Estimated Glycated albumin' levels early in pregnancy could detect women at risk to develop gestational diabetes mellitus

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Abstract

Background: Gestational diabetes mellitus (GDM) is characterized by dysfunction in maintaining glucose homeostasis leading to adverse maternofetal outcomes and this necessitates the use of markers for its early prediction.

Objectives: To determine the ability of the estimated percentage of glycosylated hemoglobin (HbA1c%) and glycated albumin (GA%) at the 6th gestational week (GW) to define women liable to develop GDM.

Patients and methods: 402 women were clinically evaluated and gave blood samples for estimation of fasting blood glucose (FBG) and HbA1c% and GA% at the 6th-8th GW. At the 24th GW, all women underwent the evaluation of insulin resistance (IR) using the Homeostasis model assessment of IR score and the 75-Oral Glucose Tolerance Test (75-OGTT) to diagnose GDM. The levels of estimated variate at the 6th-8th GW were statistically analyzed to define the predictor for GDM.

Results: 62 women developed IR and 36 of them progressed to GDM. Statistical analyses defined FBG, GA%, HbA1c% as predictors for IR and GDM, but the Paired-sample area difference under the ROC curves defined high GA% as the significant positive predictor for GDM. Kaplan-Meier analysis defined GA% at 14% and 15% could define the risk for GDM by 20% and 40%, respectively but the evaluated performance characters at 15% were significantly (P=0.0074) higher than at 14 %.

Conclusion: Estimation of GA% in blood samples obtained at the 6th-8th GW could predict the oncoming GDM with high specificity and negative predictive value at the cutoff of 15%.

Keywords: Gestational Diabetes Mellitus; Insulin Resistance; Glycated albumin; Glycated hemoglobin; Early prediction.

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Introduction

Gestational diabetes (GDM) could be defined as glucose intolerance of varying severity that first occurs in pregnancy and is not an uncommon condition, especially with the worldwide spread of obesity **(Smyth et al., 2023)**. The development or severity of GDM was found to be related to both pre-gestational body mass index (BMI) and to inappropriate gestational weight gain, which may increase the risk for adverse maternofetal outcomes **(Santos Monte et al., 2023)**.

The glycation process is the non-enzymatic process of proteins or lipids by reducing sugars and is associated with the activation of NADPH oxidase resulting in the generation of reactive oxygen species **(Ma et al., 2017)**, activation of the apoptosis-related gene expression **(Kang et al., 2023)** and through activation of nuclear factor-κB causes the release of inflammatory cytokines **(Yan et al., 2022)**.

Coupling of the previous data concerning the possibility of the development of GDM and the harms resulting from the process of hyperglycemia-induced protein and lipid glycation assured the recently documented that these risks may be attributable to the fact that the hyperglycemia is more severe and is already present before conception **(Reitzle et al., 2023)** and necessitates early discrimination of women at high-risk for getting GDM.

Diagnosis of diabetic patients depends on the estimation of blood glucose (BG) levels, however, these estimations are subjected to multiple variations and their reliance as a predictor for the oncoming diabetic state is questionable **(Mihaela et al., 2019)** and its monitoring application is inconvenient **(Beldare & Coté, 2021)**. Further, the estimation of plasma levels of glycated hemoglobin (HbA1c), which represents the standard monitoring tool for diabetic patients, is not appreciated for pregnant women for its long turnover duration that depends on the lifespan of RBCs, and hemoglobin concentration and RBC counts **(Mendes et al., 2019)**. Recently **Shimizu et al., (2022)** compared the effect of sodium-glucose cotransporter 2 inhibitors received by diabetics and found changes in HbA1c levels underestimated the glucose-lowering effect and the diminished glycemic fluctuation induced by therapy than glycated albumin (GA) and concluded that estimation of GA% is the more applicable monitoring tool for diabetic patients. This study targeted to determine which glycated protein; HbA1c or GA could stratify newly pregnant women according to the possibility of getting GDM

Patients and methods

Design: Multicenter prospective non-randomized clinical trial.

Setting: Antenatal Care Units (ACU) at Obstetrics & Gynecology Departments, Benha & Tanta University Hospitals in conjunction with multiple private Obstetric centers

Study participants: All newly pregnant multipara women attending the ACUs for assurance of getting pregnant were evaluated for a history of manifest diabetes mellitus (DM), previous GDM, previous complicated pregnancy especially cesarean section for macrosomia, and history of maintenance on diabetogenic drugs or ketogenic diet regimen. Then, patients were clinically examined for determination of BMI data and estimation of baseline systolic and diastolic blood pressures. All women were asked to attend the clinic at the 6^{th}-8^{th} gestational week (GW) for ultrasonographic assessment for the presence of a viable fetus.

