PREVALENCE AND IDENTIFICATION OF POTENTIAL PREDICTORS ASSOCIATED WITH GESTATIONAL DIABETES MELLITUS IN NORTH MACEDONIA

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is defined as the occurrence of diabetes which is discovered during pregnancy. It is a widespread global condition with many maternal and fetal health risks.

Objective: The aim of this study was to identify the prevalence and potential predictors of GDM among a cohort of women from North Macedonia.

Patients and Method: A total number of 154 (143) participants were included in the study. The diagnosis of GDM was made using the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria. Patients with known diabetes prior to pregnancy, history of GDM, in vitro fertilization (IVF), multiple gestation and severe medical conditions were excluded from the study. The recorded variables were age, nationality, religion, education, parity, family history of diabetes (FHD), pre-pregnancy body mass index (BMI), weight gain, smoking and oral contraceptive use. The statistical analysis was done calculating exact logistic regression in "R".

Results: Significant predictors: For every one-unit increase in BMI, the odds of developing GDM increased by 8.6% (coefficient=0.086, p=0.026). Women with family history of diabetes had 2.74 times higher odds of developing GDM (coefficient=1.008, p=0.011). The Orthodox participants had significantly lower odds of developing GDM compared to the Muslim ones (coefficient=-2.528, p=0.011). Two prior pregnancies raised the odds to 4.70 times higher compared to no prior pregnancies (coefficient=1.547, p=0.042).

Conclusion: The study emphasizes the importance of addressing pre-pregnancy BMI and screening individuals with family history of diabetes. The high prevalence of GDM suggests a need for public health strategies focusing on preconception care, lifestyle interventions and regular screening during pregnancy.

Key Words: *Gestational diabetes mellitus; prevalence; risk factor.*

Introduction

Gestational Diabetes Mellitus (GDM) is a common pregnancy complication that affects a significant number of women, with serious short and long-term health implications, including an increased risk of preeclampsia, preterm birth and macrosomia, as well as the future development of type 2 diabetes in both mothers and children.

Worldwide, the prevalence of GDM ranges from 5% to 25.5% and is dependent on many socio-demographic factors, as well as screening and diagnostic criteria. According to the International Diabetes Federation (IDF), the prevalence of GDM is expected to be on the rise year by year (1).

Since 2013 GDM has been defined as the **development** of diabetes during pregnancy (2). The Scientific Association of Endocrinologist and Diabetologists of Macedonia has accepted the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria (2) shown in Table 1, which are based on the 2008 Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study findings (3).

Table 1. IADSPG criteria:

Glucose measurement	Plasma glucose concentration (mmol/l)
Fasting	≥5.1
1 h	≥10
2 h	≥8.5

GDM is diagnosed if one or more of the following glucose values exceed the threshold during a 75g Oral Glucose Tolerance Test (OGTT) at 24–28 weeks of gestation.

Despite increasing awareness of GDM, studies exploring the predictors of its occurrence, particularly in specific populations, remain limited. Few studies have investigated the role of socio-cultural factors in non-Western populations, leaving a gap in understanding the predictors of GDM in other regions, particularly in Eastern Europe. The majority of the non-Western studies are done among the Asian, African and Middle Eastern population (4–7). This is especially true for North Macedonia (8).

This study seeks to identify the prevalence and some of the predictors of GDM in a cohort of women from Republic of North Macedonia, with an emphasis on demographic, clinical, and socio-cultural factors.

Materials and Method

This cross-sectional study was performed at the Obstetrics & Gynecology office “INA” in Skopje from 01.01. to 31.12.2022. From a total number of 154 consecutive pregnant patients, the ones with a history of GDM in previous pregnancies, IVF, multiple gestation and severe medical conditions were excluded from the study, which left 143 women. The diagnosis of GDM was made using the criteria of the IADPSG after a 75mg OGTT from 24-28 gestational weeks (2).

Their demographic data, past medical, obstetrical and family history, obtained by semi-structured one-on-one, face-to-face interviews included: age, nationality, religion, education, parity, family history of diabetes, pre-pregnancy BMI, smoking, and use of oral contraceptives. The OGTT was done at the "Biotek" laboratory in Skopje. The statistical analysis was done by calculating exact logistic regression in R statistical software.

Results

Out of 143 women who participated in the study, 56 (39.1%) had GDM. The median age was 31 years, with an interquartile range of 7 years. The majority were Macedonian Christian Orthodox (118; 82.5%). More than half of the participants (64.9%) had university education or higher. More than half had none or one child (46.2% and 39.2%, respectively). The family history of diabetes was present in 39.2% and more than half had normal pre-pregnancy BMI (65%). Only 22.4% were still smoking and 45.5% had never smoked. The absolute majority (96.5%) had never used oral contraceptives.

