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Correlation of Maternal Blood Glucose Level to Maternal Delivery and Fetal Outcome in Hasan Sadikin General Hospital

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ABSTRACT

Introduction: Increase of blood glucose level In pregnant woman correlated with increased risk of maternal morbidity, and problems in labour also affect child outcome. This phenomena cause by physiological changes occur in pregnancy such as placental factor and inflammation factor in circulation. Changes in inflammation factor like *tumor nerosis factor* (TNF-α) and beta-cell correlated gene disfunction (*potassium voltage-gated channel KQT-like 1* (*Kcnq1*) and *glucokinase* (*Gck*)) could affect blood glucose level. Blood glucose control in pregnant woman known to be effective to decrease and prevent complication in mother and fetus, such as preeclampsia, prematurity, low birth weight, and asphyxia baby. This research wish to know correlation of maternal blood glucose level to maternal delivery and fetal outcome.

Methods: This research use seconder data from medical records as retrospective cohort study. Subject of this study are pregnant mother which given birth in Hasan Sadikin Hospital (RSHS) sbetween January 2018 – December 2021 and has been performed blood glucose test when first time administered in Hasan Sadikin Hospital. Analitic statistic was performed with contingency correlation test, association test with chi-square and continued with multivariate logistic regression.

Results: From 8996 subjects, positive correlation was founded between high random blood glucose with preeclampsia (r=0.154, p<0.001), premature labour (r=0.020, p=0.052), and low birth weight (r= -0.034, p=0.003). Correlation between random blood glucose and asphyxia was unfounded (r=0.003, p=0.809).

Conclusion: There's weak positive correlation between random blood glucose to preeclampsia and prematurity incidence. There's also weak negative correlation between random blood glucose and baby birth weight. Correlation between blood glucose and APGAR score was unfounded.

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KEYWORDS: random blood glucose; pregnancy; maternal outcome; fetal outcome

INTRODUCTION

Maternal mortality rate (MMR) and neonatal mortality rate (NMR) are primary indicator for civil health and stated as one of the goals in Sustainable Development Goals (SDGs). According to *Survei Demografi Keluarga Indonesia* (SDKI) in 2012, Indonesian MMR reach 305/100.000 life birth and NMR reached 32 per 1.000 life birth. These numbers had make Indonesia has highest rank in Southeast Asia. One of the solution for these problems and to increase quality of mother and child is to do early detection and prevention also correct management is mandatory to prevent complication in pregnancy.

Different with gestational diabetes (GDM) incidence globally, GDM incidence in Indonesia only 1,9 - 3,6%. This number is relatively low compared GDM incidence in South East Asia which reach 24,2%. Some anomalies felt by the author seeing that number. First, in Indonesia GDM early screening was not perform yet in primary health care, and there's no guideline about antenatal care in primary and secondary health facility establish yet.

Until now, authors haven't found about correlation between maternal blood glucose and maternal and fetal outcome. This insight made authors to this research.

METHODS

This research use secondary data from medical records as retrospective cohort study. Total subject was 8996 subject, which analitic statistic was performed with contingency correlation test, association test with chi-square and continued with multivariate logistic regression.

Independent variable on this research is random blood glucose level, meanwhile dependent variable are maternal delivery outcome and fetal outcome. Correlation between two variables was assess with contingency correlation continued by multivariate logistic regression to determine the relation between variable (P <0.005).

RESULTS

From 8996 subjects, 1934 subjects were preeclampsia. Analytical statistics show positive correlation between random blood glucose level and preeclampsia (r=0.154, p<0.001), on subject with random blood glucose level ≥140 g/dl, incidence of preeclampsia increase by 27% with risk ratio (RR) 1.93. Based on multivariate analysis, found between random blood glucose, ages and parity affect the incidence rate of preeclampsia. Age ≥35, multiparity, and grande multiparity affect the risk of developing preeclampsia with adjusted RR 1.83.

Table.1 Correlation Between Random Blood Glucose and Preeclampsia

Variable	Total n=8996	Preeclampsia		P value	r-Coefficient	RR (95% CI)
		Yes n=1934	No n=7062			
Random Blood Glucose Level						
≥ 140 g/dL	5167	1396 (27.0)	3771 (73.0)	<0.001*	0.154	1.93 (1.76 – 2.10)
< 140 g/dL	3829	538 (14.1)	3291 (85.9)			

* r-coefficient calculated by contingency correlation, RR=Risk Ratio

Table 2. Multivariate Analysis on Random Blood Glucose with Preeclampsia

Variable	Adjusted RR (95% CI)	P value
Random Blood Glucose Level		
≥ 140 g/dL	1.87 (1.71 – 2.04)	<0.001*
< 140 g/dL	Ref	
Age		
≤ 17 y.o	0.91 (0.70 – 1.17)	0.449
18-34 y.o	Ref	
≥ 35 y.o	1.67 (1.28 – 2.17)	<0.001*
Parity		
Primiparity	Ref	
Multiparity	1.26 (1.15 – 1.39)	<0.001*
Grande multiparity	1.60 (1.39 – 1.83)	<0.001*

