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CLINICAL ARTICLE

Obstetrics

The association between interpregnancy interval and gestational diabetes mellitus: A nationwide register-based study in Finland

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Abstract

Objective: Previous results on the association between interpregnancy interval (IPI) and gestational diabetes mellitus (GDM) have been contradictory. Hence, the aim of this study was to examine the association between IPI and GDM using high-quality nationwide register data.

Methods: All women with first and second pregnancies during our study period from the National Medical Birth Register during 2004–2018 were considered. A logistic regression model was used to assess the association between the length of the IPI and development of the GDM in the second pregnancy. Women were divided into three groups based on the length of the IPI: short IPI (0–11 months), normal IPI (12–47 months), and long IPI (48+ months). Adjusted odds ratios (aOR) with 95% CI were compared between the groups.

Results: A total of 47 078 women were included in the study. We found no evidence of difference when women with short IPI were compared with women with normal IPI (aOR 0.99, 95% CI 0.93–1.05). Women with long IPI had increased odds for the development of GDM when compared with women with normal IPI (aOR 1.28, 95% CI 1.19–1.38). In the logistic regression model for continuous IPI, the total odds for the development of GDM increased as the IPI increased (aOR 1.05 per year, 95% CI 1.03–1.06).

Conclusion: The odds for the development of GDM increased as the IPI increased. This study's results serve as a clarion call for proactive measures in GDM prevention. Moreover, they advocate for intensified investigation into the underlying factors contributing to GDM among women with extended IPI. It is imperative that these insights inform both clinical practice and further research agendas, as we strive to safeguard maternal health and well-being.

KEYWORDS
epidemiology, gestational diabetes, pregnancy

1 | INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the major pregnancy complications and affects both the mother and the fetus.[1] It has been estimated, that up to 22% of European parturients might be affected by GDM. In addition to the initial complications of GDM, a substantial proportion of GDM cases initially progress to type II diabetes mellitus.[1]

The risk of developing GDM is multifactorial. The association between the length of time between previous delivery and subsequent pregnancies (interpregnancy interval [IPI]) and the risk of developing GDM has been previously reported by cohort studies from Australia and the USA.[2,3] However, the findings from those studies were not similar, and in addition to the discrepancy between the studies, there were some methodologic differences in the literature, e.g., lack of studies assessing the IPI as a continuous variable. The most recent study suggests that the literature behind this topic is likely to be influenced by background factors of the mothers, which remain stable during the time between pregnancies.[3]

As GDM is a substantial risk factor for other comorbidities and complications, more research on prevention is warranted. As there is no consensus on the association between IPI and the risk of GDM, the objective of this study is to thoroughly examine the association between IPI and GDM using high-quality nationwide register data. Given the contradictory findings in previous research, this study aims to contribute clarity to the existing knowledge by analyzing data from the National Medical Birth Register spanning the years 2004 to 2018. The primary focus is on assessing the relationship between the length of the IPI and the development of GDM in second pregnancies. The study aims to categorize women into three groups based on IPI duration (short: 0–11 months, normal: 12–47 months, long: 48+ months) and to use logistic regression models to determine adjusted odds ratios (aOR) with 95% confidence intervals (CI) for comparing the GDM risk among these groups. The overarching goal is to provide comprehensive insights into the potential impact of IPI on GDM development, offering valuable information for preventive strategies and further research on the underlying factors contributing to GDM, particularly in women with longer IPI.

2 | MATERIALS AND METHODS

In this retrospective cohort study conducted using nationwide register-based data, information from the National Medical Birth Register (MBR), managed by the Finnish Institute for Health and Welfare, was used to examine the correlation between the IPI duration and the likelihood of developing GDM. The MBR is characterized by its high quality and comprehensive coverage, with current coverage reaching nearly 100%.[4,5] The research spanned from January 1, 2004 to December 31, 2018. The MBR encompasses information regarding pregnancies, delivery statistics, and perinatal outcomes for all births with a birthweight of 500 g or greater or a gestational age of 22^{+0} weeks or greater, incorporating details about pregnancy terminations as well.

