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გესტაციური შაქრიანი დიაბეტის რისკ ფაქტორების მრავალფეროვნება

ევროპის უნივერსიტეტი; საქართველოს ეროვნული უნივერსიტეტი/სეუ; დიაბეტის კვლევის ეროვნული ცენტრი; საქართველოს დეა კავშირი; საქართველოს აგდ ალიანსი

რეზიუმე

შესავალი: გესტაციური შაქრიანი დიაბეტი (გშდ) მსოფლიოში ორსულობის ერთ-ერთ ყველაზე გავრცელებულ გართულებას წარმოადგენს. ორსულობის დროს დედის ჰიპერგლიკემიის ფონზე ყოველი 5 ცოცხლად შობილიდან ერთი ვითარდებოდა, გშდ-ზე მოდის შემთხვევათა 75%-90%. გშდ არის მდგომარეობა, რომელიც ორსულობის დროს პირველად ვლინდება და ძირითადად მშობიარობის შემდეგ ქრება.

დისკუსია: გარემოს, სოციალურ-ეკონომიკური და ინდივიდუალური რისკის ფაქტორები წამყვან როლს თამაშობენ გშდ-ის გლობალურ ზრდაში. გარემოს რისკის ფაქტორები გავლენას ახდენს ნაწლავის მიკრობიომზე, იწვევს ჟანგვით სტრესს, ანთებას, ინსულინრეზისტენტობას, ნეირო-ჰორმონალურ და β-უჯრედების დისფუნქციას და ეპიგენეტიკურ მოდიფიკაციას და იწვევს გშდ-ს და მის ახლო და შორეული გართულებების რისკის ზრდას. სხვა ისეთი ფაქტორები, როგორიცაა, ქუჩის ხმაური და ხელოვნური განათება, იწვევს ძილის და ცირკადული რიტმის დარღვევებს, რაც ზრდის გშდ-ს რისკს. სოციალურ-ეკონომიკური რისკი: დედის დაბალი სოციალურ-ეკონომიკური სტატუსი დაკავშირებულია გშდ-ის მაღალ რისკთან. ინდივიდუალური რისკები იყოფა შექცევად და შეუქცევად რისკის ფაქტორებად. რაც უფრო მეტი რისკის ფაქტორი აქვს ქალს, მით უფრო მაღალია გშდ-ის განვითარების რისკი. არადიაგნოსტირებული და არანამკურნალევი გშდ ასოცირდება დედის და ნაყოფის გართულებების ფართო სპექტრთან.

დასკვნა: სკრინინგი, მკურნალობა და მართვა აუცილებელია. მიუხედავად იმისა, რომ გშდ-ის სრული პრევენცია შეუძლებელია, არსებობს რისკის შემცირების სხვადასხვა გზა. შექცევადი გარემოს, სოციალურ-ეკონომიკური და ინდივიდუალური რისკის ფაქტორების აღმოფხვრა მნიშვნელოვანია გშდ-ის გავრცელების ზრდის შესაჩერებლად.

Introduction: According to the UNO and WHO, four basic non-communicable diseses (NCDs) are: cardiovascular diseases (CVD), diabetes mellitus (DM), including gestational diabetes (GDM), cancer and chronic respiratory diseases. All NCDs are programmed and imprinted during pregnancies. Thus, hyperglycemia during pregnancy can change the fetal programming with metabolic complications in adult life!

GDM is one of the three main types of DM, it is one of the most common complications during pregnancy globally. One in 5 live births is affected by hyperglycemia in pregnancy, and 1 in 6 is affected specifically by GDM. Its prevalence varies from less than 3% (Norway/2% and Sweden/2.5%) to more than 20% (Spain/37.6%, Malaysia/27.3%, Thailand/26.5%, Germany/26.1%, India/26.1%, UK/23.1%, South Korea/21%, Vietnam/21%) [1,4].

Classification: According to WHO and the International Federation of Gynaecology and Obstetrics (FIGO)/ International Diabetes Federation (IDF) Joint Statement (2018), hyperglycemia in pregnancy (HIP) can be classified as pregestational diabetes, gestational diabetes (GDM) or diabetes in pregnancy (DIP) [2,3].

Pre-gestational diabetes (pre-GDM) is type 1, type 2 or other rarer forms of diabetes that were diagnosed in pregnant women before conception. DIP is hyperglycemia first diagnosed during pregnancy, meeting

the WHO criteria of diabetes in non-pregnant women. Available data indicate that in 2024 globally there were 23.3 million life birth affected by maternal hyperglycemia during pregnancy; 79.2% of HIP cases were due to GDM, 11% - due to pre-GDM, and 9.9% - due to DM (type1/type2) first detected prior to pregnancy [4]. GDM may occur at any time during pregnancy and, generally, disappears after the baby is born. Though, the risk of developing T2DM in the future life or GDM in next pregnancies remains very high.

