
A crucial factor in the emergence of GDM appears to be the subclinical development of IR. In fact, research looking at IR in the 1st trimester of pregnancy shows female who have greater IR in the 1st trimester have high chance to develop GDM at 28 weeks of gestation. Higher chance of GDM at 28 weeks is linked to earlier pregnancy's higher blood insulin levels [46]. Excessive gestational weight gain (GWG), overweight or obesity, a family history of diabetes, a westernized diet, an older mother age, and intrauterine nutrition status are important factors of IR [47].

7. Maternal complications associated with gestational diabetes:

According to the HAPO study, 52% of pregnant females with gestational diabetes, as defined by the International Association of Diabetes and Pregnancy Study Groups [IADPSG] and the 2013 WHO criteria, had impaired glucose metabolism after 10-14 years of follow-up, compared to 20% of pregnant females with normal glucose tolerance [48]. According to Sarli D et al, females with gestational diabetes mellitus may experience labor complications by 2.9 times [49].

Table 3 Major Maternal complications of Gestational Diabetes (GDM)	
Hypertension	It is more common in pregnant female that have GDM than in control pregnant women in one retrospective analysis of 143 GDM women(50).A meta-analysis of 99415 female found that preeclampsia (PE) and gestational hypertension (GH) affect 14% and 9% of future pregnancies, respectively, and may be indications of hypertensive disease recurrence.(51)
Preeclampsia	PE is the medical term for newly detected hypertension with proteinuria or at least one additional organ malfunction that was discovered at or after 20 weeks of pregnancy.(52) The appropriate cause of PE is not known, that is accepted that its primary pathophysiology is vascular endothelial damage brought on by oxidative stress brought on by elevated placental ROS or diminished antioxidant activity.(53)
T2DM	T2DM and GDM are associated. In fact, O'Sullivan and Mahan reported in 1964 that in pregnancy, glucose thresholds on the 3-hour one hundred grams oral glucose tolerance test (OGTT) might forecast a female may develop T2DM in the years that followed, therefore creating the first diagnostic criteria for GDM.(54) According to a population-based study, women with a history of GDM had an 18.9% chance of developing type 2 diabetes within 9 years of the index pregnancy, while the control group of women without a history of GDM only had a 2% chance.(55)
Polyhydramnios	Polyhydramnios that is defined as an elevation in amniotic fluid during pregnancy. Women who experienced polyhydramnios were more likely to give birth through caesarean section. The primary risk factors for polyhydramnios include gestational diabetes as well as type 2 diabetes. Neonatal birth weights over 2.5 kilograms and higher rates of NICU hospitalization were risks for neonates born to mothers with polyhydramnios.(56)
Cancer	In GDM higher levels of insulin-like growth factor 1, which may promote uncontrolled cell proliferation and malignancy. According to Yun-Shing Peng et al. in comparison to the non-GDM group, the rates of cancer development were noticeably high in women with GDM.(57) Gestational diabetes in mother all seem to be linked to childhood cancer in the offspring. Acute lymphoblastic leukemia (ALL) is the malignancy for which the link between maternal diabetes and pediatric cancer is most conclusive.(58)
Chronic kidney disease	In high-income nations, it is estimated that 3% of pregnant women have chronic kidney disease (CKD).As maternal age and obesity increase, it is expected that the prevalence of CKD in pregnancy would grow.(59) BUN may be a possible indicator of GDM since higher BUN levels in the 1st trimester of pregnancy were associated to higher chance of GDM(60)

Figure 3 Major Offspring Complications



The most common fetal complication was found to be macrosomia. The major reason of this weight rise is the mother's insulin resistance, since more glucose flows through the placenta to enter the fetal circulation, and the additional glucose is stored as body fat in the fetus, resulting in macrosomia [61] . GDM female are more likely to have a history of early foetal loss, and GDM may be the connection between spontaneous abortions, PCOS, and insulin resistance [62]. In short term risk elevated mother glucose levels were linked to higher incidence of LGA, shoulder dystocia or birth damage , new born hypoglycemia in the HAPO research. Recent findings indicating greater glucose-linked hypothalamus activity in kids aged seven to eleven years who had previously been sensitised in utero to mother's obesity and GDM, which indicated a higher ultimate BMI , suggests a plausible explanation for this elevated childhood obesity risk [63].

