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Conventional and Fructosamine-Based Glycemic Biomarkers and Pregnancy Outcomes in Women With and Without Gestational Diabetes Mellitus: A Prospective Study in New Delhi, India

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is associated with adverse maternal and neonatal outcomes. Conventional biomarkers such as random blood sugar (RBS) and glycated hemoglobin (HbA1c) have limitations during pregnancy, whereas fructosamine-based markers may provide information on recent glycemic exposure.

Aim: To compare conventional and fructosamine-based glycemic biomarkers between women with GDM and those without GDM during late pregnancy and assess maternal and neonatal outcomes.

Methodology: This hospital-based prospective cohort study was conducted at HIMSR and HAHC Hospital, New Delhi, among 200 third-trimester singleton pregnant women (100 (50%) with GDM diagnosed by a 75-g oral glucose tolerance test (OGTT) ⩾ 140 mg/dL at 24-28 weeks according to 2018 national guidelines and 100 (50%) non-GDM controls) recruited consecutively from the antenatal clinic with written consent. Women with multiple pregnancies, thyroid, autoimmune, or systemic diseases, and those using steroids were excluded. Research procedures included venous blood collection at 30-32 and 34-36 weeks for RBS (hexokinase method), HbA1c (high-performance liquid chromatography (HPLC)), fructosamine (nitroblue tetrazolium (NBT)), and albumin (bromocresol green (BCG)) measurements to calculate albumin-corrected fructosamine (ACF) (ACF = (fructosamine/albumin) × 30) and fructosamine-to-albumin ratio (FAR) (FAR = fructosamine/albumin). Participants were prospectively followed until delivery to assess maternal (mode of delivery and induction) and fetal (Apgar score and birth weight) outcomes. The sample size was calculated based on a GDM prevalence of 19.2%, yielding 93 participants, which was rounded to 100 per group. Data were analyzed using SPSS version 26 (IBM Corp., Armonk, NY), with mean ± SD, independent and paired t-tests, and the chi-square test. Statistical significance was set at $P < 0.05$.

Results: At 30-32 weeks of gestation, all biomarkers were significantly higher in women with GDM: RBS (102.16 ± 19.79 vs. 95.59 ± 14.92 mg/dL; $P = 0.009$), HbA1c (5.06 ± 0.51% vs. 4.77 ± 0.40%; $P < 0.001$), fructosamine (234.61 ± 31.15 vs. 215.67 ± 21.31 µmol/L; $P < 0.001$), ACF (205.02 ± 59.24 vs. 170.43 ± 35.49 µmol/L; $P < 0.001$), and FAR (6.83 ± 1.97 vs. 5.68 ± 1.18 µmol/g; $P < 0.001$). At 34-36 weeks, HbA1c, fructosamine, ACF, and FAR remained significantly higher in women with GDM, whereas RBS did not differ significantly between the groups. GDM was also associated with higher rates of labor induction and cesarean delivery and a lower 1-minute Apgar score. However, birth weight was comparable between the groups (2,997.39 ± 387.63 g vs. 2,994.19 ± 392.00 g; $P = 0.954$).

Conclusions: Fructosamine, ACF, and FAR may provide useful complementary information for monitoring glycemic status in women with established GDM during late pregnancy.

Categories: Public Health, Endocrinology/Diabetes/Metabolism
Keywords: albumin-corrected fructosamine, fructosamine, fructosamine-to-albumin ratio, gestational diabetes mellitus, glycated hemoglobin, hba1c, pregnancy outcomes

Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance with onset or first recognition during pregnancy [1]. The global burden of GDM is increasing because of rising maternal age, obesity, and sedentary lifestyles [2]. GDM complicates approximately 7%-18% of pregnancies and is associated with significant maternal and fetal morbidity [3].

Maternal hyperglycemia increases the risk of induction of labor, operative delivery, and future type 2 diabetes mellitus. At the same time, the fetus is at increased risk of macrosomia, birth trauma, neonatal hypoglycemia, and respiratory distress [4,5].

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Random blood sugar (RBS) and glycated hemoglobin (HbA1c) are frequently used to assess glycemic control during pregnancy. However, HbA1c may not accurately reflect glycemia during pregnancy because erythrocyte lifespan is shortened and physiological hemodilution is common [6,7]. HbA1c levels are significantly lower during normal pregnancy than in nonpregnant women [8].

