

## Research Article

## Role of Glycated Albumin during Pregnancy

*Albumin Glikat pada Kehamilan*Suzanna Immanuel<sup>1</sup>, Thoeng Ronald<sup>1</sup>, Kanadi Sumapradja<sup>2</sup>, Arini Setiawati<sup>3</sup><sup>1</sup>Department of Clinical Pathology<sup>2</sup>Department of Obstetrics and Gynecology<sup>3</sup>Department of Pharmacology and Therapeutics

Faculty of Medicine Universitas Indonesia/

Dr. Cipto Mangunkusumo Hospital

Jakarta

## Abstract

**Objective:** To determine the glycated albumin profile during pregnancy with normal glycemic status.**Methods:** We recruited 60 pregnant women between 21 and 36 weeks of gestation. We conducted several laboratory tests, such as glycated albumin, blood glucose, and albumin. These parameters were compared among four groups of gestational age (21-24 weeks, 25-28 weeks, 29-32 weeks, and 33-36 weeks) using ANOVA or Kruskal-Wallis test continued by Post-hoc test.**Results:** Glycated albumin was not statistically different among the groups. Albumin level of 33-36 weeks of gestation women (3.6 (SD 0.2) g/dl) was lower than 21-24 weeks of gestation women (3.8 (SD 0.2) g/dl).**Conclusion:** Glycated albumin level is not affected by gestational age. Therefore, glycated albumin may be used as glycemic status indicator during pregnancy from 21 to 36 weeks.

[Indones J Obstet Gynecol 2017; 5-1: 16-18]

**Keywords:** HbA1c, glycated albumin, glycemic status, pregnancy

## Abstrak

**Tujuan:** Mengetahui karakteristik albumin glikat pada kehamilan dengan status glikemik normal.**Metode:** Enam puluh perempuan hamil 21-36 minggu. Dilakukan pemeriksaan albumin glikat, glukosa darah, dan albumin. Parameter-parameter tersebut dibandingkan antara empat kelompok usia kehamilan (21-24 minggu, 25-28 minggu, 29-32 minggu, dan 33-36 minggu) menggunakan uji ANOVA atau Kruskal-Wallis dan dilanjutkan dengan uji Post-hoc.**Hasil:** Kadar albumin glikat tidak berbeda antara keempat kelompok usia kehamilan. Kadar albumin pada kelompok kehamilan 33-36 minggu (3.6 (SB 0.2) g/dl) lebih rendah dibandingkan kelompok kehamilan 21-24 minggu (3.8 (SB 0.2) g/dl).**Kesimpulan:** Kadar albumin glikat tidak terpengaruh dengan usia kehamilan. Albumin glikat dapat menjadi penanda status glikemik pada usia kehamilan 21-36 minggu.

[Maj Obstet Ginekol Indones 2017; 5-1: 16-18]

**Kata kunci:** albumin glikat, HbA1c, kehamilan, status glikemik**Correspondence:** Thoeng Ronald; thoeng\_ronald@hotmail.com

## INTRODUCTION

In 2013, International Diabetes Federation (IDF) estimated that 21.4 million women in the world suffering from hyperglycemia in pregnancy. It was estimated that 16% of them suffered from gestational diabetes mellitus (GDM); thus, it required close monitoring during pregnancy and after childbirth. Southeast Asia had the highest prevalence of hyperglycemia in pregnancy at 25.0% compared with Europe at 12.6% (table 1).<sup>1</sup>

Untreated hyperglycemia can lead to several complications both to the mother and fetal, such as impaired invasion of cytotrophoblast that causes placental hypoxia releasing antiangiogenic factors, such as soluble fms-like tyrosine kinase-1 (sFlt-1)

resulting to preeclampsia, premature birth, fetal hyperinsulinemia that causes diabetic fetopathy including macrosomia, increasing the cesarean section rate, perinatal trauma, neonatal hypoglycemia, and fetal death. International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommends screening for diagnosis of GDM using oral glucose tolerance test (OGTT) at 24-28 weeks of gestation. The procedure is through dissolving 75 grams of glucose to 200 ml water for all pregnant women.<sup>1-5</sup>

We need an indicator not only as a tool for monitoring the glycemic status during pregnancy, but also to predict about possible complication for mother and baby.

**Table 1.** Prevalence of Hyperglycemia in Pregnancy (20-49 years) in 2013<sup>1</sup>

Region	Number of Cases per Live Births (Million)	Prevalence (%)
Africa	4.6	14.4
Europe	1.7	12.6
Middle East and North Africa	3.4	17.5
North America and the Caribbean	0.9	10.4
Central and South America	0.9	11.4
Southeast Asia	6.3	25.0
Western Pacific	3.7	11.9

Glycosylated albumin is a new indicator for monitoring glycemic status which is not affected by the condition of anemia. Glycosylated albumin is formed through a process of non-enzymatic glycation, in which glucose is covalently bonded to the amino acid residues such as lysine, arginine, cysteine of albumin. Through Amadori reaction, it forms ketoamine stable form. Glycosylated albumin can indicate glycemic status for the previous 2 weeks because albumin half-life is only 15-20 days. Therefore, glycosylated albumin can be used to monitor short-term glycemic status. Study by Hashimoto, et al. on 47 pregnant women with gestational age of 21-36 weeks found glycosylated albumin level was not influenced by gestational age.<sup>6-9</sup> This study aims to determine the profile glycosylated albumin during pregnancy with normal glycemic status.

## METHODS

This was a cross-sectional study design which recruited 60 pregnant women with 21 to 36 weeks of gestation. The study was conducted from April to May 2016 and it was approved by the ethics committee of the Dr. Cipto Mangunkusumo Hospital/Faculty of Medicine, Universitas Indonesia with the approval number of 260/UN2.F1/ETHICS/2016.