8.Management of Gestational Diabetes:

1.1. Lifestyle modifications

A. Dietary therapy

Understanding how nutrition affects blood sugar is crucial for avoiding including caesarean sections, delivery difficulties, LGA babies, and type 2 diabetes. Special attention should be paid to carbohydrate consumption [64]. The diet should be calorie-sufficient and tailored to the nutrient needs of pregnancy. Suggested nutritional distribution: 40–50% Carbohydrates.20% protein.Fat: 30–35%.

B. Glucose monitoring

Constant Glucose tracking the first trimester's potential clinical value for predicting GDM and unfavourable pregnancy outcomes, especially in people who are overweight or obese [65]. Fasting glucose of 95 mg/dL (or 90 if attained without hypoglycemia), 1-hour post-prandial glucose of 140, and 2-hour post-prandial glucose of 120 are all glycemic objectives [9].

C. Physical Activity

Physical activity improves glycemic management and improve insulin sensitivity through enhanced muscle glucose absorption and reducing excessive GWG. The American Diabetes Association (ADA) advises 20-50 minutes of moderate intensity physical activity each day, 2-7 days per week [66].

2.1 Drug Therapy

When lifestyle measures fail to achieve blood glucose objectives, the inclusion of glucose-lowering treatment is suggested. In the United States and Canada, insulin is used as the 1st line pharmacological therapy for GDM; however, oral medication is preferred in the United Kingdom until blood glucose levels are exceedingly high [67].

1) ORAL HYPOGLYVEMIC AGENTS

Oral medicines are not advised as the first line of treatment for persistent hyperglycemia in individuals with GDM since their potential long-term consequences on neonatal outcomes have not been sufficiently investigated. Oral medicines may be provided to patients who refuse or are unable to receive insulin.

1. Glyburide :

Starting at 2.5 mg daily or every 12 hours, glyburide is gradually increased to a maximum of 10 mg twice day, depending on glycemic control. However, there is a risk of shoulder dystocia and the requirement for a caesarean delivery due to neonatal hypoglycemia and larger birth weight [68].

2. Metformin:

Metformin is an affordable oral medication for insulin resistance that has benefits over insulin, such as preventing hypoglycemia and weight gain. Unlike insulin or glyburide, metformin lowers the risk of newborn hypoglycemia and macrosomia in GDM while reducing maternal weight gain and gestational hypertension [69]. Take 500 mg with food once or twice a day to start. To reach glycemic targets, raise every 1-2 weeks, up to a maximum of 2,500 mg [70].

3.Insulin Regime

Researches show insulin therapy as the safest type of treatment, and OAD (orally administrated medications) treatment should be started only in the case of the patient's lack of consent to insulin therapy or its unavailability [71]. It is the first-choice medication for treating gestational diabetes mellitus because it effectively regulates blood sugar levels [72]. The dosage and timing of insulin delivery for individuals who need it are determined by the patient's body weight, gestational age, and the time of day when hyperglycemia is happening. After starting, insulin dosages are regularly modified during pregnancy in response to blood glucose readings, hypoglycemic symptoms, physical activity, food intake, infection, and adherence. Short-acting insulin has been shown to raise the risk of hypoglycemia and may result in changes in glycemic control in people with GDM. While lispro has been linked to higher birth weight and a higher incidence of big for gestational age newborns, recent experience with aspart has been comforting [68]. Women who only experience hyperglycemia during the morning fasting state should get a single dosage of intermediate insulin, such as NPH or detemir, before bed. Rapid-acting insulin should be taken before a meal in women who have postprandial hyperglycemia after just certain meals. A combination of intermediate- or long-acting and short-acting insulin should be used to treat women who experience hyperglycemia during the day. The daily dose of insulin should be 0.7–1.0 units/kg, with rapid-acting insulin administered prior to meals and intermediate- or long-acting insulin administered in the morning or before bed [73].

