

Prevalence and Associated Factors of Prediabetes in Postpartum Gestational Diabetes Mellitus Mothers in the East Coast of Malaysia

Mohamed Yusof SA^a, Tengku Ismail TA^{a*}, Anuar Roselan MK^b, Ismail AF^a

^aDepartment of Community Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

^bBesut District Health Office, Jalan Keluang Kampung Raja, 22000 Besut, Terengganu, Malaysia

ABSTRACT

INTRODUCTION: Majority of gestational diabetes mellitus (GDM) mothers resume normal glycaemic state after delivery. However, this hyperglycaemic condition may persist in some women. Postpartum GDM mothers have a higher risk of progression to diabetes and prediabetes than those with normal pregnancy. This study was aimed to determine the prevalence of prediabetes among postpartum GDM mothers and its associated factors during six weeks of postpartum glucose testing. **MATERIALS AND METHOD:** A cross-sectional secondary data review was conducted from January 2021 until May 2021 among postpartum mothers with history of GDM who performed postpartum glucose testing in all government health clinics in Besut, Terengganu from January 2018 until December 2019. A descriptive and multiple logistic regression analysis were performed using IBM SPSS Statistics version 26 software. **RESULT:** A total of 429 cases were included. Prevalence of diabetes and prediabetes was 2.3% (95% CI 1.6%, 3.0%) and 13.8% (95% CI 12.1%, 15.5%), respectively. There was significant associations found between previous history of GDM (Adj. OR 3.28; 95% CI 1.83, 5.87; $p < 0.001$) and insulin usage (Adj. OR 2.75; 95% CI 1.51, 4.99; $p = 0.001$) with development of prediabetes at postpartum period. **CONCLUSION:** The prevalence of diabetes and prediabetes among postpartum GDM mothers in Besut district was as high as other studies in Malaysia and globally. Women with a previous history of GDM and insulin usage should be focused on prevention strategies as they were at higher risk of developing prediabetes in the postpartum period.

Keywords

Prediabetic state, diabetes mellitus, postpartum period, gestational diabetes mellitus, insulin

Corresponding Author

Dr. Tengku Alina Tengku Ismail
Department of Community Medicine, School of
Medical Sciences, Health Campus, Universiti
Sains Malaysia,
16150 Kubang Kerian, Kelantan, Malaysia
Email : dralina@usm.my

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INTRODUCTION

Prediabetes is a metabolic disorder in which a blood sugar levels exceed the normal range but not severe enough yet to be classified as diabetes. It is characterized by impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or a combination of both.¹ The pathophysiologic determinants that lead to development of prediabetes were insulin resistance and deterioration in β - cells function in which there is lack of insulin to overcome insulin resistance in both liver and the skeletal muscle. Besides that, certain factors including lipotoxicity, inflammation and oxidative stress, hyperglycaemia and genetic factors may contribute to β - cells destruction.²

GDM is a kind of carbohydrate intolerance that results in different degrees of hyperglycaemia and is caused by an inadequate β -cells composition for the body's insulin

needs. Majority of the time, GDM develop because β -cells are unable to satisfy the excessive demands of insulin when insulin resistance increases during pregnancy.³ Mothers with history of GDM are at significant risk of developing prediabetes, particularly IGT, due to decreased β -cells activity and the pathophysiology of insulin resistance.⁴ The likelihood of getting diabetes following GDM was 3.7% at nine months and 18.9% nine years later.⁵ Kim *et al*⁶ reported that mothers with a history of GDM had at least seven times higher risk to develop type 2 DM as compared to those with normal pregnancies.

Prevalence of diabetes and prediabetes in postpartum mothers with a previous experience of GDM varies widely across countries in the world, from 18% to 60%.⁷ A cross-sectional study conducted at University Malaya

Medical Centre reported the prevalence of type 2 DM and prediabetes were 35.5% and 26.2%, respectively.⁸ However, there is still a scarcity of evidence in Malaysia on the prevalence of abnormal glucose tolerance in women following GDM. Studies in Asean and non-Asean countries have shown that among the frequently reported factors contributing to persistent abnormal postpartum glucose outcome were advanced maternal age, multiparity, family history of diabetes, previous history of GDM, early gestational age at diagnosis of GDM, higher body mass index (BMI), and insulin requirement during pregnancy.⁹⁻¹¹ Identifying and understanding the associated factors might enhance patient risk assessment during pregnancy.¹²

