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DETERMINANTES DO DIABETES MELLITUS GESTACIONAL

DETERMINANTS OF GESTATIONAL DIABETES MELLITUS

DETERMINAN DIABETES MELITUS GESTASIONAL

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RESUMO

Introdução: O Diabetes Mellitus Gestacional (DMG) é um distúrbio de tolerância à glicose que aparece pela primeira vez durante a gravidez. DMG pode causar uma variedade de complicações obstétricas e perinatais para mulheres grávidas e seus fetos. A prevalência de GDM na cidade de Surabaya em 2015 era de 2,29%, passando para 3,88% em 2018. **Objetivo.** O objetivo deste estudo foi analisar os determinantes (história familiar de diabetes mellitus, IMC, história de peso ao nascer, paridade e idade da gestante) que influenciam no DMG. **Métodos:** Esta pesquisa é um estudo analítico com abordagem observacional. O desenho da pesquisa foi realizado por meio de um estudo de caso-controle. O número de amostras neste estudo foi de 36 pessoas, 6 casos e 30 pessoas como controles, e foram retiradas aleatoriamente. A fonte de dados veio de dados secundários (prontuários de mulheres grávidas) no Centro de Saúde de Mulyorejo Surabaya. A análise utilizada neste estudo foi um teste de regressão logística simples. **Resultados e Discussão:** A análise mostrou que houve efeito da história familiar de diabetes mellitus (p = 0,035) sobre a incidência de DMG. A paridade é uma variável potencial (p = 0,077) na incidência de DMG. Enquanto isso, IMC, história de peso ao nascer e idade materna não tiveram efeito sobre a incidência de DMG. **Conclusões:** Mulheres grávidas com histórico familiar de diabetes que não estão em equilíbrio com um bom estilo de vida podem ter complicações quando experimentam o DMG.

Palavras-chave: *História Familiar de DM, Paridade, Diabetes Mellitus Gestacional (DMG).*

ABSTRACT

Background: Gestational Diabetes Mellitus (GDM) is a glucose tolerance disorder that first appears during pregnancy. GDM can cause a variety of obstetric and perinatal complications for pregnant women and their fetuses. The prevalence of GDM in the city of Surabaya in 2015 amounted to 2.29%, increasing to 3.88% in 2018. **Aim:** The purpose of this study was to analyze the determinants (family history of diabetes mellitus, BMI, history of birth weight, parity, and the age of the pregnant woman) that influence the GDM. **Methods:** This research is an analytical study with an observational approach. The research design was carried out using a case-control study. In this study, the number of samples was 36 people, 6 cases, and 30 people as controls, and were taken randomly. The data source obtained from secondary data (medical records of pregnant women) at Mulyorejo Health Center Surabaya. The analysis used in this study was a simple logistic regression test. **Results and Discussion:** The result showed an effect of a family history of diabetes mellitus (p = 0.035) on the incidence of GDM. Parity was a potential variable (p = 0.077) on the incidence of GDM. Meanwhile, BMI, history of birth weight, and mother's age did not affect the incidence of GDM. **Conclusion:** Pregnant women with a family history of diabetes who are not balanced with maintaining a good lifestyle can experience complications of developing GDM.

Keywords: *History of DM in the Family, Parity, Gestational Diabetes Mellitus (GDM).*

ABSTRAK

Latar Belakang: Diabetes Melitus Gestasional (DMG) adalah gangguan toleransi glukosa yang pertama kali muncul selama kehamilan. DMG dapat menyebabkan berbagai komplikasi kebidanan dan perinatal bagi ibu hamil dan janinnya. Prevalensi DMG di Kota Surabaya pada tahun 2015 sebesar 2,29% meningkat menjadi 3,88% pada