What Is GDM? The World Health Organization (WHO) defines GDM as "any level of the early or first detection of glucose intolerance in pregnancy". GDM is a non-communicable disease, affecting pregnant women, it is a condition in which human placental lactogen (HPL) prevents the body from using insulin effectively. It leads to hypergycemia and to gestational diabetes. GDM is a condition in which a woman without diabetes develops high blood sugar levels, that is first diagnosed during pregnancy and, generally, resolves at birth. There are 2 types of GDM which are categorized based on the treatment required to keep blood sugar levels in an optimum range: 1) *A1GDM* - known as "diet-controlled gestational diabetes," (it can be managed without medication), and 2) *A2GDM* - this type needs to be treated with medicine [5]. Although the cause of GDM is not known, there are some theories as to why the condition occurs. And risk factors, without doubt, play an important role.

What Are the Risks Factors Associated with GDM? The environmental, socioeconomic and individual risk factors associated with GDM play pivotal role, causing constant global rise of GDM prevalence over the past two decades, and are associated with the wide range of maternal and fetal/child short-term and long-term complications [6].

GDM and Environmental Risk Factors: Experimental studies suggested that the potential biological mechanisms of environmental pollutants**,** such as ratio of grey space-to-green space, buildings and city planning,walking and recreation spaces; food environment; soil and water pollution, air pollution with, such polutants as oxinitrides; climate factors (seasons, high seasonal ambient temperature, hot weather); chemicals and metals in sea food; persistent organic pollutants - all affect gut microbiome, cause oxidative stress, inflamation, insulin resistance, neurohormonal and β-cell dysfunction, and epigenetic modification, leading to an increased risk of GDM, and its short-term and long-term complications [7]. Bisphenol A (BPA) is an endocrine-disruptor, that is used in the production of polycarbonate plastics. There is evidence that maternal exposure to BPA even among pregnant women of normal weight, is associated with the increased risk of GDM [8-12]. Artificial light and street noise are "*neglected pollutants*" that cause significant damage to human, mainly, woman's health; noise affects upto 40% of the population; light pollution causes circadian rhythm and sleep disorders, disrupts glucose metabolism may be associated with GDM risk. [13]

GDM and Socio-Economic Risk Factors: According to results from the Generation R Study, low maternal educational level promoted the development of GDM [14,15]. An Italian study from Turin found that mothers with low socioeconomic position (a composite index assessing educational level and employment) were at a higher risk of developing GDM [16].

GDM and Individual Risk Factors: The leading individual risk factors of GDM are: age ≥35 years; high BMI prior pregnancy (>25 kg/m²); gaining too much weight (>10kg) in the 1-st trimester of the current pregnancy; family history of type 2 DM/GDM (in the 1-st-degree relatives); pre-diabetes; history of GDM, previous infant with birth weighing >4000 g, previous stillbirth and/or recurrent abortions (>3 in previous pregnancies), fetal malformations, preterm delivery (<37 gestational week), Cesarean section, multiple pregnancy (2-3 fetuses); HbA1c >5.7; dyslipidemia (low HDL-CH,TR >200 mg/dl); hypertension

(chronic and pregnancy induced); conditions associated with insulin resistance; polyhydramnios; glucocorticoid administration, etc.

Such individual, habbitual risk factors as low physical activity, stress of any form and smoking play important role in the development of all non-communicable diseases, including GDM! [17-19]. Smoking specifically causes insulin resistancet, leading to obesity and pre-diabetes, thus aggrevationg the risk of GDM. It carries triple risk: for a woman, especially, pregnant one; fetus, and future generations [20]. The more risk factors a woman has, the higher is the risk of developing GDM. In the presence of multiple risk factors, supervision by a multidisciplinary team is required. Supervision should be initiated well before conception.

Hyperglycemia in Pregnancy and Maternal Age: Risk of hyperglycemia during pregnancy increases with maternal age, reaching its peak at the age of 45-49 years (42.3%). Since the majority of pregnancies and births occur at <30 years of age, (46.3%, or 9.8 million) the most cases of hyperglycemia in pregnancy occurs in this age group. One of the meta-analyses, published in 2020, demonstrates that the risk of GDM increases linearly with successive age-groups [21]. Though, in the last decades, there is an increase in the number of primigravida aged 35years and older.

Risks Categories of GDM: Risk of GDM development falls into three categories: 1) high risk (pre-diabetes, history of GDM, pre-existing CVD, obesity (BMI ≥30 kg/m²); 2) moderate risk (unhealthy lifestyle, smoking, family history of DM, hypertension, PCOS, MASLD, low socio-economic status, age >45 years); 3) low risk (age <45 years, with absence of the any above)

GDM and Conditions, That Increase the Risk of GDM:

Duration and Quality of Sleep - Evidence demonstrates that sleep disorders may increase pregnancy complications including GDM. Obstructive sleep apnea (OSA) is the most common form of sleep-disordered breathing, that increases the risk of GDM. There is Association between poor sleep quality and GDM, though it is not yet proved whether improved sleep duration and/or quality will result in amelioration of glucose metabolism [22-24].

