Research Article

Glycated Albumin as an Outcome Predictor in Pregnant Women with Diabetes Mellitus

Glycated Albumin sebagai Prediksi Hasil pada Perempuan Hamil dengan Diabetes Melitus

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Abstract

Objective: To determine the correlation between Glycated Albumin concentrations with the outcome of pregnant women with Type 2 Diabetes Mellitus in Zainoel Abidin Hospital, Banda Aceh.

Methods: This was an observational correlational study using a cross-sectional design. Subjects include pregnant women with a history of Type 2 Diabetes Mellitus who are examined for serum GA levels using colorimetric enzymatic methods and the outcomes will be assessed during pregnancy. Data analysis was performed using the ETA test and Receiver Operating Characteristic (ROC) curve.

Results: A total of 29 subjects with a mean age of 33.25 years had normal maternal outcome and those with a mean age of 34.92 years had abnormal maternal outcome. Statistically there was a significant correlation between GA levels and the maternal outcome of pregnant women with Type 2 Diabetes Mellitus (p = 0.009) with a moderate degree of negative correlation (r = 0.477). The GA cut-off for pregnancy outcome is 16.77% with a sensitivity and specificity of 76% and 75% respectively.

Conclusions: Examination of GA concentration can be used as a predictor to assess maternal outcomes during pregnancy with moderate correlation and a cutoff point of 16.77%.

Keywords: diabetes mellitus, glycated albumin, maternal outcome, pregnancy.

Abstrak

Tujuan: *Untuk mengetahui korelasi kadar Glycated Albumin terhadap outcome pada ibu hamil yang menderita diabetes melitus tipe I dan untuk mengetahui berapa kadar Glycated Albumin yang dapat memberikan hasil buruk pada ibu hamil yang menderita diabetes melitus tipe II di RSUD dr. Zainoel Abidin Banda Aceh.*

Metode: *Penelitian ini merupakan studi korelatif observasional menggunakan desain potong lintang. Perempuan hamil dengan riwayat DMT2 akan diperiksan kadar GA serum menggunakan metode enzimatik kolorimetri serta akan dinilai outcome selama kehamilan. Analisis data dilakukan menggunakan uji Eta dan kurva Receiver Operating Characteristic (ROC) dengan tingkat kepercayaan 95%.*

Hasil: *Sebanyak 29 subjek dengan rerata usia 33,25 tahun (hasil normal) dan 34,92 tahun (hasil kelainan). Secara statistik terdapat korelasi yang bermakna antara kadar GA dan outcome ibu penderita DMT2 (p = 0,009) dengan derajat korelasi sedang (r = 0,477) dengan arah korelasi negatif. Titik potong GA terhadap outcome kehamilan adalah 16,77% dengan sensitifitas dan spesisitas secara berurutan 76% dan 75%.*

Kesimpulan: *Pemeriksaan GA dapat dijadikan sebagai prediktor untuk menilai outcome ibu selama kehamilan dengan tingkat korelasi sedang dan titik potong 16,77%.*

Kata kunci: *diabetes melitus, glikasi albumin, hamil, luaran ibu.*

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INTRODUCTION

Type 2 diabetes is characterized by hyperglycemia and results from a combination of insulin resistance, inadequate insulin secretion, and excessive or inappropriate glucagon secretion. Uncontrolled type 2 diabetes is associated with various microvascular, macrovascular and neuropathic complications. Unlike patients with type 1 diabetes mellitus, patients with type 2 are not completely dependent on insulin for life. Diabetes mellitus is a chronic disease that requires long-term medical attention in order to prevent complications which may occur.[1]

The prevalence of diabetes is increasing worldwide. The International Diabetes Federation predicts that the number of people living with diabetes will increase from 366 million in 2011 to 552 million in 2030.[2] The top ten countries with leading incidences of diabetes today include India, China, the United States, Indonesia, Japan, Pakistan, Russia, Brazil, Italy and Bangladesh. The biggest increase in diabetes will occur in Africa over the next 20 years. About 80% of people in Africa with diabetes are undiagnosed and many cases occur at the age of 30 to 60 years with high mortality rates.[1]

