Seasonal variation in gestational diabetes mellitus among women in Norway: a national population-based study

Astrand Melteig Stalheim,1,2 Marjolein Memelink Iversen,1 Anne Karen Jenum,3 Line Sletner,5,7 Signe N Stafne,6,7 Elisabeth Qvigstad,5,8 Linda Sagedal,9 Roy Miodini Nilsen,10 Vigdis Aasheim,1 Ragnhild B Strandberg1

ABSTRACT

Objectives Previous research on seasonal variation in the incidence of gestational diabetes mellitus (GDM) has shown inconclusive results. Furthermore, little is known about whether a seasonal variation in GDM might be associated with the maternal country of birth. We examined whether there was seasonal variation in GDM incidence by the maternal country background.

Design National population-based registry study.

Setting and participants We used national population-based data from the Medical Birth Registry of Norway (MBRN), n=1 443 857 (1990–2016) and data from four merged community-based studies (4GDM) with universal screening for GDM, n=2 978 (2002–2013).

Outcome measures The association between season of pregnancy onset with incidence of GDM was examined separately in both datasets using logistic regression analyses, stratified by the mother’s country background using two broad geographical categories (MBRN: Norwegian and immigrant; 4GDM: European and African/Asian ethnicity). Winter season was used as reference category.

Results The incidence of GDM in MBRN was highest when the pregnancy started during the winter (Norwegian-born: 12.1%; immigrants: 3.32%) and lowest when pregnancy started during the summer for both Norwegian and immigrant women (Norwegian-born: 1.03% (OR 0.85, 95% CI 0.81 to 0.98); immigrants: 2.99% (OR 0.90, 95% CI 0.84 to 0.96)). The 4GDM data showed that women with European ancestry had the highest incidence of GDM when pregnancy started during autumn (10.7%, OR 1.01, 95% CI 0.69 to 1.46) and winter (10.6%), while ethnic African and Asian women had the highest incidence when pregnancy onset was during the summer (15.3%, OR 1.17, 95% CI 0.54 to 2.53).

Conclusions Based on national population-based data, this study suggests that GDM incidence varies by season in both Norwegian-born and immigrant women. The 4GDM dataset did not show a clear seasonal variation in GDM incidence, possibly due to the relatively small sample. Causes for the seasonal variation in GDM should be explored further.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first detected during pregnancy.1 The condition is due to a reduced ability to increase insulin production to meet the physiological increase in insulin resistance that occurs during pregnancy.2 GDM poses a risk for several adverse maternal and fetal outcomes. Women with GDM have an increased risk of pre-eclampsia, caesarean section3 and type 2 diabetes mellitus (GDM) diagnosis.4 The Medical Birth Registry of Norway data underestimated the incidence of milder cases of GDM treated only with lifestyle advice.5

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study used data from a large national population-based registry, supplemented with data from four merged community-based studies.

⇒ The two datasets complement each other regarding study size, ethnic groups and gestational diabetes mellitus (GDM) diagnosis.

⇒ The Medical Birth Registry of Norway data underestimated especially the incidence of milder cases of GDM treated only with lifestyle advice.

⇒ We could not classify the mother’s country background in the same way in both datasets.
season at the time of performing the oral glucose tolerance test (OGTT). Furthermore, one study reported the highest fasting glucose values in winter and the highest 2-hour glucose values in summer. Finally, an Australian study examined the association between the season of pregnancy onset and incidence of GDM. Their study showed the highest incidence of GDM when pregnancy started in winter. If the outdoor temperature at time of testing causes the seasonal variation in GDM, we would assume to find a similar trend for seasonal variation independent of the individuals’ geographical origin. However, levels of physical activity, nutrient intake or vitamin D status, which can vary by season, may also be involved in the development of GDM. Two meta-analyses reported that physical activity before and during pregnancy may reduce the incidence of GDM. Moreover, other studies indicate that physical activity is seasonal in many countries. Therefore, seasonal variation in physical activity could potentially be associated with seasonal variation in GDM. The divergent results across studies suggest that more research is needed to examine seasonality in GDM incidence, and potential mechanisms involved.

