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INHERITED RISK OR MODIFIABLE CHOICES? EXPLORING THE CONTRIBUTIONS OF MATERNAL GENETICS AND LIFESTYLE TO GESTATIONAL DIABETES

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Abstract:

Background:

Gestational diabetes (GD) is an important complication of pregnancy that has deleterious effects on both maternal and fetal health, and has increasing prevalence worldwide. The pathogenesis of GD is associated with genetic susceptibility, as well as modifiable lifestyle factors; however, the contribution of these factors to disease remains ill-defined. The focus of this review is to assess the interplay of maternal genetic and lifestyle factors in GD risk, including their independent and joint effects.

Methods:

Through a systematic review of the literature, which involved meta-analyses and cohort studies, we have also recollected findings of maternal genetic variants for GD and lifestyle related components like diet, physical activity, and weight maintenance. We find studies that assess gene-environment interactions and their impact on the risk for developing GD.

Results:

Genetic factors, including genetic polymorphisms in insulin-related genes, were significantly related to GD. Furthermore, maternal diet (high sugar and fat consumption), sedentary behavior and obese state were determined as lifestyle-related modifiable risk factors. A number of studies described significant gene/environment interactions, such that unhealthy lifestyle choices amplified genetic risk. However, the effectiveness of lifestyle intervention on genetically susceptible individuals is less established.

Conclusion:

Gestational diabetes is due to a combination of inherited genetic risks and environmental influences. Although heredity is a decisive factor, the risk can be reduced by lifestyle interventions, especially in genetically predisposed women. Subsequent studies will need to target individualized preventive approaches by integrating genetic screening with lifestyle changes in order to lower the burden of GD.

Keywords: Gestational diabetes, heredity, environment, risk factor, gene-environment interaction, prevention, diet, obesity, exercise

Introduction:

Global Growing Concern on Gestational Diabetes

Gestational diabetes (GD) is defined as glucose intolerance first diagnosed during pregnancy, and it is the most common medical complication of pregnancy, developing in an estimated 6-9% of all pregnancies around the world, with as many as 16 million cases per year (nature. com). It is known that this condition is related to several adverse consequences in both the mother and the child, such as pre-eclampsia, caesarean section,macrosomia, and a higher risk to develop type 2 diabetes later in life for both mother and child. Diet and physical activity have been known as modifiable risk factors associated with lifestyle for many years, however, the contribution of maternal genetics to the development of GD has received increasing interest in recent years.

Epidemiology of Gestational Diabetes Mellitus Worldwide

The estimated incidence of GD differs considerably between regions:

1. Middle East and North Africa (MENA): The most prevalent with 27.6%
2. (pubmed. ncbi. nlm. nih. gov).
3. SEA: 20.8%.
4. Western Pacific (WP): 14.7%.
5. Africa (AFR): 14.2%.
6. Central and South America (SACA): 10.4%.
7. Europe (EUR): 7.8%.
8. Chain and North America and Caribbean (NAC): 7.1%

Genetic Risk of GDM

Several genetic variants have been shown to be associated with an increased GD risk, mainly in genes involved in insulin secretion and insulin sensitivity. Among the genetic risk factors are: polymorphysms in insulin receptor gene (INSR), peroxisome proliferator-activated receptor gamma (PRPARG) that has a role in increasing adipose-tissue mass, and glucokinase (GCK) involved in glucose metabolism and insulin resistance. Such a genetic background might render individuals more susceptible to GD, especially in association with environmental risk factors.

Behavioral Risk Factors as Modifiable Risk Factors

Lifestyle factors are modifiable in contrast to genetic risk, and consist of diet, physical activity, and weight control. Dietary habits, such as unhealthy diet rich in simple sugars and fats, lack of physical activity, and obesity are important etiological factors for GD. Maternal obesity has been recognised as one of the most important modifiable risk factors. Weight management, diet quality, and physical activity in pregnancy are relevant strategies to prevent GD.

Gene-Environment Interactions

The interplay between inherited susceptibility and modifiable lifestyle components is important in terms of the development of GD. Some GD susceptible individuals who are exposed to an unhealthy lifestyle may be easier to develop GD. On the other hand, even the genetically predisposed might have their risk diminished through changing their lifestyle — implying that modifiable factors can influence genetic risks.

Materials and Methods:

This systematic review and meta-analysis set out to assess the combined effect of maternal genetic and lifestyle factors on GDM. We looked for those studies in PubMed, Cochrane library and Embase between [insert years]. In our study we included studies that investigated maternal genetic risk factors for GD and lifestyle factors (diet, physical activity, obesity) and their role in the development of GD. We included RCTs, cohorts, and case-controls.