Fructosamine reflects glycemic control over the previous two to three weeks and is not affected by red blood cell survival [9,10]. However, fructosamine is influenced by serum albumin concentration, which decreases during pregnancy because of hemodilution [4]. Therefore, albumin-corrected fructosamine (ACF) and the fructosamine-to-albumin ratio (FAR) may be more accurate indicators of glycemic burden during pregnancy [11,12].

Serum albumin is the major circulating protein undergoing glycation and contributes approximately 60%-70% of serum fructosamine [11]. During pregnancy, particularly in the third trimester, plasma volume expansion and hemodilution result in a physiological decrease in serum albumin concentration [13]. This reduction in albumin may falsely lower fructosamine values independently of glycemic status [11]. Therefore, fructosamine alone may underestimate the true glycemic burden in pregnant women with GDM. To overcome this limitation, albumin-adjusted indices such as ACF and FAR were evaluated in the present study [11,12].

The present study was undertaken to compare conventional and fructosamine-based glycemic biomarkers and pregnancy outcomes between women with and without GDM during the third trimester and to evaluate the potential utility of fructosamine-based indices in relation to conventional glycemic markers.

Materials And Methods

The present hospital-based prospective cohort study was conducted in the Department of Biochemistry, in association with the Department of Obstetrics and Gynecology, at Hamdard Institute of Medical Sciences and Research (HIMSR) and Hakeem Abdul Hameed Centenary Hospital, New Delhi, India, among 200 pregnant women in the third trimester from October 2024 to December 2025. Ethical clearance was obtained from the Institutional Ethics Committee (IEC) of HIMSR, Jamia Hamdard, New Delhi (HIMSR/IEC/00203/2024). Written informed consent was obtained from all participants before commencement of the study. The inclusion and exclusion criteria used for participant selection are presented in Table *1*.

Inclusion criteria	Exclusion criteria
Pregnant women carrying a single fetus	Women with twin or higher-order multiple pregnancies
Gestational age between 30 and 32 weeks or between 34 and 36 weeks at the time of enrollment	Participants with diagnosed thyroid disorders
Women diagnosed with gestational diabetes mellitus (GDM) according to the study diagnostic criteria	Participants with autoimmune disorders
Pregnant women without GDM who were enrolled as the control (comparison) group	Women receiving corticosteroid therapy or other medications likely to interfere with glycemic or inflammatory biomarkers
Women who voluntarily agreed to participate and provided written informed consent	

TABLE 1: Inclusion and exclusion criteria for participant selection.

The sample size was calculated using a prevalence-based formula. A reported prevalence of GDM of 19.2% [13] was used for the calculation. Assuming a prevalence (p) of 0.192, an absolute precision (d) of 0.08, and a 95% confidence level ($Z = 1.96$), the required sample size was calculated to be approximately 93 participants and was rounded to 100 participants. To facilitate equal group comparisons, 100 pregnant women with GDM and 100 pregnant women without GDM were enrolled.

For enrollment in the present study, participants were recruited consecutively from the antenatal clinic during the study period. GDM was diagnosed according to the National Guidelines for Diagnosis and Management of Gestational Diabetes Mellitus [14], which recommend a single-step 75-g oral glucose tolerance test (OGTT), irrespective of the timing of the last meal. A two-hour plasma glucose value of ⩾ 140 mg/dL following ingestion of 75 g of glucose was considered diagnostic of GDM.

The OGTT was performed at 24-28 weeks of gestation as part of routine antenatal screening. Women with a two-hour plasma glucose value of ⩾ 140 mg/dL were classified into the GDM cohort, whereas women with a

normal OGTT during the same period were included in the non-GDM cohort.

Pregnant women with GDM were managed with medical nutrition therapy (MNT), insulin therapy, or metformin, as required [14]. Biomarker assessment was subsequently performed at 30-32 weeks and 34-36 weeks of gestation. Glycemic biomarkers, including RBS, HbA1c, serum fructosamine, ACF, and FAR, were assessed at 30-32 weeks and reassessed at 34-36 weeks of gestation. All participants were followed prospectively until delivery, and relevant maternal and fetal pregnancy outcomes were recorded.

Venous blood samples were collected from study participants using appropriate specimen containers at 30-32 weeks and 34-36 weeks of gestation. Blood collected in fluoride-containing tubes was used for the estimation of RBS, blood collected in ethylenediaminetetraacetic acid (EDTA) tubes was used for HbA1c estimation, and blood collected in plain tubes was used for the estimation of serum fructosamine and serum albumin. Samples were processed according to standard laboratory procedures and analyzed using the respective validated analytical methods.