The existing literature has found that the mother’s country background is related to the risk of GDM. Studies report that immigrant women have a higher GDM prevalence than non-immigrant women, in particular women with Asian or African ancestry. Two previous studies have examined seasonal variation in GDM based on the mother’s country background. Insights about seasonal differences in GDM incidence by mother’s country background may point to possible mechanisms involved in the development of GDM, and ethnic differences in GDM. This knowledge can be used to inform new studies and as a small step towards developing targeted interventions to promote a healthy lifestyle in the diverse group of women in reproductive age, and specifically for pre-pregnancy or early pregnancy follow-up consultations. In this study, we used two datasets, first data from a large national population-based registry. Second, we used an additional dataset from studies performing universal screening for GDM, which gave us the possibility to investigate our aim more in-depth. The aim of this study was to examine whether there was seasonal variation in the incidence of GDM when stratified by the mother’s country background using two broad geographical categories (Medical Birth Registry of Norway (MBRN): Norwegian and immigrant; 4GDM: European and African/Asian ethnicity).

**METHODS**

**Study design, setting and samples**

The main analyses for the present study were based on the MBRN, which is a large perinatal database in which the registration of all births in Norway has been compulsory since 1967. The current dataset consisted of deidentified pregnancy data linked with sociodemographic and immigrant data obtained from Statistics Norway for the period 1990–2016. From this dataset, we selected all pregnancies in which the maternal country of birth and month of pregnancy onset were available among first-generation immigrants only (foreign-born women with two foreign-born parents) and all Norwegian-born women (of Norwegian-born parents). Thus, to retain more homogenous groups, we excluded 85,066 pregnancies of Norwegian-born women with two foreign-born parents; foreign-born women with one Norwegian-born parent; Norwegian-born women with one foreign-born parent; and foreign-born women with two Norwegian-born parents. Moreover, we excluded any women with pregestational diabetes registered in the MBRN, leaving a sample size of n=1,433,857 pregnancies (online supplemental figure S1). Midwives or general practitioners register if a woman has type 1 diabetes, type 2 diabetes or gestational diabetes in a standard antenatal form during the follow-up consultations in pregnancy, and this information is sent to the Medical Birth Registry after birth along with the other pregnancy-related information.

Our additional dataset was obtained from the 4GDM consortium, with merged data from four Norwegian pregnancy studies (two cohort studies and results from two randomised controlled trials (ClinicalTrials.gov Identifier: NCT01001689 and NCT00476567): ‘STORK Grouddalen’, ‘STORK Rikshospitalet’, ‘Norwegian Fit for Delivery’ and ‘Training in Pregnancy’. The data were collected in the period 2002–2013 on 391,5 women from several cities in central and southern Norway, including the capital. We included n=2978 pregnancies in total for analyses of seasonal variation of GDM, after having excluded pregnancies with missing data at the time of pregnancy onset (n=265) and GDM diagnosis (n=72) (online supplemental figure S2).

**Variables**

**Gestational diabetes mellitus**

In the MBRN dataset, the GDM diagnosis was based on traditional high-risk screening using maternal characteristics to select women for a 75 g glucose OGTT (recommended gestational week 28–30), including family history of diabetes, ethnicity from non-European countries with high risk for GDM, previous GDM, high maternal age and body mass index (BMI). In contrast, the information about GDM diagnosis in the 4GDM dataset was based on the results from universal screening in which all women were offered OGTT. In both datasets, the GDM diagnosis was made using the diagnostic criteria specified by WHO at the time of these studies, with fasting plasma glucose ≥7.0 mmol/L and/or a 2-hour plasma glucose of ≥7.8 mmol/L. In addition, we further analysed 4GDM data using GDM classified according to two additional diagnostic criteria. First, WHO 2013 criteria (slightly modified as 1-hour values are missing) with fasting plasma glucose ≥5.1 mmol/L and/or 2-hour plasma glucose of ≥8.5 mmol/L. Second, the criteria presently used in Norway (Nor2017) with fasting plasma glucose ≥5.3 mmol/L and/or a 2-hour plasma glucose of
≥9.0 mmol/L. GDM was a dichotomous variable (yes/no).