Vitamin D Deficiency – VitD deficiency has been increasingly recognized as a potential risk for GDM. The relation between GDM and VitD level seems to be a two-way street - its low values appear to increase the risk GDM; while women with GDM were more likely to experience VitD deficiency compared to those with normal Vit D levels [25-28].

GDM and Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD): There is a bilateral positive association between MASLD and GDM: some studies reported that MASLD risk is significantly higher in women with GDM; still others reported that GDM risk was substantially higher in women, who, independent of their BMI (normal or elevated) were diagnosed with MASLD. GDM is associated with increased postpartum risk for MASLD [29,30].

Feto-Maternal Complications of GDM: GDM is associated with a wide range of both maternal complications during pregnancy, labor, postpartum and beyond, and fetal congenital and neonatal complications and poor long-term outcomes [31].

Feto-Maternal Outcomes of GDM and the Role of GDM Screening: GDM is a major pregnancy complication associated with increased morbidity and mortality for the mother, fetus and baby. A fetal and neonatal mortality rate was as high as 65% before the development of specialized maternal and neonatal care. Undiagnosed and untreated GDM leads to adverse pregnancy outcomes.

Thus, the purpose of screening, treatment, and management of GDM is to: 1) reduce maternal, fetal and newborn mortality and morbidity; 2) reduce its risk in women with GDM in anamnesis; 3) prevents the transmission of DM and metabolic disorders from one generation to another.

Prevention of GDM: GDM is not totally preventable, but there are ways to help lower the risk! Control and elimination of environmental and socioeconomic risk factors comprise population strategy and are the responsibility of the State and Government [18]. High-risk strategy is aimed at high-risk population. Elimination of reversible individual risk factors, such as obesity, waist circumference, unhealthy diet, physical inactivity, smoking, etc. are mostly the responsibility of each individual.

Measures to reduce potential risks of GDM development include: 1) elimination of reversible individual risks means; 2) maintenance of healthy body weight; 3) in case of overweight, losing 5-7% of body weight; 4) if woman's condition allows, performing regular physical activity; 5) healthy eating; 6) blood sugar testing as early as three months before conception, if a woman with history of GDM is planning a pregnancy; 7) planning of each next pregnancies, if a woman had GDM in a prior pregnancy; 8) if GDM risk factors are present, screening tests should be performed in the first trimester to see if the condition has developed again.

According to 2019 Research Trusted Source, it is recommended to influence individual risk factors around pregnancy [32]. The best time to lower the risk of GDM and make lifestyle changes is during family planning or long way before getting pregnant!

Treatment of GDM: If during screening GDM is revealed, treatment should be initiated immediately! Treatment of GDM includes: special meal plans; scheduled physical activity; daily blood glucose testing (in GDM); insulin injections (in GDM, if needed); metformin (if needed) [33].

Conclusion: Aggressive influence of risk factors, mainly reversible environmental, socio-economic and individual ones, has lead to critical increase in GDM prevalence in high-, middle- and low-income countries. GDM that is not diagnosed, or is diagnosed late, or if proper treatment is nor provided show high feto-maternal morbidity and mortality. Timely and correct screening is essential for prevention of GDM complications and fetal programming in adult life. Though GDM cannot be totally prevented, a lot can be done to lower the risk, as what happens in the womb lasts all life!

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SUMMARY

Background: Gestational diabetes mellitus (GDM) is one of the most common complications during pregnancy globally. One in 5 live births is affected by hyperglycemia in pregnancy (HIP), and 75% to 90% of HIP cases are GDM. GDM is first diagnosed during pregnancy and, generally, resolves at birth.

Discussion: The environmental, socioeconomic and individual risk factors associated with GDM play pivotal role, causing constant global rise of GDM prevalence over the past two decades. Environmental risks affect gut microbiome, cause oxidative stress, inflammation, insulin resistance, neurohormonal and β-cell dysfunction, and epigenetic modification. They might be associated with an increased risk of GDM, and its short- and long-term complications. Other "neglected pollutants" that cause significant damage to human health are street noise and artificial light, light pollution causes circadian rhythm and sleep disorders that increase the risk of GDM. Socio-economic position of a mother is also associated with elevated risk of GDM. Individual risks: there is a large number of individual risks, that can be divided into2 groups: reversible and irreversible ones. The more risk factors a woman has, the higher is the risk of developing GDM. Undiagnosed and untreated GDM is associated with maternal complications during pregnancy, labor, postpartum and beyond, and fetal congenital and neonatal complications and poor long-term outcomes.

Conclusion: Screening, treatment, and management of GDM are essential. Though GDM is not totally preventable, there are ways to help lower the risk: Elimination of the negative effect of reversible environmental, socio-economic and individual risk factors, is important to halt the rise of GDM prevalence in high-, middle- and low-income countries.

Keywords: gestational diabetes mellitus, risk factors, feto-maternal outcomes, screening, prevention