tahun 2018. **Tujuan:** Tujuan penelitian ini adalah untuk menganalisis determinan (riwayat diabetes melitus dalam keluarga, IMT, riwayat berat bayi lahir, paritas, dan usia ibu hamil) yang mempengaruhi kejadian DMG. **Metode:** Penelitian ini merupakan penelitian analitik dengan pendekatan observasional. Desain penelitian dilakukan dengan menggunakan studi kasus kontrol. Jumlah sampel dalam penelitian ini berjumlah 36 orang, 6 kasus dan 30 orang sebagai kontrol, dan diambil secara acak. Sumber data berasal dari data sekunder (rekam medis ibu hamil) di Puskesmas Mulyorejo Surabaya. Analisis yang digunakan dalam penelitian ini adalah uji regresi logistik sederhana. **Hasil dan Diskusi:** Hasil analisis dalam studi ini menunjukkan ada pengaruh riwayat keluarga diabetes mellitus (p = 0,035) terhadap kejadian DMG. Paritas merupakan variabel potensial (p = 0,077) terhadap kejadian DMG. Sedangkan BMI, riwayat berat badan lahir, dan umur ibu tidak berpengaruh terhadap kejadian DMG. **Kesimpulan:** Ibu hamil dengan riwayat keluarga diabetes yang tidak seimbang dengan mempertahankan gaya hidup yang baik dapat mengalami komplikasi berkembangnya DMG.

Kata kunci: *Riwayat DM dalam Keluarga, Paritas, Diabetes Melitus Gestasional (DMG).*

1. INTRODUCTION:

Gestational Diabetes Mellitus (GDM) is a glucose tolerance disorder that first appears during pregnancy (American Diabetes Association, 2004). The GDM condition applies to women who have never previously detected diabetes and are diagnosed with an increase in glucose during pregnancy or as a result of pregnancy. The International Diabetes Federation estimates in its research results that 20.9 million or 16.2% of live births by women in 2015 had some form of hyperglycemia in pregnancy. These hyperglycemia forms account for 85.1% of cases due to gestational diabetes mellitus (International Diabetes Federation, 2015). The prevalence of gestational diabetes mellitus in Indonesia is 1.9% -3.6% in general pregnancies (Soewondo and Pramono, 2011). The prevalence of GDM in Surabaya as described by the Dr. Soetomo General Hospital in 2015 was 2.29% (Sholehudin, 2015), increasing to 3.88% in 2018 (Brina, 2019).

Women with GDM are at high risk of developing type 2 diabetes after pregnancy (Bao *et al*., 2016). Other risk factors can occur in pregnant women over 30 years of age, obesity (BMI> 30), excessive weight gain during pregnancy, which is more than 11-12 kg, there is a family history of DM, a history of GDM in a previous pregnancy, parity, multiparity, hypertension, history of stillbirth (death of a baby in the womb), history of giving birth to a baby with congenital abnormalities, glucosuria (excess sugar levels in urine) during pregnancy, history of giving birth to large babies (>4000 grams) (Ferrara, 2007). Obesity and other factors that promote insulin resistance appear to increase the risk of type 2 diabetes. Offspring of women with GDM have an increased risk of obesity, glucose intolerance, and Diabetes Mellitus. (Wahab *et al*., 2020).

The classification of GDM in pregnant women has been a matter of debate on the cut-off point or when the mother can be diagnosed with gestational diabetes mellitus (Koning *et al*., 2016). In simple terms, the classification of Diabetes Mellitus or Gestational Diabetes Mellitus can be done according to when the mother was diagnosed with diabetes. If the mother acquires diabetes before pregnancy, the classification is pregestational diabetes Mellitus; if the mother is diagnosed for the first time during pregnancy, she is classified as diabetes Mellitus.

The incidence of diabetes Mellitus at Mulyorejo Health Center was the 7th most disease category with 647 incidents. Women with GDM are often asymptomatic, so screening is important for detection. Screening in women with GDM also needs to be done 6 or 12 weeks after delivery. Carry out lifelong diabetes screening in women with a history of GDM at least once every three years (Garrison, 2015).