Season and month of pregnancy onset
In the MBRN data set, we estimated the calendar time of pregnancy onset based on the year and month of delivery minus the gestational age based on ultrasound derived term. In the 4GDM data set, the time of pregnancy onset was based on the year and month of OGTT minus the gestational age based on ultrasound derived term. In the 4GDM data set, the time of pregnancy onset was based on second trimester ultrasound measurements or, if missing, on the last reported menstrual period. In keeping with previous studies, the season variable was categorised as follows: winter (December–February), spring (March–May), summer (June–August) and autumn (September–November). In addition, due to a large MBRN sample size, we also performed analyses for each individual month.

Mother’s country background
The mother’s country background in the MBRN dataset was categorised as Norwegian-born or immigrant women (first-generation; foreign-born women with two foreign-born parents). In the 4GDM dataset, the mother’s country background was categorised as European or African/Asian ancestry, based on the birthplace of the mother of the participating woman. The merging of larger categories of ethnic origin in 4GDM was made due to the small sample size and confidentiality concerns. In the European category, 97.6% were Norwegian-born or born in other Western European countries.

Other variables
Other variables involved in the analyses were maternal age (continuous), parity (primipara or parous), marital status (married/cohabitant or single/other) and education level (primary or less, high school or higher).

Statistical analyses
The GDM diagnosis was the dependent (outcome) variable, while season/month of pregnancy onset was the independent (exposure) variable. We first produced descriptive statistics for the dependent and independent variables, as well as for ‘other variables’. We used logistic regression for examining the association between GDM and season, and GDM and ethnicity. In addition, we used logistic regression analysis to investigate, when stratified by the mother’s country background, the association between season as categorical exposure and GDM as a binary outcome. The results were reported as ORs with 95% CIs. For each dataset, we stratified analyses by the mother’s country background (MBRN: Norwegian-born and immigrants; 4GDM: European and African/Asian). We used winter and the month of January as references because this was the time of pregnancy onset with the highest incidence of GDM in the MBRN dataset. We used Stata IC V.16.0 for the statistical analysis (StataCorp, Texas, USA).

Patient and public involvement
This study used existing national population-based register data (1990–2016) and data from four merged community-based studies performed in the period 2002–2013. Patient and public involvement in the current study were therefore not applicable.

RESULTS
Sample characteristics and incidence of GDM
Table 1 shows data from the MBRN (n=1 443 857) for the period 1990–2016 and data from the 4GDM (n=2978) for the period 2002–2013. Compared with the MBRN dataset, the 4GDM dataset had a higher proportion of primipara (61.1% and 43.3%, respectively), a higher proportion of women with a ‘higher education’ (73.5% and 42.3%) and a lower proportion of women with an educational level of ‘primary or less’ (4.9% and 22.0%). The two samples had a similar mean maternal age (30.1 and 29.2 years, respectively).

The overall incidence of GDM in the MBRN dataset was 1.4%, with an increasing trend over time, particularly after 2009 (figure 1). The overall incidence of GDM in the 4GDM dataset was 10.8%. Table 1 shows that, for both datasets, women with GDM had a higher mean maternal age compared with women without GDM and a lower educational level. We also found a slightly higher incidence of GDM among parous women compared with primipara (mainly in MBRN) and a higher incidence of GDM in the immigrant group in the MBRN dataset, as well as African/Asian women in the 4GDM dataset.

Seasonal variation of GDM
In the MBRN dataset, both Norwegian-born and immigrant women had the lowest incidence of GDM when pregnancy started during the summer season (1.05%, crude OR 0.85, 95% CI 0.81 to 0.89 and 2.99%, crude OR 0.90, 95% CI 0.84 to 0.96) (table 2, figure 2). When investigating calendar time in more detail, the monthly variation showed a lower incidence of GDM when the month of pregnancy onset was between May and October (0.99%–1.07%) for Norwegian women and between May and July (2.80%–2.97%) for immigrant women (online supplemental table S1).