Optimal control of blood sugar levels in the first and second trimesters of pregnancy is important to prevent complications in both the mother and fetus. The American Diabetes Association and the UK National Institute for Health and Care Excellence encourages proper glycemic control for women with type 1 diabetes during early pregnancy (recommended HbA1c levels <48 mmol / mol [<6.5%]).[3] Maternal influences due to diabetes can be subdivided during pregnancy, labor and puerperium. During pregnancy, diabetes can cause abortion, preeclampsia, polyhydramnios, premature labor and increased risk of pelvic head disproportion and malpresentation. During labor, diabetic complications include prolonged labor due to macrosomia, shoulder dystocia, increased risk for operation, rupture of the birth canal and postpartum hemorrhage. During pueperium, puerperal sepsis caused by immunocompromised conditions in pregnant women with diabetes may occur and can increase maternal morbidity. Effects of diabetes on the fetus include Fetus intrauterine death of the fetus, Macrosomia, late pulmonary maturation, birth trauma, growth retardation, congenital malfromation, and increased neonatal mortality.

Optimal maintenance of blood glucose levels is known to be associated with decreased complications in diabetes mellitus. In 2010 the American Diabetes Association (ADA) included HbA1c levels in the diagnostic criteria of Diabetes and recommend that HbA1C examination should be performed to control diabetic complications.[4-6] It has recently been reported that there are biomarkers that are more sensitive than HbA1C to indicate diabetes, namely Glycated Albumin (GA). Glycated Albumin was declared 10 times more sensitive than HbA1C in a study which examined a group of diabetics before and after undergoing diabetes therapy. The aim of this research is to find out whether glycated albumin levels is correlated with maternal outcome in pregnant women suffering from type II diabetes mellitus at the Regional General Hospital (RSUD) Dr. Zainoel Abidin Banda Aceh.

METHODS

This was a cross sectional design. The aim of this study is to determine the correlation between Glycated Albumin levels and the maternal outcome of pregnant women with Type 2 Diabetes. This research was conducted in the delivery suite of the Dr. Zainoel Abidin (RSUZA) General Hospital Banda Aceh from 4th January 2019 to 4th January 2020. Laboratory tests for Glycated Albumin levels were conducted at the Prodia Laboratory in Banda Aceh.

Inclusion criteria include a diagnosis of Diabetes Type 2 in pregnant women aged between 18 to 39 years old which is confirmed by an Internal Medicine Specialist. Exclusion criteria include: twin pregnancies, consumption of medication which affect pregnancies (for example, drugs which cause abortion and disruption of fetal organ development), pregnant women with congenital heart defects, autoimmune disease, malnutrition and placental and uterine abnormalities.

Blood specimens for examination of Glycated Albumin levels were taken from mediana cubital vein. About 3 ml was inserted into a serum separator tube and sent to the Banda Aceh Prodia Laboratory. Glycated albumin levels were assessed using colorimetric enzymatic method. The diagnosis of Diabetes Type 2 is made by an Internal Medicine Specialist. All data collected are analysed further using the ETA test and Receiver Operating Characteristic (ROC) curve.

RESULTS

There were 29 pregnant women suffering from type 2 diabetes mellitus who fulfilled the subject inclusion criteria. General characteristics of respondents and its respective maternal outcome are as follows:

Table 1. General Characteristics of Respondents and its Respective Maternal Outcome

Variable	Maternal Outcome	
	Normal (n=5)	**Abnormal (n=24)**
Age of Mother (years)	36 ± 3.16	34.42 ± 4.12
Gestational Age (weeks)	38.4 ± 0.89	29.25 ± 10.13
Body Mass Index (Kg/m2)	29.82 ± 1.18	30.23 ± 4,52
Fasting Blood Glucose Concentration (mg/dL)	99.6 ± 19.55	164.88 ± 70.01
2 hours Post Prandial Blood Glucose Levels (mg/dL)	143 ± 32.57	236.08 ± 92.73
HbA1C Concentrations (%)	6.02 ± 0.24	8.22 ± 1.58
Gestational		
G1	0	3 (12.5)
G2	2 (40)	4 (16.7)
G3	1 (20)	8 (33.3)
G4	0	5 (20.8)
G5	2 (40)	2 (8.3)
G6	0	1 (4.2)
Parity		
P0	0	3 (12.5)
P1	2 (40)	8 (33.3)
P2	1 (20)	7 (29.2)
P3	1 (20)	4 (16.7)
P4	1 (20)	2 (8.3)
Abortus		
A0	4 (80)	16 (66.7)
A1	1 (20)	5 (20.8)
A2	0	2 (8.3)
A3	0	1 (4.2)
Diagnosis upon first visitation		
Incomplete Abortion	0	3 (12.5)
Severe Preeclampsia	0	8 (33.3)
Normal Delivery	5 (100)	0
Preterm Labour	0	2 (8.3)
Complete Abortion	0	1 (4.2)
IUGR	0	2 (8.3)
Macrosomia	0	4 (16.7)
Threatened Premature Labour	0	2 (8.3)
Missed Abortion	0	1 (4.2)