Exclusion criteria : These included a history of pregnancy-related complications other than GDM, the presence of manifest DM, essential hypertension, chronic kidney and liver diseases, manifestations of hypo-albuminemia or severe weight loss or cutaneous manifestations of hypovitaminosis, and obesity of grades II or III. Also, patients who refused or will be unable to attend the follow-up visits were excluded from the study. Further, all pregnant women who developed pregnancy-related complications other than GDM during the study duration were excluded from the study.

Inclusion criteria: Newly pregnant normoglycemic multipara women who were free of exclusion criteria and attended the ACU at the 6^{th}-8^{th} GW and gave blood samples during the preliminary evaluation were enrolled in the study.

Ethical considerations and blindness : The study protocol was preliminarily approved in Jan 2020 and the final approval was obtained at the end of case collection; i.e. when the last enrolled case had passed her 24^{th} GW. All women who attended the ACU at the 6^{th}-8^{th} GW gave blood samples that were collected by an assistant in tubes arranged according to the investigations to be done. The assistant who collected the blood samples was blinded about the investigations and their indications and numbered the tubes by patient' serial number and date of attendance, while patients' informative data were registered in a file carrying the same serial number and date. The biochemist was blinded about the indications for these investigations and the obstetrician was also blinded about the results of these investigations till the 24^{th} GW of the last case enrolled in the study.

Blood sampling & investigations

At the 6^{th}-8^{th} GW, blood samples were collected after skin sterilization from the antecubital vein and distributed into the following tubes:

1. Tube-1 contained sodium fluoride (2 mg sodium fluoride/ ml blood) to prevent glycolysis for estimation of fasting blood glucose (FBG) levels using the glucose oxidase method.
2. Tube-2 is EDTA containing tube to collect plasma for estimation of plasma HbA1c and GA levels.
3. Tube-3 is a plain tube; blood was allowed to clot and centrifuged to collect serum for estimation of fasting serum insulin (FSI).

Diagnosis of insulin resistance (IR) and GDM

1. Diagnosis of IR was dependent on the calculation of the Homeostasis model assessment of IR (HOMA-IR) score and if it equals two, the woman was considered IR **(Matthews et al., 1985)**.
2. GDM was diagnosed after performing the 75-Oral Glucose Tolerance Test (75-OGTT) which entails the estimation of FBG and estimation of 1-h and 2-h postprandial BG (PPBG). GDM was diagnosed if FBG ≥92 mg/dl, 1-h PPBG ≥180 mg/dl and 2-h PPBG ≥153 mg/dl **(IADPSG, 2010)**.

Study outcomes

1. The ability of the estimated variate to point out women vulnerable to developing GDM
2. The best cutoff point for the variate with high predictability for GDM

Statistical analysis

The results were presented, analyzed, and tabulated as means and numbers with representative P-value that indicates significance if <0.05. The multivariate regression and ROC curve analyses curve were performed

to stratify the variate according to its ability to predict the development of GDM at the 24th GW. The paired analysis for the differences of the area under the ROC curve (AUC) was applied to discriminate between variate of significant AUC in comparison to the area under the reference line of the curve. All statistical analyses were performed using the SPSS program (IBM, USA, 2017).

Results

During the study duration, 73 women were excluded at the time of enrolment and 51 women were missed, these 124 women were excluded from the study. Unfortunately, 18 women developed pregnancy-related complications; 11 had an abortion, and 7 women developed early preeclampsia, these women were excluded from the statistical analyses (**Fig. 1**) and the data of 402 women were analyzed and shown in (**Table .1**).