Prediabetes means that the affected person still did not develop the disease. In other words, the condition is still reversible. It can be reverted to normal following specific healthy lifestyle measures such as increasing physical activity and consuming a balanced and healthy diet.¹³ Therefore, it is crucial to identify persons at risk of prediabetes by recognizing contributing or associating factors. By then, healthcare providers can provide appropriate measures and advice for the high-risk group. Realizing the importance of early recognition of prediabetes conditions and prevention towards further progression to diabetes, this study aimed to determine the prevalence of diabetes and prediabetes among postpartum GDM mothers, as well as factors associated with prediabetes among postpartum mothers in Besut, Terengganu in 2018-2019.

MATERIAL AND METHODS

Study Design and Participants

The study was a cross-sectional secondary data review which lasted from January 2021 until May 2021. The study was conducted among all postpartum mothers with a history of GDM who performed postpartum glucose testing in all government health clinics of Besut, Terengganu in 2018-2019. Besut is one of Terengganu's districts bordering to the north and west by the state of Kelantan, and to the east by the South China Sea. Notably, Besut have recorded increment in the number of registered GDM cases.¹⁴

Sample size was calculated using the single proportion formula to address the prevalence of diabetes and prediabetes while Power and Sample Size (PS) Software version 3.0 (two proportion formula) was used for the associated factors of prediabetes. The prevalence data of diabetes (36%) and prediabetes (26.2%) in Malaysia was based on the finding from Chew *et al*⁸, where 'n' was the required sample size, 'Z' was the Z statistics for 95% confidence interval which equal to 1.96, 'p' was the estimated prevalence of diabetes and prediabetes among postpartum GDM mothers and 'd' was the 5% absolute precision of margin of error. Hence, after considering 10% possibility of data entry error, the required sample size was 450, which was biggest sample size obtained for this study.

All postpartum GDM mothers who were registered in GDM Mothers Registry Book 101 (AN)/16 at all government health clinics of Besut district between 1 January 2018 and 31 December 2019 were eligible for this study. Mothers who were non-Malaysians and whose records contain absence more than 10% of the required information were excluded from the study. Thus, the sampling frame involved all postpartum mothers with history of GDM who performed postpartum glucose testing in government health clinics of Besut district, Terengganu who met the study criteria. A convenience sampling was done, where all sample was selected as there was only 429 sample which met the study criteria.

Research Tool and Data Collection

After delivery, all postpartum mothers with history of GDM must undergo postpartum glucose testing using 75-gram oral glucose which usually be scheduled on six weeks postpartum or more. Results of the postpartum glucose testing were then evaluated based on the guideline of management of diabetes in pregnancy. Criteria for diabetes (FPG \geq 7.0 mmol/L and/or 2 hour PG \geq 11.1 mmol/L and prediabetes when isolated IFG (FPG \geq 5.6 mmol/L to < 7.0 mmol/L), isolated IGT (FPG<5.6 mmol/L and 2 hour PG \geq 7.8mmol/L) and combined IFG/IGT (FPG \geq 5.6 mmol/L to < 7.0 mmol/L and 2 hour PG \geq 7.8 mmol/L to < 11.1 mmol/L). These results were recorded in the Maternal Health Record Book [KIK

1/(b)/96 (Vol.2012)] and GDM Mothers Registry Book [101 (AN)/16].

This study utilised the secondary data which were obtained from these record book and registry book, as well as the list of antenatal GDM mothers. The list consists of brief information on sociodemographic and obstetric factors such as age, parity, date of oral glucose tolerance test (OGTT) taken and the result of OGTT. The record book was the copy records of maternal health which were kept at the health clinics. This record book provided details data on the maternal health concerns such as sociodemographic data, information on the current pregnancy, foetal growth, birth, new-born and postnatal. All maternal health record books of postpartum GDM mother listed from the first tools where then collected from each respective clinic and sent to Maternal Child Health (MCH) unit at district health office to be reviewed. In addition, the registry book serves as the complement if the data from the record book was not available or incomplete. All relevant data was collected using proforma checklist, which was then imported into SPSS. The proforma checklist has three parts: i) women's socio-demographic information, ii) obstetric information, and iii) clinical information.

This study was conducted in line with the ethics and principle and the ethical approval was obtained from the Human Research and Ethics Committee, Universiti Sains Malaysia (USM/JEPeM/20110592) and the Medical Review and Ethical Committee from National Institute of Health, Ministry of Health Malaysia NMRR-20-2603-5725 (IIR).