From 2004 to 2018, Finland recorded a total of 843 466 pregnancies. For our study, we specifically chose women who experienced their first and second pregnancies within this timeframe using the MBR. Among these women, only those who underwent the 75-g 2-h oral glucose tolerance test in both pregnancies were included in our analysis. In Finland, the screening for GDM started in 2004, but the screening methods for GDM changed after 2008 to comprehensive screening, meaning that the GDM testing rates increased towards the end of the study period. Exclusion criteria encompassed women with confirmed GDM in their initial pregnancy ($n = 16\,264$), as a history of GDM serves as a robust indicator for the likelihood of GDM recurrence in subsequent pregnancies. Third or later pregnancies of the women included in this study were removed from the data. Therefore, the remaining study sample consisted of 47 078 women with first and second pregnancies. The IPI from the day of giving birth in the first pregnancy, and the beginning of the second pregnancy for these women were calculated, and the association between the length of the IPI and the development of GDM in the second pregnancy was evaluated. The beginning date of the pregnancy was calculated using the date of giving birth and the length of the pregnancy registered in the MBR. The forming of the study sample is shown as a flowchart in Figure 1.

2.1 | Statistics

The continuous variables were analyzed either as means accompanied by standard deviations or as medians along with interquartile ranges, depending on the data distribution. Categorical variables were depicted using absolute numbers and corresponding percentages. Student *t* test, Mann–Whitney *U* test and χ^2 tests were used for group comparisons. Rates were displayed with their respective 95% CI, calculated using Poisson regression. A logistic regression model was used to assess the association between the length of the IPI and the development of GDM in the second pregnancy leading to birth. As the literature suggests, the risk for GDM might be higher in short IPI, and long IPI.[2,3] Therefore, we divided women into three groups based on the length of the IPI: short IPI (0–11 months), normal IPI (12–47 months), and long IPI (48+ months). Women with short IPI and long IPI were compared with women with normal IPI. In addition, logistic regression using continuous IPI was used separately for all women, women with IPI over 11 months, and women with IPI over 47 months. With these time periods, we were able to study the odds of GDM, when the most common IPI were included, and also to study the odds in the group of pregnancies with the longest IPI. The aOR with 95% CI were compared between the groups. The model was adjusted for covariates that were found to be risk factors for GDM based on the previous studies and these were included in our data. The selected covariates included the following: maternal age, continuous maternal body mass index (BMI; calculated as weight in

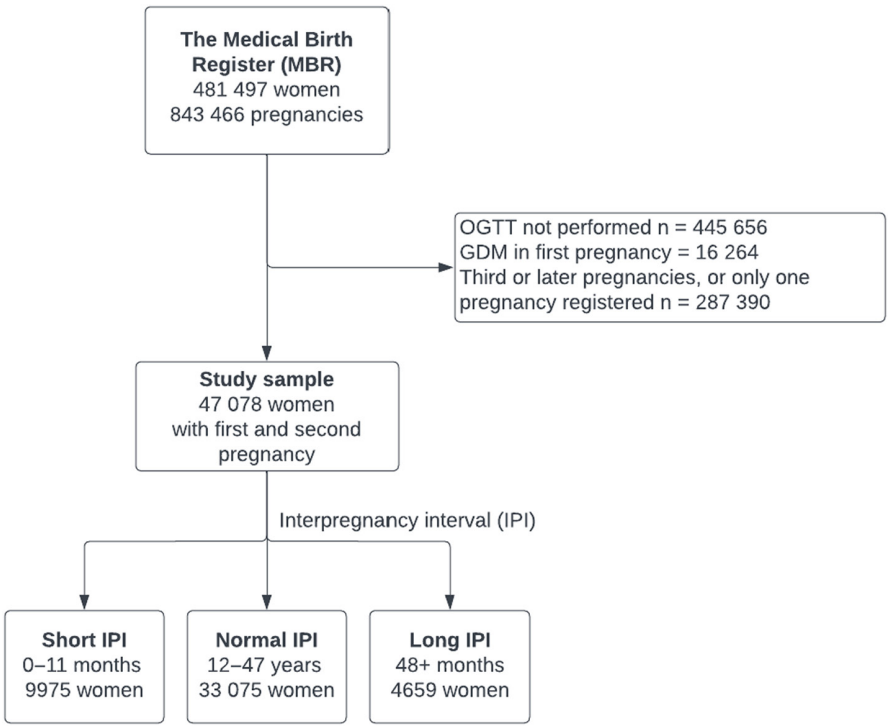

FIGURE 1 Flowchart of the study population. Pregnancies in which 2-hour oral glucose tolerance tests (OGTTs) were not performed ($n = 445\,656$), gestational diabetes (GDM) was diagnosed in the first pregnancy ($n = 16\,264$), and third or later pregnancies, or only one pregnancy during our study period ($n = 287\,390$) were excluded from the analysis. IPI, interpregnancy interval.

kilograms divided by the square of height in meters), maternal smoking status, in vitro fertilization, and multiple pregnancies.[6–10] An α of 0.05 was used as the cut-off for significance. Statistical analysis was performed using R version 4.0.3.