Table 1. Enrolment data

Variables		Findings
Mean (±SD) of age (years)		29.2±3
Mean (±SD) of body mass index (kg/m^2)		29.4±2
Gravidity		2.7±0.7
Parity		1.5±0.6
Blood pressure (mmHg)	**Systolic**	114.7±5.6
	Diastolic	77.3±4.3
Fasting blood glucose (mg/dl)		83.3±4.1
HbA1c (%)		4.9±0.6
GA (%)		12.3±1.5
HOMA-IR score		0.95±0.18

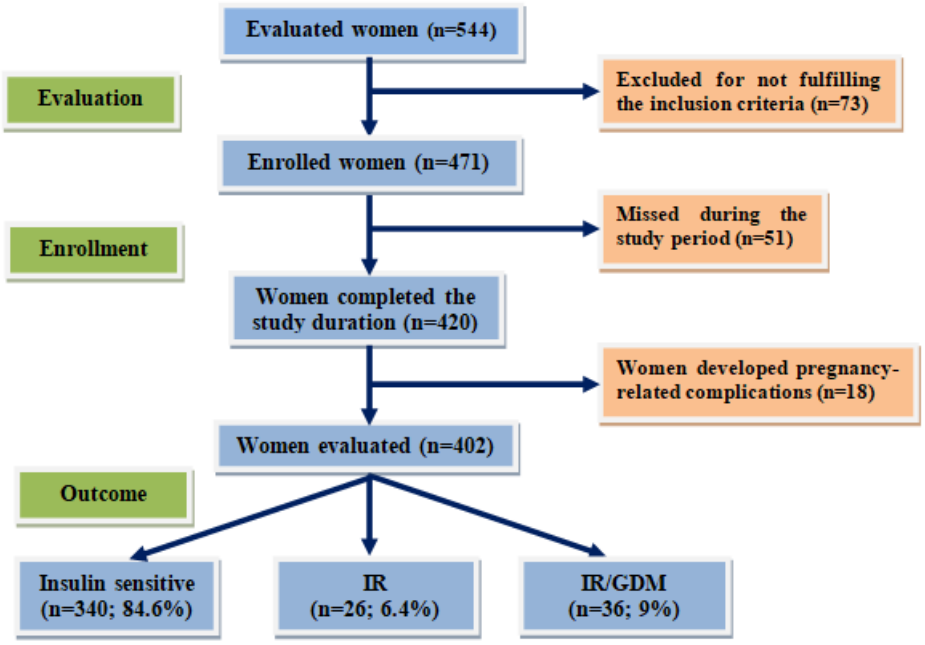

Fig.1. The study flow sheet

The 75-OGTT detected 62 women had developed IR with HOMA-IR score ≥2 and 36 women of these IR women had FBG diagnostic of GDM for an incidence of 15.4% and 9% for IR and GDM, respectively. Mean levels of fasting and PPBG levels estimated at the 24th GW were significantly (P<0.001) higher in samples of GDM women compared to insulin sensitive with non-significantly higher levels in samples of IR women than insulin-sensitive women. Samples of both IR and GDM women showed significantly higher HOMA-IR scores than insulin-sensitive women with a significantly higher score for GDM women (**Table. 2**).

Table 2. The results of 75-OGTT performed at the 24th GW for studied women according to their homeostatic outcomes

Variables	Insulin sensitive	Insulin resistant	GDM	Total
FBG (mg/dl)	83.4±3.9	89.7±3.3	99.1±5.7	85.2±6.2
1-h PPBG (mg/ml)	159.4±9.4	165.4±9.1	201.3±10.6	163.5±15.3
2-h PPBG (mg/dl)	123.1±10.7	129.9±12.1	162.2±6.3	127±15.3
Fasting plasma insulin (mg/dl)	4.94±0.4	9.7±0.58	9.8±0.8	5.58±2.3
HOMA-IR score	1.11±0.4	2.19±0.11	2.36±0.2	1.3±0.57

The incidence of IR and GDM at the 24th GW showed positive significant correlations with the 6th GW BMI, FBG, GA, HbA1c, and GA/HbA1c (**Table .3**).

Table 3. Pearson's correlation between the incidence of IR and GDM and BMI and laboratory variable determined at the 6th GW

Independent variables / Dependent variables	Insulin resistance		Gestational Diabetes Mellitus	
	Pearson's correlation (r)	P-value	Pearson's correlation (r)	P-value
Body mass index (BMI)	0.114	0.023	0.166	0.001
Fasting blood glucose (FBG)	0.237	<0.001	0.231	<0.001
Glycated albumin (GA)	0.253	<0.001	0.374	<0.001
Glycated hemoglobin (HbA1c)	0.176	<0.001	0.213	<0.001
GA/HbA1c ratio	0.181	<0.001	0.233	<0.001

Multivariate Regression analysis of the correlated variate excluded BMI and GA/HbA1c ratio as predictors for both IR and GDM (**Table .4**).