2) VITAMINS

The most widely utilized nutrient in the therapy of GDM is vitamin D; yet, there is ongoing debate on how vitamin D supplementation affects glycemic control in GDM. Vitamin D supplementation has been shown in several studies to improve glycaemia in women with GDM [74] Vitamin B12 deficiency (serum vitamin B12 concentration 150–220 pmol/L) was linked to an elevated risk of GDM in different studies including the most current one with 4,746 samples [75]. GDM is more strongly linked to abnormalities in serum folic acid and vitamin B12. A vital vitamin during pregnancy, folic acid plays a role in DNA methylation and the manufacture of proteins and nucleic acids needed for cell division and foetal development [76].

3)INOSITOLS

The majority of plant and animal cells create inositol, a carbocyclic polyol that accumulates in the kidneys, brain, liver, placenta, and other organs. Inositol promotes cell signaling and is involved in a range of physiological functions such as glucose and calcium metabolism, endocrine control, and the stress response. Myoinositol (MI) and D-chiro inositol (DCI) are the most frequent and therapeutically relevant forms found in nature and food. MI and DCI have insulin-like properties that aid in glycemic management. Supplementing Myoinositol 2000 mg with folic acid 200 mcg BD in early pregnancy (12-13 weeks of gestation) has been proven to decrease the effect of GDM in at-risk female [77].

4)PROBIOTICS

In GDM counteract the impact of abnormal indigenous microbiota, as well as the secretion of pro inflammatory mediators like as leptin. As a result, as noted in a clinical study, certain probiotics utilized as dietary adjuncts to lower the chance of disorders such as GDM that are linked with changed gut microbiota composition, elevated intestinal permeability, or altered immunological or metabolic balance. Indeed, the effect of probiotics on GDM may be stronger in a high-risk group (e.g., obesity) [78].In women with GDM, probiotic supplementation may improve blood pressure, oxidative stress, inflammation, glucose metabolism, and lipid profiles. Gut dysbiosis may also play a role in the pathophysiology of GDM by promoting changes in metabolic processes like insulin resistance, glucose intolerance, inflammation, oxidative stress, and hormone dysregulation, including GLP-1 [79].

Current gaps in gestational diabetes research:

The precise OGTT method is a significant research gap since the Hyperglycemia and Adverse Pregnancy Outcomes Study (HAPO) indicated that a single step glucose tolerance test (75 g 2 h OGTT) in the late second and early third trimesters achieved a superior positive result. However, the American College of Obstetricians and Gynaecologists and the American Diabetes Association currently accept the standards for the two-step process (the 100 g 3-hour OGTT is carried out after the 50 g glucose challenge test).The relative efficacy, safety, acceptability, and long-term results of oral hypoglycemic and insulin treatment remain unknown. This has caused authorities to disagree and patients and clinicians to be confused. Future research should compare therapy while evaluating both mother and baby outcomes.

CONCLUSION

This review article gives an in-depth look at gestational diabetes, including its the field of epidemiology risk factors, diagnosis, treatment, and influence on mother and fetal health. The current literature synthesis demonstrates that gestational diabetes is a complicated and multifaceted illness with potential future effects for both maternal and neonates. The study emphasizes the importance of early identification and intervention, since prompt care can lead to better results and lower the risk of problems throughout pregnancy and afterwards. Furthermore, it emphasizes the significance of a multidisciplinary approach comprising healthcare practitioners, nutritionists, and educators in providing optimal treatment to

pregnant women with gestational diabetes .While there has been progress in understanding and controlling gestational diabetes, there are still certain areas that require additional research. Continued research into personalized treatment options, the role of genetics in disease progression, and the possible influence of the microbiome on gestational diabetes is warranted. It is important to conduct a randomized controlled study to see if utilizing real-time CGM during pregnancy in patients with GDM improves maternal and baby results. Furthermore, the use of insulin pumps or new insulin formulations such as fast-acting insulin aspart, which may assist certain women with GDM, has not been studied in this population. It is envisaged that future studies in the field of GDM will result in the normalization of women's and their offspring's short- and long-term results.