In a normal pregnancy, insulin resistance increases in mid-pregnancy and continues until birth (Kampmann *et al*., 2019). This is the reason why GDM can only be detected in the second and third trimesters of gestation. The impact caused by mothers with GDM is that they are at high risk of experiencing excess weight gain, preeclampsia, eclampsia, cesarean section, cardiovascular complications, and death. (Perkins *et al*., 2007). The factors that cause the incidence of GDM are history of GDM in a previous pregnancy, the history of diabetes mellitus (DM) in the family (parents, siblings, grandparents), multiparity, BMI, and age of pregnant women (Agussalim *et al*., 2018). Macrosomia is one of the high risks of neonatal mortality. Macrosomics is a condition in which the fetus is born outside a certain body weight, usually more than 4000g or 4500g, regardless of the gestational age of the fetus (Said and Manji, 2016). Previous macrosomic babies weighing 4.5 kg or more are also at risk for gestational diabetes (NICE, 2015). Likewise, mothers with GDM are at risk of giving birth to macrosomic babies (KC *et al.,* 2015).

Therefore, this study aimed to analyze the factors of the occurrence of GDM to do prevention early and minimize the incidence of complications and maternal death.

2. MATERIALS AND METHODS:

2.1. Study Design

This study was an analytical study with an observational approach. The research design was carried out with a case-control study. This study group samples were pregnant women registered at Primary Health Care of Mulyorejo Surabaya from 2017 to May 2018. The total sample in this study was 36 people, 6 people as cases and 30 people as controls, and was taken randomly. The data source comes from secondary data (medical records of pregnant women) at Primary Health Care of Mulyorejo Surabaya.

The sample was calculated using the sample size formula for case control studies with propotion value for diabetes cases (Bener *et al*., 2011). Calculate the sample size with a ratio of cases and controls 1: 5 as follows:

$$N = (1+1/c)\ p\ q\ (Z_{1-\alpha/2} + Z_{1-\beta})^2 / (p_1 - p_0)^2$$
$$N = (1+1/5)\ 0{,}759\ (0{,}241)\ (1{,}96 + 0{,}842)^2 / (0{,}8 - 0{,}718)^2 = 5{,}4409$$

The calculation results show the minimum case sample is 5.4409 then rounded to 6. Because it uses a ratio of 1: 5, the number of samples of cases was 6 and controls was 30.

2.2. Data Collection

Data collection techniques used secondary data taken through patient medical records by asking the mothers about their visit. The data categorized the factors that affect the health risks of pregnant women into two. The first was health status factors that contain family history of diabetes mellitus sufferers by asking the mother whether there is a family who has diabetes mellitus (Yes or No), BMI was calculated from the ratio of height and weight (<25: normal, 25-29.9: overweight, ≥30: obesity). The second one was the reproductive status factor which contains history of birth weight (<2500 grams; 2500-3900 grams; ≥4000 grams) the birth weight which was more than 4000 grams is considered a macrosomic baby, parity was indicated by how many children have been born of the mother (>2 or ≤2) and the age of the pregnant woman (<20 years; 20-35 years;>35 years).

2.3. Ethics

This study has received ethical approval from the Health Research Ethics Committee of the Faculty of Public Health, Airlangga University, with number 441-KEPK.

2.4. Data Analysis

The data analysis used in this research was a simple logistic regression test. The initial stage of this analysis was to use variables for candidate selection. All independent variables were analyzed using a simple logistic regression selection test. If an independent variable has p ≤0,250, it becomes a candidate and can be continued to the multivariable test. The next stage is to test to see the effect of the variables together using multiple logistic regression. The independent variable is said to significantly influence the dependent variable if the p-value is <0.05.

3. RESULTS AND DISCUSSION:

The results showed that 11 mothers had a history of DM in the family and 36.4% who had GDM, while 8% of other mothers had GDM but there was no family history of DM. Not all mothers who have a family history of DM can experience GDM or vice versa. This might be influenced by the aware attitude of the mother, who already knows that she has a risk factor for a family history of DM in maintaining her lifestyle, either from food or physical activity. On the other hand, mothers who do not have a family history of diabetes will not necessarily avoid GDM if they do not maintain their lifestyle. In this study, respondents were divided based on 3 categories, namely BMI <25 (normal), 25≤IMT≤ 29.9 (overweight), and BMI ≥30 (obesity). Based on the study results, the BMI of women before pregnancy was in the overweight category, namely 18 people. Mothers with GDM who had a BMI before pregnancy were in the overweight category of 22.2%, and a normal BMI of 13.3%. Mothers who did not have GDM but had BMI in the obesity category were 3 people. In this study, it was found that mothers experienced the majority of GDM events with BMI in the range of 25≤IMT≤ 29.9. Mothers who have a BMI who are overweight are more at risk of experiencing GDM.