The distribution of parity and diagnosis are presented in the table above. The group with normal outcomes is dominated by the parity G1 and G5, P1 and A0, while the group with abnormalities is dominated by G3P1A0. Most groups of pregnant women with abnormalities had a diagnosis of severe preeclampsia (33.3%) and macrosomia (16.7%) and also Preterm Labor, IUGR and premature labor with an incidence percentage of 8.3% each.

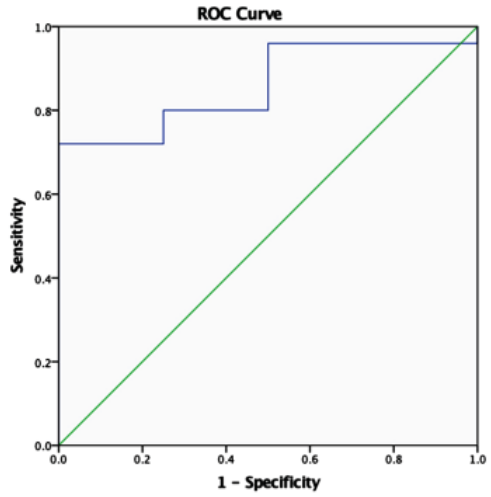

Figure 1. ROC Curve showing the correlation between Glycated Albumin and Maternal Outcome

The diagram above shows the Receiver Operating Characteristic (ROC) curve which shows the Area Under Curve (AUC) of 0.860. Based on these values it can be concluded that GA examination can be used as a predictor of pregnancy outcome in women suffering from type II DM with a discrimination rate of 86%. Furthermore, by using the coordinate of the curve, the GA intersection point is statistically 16.77%. The sensitivity and specificity values of the cut points are 76% and 75% respectively.

Table 2. Analysis of the Correlation of Study Variables

Glycated Albumin	Mean (Min – Max)	R*	*P-value*
Normal	12.54 (7.2 – 16.67)	-0.477	0.009
Abnormal	20.56 (7.1 – 38.2)		

Based on the ETA correlative test results above, it can be concluded that there is a correlation between glycated albumin levels and the outcome of mothers suffering from type II diabetes with a significance level of 0.009. Correlation coefficient values between the two variables indicate medium strength with a value of R = 0.477 with a negative correlation.

DISCUSSION

Infants of diabetic mothers generally experience various complications related to fetal hyperinsulinemia induced by maternal hyperinsulinemia. In the first trimester, maternal hyperinsulinemia can cause hyperinsulinemia embryopathy which can cause major disability and spontaneous abortion. Furthermore, in the second and third trimesters, maternal hyperinsulinemia can cause fetal hyperglycemia, hyperinsulinemia, myocardial hypertrophy, delay of pulmonary maturation and macrosomia.[7]

At present the gold standard for checking glucose levels is by measuring the levels of glycated hemoglobin (HbA1C). This examination provides information of varying blood glucose levels during the last 2 to 3 months. However, HbA1C levels are as dependent on the abnormal life span of erythrocytes as they are with iron deficiency anemia. Pregnant women with diabetes mellitus or gestational diabetes mellitus often have iron deficiency anemia, making the HbA1C examination inaccurate.[8,9]

In general, maternal outcomes can be divided into three, namely during pregnancy, labor and puerperium. Outcome during pregnancy can be in the form of abortion, preeclampsia, polyhydramnios, preterm labor. During labor in the form of prolonged labor due to a large baby, shoulder dystocia, ruptured birth canal and postpartum hemorrhage. Puerperal sepsis caused by immunocompromised conditions in pregnant women with diabetes can increase meternal morbidity. Furthermore, negative effects which may occur to the fetus include IUFD, macrosomia, late lung maturation, birth trauma, growth retardation, congenital malfromation, and increased neonatal mortality.[4]