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Multi-Lingual Abstracts

Abstract in عربى (Arabic)

ملخص

يُعرّف سكري الحمل بأنه ارتفاع سكر الدم الذي يحدث لأول مرة أثناء الحمل. تتزايد حالات سكري الحمل عالميًا بوتيرة مثيرة للقلق، لا سيما في دول جنوب آسيا. ويرتبط بنتائج سلبية على الأم والوليد. سيساعدنا فهم عوامل الخطر العديدة، والعمليات الفيزيولوجية المرضية، والمكونات الجينية لسكر الحمل في تحديد النساء المعرضات للخطر، ووضع استراتيجيات وقائية فعالة، وتوفير إدارة سليمة للمرض. تكمن المشكلة الرئيسية في غياب توافق آراء ممارسي الرعاية الصحية حول إجراءات الفحص. تُلخص هذه المقالة الشاملة المعارف المتوفرة والتطورات الحالية في مجال سكري الحمل، بهدف توفير فهم شامل لفيزيولوجيا المرض، وعوامل الخطر، وتشخيصه، وعلاجه، وتأثيره على صحة الأم والجنين. كما تُركز على الطبيعة المعقدة لسكري الحمل من خلال دراسة شاملة للأبحاث الحالية، واكتشاف عوامل خطر مهمة مثل العمر، والتاريخ العائلي، والسمنة. وتُوصف أدوات التشخيص، بما في ذلك اختبارات تحمل الجلوكوز الفموية، والتطورات في تقنيات الفحص، في سياق الكشف المبكر والتدخل في الوقت المناسب. وتُناقش استراتيجيات المراقبة الذاتية لتركيزات الجلوكوز في الدم، والعلاج بالغذاء، والأدوية الفموية، وحقن الأنسولين. ويهدف المقال الرئيسي إلى تخفيف عبء سكري الحمل، وتمهيد الطريق لحالات حمل أفضل، وللأجيال القادمة، والتفاني المستمر في تحسين صحة الأم والطفل.

الكلمات المفتاحية:

سكري الحمل (GDM)، مقاومة الأنسولين، خلل خلايا بيتا

Abstract in اردو (Urdu)

خلاصہ

حمل کی ذیابیطس mellitus (GDM) کو ہائپرگلیسیمیا کے طور پر بیان کیا جاتا ہے جو حمل میں پہلی بار ہوتا ہے۔ عالمی سطح پر حاملہ ذیابیطس میلیتس (GDM) کے واقعات خاص طور پر جنوبی ایشیائی ممالک میں تشویشناک رفتار سے بڑھ رہے ہیں .اس کا تعلق زچگی اور نوزائیدہ بچوں کے ناموافق نتائج سے ہے۔ بہت سے خطرے والے عوامل، پیتھو فزیولوجیکل عمل اور جی ڈی ایم کے جینیاتی اجزاء کو سمجھنا خطرے میں پڑنے والی خواتین کی شناخت، مؤثر روک تھام کی حکمت عملی تیار کرنے، اور بیماری کا مناسب انتظام فراہم کرنے میں ہماری مدد کرے گا۔ بنیادی مسئلہ اسکریننگ کے طریقہ کار پر ہیلتھ کیئر پریکٹیشنرز کے درمیان اتفاق رائے کی عدم موجودگی ہے۔ یہ جامع مضمون حاملہ ذیابیطس کے میدان میں موجودہ علم اور موجودہ پیش رفتوں کی ترکیب کرتا ہے، جس کا مقصد اس کی پیتھوفیسولوجی، خطرے کے عوامل، تشخیص، علاج، اور زچگی اور جنین کے نتائج پر اثر و رسوخ کی مکمل تفہیم فراہم کرنا ہے کیونکہ یہ حاملہ ذیابیطس کے پیچیدہ خطرے پر زور دیتا ہے جیسا کہ ایک مکمل تحقیق کے ذریعے خاندانی تاریخ کے اہم معائنے، موجودہ عمر کے مختلف معائنے کے ذریعے۔ موٹاپا، تشخیصی ٹولز، بشمول زبانی گلوکوز رواداری کے ٹیسٹ، اور اسکریننگ کی تکنیکوں میں پیش رفت کو ابتدائی شناخت اور بروقت مداخلت کے تناظر میں بیان کیا گیا ہے۔ خون میں گلوکوز کے ارتکاز کی خود نگرانی کرنے کی حکمت عملیوں اور خوراک، منہ کی دوائیوں اور انسولین کے انجیکشن کے ساتھ علاج پر بات کی گئی ہے۔ اس کا بنیادی مقصد حمل ذیابیطس کے بوجھ کو کم کرنا اور بہتر حمل اور آنے والی نسلوں کے لیے راہ ہموار کرنا اور ماں اور بچے کی صحت کو بہتر بنانے کے لیے مسلسل لگن دینا ہے۔