It could also be observed that of the 6 mothers who experienced GDM, only one mother had a history of birth weight more than 4000 grams (macrosomia). Most mothers have a history of giving birth to babies with normal weight 2500-3900 grams. There were 11.8% of mothers who

had GDM with a history of giving birth to babies weighing between 2500-3900 grams. The results showed that mothers who had a history of giving birth to babies weighing ≥4000 grams had no risk of developing GDM because most mothers who had GDM had babies with a history of normal birth weight, and only one mother with a history of macrosomic babies.

The distribution of the parity variable showed that almost all pregnant women had parity ≤2. Mothers with GDM with parity ≤2 were 14.7% of the total 34. Mothers with GDM with parity> 2 were only one person. The results in this study only found 2 mothers with multiparity, while only one mother developed GDM. Most of these mothers with parity ≤2 were probably due to the family planning program run well by the government.

The distribution of mothers in this study showed that the mean age of mothers is in the range of 20-35 years. The results of the study were only three mothers aged> 35 years. Mothers who have GDM 5 people have an age range of 25 to 35 years and mother ages> 35 years. The results of this study indicate that mothers who were susceptible to GDM were those between 25-35 years of age. This might happen because she felt that she was still young, so she ignored her diet and lifestyle.

3.1 Health Status Factors

The health status factor is a factor that is an intermediate determinant of influencing pregnancy complications and death in the mother (McCarthy and Maine, 1992). Health status factors include the family history of DM and the body mass index (BMI) of a mother before pregnancy. The study respondents were 6 pregnant women with GDM and 30 pregnant women who did not experience GDM. The following is a discussion of health status factors that influence GDM.

3.1.1 History of Diabetes Mellitus (DM) in the Family

The results showed that 4 mothers had a history of DM in the family and experienced GDM, while the other 2 mothers had GDM, but there was no family history of DM. Based on the multiple logistic regression test results, it was found that significant results were that the family history of DM affects the incidence of GDM in pregnant women. The analysis results also obtained an OR value that indicates that a family history of DM in pregnant women has a 22,000 times chance of causing GDM compared to pregnant women who do not have a history of DM in the family. This study is in line with a previous study that mothers with a family history of DM have a 1.481 fold increased risk for GDM compared with no family history of DM (Zhu *et al*., 2017).

History has a very strong influence on the incidence of GDM, because according to a study about 50 percent of patients with type 2 diabetes have a parent who has diabetes, and more than a third of diabetes patients have a sibling with diabetes (Tandra, 2008). So when a mother has a family history of DM, the mother has a greater risk of experiencing GDM during pregnancy. Research by Cong Luat Nguyen, *et al* (2018) on the prevalence of GDM from January 2000 to December 2016 states that the prevalence of GDM varies across countries, including identification of pregnant women during the first and second trimesters. Besides that, it is influenced by several factors, one of which is genetic factors. As a result of this gestational diabetes mellitus, the impact will only be visible after a few years; if it is not handled now, it will trigger an increase in the incidence of GDM. Mothers with GDM are at high risk for excess body weight gain, preeclampsia, eclampsia, cesarean section, and cardiovascular complications to maternal death. Even in the world, the incidence is up to 1.3%. After giving birth, mothers with GDM are at risk of developing type 2 diabetes. For example, in India, it is stated that 6.3% of 811 pregnancies in the Indian Prima tribe of Arizona even occur recurrent GDM in the future. Meanwhile, babies born to mothers with gestational diabetes are at high risk for macrosomia, while the prevalence in pregnant women with a family history of diabetes is 1.5% (Sheen YJ, *et al.*, 2019).

3.1.2 Body Mass Index (BMI) Before Pregnancy

BMI before pregnancy is a major determinant of pregnancy outcome. Increased BMI was associated with an increased risk of preeclampsia, GDM, gestational hypertension, and cesarean delivery (Nelson *et al*., 2009). According to the National Health and Nutrition Examination Survey, 33.4% of women aged 20 to 34 were obese (body mass index (BMI) ≥30), and 58.4% were overweight (BMI ≥25)(Riley *et al*., 2018).