Main outcome and variables

The first outcome was looking on the prevalence of diabetes and prediabetes. The numerator referred to the number of mothers diagnosed with diabetes or prediabetes, while the denominator was all postpartum GDM mothers involved in this study. The second outcome focused on the factors associated with prediabetes, thus those with the diagnosis of diabetes were not included in the analysis. The dependent variable for this outcome was a dichotomous variable (prediabetes

and normal). The prediabetes collectively refers to the diagnosis of either IFG, IGT or combined of IFG/IGT which were detected from the postpartum glucose testing and recorded in the registry book.

Sociodemographic, obstetric and clinical characteristics of postpartum GDM mothers were obtained. The sociodemographic data include age, ethnicity, marital status, educational level and employment status. The number of parities, previous history of GDM, family history of GDM, gestational age at diagnosis of GDM, insulin usage and BMI at booking were the considered obstetric and clinical characteristics for the study. Gestational age at diagnosis referred to the age of the pregnancy at the time of GDM diagnosis, while history of GDM means any previous experienced of GDM in the pregnancies preceding the latest pregnancy. Family history of DM means any related history of DM in the woman's first-degree relatives. Insulin usage referred to the use of insulin as a method of treatment for the GDM during most recent pregnancy.

Data analysis

IBM SPSS version 26 software was used to enter data and for the statistical analysis. All variables were summarized using descriptive statistics. Numerical values were reported as mean (SD) or median (IQR), while categorical data were displayed as frequency (percentage). Factors associated with prediabetes were determined through simple and multiple logistic regression analysis. Simple logistic regression was performed to obtain the preliminary variables associated with prediabetes among postpartum GDM mothers and presented as crude odd ratio. The criteria for the selection of variables to be included in multiple logistic regression were variables with p -value < 0.25 or that were clinically relevant and important. Thus, the preliminary main effect model was gained by comparing the models using the backward likelihood ratio (LR) and forward LR. Multicollinearity and interaction between were checked. Goodness of fit model was checked by using the Hosmer and Lemeshow goodness of fit test, a classification table, and the receiver operating characteristic (ROC) curve. The p -value of 0.05 was set as significance level.

RESULTS

Characteristics of participants

Out of 450 cases of postpartum GDM mothers who performed postpartum glucose testing, only 429 cases fulfilled all the study criteria and was incorporated in the study. Majority of the mothers' age were less than 35 years old, 295 (68.8%) and most of them were from Malay ethnic group, 427 (99.5%) and were married, 428 (99.8%). As for the educational level, more than half of the mother's achieved secondary educational level, 240 (55.9%), however most of them were unemployed, 231 (53.8%). Approximately, 108 (25%) have experienced of previous history of GDM and 252 (60%) did not have any related family history of DM. A total of 99 out of 429 mothers (23.1%) were treated with insulin during their recent pregnancy. Details of the characteristics are shown in Table 1.

Table 1. Sociodemographic, obstetric and clinical characteristics of postpartum GDM mothers in Besut Terengganu, 2018-2019 (n=429)

Characteristics		Total, n (%)
Age (year)	Less than 35	295 (68.8)
	More than 35	134 (31.2)
Ethnicity	Malay	427 (99.5)
	Non-Malay	2 (0.5)
Marital status	Married	428 (99.8)
	Unmarried	1 (0.2)
Educational level	Primary	19 (4.4)
	Secondary	240 (55.9)
	Tertiary	170 (39.7)
Employment status	Employed	142 (33.1)
	Unemployed	231 (53.8)
	Self Employed	56 (13.1)
Parity	Less than 5	341 (79.5)
	5 and more	88 (20.5)
Previous history GDM	No	321 (74.8)
	Yes	108 (25.2)
Family history of DM	No	252 (58.7)
	Yes	177 (41.3)
Gestational age at diagnosis of GDM	First trimester	116 (27.0)
	Second trimester	169 (39.4)
	Third trimester	144 (33.6)
Insulin usage	No	330 (76.9)
	Yes	99 (23.1)
BMI at booking (kg/m ²)*		27.47 (5.59)

*mean (SD)

Prevalence of diabetes and prediabetes among postpartum GDM mothers

From the 429 cases of GDM mothers who came for postpartum glucose testing, there were 2.3% (95% CI 1.6%, 3.0%) of them who developed DM and 13.8% (95% CI 12.1%, 15.5%) were diagnosed as prediabetes (Figure 1). The majority of the mother, 83.9% (95% CI 82.1%, 85.7%), have gained normal reading of the OGTT at the postpartum period.