Dependent variable: Preeclampsia, RR=Risk Ratio

Random blood glucose level and age also affect the incidence of prematurity, meanwhile parity didn't affect prematurity incidence. Age ≤ 17 years old with random blood glucose level ≥ 140 g/dL affect the risk of prematurity with *adjusted* RR 1.05. Preeclampsia and prematurity also corelated with low birth weight, meanwhile random blood glucose level and age didn't affect incidence of low birth weight

Table 3. Correlation of Random Blood Glucose and Prematurity

Variable	Total n=8996	Prematurity		P value	r-Coefficient	RR (95% CI)
		Yes n=4096	No n=4900			
Random Blood Glucose Level						
≥ 140 g/dL	5167	2398 (46.4)	2769 (53.6)	0.052	0.020	1.05 (1.00 – 1.10)
< 140 g/dL	3829	1698 (44.3)	2131 (55.7)			

* r-coefficient calculated by contingency correlation, RR=Risk Ratio

Table 4. Multivariate Analysis on Random Blood Glucose with Prematurity

Variable	Adjusted RR (95% CI)	P value
Random Blood Glucose Level		
≥ 140 g/dL	1.05 (1.00 – 1.10)	0.042*
< 140 g/dL	Ref	
Age		
≤ 17 y.o	1.17 (1.05 – 1.30)	0.004*
18-34 y.o	Ref	
≥ 35 y.o	1.04 (0.98 – 1.09)	0.252
Parity		
Primiparity	Ref	
Multiparity	1.00 (0.95 – 1.06)	0.874
Grande multiparity	0.92 (0.83 – 1.02)	0.118

Dependent variable: Prematurity, RR=Risk Ratio

Table 5. Correlation of Random Blood Glucose and Birth Weight

Variable	Total n=7855	Birth Weight		P value	r-Coefficient	RR (95% CI)
		Low Birth Weight n=4010	Normal n=3845			
Random Blood Glucose Level						
≥ 140 g/dL	4420	2322 (52.5)	2098 (47.5)	0.003*	-0.034	1.07 (1.02 – 1.12)
< 140 g/dL	3435	1688 (49.1)	1747 (50.9)			

* r-coefficient calculated by contingency correlation, RR=Risk Ratio

Table 6. Multivariate Analysis on Random Blood Glucose with Birth Weight

Variable	Adjusted RR (95% CI)	P Value
Random Blood Glucose Level		
≥ 140 g/dL	1.00 (0.98 – 1.03)	0.733
< 140 g/dL	Ref	
Age		
≤ 17 y.o	1.03 (0.98 – 1.08)	0.199
18-34 y.o	Ref	
≥ 35 y.o	1.00 (0.98 – 1.08)	0.982
Preeclampsia		
Yes	4.78 (4.49 – 5.10)	<0.001*
No	Ref	
Prematurity		
Yes	1.03 (1.00 – 1.05)	0.027*
No	Ref	

Dependent Variable: Low birth weight, RR=Risk Ratio

Preeclampsia and prematurity increase the incidence risk of low birth weight. The adjusted RR value for preeclampsia is 4.78. Age and prematurity have an effect on the incidence of asphyxia, while blood glucose and parity have no effect on prematurity. Age ≤ 17 years and ≥ 35 years increases the risk of asphyxia. The adjusted RR value for age ≤ 17 years is 1.49 and for age ≥ 35 years is 1.22, and the adjusted RR value for prematurity is 2.88.

Table 7. Correlation of Random Blood Glucose with APGAR Score

Variable	Total n=8996	APGAR		P value	r-Coefficient	RR (95% CI)
		Asphyxia n=889	Normal n=8107			
Random Blood Glucose Level						
≥ 140 g/dL	5167	514 (9.9)	4653 (90.1)	0.809	0.003	1.06 (0.90 – 1.15)
< 140 g/dL	3829	375 (9.8)	3454 (90.2)			

* r-coefficient calculated by contingency correlation, RR=Risk Ratio

Table 8. Multivariate Analysis on Random Blood Glucose with Asphyxia

Variable	Adjusted RR (95% CI)	P value
Random Blood Glucose Level		
≥ 140 g/dL	0.99 (0.88 – 1.13)	0.926
< 140 g/dL	Ref	
Age		
≤ 17 y.o	1.49 (1.15 – 1.92)	0.003*
18-34 y.o	Ref	
≥ 35 y.o	1.22 (1.06 – 1.40)	0.005*
Prematurity		
Yes	2.88 (2.51 – 3.32)	<0.001*
No	Ref	

Dependent variable: Asphyxia, RR=Risk Ratio

DISCUSSION

Of the 8996 subjects in this study, there were 54.6% of the subjects who had spontaneous deliveries and 45.4% had caesarean section deliveries. The highest parity was grande multipara (54.0%), then primipara (38.6%) and multipara 7.4%. The average blood glucose level in the subjects of this study was 158 g/dL (SD: 64 g/dL), random blood glucose level <140 g/dl was 42.6%, and random blood glucose level ≥140 g/dl was 57.4%.