In the 4GDM dataset, the GDM incidence for European women ranged from 9.61% (crude OR 0.89, 95% CI 0.64 to 1.25) when the pregnancy onset was during spring to 10.68% (crude OR 1.01, 95% CI 0.69 to 1.46) in the autumn (table 2, figure 2). For women of African/Asian origin, the incidence increased from 13.30% (OR 1.0, reference) when pregnancy onset was during winter to 15.31% (crude OR 1.17, 95% CI 0.54 to 2.53) in the summer (table 2, figure 2). When examining seasonal variation in GDM incidence using the WHO2013 and Nor2017 diagnostic criteria, with greater emphasis on elevated fasting glucose values, we found that the lowest incidence of GDM in the European women was in the group with pregnancy onset in summer (WHO2013...
11.05% and NOR2017 5.53%). (online supplemental table S2). The results in these analyses from the 4GDM did not reach statistical significance.

The bivariate results from the association between GDM and immigration (without season) and GDM and seasons (without mother’s country background) are presented in online supplemental table S3 (both datasets). In the MBRN dataset, the ORs were lower for all seasons than the reference season (winter). Further, there was a significant higher risk for GDM among immigrants in the MBRN dataset (OR 2.92, 95% CI 2.84 to 3.00) and among Asian/African immigrants in the 4GDM dataset (OR 1.49, 95% CI 1.10 to 2.03), compared with Norwegians and Europeans, respectively.

**DISCUSSION**

We found a seasonal variation in GDM incidence (using WHO 1999 diagnostic criteria) in the national population-based data (MBRN). Both Norwegian-born and immigrant women had the highest incidence of GDM when pregnancy started during the winter season, while the incidence was lowest when pregnancy started during the summer. In the 4GDM consortium, the highest GDM incidence (using WHO 1999 criteria) was in pregnancies with an onset during autumn and winter for women from Europe, while women from Africa and Asia had the highest incidence when pregnancy started during the summer (although results in the 4GDM were not statistically significant).

**Strengths and limitations**

As far as we are aware, this is the first study to identify a seasonality of GDM by the mother’s country background. We had the opportunity to examine seasonality in the two datasets, one nation-wide registry and another dataset with universal screening procedures. The use of the two datasets therefore complements each other, however, both datasets have strengths and limitations. Using MBRN data may improve internal validity because it is a national registry and therefore has a low risk of selection bias due to participation. On the other hand, there are limitations when using national registry data. Although Norway used the same guidelines for risk factor screening during...
most of the sample period (1999–2016), the classification criteria might have been implemented differently across time. As the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, which was published in 2008, may have increased the awareness on the diagnosis in the subsequent years. Moreover, the GDM diagnosis was dichotomous and based on documentation made by midwives in the maternity wards. The GDM diagnosis in the MBRN has shown a very good sensitivity, but it is likely that the MBRN data underestimated the incidence of GDM, especially milder cases treated only with lifestyle advice. We do not consider these limitations to introduce systematic bias for the MBRN registry data regarding the research questions in our study. Another possible limitation in our study was that we could not classify the mother’s country background in the same way in both datasets. As an Asian/African origin is known to be associated with an increased risk of GDM, and due to a small sample size, we chose to contrast our results by whether the woman had a European or African/Asian background in the 4GDM dataset. On the other hand, in the MBRN dataset, the immigrant group will also include immigrants from other European countries. Finally, in the MBRN dataset, we only included first-generation immigrant women, while in the 4GDM, in addition to first-generation immigrant women, were second-generation immigrants. Importantly, however, there is no reason to believe that these differences have varied throughout the year and it is therefore unlikely to affect our analyses of seasonality.

Despite these limitations, we consider the two datasets to be complementary and that they offer a broader perspective on GDM seasonality.