کلیدی الفاظ:

حملاتی ذیابیطس میلیتس (GDM)، انسولین مزاحمت، β-خلیہ کی خرابی

Abstract in 中国人 (Chinese)

抽象的

妊娠糖尿病（GDM）定義為懷孕期間首次出現的高血糖。全球妊娠期糖尿病 (GDM) 發生率正以令人擔憂的速度增長，尤其是在南亞國家。它與不良的產婦和新生兒結果有關。了解 GDM 的許多風險因素、病理生理過程和遺傳成分將有助於我們識別高風險女性、制定有效的預防策略並提供適當的疾病管理。主要問題是醫療保健從業者對篩檢程序缺乏共識。這篇綜合性的文章綜合了妊娠期糖尿病領域的現有知識和當前發展，旨在全面了解其病理生理學、風險因素、診斷、治療以及對母嬰結果的影響，通過詳盡檢查當前研究強調妊娠期糖尿病的複雜性，發現年齡、家族史、肥胖等重大風險變量，診斷工具（包括口服葡萄糖耐量測試）以及在早期篩選技術的發展，並在早期識別和及時描述的背景下進行描述。討論了自我監測血糖濃度的策略以及透過食物、口服藥物和胰島素注射進行治療的策略。其主要目的是減輕妊娠糖尿病的負擔，為更好的懷孕和子孫後代鋪平道路，並持續致力於改善母嬰健康。

關鍵字：

妊娠糖尿病（GDM）、胰島素抗性、β細胞功能障礙

Résumé **Abstract in française (French)**

Le diabète gestationnel (DG) se définit par une hyperglycémie survenant pour la première fois pendant la grossesse. Les cas de diabète gestationnel (DG) se multiplient à un rythme inquiétant dans le monde, notamment dans les pays d'Asie du Sud. Ce diabète est associé à des complications maternelles et néonatales. Comprendre les nombreux facteurs de risque, les processus physiopathologiques et les composantes génétiques du DG nous aidera à identifier les femmes à risque, à développer des stratégies préventives efficaces et à assurer une prise en charge adaptée de la maladie. Le principal problème réside dans l'absence de consensus parmi les professionnels de santé sur les procédures de dépistage. Cet article complet synthétise les connaissances existantes et les avancées actuelles dans le domaine du diabète gestationnel. Il vise à mieux comprendre sa physiopathologie, ses facteurs de risque, son diagnostic, son traitement et son influence sur l'évolution maternelle et fœtale. Il met en évidence la complexité du diabète gestationnel grâce à un examen exhaustif des recherches actuelles, à l'identification de variables de risque significatives telles que l'âge, les antécédents familiaux, l'obésité, ainsi qu'à la description des outils diagnostiques, notamment les tests d'hyperglycémie provoquée par voie orale, et à l'évolution des techniques de dépistage, dans le cadre d'une identification précoce et d'une intervention rapide. Les stratégies d'autosurveillance glycémique et le traitement par l'alimentation, les médicaments oraux et les injections d'insuline sont abordés. L'objectif principal est d'alléger le fardeau du diabète gestationnel et d'ouvrir la voie à de meilleures grossesses pour les générations futures, ainsi qu'à un engagement continu en faveur de l'amélioration de la santé maternelle et infantile.