The condition of hyperglycemia in the fetus occurs when the maternal pancreatic insulin response is inadequate, this manifests as a recurring postprandial hyperglycemic episode. This postprandial episode is a major cause of rapid growth in the fetus. Maternal and fetal blood glucose levels are accompanied by episodic fetal hyperinsulinemia. Fetal hyperinsulinemia causes an increase in the storage of excess nutrients, causing macrosomia. Energy expenditure associated with the conversion of excess glucose into fat causes depletion of fetal oxygen levels. These episodes of fetal hypoxia are accompanied by increased adrenal catecholamines, which cause hypertension, cardiac remodeling and hypertrophy, erythropoietin stimulation, red blood cell hyperplasia, and increased hematocrit concentration. Polycythaemia occurs in 5-10% of newborns of diabetic mothers. High hematocrit values in neonates cause vascular sludging, poor circulation, and postnatal hyperbilirubinemia.[10]

Adverse effects due to abnormal maternal metabolism in offspring have also been observed. Glucose intolerance and higher serum

insulin levels are more common in children of diabetic mothers. Several literature supports the relationship between intrauterine exposure with diabetic mothers and the risk of metabolic syndrome later in life. Metabolic syndromes in childhood include obesity, hypertension, dyslipidemia, and glucose intolerance. Fetuses of diabetic women born with a large age for gestation appear to be at greatest risk.[11]

Children born to mothers with diabetes exhibit higher levels of cardiac biomarkers for endothelial damage, as well as higher levels of leptin, BMI, waist circumference, and systolic blood pressure. This relationship remained significant even in pregnant women with a previously normal BMI.[7]

Diabetes management during pregnancy with continuous glucose monitoring (CGM) can reduce maternal hyperglycemia and macrosomia.[12] Maintaining normal blood glucose levels has been known to reduce the risk of maternal and neonatal complications during pregnancy. Referring to the study, monitoring of glucose levels using appropriate modalities is needed to improve neonatal and maternal outcomes during pregnancy and childbirth. A multicenter study concluded that GA examination is more superior for diabetes management during pregnancy than HbA1C.[13]

Glycated albumin (GA) is a ketoamine formed from albumin and glucose binded by non-enzymatic oxidation reaction, it is considered as an index of glycemic control that is not influenced by abnormalities in hemoglobin metabolism. Glycated albumin is able to monitor the administration of diabetes therapy and also anticipate earlier complications of DM. GA is not affected by albumin concentration because GA calculates the ratio of total serum albumin.[12]

However, before carrying out a GA examination on pregnant women, several factors which can affect serum albumin need to be considered. Serum GA levels are influenced by several factors associated with albumin regulation regardless of diabetes status such as thyroid dysfunction and cirrhosis. For example, thyroid hormone is known to play a role in albumin catabolism. Serum GA levels are positively correlated with serum TSH and negatively correlated to free T3 and T4. In addition, GA levels are also influenced by age and nutritional status.

Recent studies have reported the effectiveness of examining glycated albumin (GA) as a marker (biomarker) of glucose control in pregnant women. Compared to HbA1C, GA describes blood glucose levels with a shorter duration of 2 to 3 weeks. GA is not affected by the life span of erythrocytes like HbA1C, so it is very useful during pregnancy.[14] In addition to acting as a control of blood glucose levels, this study proves the correlation between GA levels on pregnancy outcomes in women suffering from type 2 diabetes mellitus.

Similar to this study, Sugawara et al in 2016 reported that GA examination served as a predictor of fetal complications during pregnancy. With a GA cutoff of 15.8% in the study, it was known that various neonatal complications such as hyperglycemia, respiratory distress, hypocalcemia, myocardial hypertrophy and macrosomia were identified.[15] However, the GA cutoff point obtained from this study which predicts maternal pregnancy outcomes with DMT2 was found greater than 16.7%.

CONCLUSION

Our study concludes that examination of Glycated Albumin concentration can be used as a predictor to assess maternal outcomes during pregnancy with a moderate correlation level and a cutoff point of 16.77%.

SUGGESTION

Hopefully, this research can inspire more researchers to conduct more studies which reaffirm the importance of Glycated Albumin as a screening modality and its ability to predict maternal outcome in pregnant women with Type 2 Diabetes Mellitus.

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