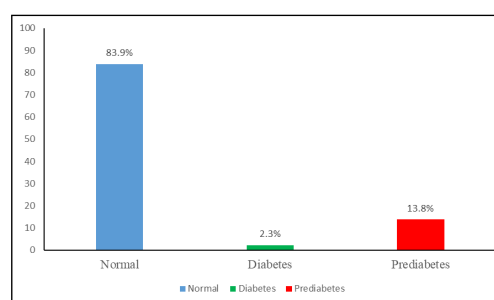


Figure 1 : Prevalence of diabetes and prediabetes among postpartum GDM mother who performed postpartum glucose testing in Besut, Terengganu in 2018-2019

Factors associated with prediabetes

In the univariate analysis of factors associated with prediabetes among postpartum GDM mothers, gestational age at diagnosis of GDM, previous history of GDM, insulin usage and BMI at booking were the significant factors identified with p- value <0.05. Age and educational level were also included in the multivariable analysis since their p- values were between $0.05 \leq p < 0.25$ (Table 2).

Multivariable analysis showed that, there were significant association between prediabetes among postpartum GDM mothers with previous history of GDM (Adjusted OR 3.28; 95% CI 1.83,5.87; $p < 0.001$) and insulin usage during the pregnancy (Adjusted OR 2.75; 95% CI 1.51,4.99; $p = 0.001$). The postpartum mothers with a previous history of GDM had 3.28 times the odds of having prediabetes, as compared to those with no prior history of GDM when adjusted for the insulin usage. Those who were prescribed with insulin for the treatment of GDM during pregnancy had almost 2.75 times higher odds of getting prediabetes as compared to those who did not receive insulin treatment during pregnancy (Table 3).

Table 2. Simple logistic regression for factors associated with prediabetes among postpartum GDM mothers in Besut, Terengganu in 2018-2019 (n=419)

Variables	Prediabetes		Normal		Crude OR (95% CI)	Wald statistic (df)	P-value
	n (%)	Mean (SD)	n (%)	Mean (SD)			
Age							
Less than 35	36 (61.0)		250 (69.4)		1		
More than 35	23 (39.0)		110 (30.6)		1.45 (0.82,2.57)	1.65 (1)	0.199
Educational level							
Tertiary	18 (30.5)		149 (41.4)		1		
Primary	3 (5.1)		14 (3.9)		1.77 (0.47, 6.77)	0.70 (1)	0.402
Secondary	38 (64.4)		197 (54.7)		1.60 (0.88, 2.91)	2.34 (1)	0.126
Employment status							
Employed	18 (30.5)		121 (33.6)		1		
Unemployed	34 (57.6)		191 (53.1)		1.20 (0.65, 2.21)	0.33 (1)	0.567
Self employed	7 (11.9)		48 (13.3)		0.98 (0.39, 2.50)	0.002 (1)	0.967
Gestational age at diagnosis of GDM							
First trimester	20 (33.9)		92 (25.6)		1		
Second trimester	27 (45.8)		136 (37.6)		0.91 (0.48, 1.73)	0.08 (1)	0.780
Third trimester	12 (20.3)		132 (36.8)		0.42 (0.20, 0.90)	5.01 (1)	0.025
Parity							
Less than 5	47 (79.7)		286 (79.4)		1		
5 and more	12 (20.3)		74 (20.6)		0.99 (0.50, 1.96)	0.001 (1)	0.970
Previous history of GDM							
No	30 (50.8)		284 (78.9)		1		
Yes	29 (49.2)		76 (21.1)		3.61 (2.04, 6.39)	19.52 (1)	<0.001
Family history of DM							
No	38 (64.4)		208 (57.8)		1		
Yes	21 (35.6)		152 (42.2)		0.76 (0.43, 1.34)	0.92(1)	0.339
Insulin usage							
No	34 (57.6)		291 (80.8)		1		
Yes	25 (42.4)		69 (19.2)		3.10 (1.74, 5.53)	14.67 (1)	<0.001
BMI at booking		28.9 (6.80)		27.3 (5.40)	1.05 (1.00, 1.10)	4.23 (1)	0.040