Although this study used random blood glucose variables, it is possible that pregnant women with high random blood glucose have experienced chronic hyperglycemia which plays a role in the pathogenesis of complications that occur in both mother and baby. The impact of acute hyperglycemia can be seen in an in vitro study conducted by Spindler et al in 2016, in healthy subjects who were given dextrose and ocreotide intravenously for 2 hours in a row, showing a decrease in IL-6 expression in intermediate mosocytes. Hyperglycemia conditions will initially cause a non-enzymatic reaction of glucose with amino acids which will form the formation of amadori product which is reversible. This amadori product will then undergo more complex reactions such as rearrangement, dehydration and condensation processes to form irreversible bonds called advanced glycation end products (AGEs) which have an important role in various complications of hyperglycemia.

In this study, it was shown that there was a weak positive correlation between transient blood glucose levels and the incidence of preeclampsia (r=0.154, p<0.001). It was seen that 14.1% of subjects with random blood glucose level <140 g/dl had preeclampsia. then in subjects with random blood glucose level ≥140 g/dl, the incidence of preeclampsia increased to 27.0%, the Risk Ratio (RR) was 1.93, meaning that subjects with current blood glucose levels ≥140 g/dl had 1.93 times the risk of experiencing preeclampsia.

In multivariate analysis, it was found that random blood glucose level, age and parity had an influence on the incidence of preeclampsia. Random blood glucose level ≥ 140, age ≥ 35 years, multipara and grande multipara types of parity increase the risk of preeclampsia with RR 1.87, 1.67, 1.26, and 1.6. With relative risks that are not much different (1.60 and 1.67), we can see that grande multipara occurs mostly in the age group > 35 years, so it is very likely that in addition to high blood glucose, the incidence of preeclampsia in the subjects of this study is also influenced by the mother's metabolic condition. before pregnancy or the possibility of chronic diseases that have been owned by the mother before pregnancy.

In multivariate analysis, it was found that random blood glucose level ≥ 140 g/dL and maternal age ≤ 17 years had a risk for the occurrence of prematurity with RR 1.05 and 1.17. Prematurity itself is influenced by many factors, based on a literature search it is said that hyperglycemia in pregnancy directly causes an increase in oxidative stress which is the basic mechanism that causes preterm labor. Indirectly, the condition of preeclampsia which increases at the age of ≤ 17 years can also affect prematurity, one of the treatments for

preeclampsia in pregnant women is by termination of pregnancy.

There is a negative correlation between maternal blood glucose levels and baby's birth weight (r= -0.034, p=0.003), in subjects with random blood glucose level <140 g/dl, 49.1% had low birth weight, then in subjects with random blood glucose level S ≥140 g/dl, 52.5% had low birth weight. RR value was 1.07. Based on multivariate logistic regression analysis, it was found that preeclampsia and prematurity had an influence on the incidence of low birth weight babies, while random blood glucose level and age had no effect on low birth weight babies. Preeclampsia and prematurity increase the risk of low birth weight incidences. The adjusted RR value for preeclampsia was 4.78, meaning that subjects with preeclampsia had 4.78 times risk of having a low birth weight baby compared to normal subjects after controlled for blood glucose levels, age and prematurity. The adjusted RR value of prematurity was 1.03, meaning that subjects with prematurity had 1.03 times risk of having a low birth weight baby compared to normal subjects after controlled for blood glucose levels, age and preeclampsia. In addition, there are other physiological factors that affect the baby's birth weight, which is preterm gestational age.

From the results of this study, it was found that there was no correlation between random blood glucose levels with the incidence of asphyxia (r=0.003, p=0.809). From the multivariate test, it was found that age and prematurity had an effect on the incidence of asphyxia, while random blood glucose and parity had no effect on prematurity. Age ≤17 years and ≥35 years increases the risk of asphyxia. The adjusted RR value for age ≤17 years was 1.49 and age ≥ 35 years was 1.22, meaning that subjects aged ≤17 years had 1.49 times and age ≥35 years had 1.22 times risk of having an asphyxia baby compared to ages 18-35 years. The adjusted RR value of prematurity was 2.88, meaning that subjects with prematurity had 2.88 times risk of having an asphyxia baby.

Based on the results of this study, it was found that there is a correlation between maternal blood glucose levels and the occurrence of poor birth outcomes, so that random blood glucose test during pregnancy is a practical and efficient alternative method of choice for now in screening gestational diabetes mellitus and controlling blood glucose levels in pregnant women in Indonesia if the OGTT is difficult to do, but still inferior when compared to fasting blood glucose and 2 hours post prandial blood glucose test.

CONCLUSION

There is a weak positive correlation between random blood glucose levels with the incidence of preeclampsia and prematurity. There is a weak negative correlation between random blood glucose levels and birth weight, there is no correlation between random blood glucose levels and poor APGAR scores.

ETHICAL APPROVAL

Research have been permitted by Ethical Comitte of RSUP Dr. Hasan Sadikin Bandung
(*Nomor*: LB.02.01/X.6.5/220/2022)

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