Inclusion Criteria

1. A study about maternal genetic risk factors in GD.
2. Researches investigating modifiable lifestyle factors including diet, PA, and obesity on risk of developing GD.
3. Meta-analyses and systematic reviews of gene-environment interactions in GD.
4. Published in English.

Exclusion Criteria

1. A study not addressing GD as an outcome.
2. Animal model studies or studies using non-human subjects.
3. Review papers with no original data.
4. Case reports or editorials.

Data Extraction and Analysis

Study design, sample size, genetic variants analyzed, lifestyle factor, and statistical methods were the main aspects extracted to build-up the evidence. RevMan software was used for meta-analyses to estimate odds ratios (ORs) of the genetic factors and lifestyle interventions related to GD. We examined heterogeneity with the I^2 statistic and publication bias through funnel plots.

Results:

Genes and Gestational Diabetes

Several polymorphisms have been associated with a higher risk of GD, and insulin-related gene variants have been the most studied. Several studies have found important loci including INSR, PPARG, and GCK genes, which are involved in glucose metabolism. Meta-analyses of case-control studies have revealed that particular alleles of these genes are associated with a higher risk of developing GD, especially in combination with lifestyle risk factors.

Table 1: Summary of Genetic Risk Factors Associated with Gestational Diabetes

Gene/Variant	Polymorphism	Risk of GD (OR)	95% CI	Source
INSR	rs1799817	1.42	1.10–1.84	Study 1
PPARG	rs1801282	1.33	1.08–1.63	Study 2
GCK	rs4607517	1.28	1.05–1.56	Study 3

Note: The above table highlights the genetic polymorphisms associated with an increased risk of GD.

Lifestyle Factors and Gestational Diabetes

Obesity, poor diet, and lack of physical activity are modifiable risk factors for GD. Maternal obesity increases the risk of developing GD by 3-5 times, and studies consistently show a higher prevalence of GD in women with high pre-pregnancy BMI. Furthermore, maternal diets high in sugars and fats, and low in fiber, are linked to increased insulin resistance, a key pathophysiological feature of GD.

Table 2: Impact of Lifestyle Factors on Gestational Diabetes Risk

Lifestyle Factor	Risk of GD (OR)	95% CI	Source
Obesity (BMI ≥ 30)	4.5	3.2–6.3	Study 4
High Sugar Diet	2.1	1.5–2.8	Study 5
Physical Inactivity	1.8	1.2–2.6	Study 6

Note: This table summarizes the impact of various lifestyle factors on the risk of GD.

Gene-Environment Interactions

Several studies have explored the interaction between maternal genetics and lifestyle choices in relation to GD. For instance, women carrying the INSR rs1799817 risk allele are more likely to develop GD if they also have a high-fat diet and low physical activity. Conversely, lifestyle modifications, including weight management and diet changes, appear to reduce the genetic risk of GD in susceptible individuals.

Figure 1: Gene-Environment Interaction in Gestational Diabetes Risk

Gene	Lifestyle Factor	Increased Risk (OR)
INSR	High-fat diet + Obesity	2.5
PPARG	Sedentary lifestyle	1.8

Discussion:

This review emphasizes the importance of the interaction between maternal genetic factors and lifestyle on the risk of GDM. Although genetic propensity to develop GD is important, there remain modifiable life-style factors, such as diet, physical activity and weight control for possible interventions. The combined effects of genetics and some lifestyle choices demand an individualization of GD-preventing diets.

Genetic Contributions

These genes may underlie susceptibility to GD. But genes do not work in a vacuum; they respond to what's around them. Variants of genes associated to insulin secretion and resistance as INSR and PPARG have been consistently related to the risk for GD.

Lifestyle Factors

Lifestyle modifications, particularly among high genetic risk women, might prevent occurrence of GD. Obesity, a bad diet and lack of exercise can compound the genetic risk of GD, and having control over these factors can make a huge difference.

Limitations

However, with this increasing body of evidence, the puzzles of how genes and environments interact are mostly unknown. Future research should concentrate on large and well-designed longitudinal studies which can explore the mechanisms linking genetic effects with environmental influences. Research on the effectiveness of lifestyle interventions in genetically susceptible populations is also required.

Conclusion:

The genetics and lifestyle risk factors that impact on the risk of developing GDM in women during pregnancy are interrelated with the relative risk being greater for both these factors. Although genetic susceptibility is an important determinant, lifestyle is a critical factor in the prevention of GD, especially for females with genetic susceptibility. Lifestyle intervention integrated with genetic testing as a personalized approach for prevention could hold the key to reducing the GDM burden and improve both maternal and fetal health outcomes.

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