Table 4. Multivariate Regression analysis of the correlated variate for prediction of IR and GDM

Independent variables / Dependent variables	Insulin resistance		Gestational Diabetes Mellitus	
	Standardized coefficient	P-value	Standardized coefficient	P-value
Body mass index (BMI)	0.052	0.279	0.055	0.089

Fasting blood glucose (FBG)	0.200	<0.001	0.177	<0.001
Glycated albumin (GA)	0.217	<0.001	0.338	<0.001
Glycated hemoglobin (HbA1c)	0.141	0.003	0.170	<0.001
GA/HbA1c ratio	0.509	0.751	0.435	0.802

ROC curve analysis assured the predictability of GA, FBG, and HbA1c for both IR (**Fig. 2**) and GDM (**Fig. 3**).

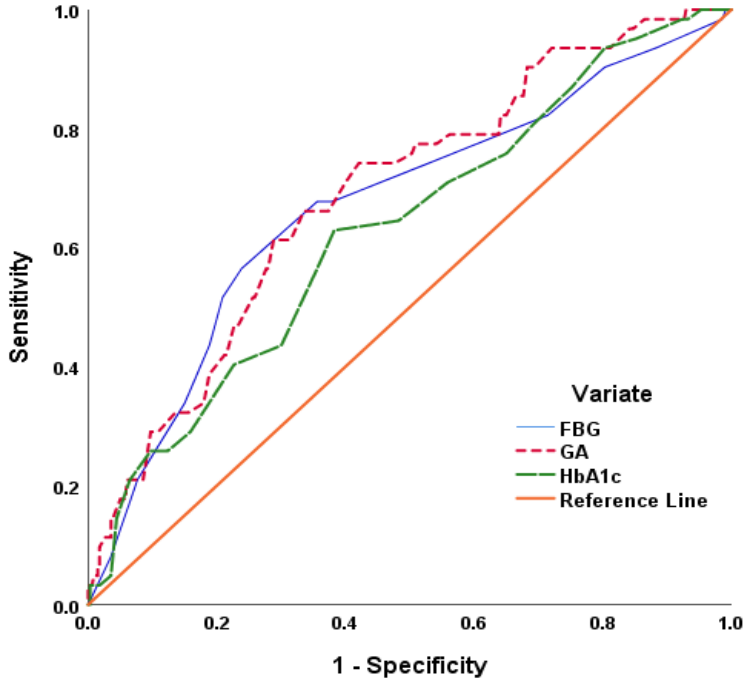

Fig.2. ROC curve for analysis of variate as predictors for the possibility of developing IR at the 24th GW

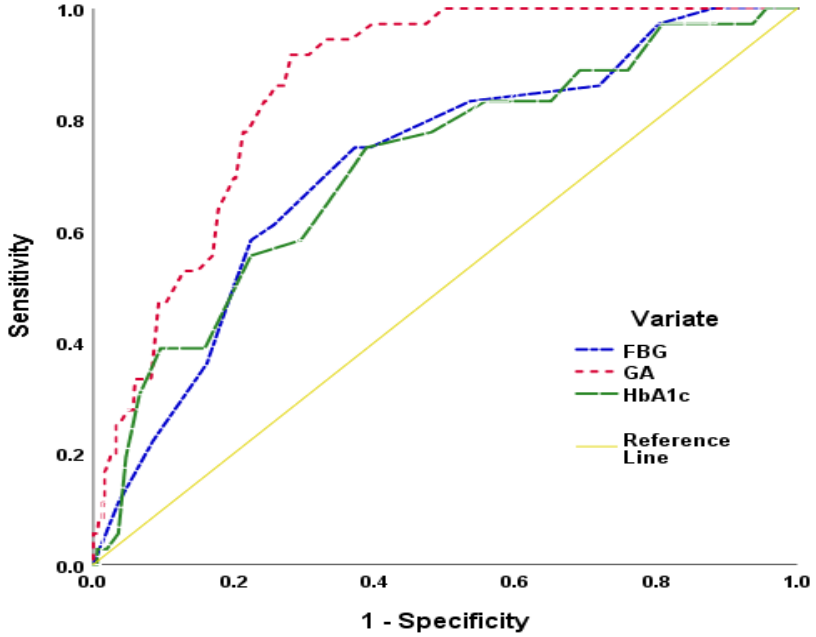

Fig.3. ROC curve for analysis of variate as predictors for the possibility of developing GDM at the 24th GW

Paired-sample area difference under the ROC curves could not define the best predictor for IR among high 6th GW FBG and GA% and HbA1c levels, while defined high GA% as the significant positive predictor for GDM with significant difference between AUC for GA% and both of FBG (P=0.001) and HbA1c% (P=0.013), while the difference between the AUC for both FBG and HbA1c% was non-significant (P=0.981) as shown in (**Table.5**).