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DISCUSSION

Prevalence of Diabetes and Prediabetes among Postpartum GDM Mothers

The progression of GDM to diabetes and prediabetes has become a global burden worldwide. The prevalence of diabetes and prediabetes among postpartum GDM mothers in Besut Terengganu in 2018-2019 was 2.3% and 13.8%, respectively. This result is nearly identical to that

of a retrospective cohort research done in Singapore, which found that 2.1% of postpartum mothers with a history of GDM acquired type 2 DM, and 16.2% had prediabetes ¹⁵. However, another local study in Kuala Lumpur reported a higher prevalence of type 2 DM

Table 3. Multiple logistic regression for factors associated with prediabetes among postpartum GDM mothers in Besut, Terengganu in 2018-2019 (n=419)

Variables	B	Adjusted OR (95% CI)	Wald Statistics (df)	P-value
Previous history of GDM				
No		1		
Yes	1.19	3.28 (1.83,5.87)	16.03 (1)	<0.001
Insulin usage				
No		1		
Yes	1.01	2.75 (1.51,4.99)	11.03 (1)	0.001

Forward LR Multiple Logistic Regression was applied
 Multicollinearity and important interaction term were checked and not found
 Hosmer Lemeshow test, *p*-value 0.801
 Classification table 85.9% correctly classified
 The area under the curve, Receiver Operating Characteristics (ROC) was 68.6%

(35.5%), and prediabetes (26.2%) among postpartum mothers as compared to our studies.⁸ The possible explanation of the difference in the figures observed in the study may be due to the differences in ethnicity. In the study done in Kuala Lumpur, there was a higher number of Indian ethnicities, which contribute to 30.6% of type 2 DM and 22.2% prevalence of prediabetes. The result was consistent with finding from the previous National Health Morbidity Survey (NHMS) in 2019, where the prevalence of diabetes among female Indian ethnicity was the highest (17.8%), followed by Malay (11.9%) and Chinese (6.5%).¹⁶

The data on the prevalence of glucose intolerance after GDM is scarce and varied across the region. In Thailand, the incidence of prediabetes among postpartum GDM mothers was approximately 27% with the characteristic age of 35 years old and above and multiparities (three or more pregnancies)¹⁷. A higher incidence was reported among Filipino women, where the incidence of prediabetes was 36.5%. Most of them developed IGT (19.4%), a combination of both IFG and IGT (9%), and IFG (8.1%).¹⁸ In contrast with a study from India whereby most the follow up women with prior GDM at six weeks postpartum diagnosed as having IFG (14.5%), 8.0% (both IGT and IFG), and 4.8% (IGT).⁹ An almost similar finding was reported in non-Asian countries ranging from 4.0% to 17.3% diabetes and from 28.8% to 36.5% for prediabetes^{19,20}. The possible postulation that may explain the inconsistency of the finding was due to the variations in cultural and lifestyle activities, which in turn determine the way of eating or dietary pattern and

daily physical activities. In addition, differences in prevalence in between countries may result from different diagnostic criteria used to diagnose GDM. Various criteria were used for the diagnosis of GDM such as based on the American Diabetes Association (ADA) 2004, National Institute for Health and Care Excellence (NICE) 2015 and International Association of Diabetes and Pregnancy Study Group (IADPSG) 2010. There has been inconsistencies and lack of consensus among health professionals pertaining to this matters which contribute to the difference in prevalence worldwide.³

Factors Associated with Prediabetes in Postpartum GDM Mothers

Previous history of GDM was found to be significantly associated with development of prediabetes among postpartum GDM mothers. Similar finding was reported by Wahabi²¹ in Saudi postpartum women. In addition, Schaefer-Graf *et al*²² and Vounzoulaki *et al*²³ reported 1.6 to 10 fold increased risk of development of DM in postpartum respectively in those with previous history of GDM as compared to those who had never experienced of GDM. Possible explanations include a more prominent β -cells dysfunction and vulnerable genetic variations in mothers with early postpartum diabetes development.²⁴

In addition, a history of GDM leads to lower insulin sensitivity, but hyperglycaemia develops due to failure of the compensatory insulin secretion mechanism.²⁵ Furthermore, insulin usage for the management of hyperglycaemia during pregnancy was reported as a strong predictor for long-term progression to prediabetes during postpartum. Our finding was consistent with study among Iranian mothers¹⁰. Another research examining the determinants of postpartum diabetes in mothers with GDM found that women who took insulin during pregnancy had a 5-fold higher chance of acquiring type 2 diabetes than women who followed a diet plan. The study also revealed that islet autoantibody-positive GDM mothers who needed insulin therapy to manage diabetes during pregnancy face with 100% risk diabetes.²⁶ On the contrary, other study found no significant connection between insulin usage at the time of pregnancy and subsequent development of diabetes and prediabetes.²⁷

Decision on starting insulin for the treatment of GDM depends on the local guidelines or protocols and the doctor's preference or patient's acceptance; therefore, this condition may contribute to the inconsistent finding in different studied populations.