All procedures were conducted in compliance with regulations established in Finland. The Ethical Committee of Tampere University Hospital exempted retrospective studies using routinely collected healthcare data from ethical committee review, pursuant to the provisions of the Medical Research Act 488/1999 and the Patient Rights Act 785/1992. As per Finnish regulations outlined in the Secondary Use of Routinely Collected Healthcare Data Act 552/2019, no written informed consent was necessary due to the retrospective nature of the register-based study, and patients were not contacted. Approval for data use was obtained from Findata following the assessment of the study protocol (Permission number: THL/1756/14.02.00/2020).

3 | RESULTS

A total of 47 078 women were included in the study. Of these, a total of 9975 women had short IPI, 33 075 had normal IPI, and 4659 women had long IPI. The mean age of the women at the time of the second pregnancy increased as the IPI increased, increasing from a mean of 28.81 ± 4.81 years (IPI 0–11 months) to a mean of 32.73 ± 4.53 (IPI 48+ months) ($P < 0.001$). The BMI of women with short IPI (28.07 ± 5.32) and long IPI (mean 28.41 kg/m^2, SD 5.71) were higher than in women with normal IPI (27.18 ± 5.18) ($P < 0.001$). Women with IPI of 48+ months (18.24%, 95% CI 17.0–19.5) had a higher proportion of smokers ($P < 0.001$). Women with IPI 48+ months had a higher rate of diagnosed GDM (27.52%, 95% CI 26.03%–29.07%), followed by IPI 11–47 months (20.01%, 95% CI 19.53%–20.49%), and IPI 0–11 months (19.91%, 95% CI 19.05%–20.82%) ($P < 0.001$) (Table 1).

In the logistic regression analysis, we found no evidence of difference when women with short IPI were compared with women with normal IPI (aOR 0.99, 95% CI 0.93–1.05). Women with long IPI had increased odds for the development of GDM when compared with women with normal IPI (aOR 1.28, 95% CI 1.19–1.38). In the logistic regression model for continuous IPI, the total odds for the development of GDM increased as the IPI increased (aOR 1.05 per year, 95% CI 1.03–1.06) (Table 2). When only women with IPI over 11 months were included, the odds for the development of GDM increased as the length of the IPI increased (aOR 1.06 per year, 95% CI 1.04–1.07) and for women with IPI of 48+ months, the odds for the development of GDM increased as the length of the IPI increased (aOR 1.04 per year, 95% CI 1.00–1.08).

4 | DISCUSSION

The main finding of this study was that the odds for the development of GDM increased as the IPI increased. Especially among women with longer IPI, the odds for GDM showed an increasing trend as the

TABLE 1 Background information at the time of second pregnancy on the study sample with different interpregnancy intervals: stratified into short IPI (0–11 months), normal IPI (12–47 months), and long IPI (48+ months).

Interpregnancy interval	Short IPI (0–11 months)[a]		Normal IPI (11–47 months)[a]		Long IPI (48+ months)[a]	
Total number of women	9975		33075		4659	
Maternal age, year	28.81 ± 4.81		30.78 ± 4.53		32.73 ± 4.48	
BMI	28.07 ± 5.32		27.18 ± 5.18		28.41 ± 5.71	
BMI unknown	13	0.13 (0.07–0.22)	371	1.11 (1.01–1.24)	182	3.91 (3.36–4.52)
Maternal smoking						
Smoker	946	9.48 (8.89–10.11)	2818	8.52 (8.21–8.88)	850	18.24 (17.0–19.5)
Unknown	203	2.04 (1.77–2.33)	702	2.12 (1.97–2.29)	107	2.30 (1.88–2.78)
Multiple pregnancies	107	1.07 (0.88–1.30)	525	1.59 (1.45–1.73)	56	1.20 (0.91–1.56)
In vitro fertilization	<5[b]	<0.10	52	0.16 (0.11–0.20)	18	0.39 (0.23–0.61)
Diagnosed GDM	1978	19.91 (19.05–20.82)	6617	20.01 (19.53–20.49)	1282	27.52 (26.03–29.07)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); GDM, gestational diabetes mellitus; IPI, interpregnancy interval.