Table 5. The Receiver Operating Characteristic curve and Paired-sample area difference under the ROC curves for variate estimated at the 6th GW as predictors for the development of IR and GDM at the 24th GW

Variables		Insulin resistance				Gestational Diabetes Mellitus			
		AUC	**Std.**	**P**	**95% CI**	**AUC**	**Std.**	**P**	**95% CI**
FBG		0.671	0.039	<0.001	0.594-0.748	0.717	0.043	<0.001	0.633-0.802
GA		0.690	0.036	<0.001	0.620-0.760	0.858	0.023	<0.001	0.813-0.904
HbA1c		0.631	0.038	0.001	0.556-0.706	0.715	0.046	<0.001	0.625-0.804
Paired-Sample Area Difference Under the ROC curves									
Variables		AUC difference	Std. difference	P	95% CI	AUC difference	Std. difference	P	95% CI
GA vs.	**FBG**	0.019	0.273	0.690	0.075-0.113	0.141	0.257	0.001	0.056-0.227
	HbA1c	0.059	0.273	0.244	0.040-0.159	0.144	0.265	0.013	0.030-0.257
FBG vs. HbA1c		0.040	0.281	0.508	0.078-0.158	0.003	0.296	0.981	0.107-0.109

Kaplan-Meier Regression analysis defined the cutoff point of 14% and 15% to define the future risk for GDM by 20% and 40% (**Fig. 4**). Evaluation of the 6th GW GA% performance characters to distinguish women liable to develop GDM at the 24th GW showed a specificity rate of 91.8% (95% CI: 88.51-94.4%), the negative predictive value of 94.65% (95% CI: 92.84-96.02%) and accuracy of diagnosis by 87.81% (95% CI: 84.21-90.84%) for using 14% as cutoff point and a specificity rate of 96.72% (95% CI: 94.34-98.29%), the negative predictive value of 92.91% (95% CI: 91.56-94.06%) and accuracy of diagnosis by 90.3% (95% CI: 86.98-93.01%) for the cutoff point at 15% with significantly (P=0.0074) higher diagnostic performance for the cutoff point at 15%

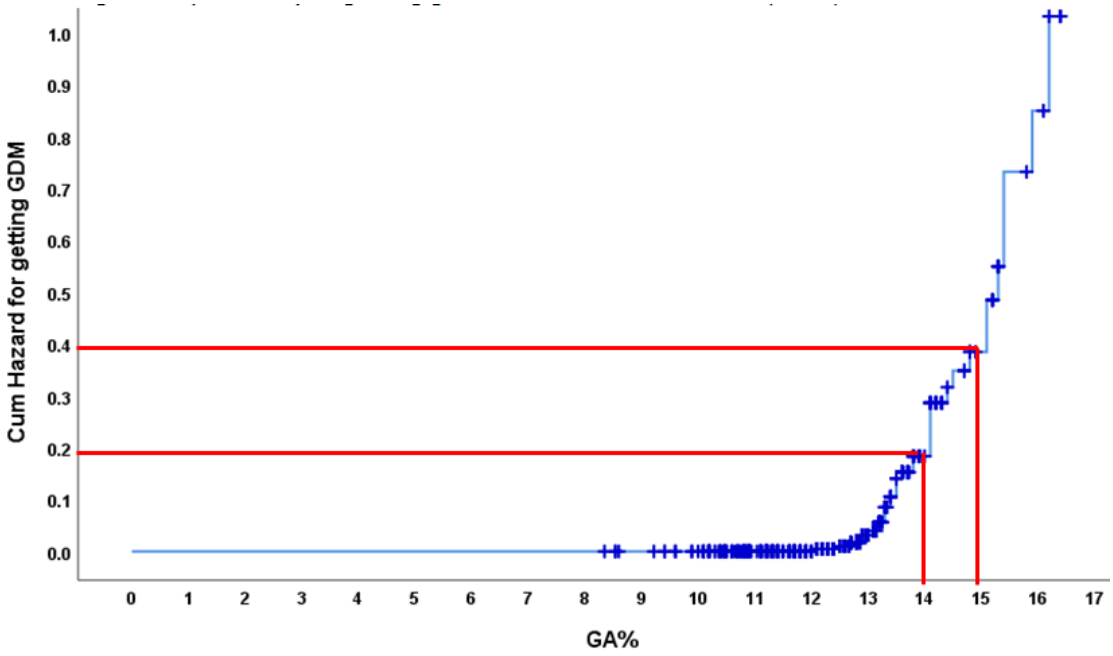

Fig.4. Kaplan-Meyer analysis of estimated GA% at the 6th GW to define the best cutoff point for prediction of GDM at the 24th GW