We divided sixty pregnant women at gestational age 21-36 weeks into four groups: 17 subjects in group I (21-24 weeks of gestation), 11 subjects in group II (25-28 weeks of gestation), 16 subjects in group III (29-32 weeks of gestation), and 16

subjects in group IV (33-36 weeks of gestation). The inclusion criteria were all pregnant women with blood glucose levels less than 200 mg/dl and we excluded women with thyroid disease, cirrhosis, diabetes, proteinuria, and corticosteroid therapy. We took 4 ml serum for assessing glycosylated albumin, albumin, and blood glucose.

Glycosylated albumin level was measured using the reagent Lucica<sup>®</sup>GA-L (Asahi Kasei Pharma). Blood glucose was measured using a Cobas C 501 (Roche Holding AG).

Differences among groups were obtained through normality test of each group. The normally distributed data were shown in mean and standard of deviation; unless the data were described in median and minimum to maximum. After that, we held the one-way ANOVA and continued by analysis of Bonferroni or Tukey multiple comparison. If distribution of data was not normal and/or its variance was not homogeneous, we did the Kruskal-Wallis test followed by Mann Whitney U post-hoc analysis between group. We performed the statistical test using SPSS version 20.

## RESULTS

Glycosylated albumin level did not differ significantly among four groups ( $p=0.061$ ). Level of albumin in group of women with gestational age 33-36 weeks (3.6 (SD 0.2) g/dl) was significantly lower than 21-24 weeks of gestation group (3.8 (SD 0.2) g/dl) ( $p=0.006$ ). Table 2 depicted the characteristics of study subjects in each gestational age.

**Table 2.** Characteristics of Study Subjects in Each Gestational Age Group

Variables	Gestational Age			
	21-24 Weeks N=17	25-28 Weeks N=11	29-32 Weeks N=16	33-36 Weeks N=16
Age (years old)	27.4 (5.4)	27.8 (6.1)	30.7 (5.6)	27.4 (4.7)
Glycated albumin (%)	11.5 (0.9)	11.6 (1.0)	11.5 (10.8-14.6)	10.8 (1.2)
Blood glucose (mg/dl)	80.7 (67.0-149.4)	81.2 (16.2)	82.6 (67.1-137.2)	78.9 (67.9-123.6)
Albumin (g/dl)	3.8 (0.2)	3.7 (0.2)	3.7 (0.2)	3.6 (0.2)

\* Mean (SD) if the variable was distributed normally

\*\* Median (min-max) if the variable was not distributed normally

## DISCUSSION

In this study, there was no significant difference in glycated albumin level between gestation groups. These results were similar to study by Hashimoto, et al. It was due to similar subjects of Asian population. This study found level of albumin in group IV (33-36 weeks of gestation) significantly was lower than the level of albumin in group I (21-24 weeks of gestation); this might be due to hemodilution. The hemodilution normally occurs because of the plasma volume increase in pregnancy.<sup>10</sup> Glycated albumin level was not influenced by hemodilution because the result in the form of glycated albumin level is a ratio of glycated albumin to albumin.<sup>11,12</sup>

## CONCLUSION

Glycated albumin level is not affected by gestational age. Therefore, glycated albumin may be used as glycemic status indicator during pregnancy from 21 to 36 weeks.

## REFERENCES

- Guariguata L, Noolan T, Beagley J, Linnenkamp U, Jacqmain O, editors. IDF Diabetes Atlas. 6<sup>th</sup> edition: Int Diabetes Fed; 2013:44-5.
- Lowe L, Metzger B, Dyer A, Coustan D, Hadden D, Hod M, et al. Hyperglycemia and adverse pregnancy outcome (HAPO) study: an overview. In: Kim C, Ferrara A, editors. Gestational diabetes during and after pregnancy. London: Springer-verlag; 2010. p. 17-34.
- Uddin MN, Beeram MR, Kuehl TJ. Diabetes mellitus and preeclampsia. Med J Obstet Gynecol. 2013; 1(3): 1016-20.
- American Diabetes Association. Standard of medical care in diabetes 2013. Diabetes Care. 2013; 36(Suppl.1): S11-66.
- Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010; 33(3): 676-82.
- Hashimoto K, Osugi T, Noguchi S, Morimoto Y, Wasada K, Imai S, et al. A1C but not serum glycated albumin is elevated because of iron deficiency in late pregnancy in diabetic women. Diabetes Care. 2010; 33(3): 509-11.
- Hashimoto K, Noguchi S, Morimoto Y, Hamada S, Wasada K, Imai S, et al. A1C but not serum glycated albumin is elevated in late pregnancy owing to iron deficiency. Diabetes Care. 2008; 31(10): 1945-8.
- Bai X, Wang Z, Huang C, Chi L. Investigation of non-enzymatic glycosylation of human serum albumin using ion trap-time of flight mass spectrometry. Mol. 2012; 17(8): 8782-94.
- Rondeau P, Bourdon E. The glycation of albumin: structural and functional impacts. Biochimie. 2011; 93(4): 645-58.
- Cunningham F, Leveno K, Bloom S, Spong C, Dashe J, Hoffman B, et al. Maternal physiology. Williams Obstetrics. 24<sup>th</sup> ed. New York: McGraw-Hill Education; 2014. p. 55-6.
- Kohzuma T, Yamamoto T, Uematsu Y, Shihabi ZK, Freedman BI. Basic performance of an enzymatic method for glycated albumin and reference range determination. J Diabetes Sci Technol. 2011; 5(6): 1455-62.
- GA-L [package insert]. Tokyo: Asahi Kasei Diagnostic; 2013. p. 1-2.