The results of statistical tests with simple logistic regression showed that the BMI of mothers before pregnancy did not significantly affect the incidence of GDM. This is contrary to research (Bener *et al*., 2011), which states that obesity was the most significant factor in the incidence of GDM.

The incidence of GDM is associated with the epidemic incidence of obesity in the past 6-8 years. The long-term impact of GDM is to increase the risk of obstetric complications of pregnancy such as hypertension, cesarean section, and increased risk of perinatal complications such as increased incidence of macrosomia, fetal miscarriage, neonatal complications (hypoglycemia, polycythemia, hyperbilirubinemia) (Takashi Sugiyama, 2011).

This study has interesting results where all mothers (3 people) who have a BMI before pregnancy in the obese category do not experience GDM. This may occur because of the many factors that can influence GDM. As the results of previous studies, it was found that 54.3% of the sample of pregnant women had a BMI in the overweight or obese category, and 32% of them had GDM (Pinheiro and Goldani, 2018). Lack of a physical activity can increase insulin resistance in pregnant women (Kampmann *et al*., 2019), mothers who regularly do physical activity can reduce their risk of developing GDM (Lin *et al*., 2020). A review study of several articles suggests that diet and physical activity interventions can help prevent GDM were inconsistent (Zhang *et al*., 2016). However, a previous review of five studies found that recreational physical activity in early pregnancy can reduce the risk of GDM by more than 20% (Tobias *et al*., 2011).

3.2 Reproductive Status Factors

Reproductive status is a factor that is an intermediate determinant of influencing pregnancy complications and maternal mortality (McCarthy and Maine, 1992). Reproductive status factors include the history of birth weight, parity, and maternal age. The study respondents were 6 pregnant women with GDM and 30 pregnant women who did not experience GDM. The following is a discussion of reproductive status factors that influence GDM.

3.2.1 History of Birth Weight

One of the agreed risk factors for GDM was a history of having given birth to a macrosomic baby in a previous pregnancy without an explanation for stillbirth or neonatal death (Shannon and Wong, 2010). Women with a history of delivering a macrosomic baby have a significantly increased risk of having another macrosomic baby in a subsequent pregnancy. For women with two or more macrosomic babies, the risk was even more significant (Aye *et al*., 2011). Delivering a baby weighing more than 3.5 kilograms was a significant predictor of T2DM development (Herath *et al*., 2017).

In this study only one mother with a history of giving birth to a macrosomic baby. According to the simple logistic regression results, there is no significant relationship between the history of birth weight and the incidence of GDM. In line with the previous study, only 3 mothers suffered from GDM out of 50 mothers who gave birth to macrosomic babies (Oroh *et al*., 2015). Macrosomia has many other causes besides diabetes mellitus, such as obesity, multiparity (Oroh *et al*., 2015). 79% of macrosomic babies were born again to mothers who were not glucose intolerant (Magenheim *et al*., 2007). Macrosomic babies born to mothers with diabetes are more at risk of hyperinsulinemia than macrosomic babies born to mothers with normal sugar levels (Siraj *et al*., 2020).

3.2.2 Parity

The multiple logistic regression test results showed that parity was not a variable affected ($p = 0.077$) on the incidence of GDM. Still, parity was a potential variable for the incidence of GDM. The distribution of the parity variable showed that almost all pregnant women had parity ≤2. Mothers with GDM who have parity> 2 are only one person.

Nurrahmani (2012) said that mothers with multiparity (more than 3) have a risk factor for diabetes mellitus in pregnancy, which is about 78% of women with multiparity (more than 3). This can happen because physiological changes affect carbohydrate metabolism due to the presence of the placental hormone lactogen that is resistant to insulin. So that insulin resistance is not only due to the due date of birth, but the hormones estrogen, progesterone, cortisol, and prolactin also affect insulin resistance. Cortisol levels in pregnant women will increase 3 times during pregnancy. So the need for insulin in pregnant women becomes high and weight gain in pregnant women is also quite easy. Besides, it is a risk factor for diabetes that is influenced by changes in the lifestyle of every human being will impact on changes in disease patterns that occur in society. In other research, several factors that are part of the lifestyle are reducing the consumption of junk food which is currently becoming very popular among children to adults, other factors such as a healthy diet, regular exercise, and other lifestyles can affect the lower risk of mothers getting diabetes in pregnancy (Irawan, 2010).