**GDM incidence**

The increase in the incidence of GDM over time in the MBRN dataset is consistent with other studies. The incidence of GDM was lower in all seasons and in both geographical categories in the MBRN dataset compared with the 4GDM dataset. These differences may be partially explained by a possible underestimation of GDM in MBRN, in particular in Norwegian women, as they were less likely to be tested. This probably also explains why the OR was almost threefold greater (2.92) in immigrants in the MBRN dataset, while only 1.49 in women with African/Asian ancestry in the 4GDM, compared with Norwegian born/ethnic European women, when using the 1999 WHO diagnostic criteria (online supplemental table S3). Furthermore, due to study protocols, 4GDM offered universal testing, which means that all respondents underwent an OGTT, even when the risk of GDM was considered low. Therefore, it is likely that the true incidence of GDM in Norway is closer to the incidence found in the 4GDM than in the MBRN. According to the American Diabetes Association, there is still no worldwide consensus regarding recommendations on which screening approach and diagnostic criteria to use for GDM.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>OR (95% CI)*</td>
</tr>
<tr>
<td>Winter</td>
<td>3376</td>
<td>1.21</td>
</tr>
<tr>
<td>Spring</td>
<td>3264</td>
<td>1.12</td>
</tr>
<tr>
<td>Summer</td>
<td>3303</td>
<td>1.03</td>
</tr>
<tr>
<td>Autumn</td>
<td>3426</td>
<td>1.09</td>
</tr>
<tr>
<td>Total</td>
<td>13 369</td>
<td>1.11</td>
</tr>
</tbody>
</table>

*Unadjusted OR.

GDM, gestational diabetes mellitus; MBRN, Medical Birth Registry of Norway.

**Figure 2** GDM incidence by season of pregnancy onset in two geographical categories in the MBRN and 4GDM datasets (WHO 1999 diagnostic criteria). GDM, gestational diabetes mellitus; MBRN, Medical Birth Registry of Norway.
GDM seasonality

A large Australian cohort study used the estimated time of conception to study the seasonal variation of GDM and found the highest incidence of GDM when pregnancy started in the coldest months. This result was consistent with our finding in the MBRN dataset of a higher incidence of GDM for pregnancies starting in winter. Moreover, previous studies suggest a higher incidence of GDM when women are tested in warmer seasons and with rising temperatures in the days prior to the OGTT. These findings were also in line with our results from the MBRN dataset, as women starting their pregnancy in the winter season were most likely tested for GDM during the subsequent summer months, as the Norwegian Society for Gynecology and Obstetrics recommended screening at 28–30 weeks gestation. Two Canadian studies found that higher air temperature on or a few weeks before the time of testing was associated with an increased risk of GDM. A change in temperature 3–4 weeks before the test was also associated with beta cell dysfunction. This evidence suggests that there may be an underlying mechanism affecting glucose metabolism. More studies are needed to explore these possible mechanisms.

Authors of prior studies recommend to examine other factors that may be involved in a possible seasonal variation, for instance level of physical activity, nutrient intake or vitamin D or even climate changes. Furthermore, a systematic review including 36 studies from Europe, America and Australia (37 studies in total), concluded that physical activity was seasonal, and that the winter season seemed to be the season with the highest prevalence of physical inactivity. Further, since some studies have shown that low physical activity and GDM are linked, seasonal variation in the levels of physical activity may be involved in the seasonality of GDM. The cold winter season in Norway may lead to less physical activity, as people may prefer to stay indoors. We could speculate that low preconceptional or early pregnancy physical activity in winter may influence the seasonality of GDM. Moreover, maternal BMI is strongly related to the risk of GDM. However, we did not adjust for BMI and physical activity as these variables may act as mediators on the causal pathway between season and GDM. The potential mediating effects of BMI and physical activity would be interesting to investigate in future studies.