Table 2. Analyzed variables and GDM.

Characteristic	Subjects (total 143)	GDM n=56 (39.1 %)	No GDM N=87 (60.8%)	Exact logistic regression analysis (95%CI) p value
Age				
<30	55 (38.5%)	22 (40%)	33 (60%)	
30-35	59 (41.3%)	24 (40.7%)	35 (59.3%)	p = 0.962
>35	29 (20.2%)	10 (34.5%)	19 (65.5%)	
Nationality				
Macedonian	118(82.5 %)	43 (36.4%)	75 (63.6%)	
Roma	11 (7.7%)	7 (63.6%)	4 (36.4%)	p > 0.05
Albanian	7 (4.9%)	3 (42.9 %)	4 (57.1%)	
Other	7 (4.9%)	3 (42.9%)	4 (57.1%)	
Religion				
Orthodox Cristian	118 (82.5%)	46 (39%)	72 (61%)	
Muslim	20 (14.0%)	10 (50%)	10 (50%)	p = 0.011
Atheist	2 (1.4%)	0	2 (100%)	
Other	3 (2.1%)	0	3 (100%)	

Education				
MSc/Doc.	22	8 (36.4%)	14 (63.6%)	
University	(15.4%)	24	46 (65.7%)	p > 0.05
Secondary school	70 (49%)	(34.3%)	25 (58.1%)	
Primary school	43	18	2 (25%)	
	(30.1%)	(41.9%)		
	8 (5.6%)	6 (75%)		
Parity				
0	66	21	45 (68.2%)	
1	(46.2%)	(31.8%)	35 (62.5%)	p = 0.042
2	56	21	4 (26.7%)	
≥3	(39.2%)	(37.5%)	3 (50%)	
	15	11		
	(10.5%)	(73.3%)		
	6 (4.1%)	3 (50.0%)		
Family history of diabetes type2				
Yes	56	30	26 (46.4%)	p = 0.011
No	(39.2%)	(53.6%)	61 (70.1%)	
	87	26		
	(60.8%)	(29.9%)		
Pre-pregnancy BMI				
Underweight	8 (5.6%)	2 (25%)	6 (75%)	
Normal	93	33	60 (64.5%)	p = 0.026
Overweight	(65.0%)	(35.5%)	17 (54.8%)	
Obese	31	14	4 (36.4%)	
	(21.7%)	(45.2%)		
	11 (7.7%)	7 (63.6%)		
Smoking				
Never	65	26 (40%)	39 (60%)	p = 0.82
Quit	(45.5%)	18 (39%)	28 (61%)	
Yes	46	12	20 (62.5%)	
	(32.2%)	(37.5%)		
	32			
	(22.4%)			
Use of oral contraceptives				
Never	138	53	85 (61.6%)	
Occasionally	(96.5%)	(38.4%)	1 (33.3%)	p > 0.05
>2 years	3 (2.1%)	2 (66.7%)	1 (50%)	
	2 (1.4%)	1 (50%)		

Socio-demographic data, past medical, obstetrical and family history of the participants.

The key findings of the exact logistic regression analysis are as follows:

Significant predictors:

- BMI before pregnancy: Coefficient: 0.086 (p=0.026). This means that a one-unit increase in BMI before pregnancy increases the odds of GDM by ~8.6%.
- Family history of diabetes type 2: Coefficient: 1.008 (p=0.011), which means that the participants with a family history of diabetes have ~2.74 times higher odds of developing GDM.
- Religion: Coefficient: -2.528 (p=0.011). The analysis showed that the Orthodox participants have significantly lower odds of GDM compared to the others.
- Parity: Coefficient: 1.547 (p=0.042). This means that participants with two previous pregnancies have ~4.70 times higher odds of GDM compared to no prior pregnancies.

The following were non-significant predictors:

- Age, nationality, education, smoking and use of oral contraceptives.

The prevalence of GDM in this cohort was 39.2% (95% CI: 31.6% – 47.3%).
Model Fit Interpretation: Likelihood Ratio Test (LRT) p-value: 0.0138; Wald Test p-value: 0.0284 (both are <0.05, thus this logistic regression model has statistical validity).