The incidence of GDM per 1000 persons per year was 3.69 in primiparous women and 4.12 in multiparous women (Almahmeed *et al*., 2017).

Women with multiparous have a higher risk of developing diabetes than women with primiparous. The odds ratio for multiparous was 1.33 times the chance of getting diabetes mellitus compared to women with primiparous. GDM had a relationship with multiparity (Huillca-Briceño and Varillas, 2016). Multiparous mothers were more likely to develop GDM than primiparous (Zhu *et al*., 2017).

3.2.3 Age of Pregnant Women

The distribution of mothers in this study shows that the mean age of mothers was in the range of 20-35 years. This is consistent with previous studies that out of 87 mothers who experienced GDM, 64 (73.6%) were aged 25 to 35 (Xu *et al*., 2017). Delivering a child after 30 years is a significant predictor of T2DM development (Herath *et al*., 2017).

According to the simple logistic regression test results, it was found that maternal age did not affect the incidence of GDM. This contradicts with the previous study, which stated that age was a risk factor for GDM. The risk of GDM will increase with age. With each increase in 1 year of age (between 17 and 46 years of age), the risk for GDM increases by 5.3% (Zhu *et al*., 2017). Although in this study age did not influence the incidence of GDM, it should be noted that six mothers experience GDM who are at risk for developing DM in the next 5 to 10 years. The ages of these mothers ranged from 30-50 years when experiencing DM. This incident showed that there will be a period of degenerative disease, in this case, DM was no longer experienced by the elderly only. Therefore, it is important to pay attention, especially in the prevention and screening of the incidence of GDM in pregnant women.

4. CONCLUSIONS:

Pregnant women with a family history of diabetes that is not matched by maintaining a good lifestyle can develop complications of GDM. Most of the mothers did not have a family history of DM even though most of the mothers BMI was in the range 25≤IMT≤29.9. The distribution of the history of birth weight for infants is mostly in the range 2500-3900 g. The majority of mothers have parity of not more than 2 children. The distribution of mother's age was mostly in the range of 20-35 years.

Based on the influence analysis results, it was found that the health status factor which was a determinant (had an influence) on the incidence of GDM was a family history of DM. The reproductive status factor, parity, is a potential factor to influence the incidence of GDM. Therefore, there were several inputs for stakeholders to be able to prevent the incidence of GDM in this study, namely as follows: Health screening (integrated ANC and laboratory health tests) must be done (prioritized) for pregnant women at Primary Health Care of Mulyorejo Surabaya who has a history of DM in families and multiparity.

Mothers need to maintain their health with regular consultations related to their pregnancy to health service centers, especially hospitals. Routinely carry out health screening after childbirth and maintain a healthier lifestyle so that the GDM incident does not develop into DM in the future.

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Table 1. *Multivariate logistic regression test for GDM risk factors (N=30)*

Factors		GDM		Non-GDM		p-value	
		n	%	n	%	Selection of candidates	Multivariate test
History of DM in the Family						.052*	.035**
	Yes	4	36.4	7	63.6		
	No	2	8.0	23	92		
BMI						.808	
	Normal	2	13.3	13	86.7		
	Overweight	4	22.2	14	77.8		
	Obesity	0	.0	3	100.0		
History of Birth Weight (grams)						1.000	
	<2500	1	100.0	0	.0		
	2500-3900	4	11.8	30	88.2		
	≥4000	1	100.0	0	.0		
Parity						.240*	.077
	≤2	5	14.7	29	85.3		
	> 2	1	50.0	1	50.0		
Age of mother (years old)						.434	
	<20	0	.0	0	.0		
	20-35	5	15.2	28	84.8		
	> 35	1	33.3	2	66.7		
Total		6	16.7	30	83.3		

Notes: *significant to a selection of candidates (<.25); **significant to multivariate test (<.05)