Discussion

Pregnancy is a diabetogenic physiological condition even in normoglycemic pregnant women; this was evidenced by the high FBG levels estimated at the 24th GW in comparison to levels estimated at the time of pregnancy diagnosis in all patients' samples. Further, the reported incidence of IR and GDM was 15.4% and 9%, respectively. These findings illustrated the vicious cycle; of pregnancy, IR, and lastly GDM. Various recent studies documented these results and suggestions and attributed them to varied mechanisms, **Hill et al., (2021)** and **Ondřejíková et al., (2021)** attributed the diabetogenicity of pregnancy to the increased blood levels of progesterone which is a diabetogenic hormone, cortisol which is released in response to the increased pituitary release of corticotropin hormones and androgens which induces a state of IR; these hormones are acting both in the genomic and non-genomic way. In another explanation, **Zapatería et al., (2021)** detected impaired expression levels of pleiotrophin, a cytokine that maintains hepatic metabolic homeostasis, regulates energy metabolism and lipid turnover, and plasticity of adipose tissue, especially during late gestation. Also, **Amabebe & Anumba (2021)** and **Mora-Janiszewska et al., (2022)** found the interaction between the gut microbiota and host gastrointestinal tract of pregnant women shifts the host metabolism in the diabetogenic direction and this was attributed to epigenetic changes among GDM women and their progeny, in association with alterations in the microbiome **(Mora-Janiszewska et al., 2022)**.

Interestingly, estimated FBG, GA, and HbA1c at the time of pregnancy diagnosis were found to point out pregnant normoglycemic women who are liable to develop IR/GDM among the studied newly pregnant women. Despite the benefit of this finding, it spotlights the fact that these women were in the prediabetic stage before getting pregnant and indicated the necessity of checking for

glucose homeostasis before getting pregnant. Further, the risk for the development of IR/GDM is positively related to BMI at the time of pregnancy diagnosis, thus this prediabetic state may be attributed to the effect of obesity which is aggravated by the gestational weight grain secondary to consumption of high-carbohydrate and fat diets and snacks. Similarly, **Mussa et al., (2021)** detected an association between being overweight and obesity and the development of GDM and found sugar-free liquids and dieting may decrease this risk. Also, **Zhang et al., (2022)** found high pre-pregnancy BMI and excessive gestational weight gain are high-risk factors for elevated HbA1c, higher OGTT, and risks of adverse pregnancy outcomes which parallel the weight gain. Further, **Punnose et al., (2022)** suggest that high HbA1c% in the 1st trimester could predict preterm birth and caesarian delivery even in absence of GDM. **Sugawara et al., (2022)** documented that GA compared with HbA1c in late pregnancy might predict infant complications arising from GDM.

Statistical analyses defined high baseline levels of GA could detect women vulnerable to developing IR/GDM with AUC higher than that for FBG and HbA1c. The superiority of GA over HbA1c was attributed by **Yuwen et al., (2017)** to the presence of multiple intramolecular disulfide bonds in albumin molecule that makes it more suitable and liable to glycation than hemoglobin. Another explanation is the short half-life of albumin that allowed turnover of GA every 2-3 wk. **(Belsare et al., 2022)**, thus reflecting the glucose homeostasis state in the preceding 2-3 wk., while the turnover of HbA1c every 3-m or according to the lifespan of RBCs and consequently it could reflect the control of blood glucose within the last three months, so it is less convenient for diagnosis or follow-up of pregnant women

These data assured the results of **Mendes et al., (2019)** and **Aleks et al., (2021)** who concluded that the short lifespan and rapid turnover of GA allow the provision of useful renewed information about glucose homeostasis whenever HbA1c does not accurately reflect the glycemic status. Further, **Sakai et al., (2021)** and **Toft et al., (2022)** found a statistically significant correlation between GA and time in range and time above the range of 63-140 mg/dl; the pregnancy glucose target with AUC for the time spent with BG level <70% and >25% of that range of 0.78 and 0.82 for GA and 0.60 and 0.72 for HbA1c, respectively and concluded that GA was more accurate than HbA1c to detect the times out of the target range.