[a]Data are presented as absolute numbers and proportions with 95% confidence intervals or as mean ± standard deviation.

[b]The Finnish legislation prevents reporting the exact event rate if the rate is lower than five.

TABLE 2 Adjusted odds ratios with 95% confidence intervals for the development of gestational diabetes mellitus.[a]

	aOR	95% CI
Short IPI versus normal IPI	0.99	0.93–1.05
Long IPI versus normal IPI	1.28	1.19–1.38
Continuous (increase per year)	1.05	1.03–1.06

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; IPI, interpregnancy interval.

[a]Women with background information at the time of second pregnancy on the study sample with different IPI. Women with short (0–11 months) and long IPI (48+ months) were compared with women with normal IPI (12–47 months). The models were adjusted by maternal age, continuous maternal body mass index, maternal smoking status, in vitro fertilization, and multiple pregnancies.

IPI increased. In shorter IPI, it appears that the odds for GDM are not markedly increased.

Previous literature reports similarly, that women with short or long IPI had higher odds for GDM.[2,3] Chou et al.[2] found that women with IPI of 6–11 months, and 12–17 months had a notably higher risk for the development of GDM, than the reference of 18–23 months. In addition, the risk of GDM among women with IPI of over 36 months was higher.[2] However, Gebremedhin et al.[3] found that short IPI were not associated with higher odds of GDM. This study questioned the hypothesis that short IPI (<6 months) increases the risk of gestational diabetes and suggested that observed associations in previous research might be attributable to confounding factors. Our results are in line with the results of that study. Among women with an IPI less than 1 year, the proportion of GDM was notably higher than for women with an IPI of 1–4 years. However, after adjusting the model, we found no evidence of a difference in the risk for the development of GDM. In addition, the proportions of background characteristics, such as higher BMI and maternal smoking, were notably higher among these women, which is most likely with other lifestyle variables not available in our data explaining the higher rate of GDM in this group. However, the absolute number of patients who had IPI was relatively low in this study, which causes some uncertainty in our results.

Interestingly, women with IPI of 4 or more years had an increased odds of GDM and the odds increased rapidly as the years increased. Chou et al.[2] had a similar finding in their study. However, it remains unknown whether long IPI as a risk factor for the development of GDM is actually caused by some pathophysiologic process, or just caused by the background factors among these women. Gebremedhin et al.[3] suggested in their study, that the observed effects of long IPI in previous similar unmatched studies likely were influenced by factors that remain stable for mothers, such as persistent lifestyle factors, and socioeconomic status, but vary much more between women. In our study, although the model was adjusted for maternal age, BMI, and smoking status, other variables that were not taken into account could be influencing the relationship between IPI and the risk for the development of GDM. Especially lifestyle factors such as diet, exercise, and socioeconomic characteristics could be playing a role in the increased odds for the development of GDM among women with longer IPI. Therefore, this topic should be further studied, possibly using prospectively collected data, which includes more background characteristics of the women included.

Our study's strength lies in the extensive nationwide registry containing comprehensive data on the oral glucose tolerance test and its results for all pregnancies throughout the study duration. The register data employed in our research are systematically gathered on a national scale through standardized forms and consistent instructions, ensuring a robust coverage exceeding 99% and minimizing potential reporting and selection biases. However, a notable limitation is the absence of clinical information regarding whether patients had a history of either type I or type II diabetes, necessitating acknowledgment of this constraint in interpreting the results. Another potential

limitation is the change in GDM screening methods post-2008, transitioning to comprehensive screening, leading to a notable increase in GDM testing rates towards the study period's conclusion.

In conclusion, the odds for the development of GDM increased as the IPI increased. Especially among women with long IPI (over 47 months), the odds for GDM had an increasing trend. In women with shorter IPI, it appears that the odds for GDM are not markedly increased. The present study's results serve as a clarion call for proactive measures in GDM prevention. Moreover, they advocate for intensified investigation into the underlying factors contributing to GDM among women with extended IPI. It is imperative that these insights inform both clinical practice and further research agendas, as we strive to safeguard maternal health and well-being.

AUTHOR CONTRIBUTIONS

MV, RL, and JT wrote the initial manuscript. IK and MV undertook the study design. VM supervised the study. Each author commented on the manuscript during the process and confirmed the final version to be submitted.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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