Mots clés :
Diabète sucré gestationnel (DSG), résistance à l'insuline, dysfonctionnement des cellules bêta

Аннотация **Abstract in русский (Russian)**

Гестационный сахарный диабет (ГСД) определяется как гипергликемия, которая возникает впервые во время беременности. Во всем мире случаи гестационного сахарного диабета (ГСД) растут тревожными темпами, особенно в странах Южной Азии. Это связано с неблагоприятными исходами для матери и новорожденного. Понимание многочисленных факторов риска, патофизиологических процессов и генетических компонентов ГСД поможет нам выявить женщин из группы риска, разработать эффективные профилактические стратегии и обеспечить надлежащее лечение заболевания. Основной проблемой является отсутствие консенсуса среди врачей по процедурам скрининга. Эта всеобъемлющая статья синтезирует существующие знания и текущие разработки в области гестационного диабета с целью предоставления полного понимания его патофизиологии, факторов риска, диагностики, лечения и влияния на исходы для матери и плода, поскольку она подчеркивает сложный характер гестационного диабета посредством исчерпывающего изучения текущих исследований, нахождения значимых переменных риска, таких как возраст, семейный анамнез, ожирение, диагностических инструментов, включая пероральные тесты на толерантность к глюкозе, и разработок в методах скрининга, описанных в контексте раннего выявления и своевременного вмешательства. Обсуждаются стратегии самостоятельного контроля концентрации глюкозы в крови и терапии с помощью пищи, пероральных лекарств и инъекций инсулина. Ее главная цель — уменьшить бремя гестационного диабета и проложить путь к лучшей беременности и для будущих поколений и постоянной преданности делу улучшения здоровья матери и ребенка.

Ключевые слова:
Гестационный сахарный диабет (ГСД), резистентность к инсулину, дисфункция β-клеток

Resumen **Abstract in español (Spanish)**

La diabetes mellitus gestacional (DMG) se define como la hiperglucemia que se presenta por primera vez durante el embarazo. Los casos de diabetes mellitus gestacional (DMG) están aumentando a un ritmo preocupante a nivel mundial, especialmente en los países del sur de Asia. Esta enfermedad se relaciona con resultados desfavorables para la madre y el recién nacido. Comprender los numerosos factores de riesgo, los procesos fisiopatológicos y los componentes genéticos de la DMG nos ayudará a identificar a las mujeres en riesgo, desarrollar estrategias preventivas eficaces y brindar un manejo adecuado de la enfermedad. El principal problema es la falta de consenso entre los profesionales de la salud sobre los procedimientos de cribado. Este artículo exhaustivo sintetiza el conocimiento existente y los avances actuales en el campo de la diabetes gestacional, con el objetivo de proporcionar una comprensión completa de su fisiopatología, factores de riesgo, diagnóstico, tratamiento e influencia en los resultados maternos y fetales, enfatizando la complejidad de la diabetes gestacional mediante un análisis exhaustivo de la investigación actual, encontrando variables de riesgo significativas como la edad, los antecedentes familiares, la obesidad, las herramientas diagnósticas, incluyendo las pruebas de tolerancia oral a la glucosa, y los avances en las técnicas de cribado, que se describen en el contexto de la identificación temprana y la intervención oportuna. Se discuten estrategias para el autocontrol de la glucemia y la terapia con alimentos, medicamentos orales e inyecciones de insulina. El objetivo principal es reducir la carga de la diabetes gestacional y allanar el camino hacia mejores embarazos, así como para las futuras generaciones y la dedicación continua a la mejora de la salud maternoinfantil.

Palabras clave:
Diabetes mellitus gestacional (DMG), Resistencia a la insulina, Disfunción de las células β