Discussion

A systematic review and meta-analysis published by Saeedi et al. in 2021 (9) states that worldwide, the prevalence of GDM varies from 1 to 28 %. This is because even when the same diagnostic criteria are used, there are differences depending on population characteristics. Data about the prevalence in the region is very limited. Paulo et al. in 2021 did a meta-analysis and systematic review of GDM prevalence studies in Europe (10) and reported 10.9%. However, in Eastern Europe it was 31.5%. Data about Republic of North Macedonia is very scarce. Papers from Katerniakova et al., Ahmeti et al. and Recica et al., published 2019-2024 have reported data about diabetes type 2 (11–13), but there is no mention of GDM. In 2016 Krstevska et al., analyzed the maternal OGTT levels in relation to large-for-gestational-age newborns and reported a prevalence of 66.1% (14).
In our study the prevalence of GDM was 39.2% (95% CI: 31.6% – 47.3%), which is higher compared to global and regional average. We believe that this is not due to the screening criteria, as the studies we have compared use the same ones. It could be a result of the population characteristics, or the lifestyle factors specific to this region, although we are aware of the fact that because of the sample size, the CI is wider, which suggests that the true prevalence lies in this range. We could not compare our results with similar studies done in our country, except the one by Krstevska et al. which shows even a higher prevalence (14).
Numerous studies have looked for potential predictors of GDM. The most commonly identified predictors are pre-pregnancy BMI (5,15,16). Pre-pregnancy BMI was identified as a significant predictor in our study, as we expected. It is especially worrying that 28.4% of the participants fell into the category of obesity. The percentage of women with a normal BMI was only 37.8%, which shows the necessity for education of women in the reproductive period about the risks of having high pre-pregnancy BMI. The observation that a one-unit increase in BMI before pregnancy increases the odds of GDM by ~8.6%,

highlights the need for pre-conception counseling and weight management programs in the general population of women.

The family history of diabetes type 2 (FHD) is the other variable which has been associated with GDM worldwide. In our study it also emerged as a significant predictor of GDM ($p=0.011$). The patients with positive family history had 2.74 times higher odds of developing GDM compared to those without such a history. This is comparable with many international studies (5,6,17). In 2008 Robitaille and Grant published a review about the genetics of GDM (18).

In our group we found 4.7 times higher odds of developing GDM in women with two previous pregnancies, compared to those with no prior pregnancies. The reports in the literature are not consistent, although there are studies suggesting that increased parity may elevate metabolic stress and insulin resistance, thereby increasing GDM risk (19–21).

Orthodox participants had significantly lower odds of developing GDM compared to others (Coefficient: -2.528). The intersection of religion and GDM has been explored in some studies. Haigh et al. performed a systematic review in 2023 (23) and concluded that women from culturally and linguistically diverse backgrounds (CALD) experienced varying cultural beliefs surrounding food, exercise and pregnancy. In 2021 a study done in Australia with South Asian women (24) found that religious and cultural dietary practices influenced adhering to medical advice. Our findings may reflect unmeasured cultural or lifestyle differences, such as dietary patterns or physical activity, which warrant further investigation. However, we have to acknowledge that 82.5% of our patients were Christian Orthodox. We believe that there is a need for a wider analysis of the differences between the dominant religion groups in our country.

Age was not a significant predictor in our group, which is different from data reported in literature (25). This may be due to the fact that most of the participants fall within a relatively narrow range (IQR = 7 years). Regarding the use of oral contraceptives, we cannot rely on the data about their prediction strength as only 3 participants reported their use.

Data in the literature about the association of maternal education level and GDM are not consistent (25–27). In our study we did not find any association between maternal education level and GDM.

The relationship between smoking and GDM has been the subject of various studies, with mixed results. Bar-Zeev et al. found that prenatal smoking is associated with higher odds of GDM, even after adjusting for known risk factors (28). On the contrary, a systematic review and meta-analysis by Athanasiadou et al. in 2023 found no association of smoking and GDM. In our study smoking was not identified as a predictor for GDM ($p>0.05$).

The exact logistic regression model used in our study demonstrated statistical validity, as evidenced by the Likelihood Ratio Test ($p=0.0138$) and Wald Test ($p=0.0284$). This is one of the strengths of our study, as well as the diverse set of predictors. The limitations are the size of the sample, which is relatively small, as well as the fact that there are confounding factors which are not measured (cultural, dietary, physical activity habits) that can influence some of the predictors (i.e. religion).

Conclusion

This study emphasizes the importance of addressing pre-pregnancy BMI and screening individuals with FHD. The high prevalence of GDM suggests a need for public health strategies focusing on preconception care, lifestyle interventions, and regular screening during pregnancy. Subsequently, identification of high-risk women before pregnancy can be very beneficial for the prevention of potential maternal and neonatal complications resulting from GDM. The results of this initial analysis show the need for further larger studies.

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