Although previous study has indicated certain sociodemographic characteristic like age Muche *et al*¹², educational level²⁸ and employment status²⁹ were associated with the development of prediabetes among postpartum mothers, our study on the contrary did not found any significant association of those characteristics with prediabetes. Our finding agreed with other studies done in Belgium where mothers' age was not connected with abnormal glucose tolerance in the early postpartum period.³⁰ As most of the postpartum GDM mothers in our study were young, we hypothesized that the risk of developing into prediabetes is lower. Other than that, the limited sample size and narrow range of maternal ages may contribute to the lack of independent predictive ability for maternal age.

The majority of the postpartum GDM mothers in our study have reached the secondary school level of education (55.9%), while only (4.4%) finished education at the primary school level. A cross-sectional research in Cape Town, South Africa, reported the primary school education of the mother as one of the associated factors with the risk of type 2 DM.²⁸ Hence, higher education levels may reflect the differences in attitude, behaviour, and appropriate action towards health care. The educated mothers will better understand their health condition and related complication of the disease that developed during their pregnancy as opposed to uneducated mothers. There was a different opinion regarding the association between a mother's occupational status and the development of prediabetes. The employment status indirectly reflects the socioeconomic status of the whole family. Low income tends to be linked with a higher incidence of diabetes and diabetes-related complications. It is also associated with higher referral to diabetes care.²⁹ In our study, 225 (53.7%) of the postpartum GDM mothers were unemployed. Out of this number, 34 (57.6%) have prediabetes, and 191 (60.0%) were normal.

However, because the study is cross-sectional, determining the causal association between socioeconomic position and diabetes is difficult.

Strength and limitations

Our study may reflect the entire Besut district population as the study focuses on mothers who came for postpartum glucose testing from all government health clinics in the districts. Apart from that, the focus of the study on the associated factors which indirectly identified the high-risk group population might help in strategized and individualized interventions. This study provides new basic knowledge for Besut population and would lead to further study in the future especially in socio-economic as this study could not find any association of socio-economic and the outcome of prediabetes. However due to limitation of the secondary data, some of the essential factors contributing to prediabetes development, such as lifestyle factors, were limitedly found in the records. Both information on dietary intake and physical inactivity may contribute to the development of the disease.

Future studies should address the limitations of our research and discover more on the lifestyle factors that could prevent the early progression of prediabetes and diabetes. In addition, it would be advantageous if further analysis could be initiated based on the results from our report and then converted into public health interventions. For example, lifestyle intervention focused on diet and physical activity during pregnancy will help reduce and control glycaemic levels and thus lead to further control of GDM and indirectly helps in preventing the development of diabetes and prediabetes. Last but not least, we advocated for larger-scale prospective studies to assess the impacts of individual patient features and related variables on the development of postpartum diabetes and glucose intolerance

CONCLUSIONS

The prevalence of diabetes and prediabetes among GDM mothers in Besut, Terengganu were 2.3% and 13.8%, respectively. This finding was consistent with international

as well as local studies. Even though our finding was lower as compared to the national prevalence of diabetes, it still indicates that our population is facing a higher burden of non-communicable disease which warrant further aggressive interventions as prediabetes is not yet considered as a disease and still have high chances of turn over towards normal glucose tolerance. The multivariable analysis identified two factors that were significantly associated with prediabetes among postpartum GDM mothers, which were the previous history of GDM and insulin usage during index pregnancy to treat hyperglycaemia. This may be linked with prolonged destruction of β -cells and severe condition of hyperglycaemia. All the associated factors identified through this study can be used to antenatally recognized mothers at higher risk of postpartum diabetes and prediabetes preceding pregnancy. The timely recognition of prediabetes is critical for preventing type 2 DM before the development of overt disease.

CONFLICT OF INTEREST

None

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