Despite a high incidence throughout the year, the weak seasonal variation found in the 4GDM may be caused by a relatively small and heterogeneous sample. Similarly, a British study with a smaller sample of 108 women with GDM found no statistically significant seasonal variation of GDM, possibly reflecting the reduced power to reach statistical significance in small samples. Furthermore, 4GDM had universal screening and showed no seasonal variation, whereas high-risk screening gave seasonal variation in the MBRN. If this result truly represents a difference between the two samples, a potential explanation could be that there might be a seasonal variation in OGTT testing, where for example fewer women are tested during the summer holidays, resulting in fewer identified GDM cases. This needs to be explored further.

A systematic review of 24 studies concluded that being an immigrant constitutes a higher risk of GDM. This finding was in line with our results from both of our datasets. It is an interesting result that in the MBRN both Norwegian and immigrant women had the lowest incidence with pregnancy start in summer, while in the 4GDM dataset the Asian/African women had the opposite trend, with the highest incidence when pregnancy started in the summer. We can only speculate about the reason for this difference. It might be partially explained by the different categorisations of the immigrant groups or by the universal screening for GDM in 4GDM. Another possible reason for such a difference may be that the immigrant category in the MBRN includes all immigrants, including Western European, which we know to have a lower prevalence of GDM compared with African and Asian immigrants. Moreover, the sample of women from Africa/Asia with GDM was small in the 4GDM, with only 12–15 women in each season.

The Australian HAPO study reported a significant increase in winter for fasting values and an increase during summer for the 2-hour glucose values. The data from 4GDM was detailed in terms of the GDM diagnosis and gave us the opportunity to examine the association between season and GDM using three different diagnostics criteria. The results when using the WHO 2013 and Nor2017 criteria showed greater variation between each season compared with the WHO 1999 criteria. This may be due to the considerable differences in how an elevated fasting glucose contributes to the GDM diagnosis compared with 2-hour glucose. More knowledge about the physiology of glucose metabolism in pregnancy is needed, as the authors of the Australian HAPO study emphasise, seasonality is a factor that should be taken into account when interpreting OGTT results.

CONCLUSION AND SUGGESTIONS FOR FUTURE RESEARCH

This study suggests seasonal variation in the incidence of GDM when using national population-based data from Norway. The GDM incidence was lowest for Norwegian-born and immigrant women when pregnancy started during the summer season. Moreover, future research is warranted to examine the potential mechanisms of seasonal variation of GDM, such as temperature during the year and physical activity levels of those studied. Such knowledge can further be used to develop targeted interventions to promote a healthy lifestyle in the diverse group of women, and specifically for pre-pregnancy or early pregnancy follow-up consultations.

Author affiliations
1 Department of Health and Caring Sciences, Western Norway University of Applied Sciences, Bergen, Norway
2 Division of Obstetrics and Gynaecology, Oslo University Hospital, Oslo, Norway
Acknowledgements The authors would like to thank everyone who participated in this study.

Contributors AMS, MM, AKJ, LSletner, SN, RMN, VA and RBS contributed to conceptualising the study, VA is the principal investigator of the MBRN registry study data. AKJ, LSletner, SN, EQ and LSagedal are principal investigators for the respective study arms in the 4GDM consortium. AMS and RMN performed statistical analyses. AMS, MM, AKJ, LSletner, SN, EQ, LSagedal, RMN, VA and RBS contributed to the interpretation of results. AMS wrote the first draft and all authors contributed with revisions of the manuscript. All authors approved the final version.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the two projects providing data for our study have been approved by the Regional Committees for Medical Research Ethics South East Norway, reference numbers 2017/2533 and 2014/1278 and the respective data protection officials. Both projects also received approval to provide data for the current study. Participants gave informed consent to participate in the studies in the 4GDM consortium before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. The data used in the current study is not publicly available due to regulatory conditions of data usage.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs Marjolein Memelink Iversen http://orcid.org/0000-0001-9954-171X Roy Miodini Nilsen http://orcid.org/0000-0002-0228-1590 Ragnhild B Strandberg http://orcid.org/0000-0003-0256-438X

References