Kaplan-Meier regression risk analysis suggested GA level of 15% is highly predictive for the development of GDM, in line with this cutoff point, **Agnello et al., (2021)** found 15.44% (90%CI 14.90-16.90) and 15.72 (90%CI 15.15-16.27) is the reference interval for healthy pregnant women during the 1st trimester, while **Zhang et al., (2021)** in large number survey, found 15.69% as a cutoff point could predict GDM that will be complicated by cesarean section and macrosomia with a significant difference in frequency of these complications between women had GA above and below this point.

Conclusion

Pregnancy is a diabetogenic physiological condition that is associated with an incidence of IR and GDM of 15.4% and 9%, respectively. Estimation of GA% in blood samples obtained at the 6th GW could predict the oncoming GDM with high specificity and negative predictive value at the cutoff of 15%.

References

- **Agnello L, Sasso B, Scazzone C, Giglio R, Gambino C, Bivona G, et al., (2021)**. Preliminary reference intervals of Glycated Albumin in healthy Caucasian pregnant women. Clin Chim Acta,519:227-230.
- **Aleks S, Shawn C, Randie L, Kuanysh K. (2021)**: Quantitation of glycated albumin by isotope dilution mass spectrometry. Clin Chim Acta, 521: 215-222.
- **Amabebe E, Anumba DO. (2021)**. Diabetogenically beneficial gut microbiota alterations in third trimester of pregnancy. Reprod Fertil. 2(1): R1-R12.
- **Belsare S, Coté G. (2021)**. Development of a colorimetric paper fluidic dipstick assay for measurement of glycated albumin to monitor gestational diabetes at the point-of-care. Talanta, 223(Pt 1):121728.
- **Belsare S, Tseng D, Ozcan A, Coté G. (2022)**. Monitoring gestational diabetes at the point-of-care *via* dual glycated albumin lateral flow assays in conjunction with a handheld reader. Analyst, 147(23): 5518-5527.
- **Dairi A, Himayda A, Moulana A, Bukhari H, Hakeem I, Elbarrany W. (2020)**. The Effect of Gestational Diabetes Mellitus on the Chorionic Villi of Human Placenta Among Saudi Arabian Mothers: A Quantitative and Comparative Study. Cureus, 12(10): e11130.
- **Hill M, Pařízek A, Šimják P, Koucký M, Anderlová K, Krejčí H, et al. (2021)**. Steroids, steroid associated substances and gestational diabetes mellitus. Physiol Res. 70(Suppl4): S617-S634.
- **International association of diabetes and pregnancy study groups (IADPSG). (2010)**. Recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care, 33:676–682.
- **Kang J, Jeong Y, Ha S, Lee H, Lee K. (2023)**. Glyoxal-derived advanced glycation end-products, Nε-carboxymethyl-lysine, and glyoxal-derived lysine dimer induce apoptosis-related gene expression in hepatocytes. Mol Biol Rep, 50(3):2511-2520.
- **Ma MW, Wang J, Zhang Q, Wang R, Dhandapani KM, Vadlamudi RK, et al.,(2017)**. NADPH oxidase in brain injury and neurodegenerative disorders. Mol Neurodegener. 12(1): 7.
- **Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. (1985)**. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 28:412–19 .
- **Mendes N, Alves M, Andrade R, Ribeiro RT, Papoila AL, Serrano F. (2019)**. Association between glycated albumin, fructosamine, and HbA1c with neonatal outcomes in a prospective cohort of women with gestational diabetes mellitus. Int J Gynaecol Obstet, 146(3):326-332.
- **Monteiro S, Santos T, Fonseca L, Saraiva M, Pichel F, Pinto C, et al. (2023)**. Inappropriate gestational weight gain impact on maternofetal outcomes in

gestational diabetes. Ann Med, 55(1):207-214.

- **Monteiro S, Santos T, Fonseca L, Saraiva M, Pichel F, Pinto C, et al. (2023)**. Inappropriate gestational weight gain impact on maternofetal outcomes in gestational diabetes. Ann Med, 55(1):207-214.
- **Mora-Janiszewska O, Faryniak-Zuzak A, Darmochwał-Kolarz D. (2022)**. Epigenetic Links between Microbiota and Gestational Diabetes. Int J Mol Sci, 23(3):1831.
- **Mussa J, Brazeau A, Peters T, Dahhou M, Sanmartin C, Ross N, et al. (2021)**. Associations of overweight and gestational diabetes mellitus with free sugars from solid and liquid sources: cross-sectional and nested case-control analyses. BMC Public Health, 21(1): 1923.
- **Ondřejíková L, Pařízek A, Šimják P, Vejražková D, Velíková M, Anderlová K, et al. (2021)**. Altered Steroidome in Women with Gestational Diabetes Mellitus: Focus on Neuroactive and Immunomodulatory Steroids from the 24th Week of Pregnancy to Labor. Biomolecules, 11(12): 1746.
- **Punnose J, Malhotra R, Sukhija K, Rijhwani R, Choudhary N, Sharma A, et al. (2022)**. Is HbA1c in the first trimester associated with adverse outcomes among pregnant Asian Indian women without gestational diabetes? J Diabetes Complications, 36(5): 108187.
- **Reitzle L, Heidemann C, Baumert J, Kaltheuner M, Adamczewski H, Icks A, et al. (2023)**. Pregnancy Complications in Women with Pregestational and Gestational Diabetes Mellitus. Dtsch Arztebl Int. (Forthcoming): arztebl.m2022.0387.
- **Sakai T, Aoyama K, Inazumi K, Kikuchi R, Sato Y, Tada A, et al. (2021)**. Time in range correlates glycated albumin measured immediately after 2 weeks of continuous glucose monitoring. J Diabetes Complications, 35(8): 107962.
- **Shimizu N, Ogawa A, Hayashi A, Shichiri M. (2022)**. Discordance in the reduction rate between glycated albumin and glycated hemoglobin levels in type 2 diabetes patients receiving SGLT2 inhibitors. J Diabetes Complications, 36(7): 108225.
- **Siricharoenthai P, Phupong V. (2020)**. Diagnostic accuracy of HbA1c in detecting gestational diabetes mellitus.J Matern Fetal Neonatal Med, 33(20):3497-3500.
- **Smyth S, Mulligan K, Rutter E, Harrington L, Hatunic M, Higgins M (2023)**: Attitudes of women with gestational diabetes toward diet and exercise: a qualitative study. J Matern Fetal Neonatal Med, 36(1): 2155045.
- **Sugawara D, Sato H, Makita E, Kuwata T, Takagi K, Ichihashi K. (2022)**. Clinical usefulness of glycated albumin and glycated albumin-to-glycated hemoglobin ratio of gestational diabetes mellitus in late pregnancy for predicting infant complications. Pediatr Neonatol, 63(3): 239-246.
- **Toft JH, Dalen I, Skadberg Ø, Gøransson L, Økland I, Bleskestad I .(2022)**. Glycated albumin and continuous glucose monitoring metrics across pregnancy in women with pre-

gestational diabetes. Endocrinol Diabetes Metab, 5(6): e376.

- **Yan M, Li X, Sun C, Tan J, Liu Y, Li M, et al. (2022)**. Sodium Butyrate Attenuates AGEs-Induced Oxidative Stress and Inflammation by Inhibiting Autophagy and Affecting Cellular Metabolism in THP-1 Cells. Molecules, 27(24): 8715.
- **Yuwen T, Huang R, Kay LE. (2017)**. Probing slow timescale dynamics in proteins using methyl 1H CEST. J Biomol NMR, 68(3):215-224.
- **ZapateríaB, Sevillano J, Sánchez -Alonso M, Limones M, Pizarro-Delgado J, Zuccaro A, et al. (2021)**. Deletion of pleiotrophin impairs glucose tolerance and liver metabolism in pregnant mice: Moonlighting role of glycerol kinase. FASEB J, 35(10): e21911.
- **Zhang Q, Lee C, Zhang L, Wu Q, Chen Y, Chen D. (2022)**. The Influence of HbA1c and Gestational Weight Gain on Pregnancy Outcomes in Pregnant Women with Gestational Diabetes Mellitus. Front Med (Lausanne), 9: 842428.
- **Zhang X, Wei Y, Fan L, Zhao Y, Li Y, Liu Y, et al. (2021)**. A multicenter all-inclusive prospective study on the relationship between glycemic control markers and maternal and neonatal outcomes in pregnant women. J Matern Fetal Neonatal Med, 34(19): 3154-3161.