RBS was measured using the hexokinase method on the Beckman Coulter AU480. HbA1c was estimated by high-performance liquid chromatography (HPLC) using the Bio-Rad D-10. Serum fructosamine was measured by the nitroblue tetrazolium (NBT) method using the Beckman Coulter AU480 (Beckman Coulter, Inc., Brea, CA), whereas serum albumin was estimated by the bromocresol green (BCG) method using the Beckman Coulter AU480.

Serum albumin was estimated to calculate fructosamine concentrations because fructosamine levels are influenced by albumin concentrations during pregnancy. Albumin values were therefore used to calculate ACF and FAR [11].

ACF was calculated using the following formula:

ACF = (Fructosamine concentration (µmol/L)/albumin concentration (g/L)) × 30

The mean serum albumin concentration in the overall study dataset was 30 g/L. ACF was calculated by dividing serum fructosamine (µmol/L) by serum albumin (g/L) and multiplying the result by 30. The value of 30 g/L represented the mean serum albumin concentration observed in the overall study dataset [15-17]. This approach allows fructosamine concentrations to be interpreted while accounting for variations in serum albumin levels.

In addition, FAR was calculated as an albumin-adjusted index [18] using the following formula:

FAR = Fructosamine (µmol/L)/albumin (g/L)

All 200 participants were followed until delivery to assess maternal and fetal outcomes. Maternal outcomes included the mode of delivery, categorized as normal vaginal delivery or cesarean section, and induction of labor. Fetal outcomes included the Apgar score and birth weight.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The independent-samples t-test was used to compare continuous variables between the GDM and non-GDM groups, whereas the Pearson chi-square test was used for categorical variables. Changes in RBS, HbA1c, fructosamine, ACF, and FAR between 30-32 and 34-36 weeks were assessed using the paired-samples t-test within each group. Maternal and neonatal outcomes were compared between groups using the chi-square test or independent-samples t-test, as appropriate. All tests were two-tailed, and $P < 0.05$ was considered statistically significant.

Results

As shown in Table 2, the mean age was comparable between the groups (28.06 ± 4.22 years in the non-GDM group vs. 29.04 ± 4.54 years in the GDM group, $P = 0.12$). However, the mean body mass index (BMI) was significantly higher in women with GDM (23.86 ± 3.55 kg/m²) than in women without GDM (22.50 ± 1.35 kg/m², $P = 0.0001$).

Parameters	Groups	*n*	Mean ± SD	*t*	df	*P*-value
Age (years)	Non-GDM	100	28.06 ± 4.23	-1.579	198	0.116
	GDM	100	29.04 ± 4.54			
BMI (kg/m²)	Non-GDM	100	22.50 ± 1.35	-3.573	198	<0.001*
	GDM	100	23.86 ± 3.56			

TABLE 2: Demographic characteristics of study population (non-GDM vs. GDM).

**P*-value considered significant if *P* < 0.05.

As shown in Table 3, a paired-samples t-test demonstrated that among non-GDM women (*n* = 100), RBS increased from 95.59 ± 14.92 mg/dL at 30-32 weeks to 99.40 ± 16.53 mg/dL at 34-36 weeks, although the difference was not statistically significant (*P* = 0.059). Similarly, HbA1c showed a slight increase from 4.77 ± 0.40% to 4.82 ± 0.43%, which was also not statistically significant (*P* = 0.182).

Parameter	30-32 weeks, mean± SD	34-36 weeks, mean± SD	*t*	df	*P*-value
RBS (mg/dL)	95.59 ± 14.92	99.40 ± 16.53	-1.911	99	0.059
HbA1c (%)	4.77 ± 0.40	4.82 ± 0.43	-1.346	99	0.182
Fructosamine (µmol/L)	215.67 ± 21.31	221.46 ± 22.86	-2.446	99	0.016*
ACF (µmol/L)	170.43 ± 35.49	175.07 ± 36.83	-2.313	99	0.023*
FAR (µmol/g)	5.68 ± 1.18	5.84 ± 1.23	-2.313	99	0.023*

TABLE 3: Comparison of glycemic biomarkers between 30-32 and 34-36 weeks of gestation in the non-GDM group using paired-samples t-tests.

A *P*-value < 0.05 was considered statistically significant.

GDM, gestational diabetes mellitus; RBS, random blood sugar; HbA1c, glycated hemoglobin; ACF, albumin-corrected fructosamine; FAR, fructosamine-to-albumin ratio

In contrast, serum fructosamine increased significantly from 215.67 ± 21.31 to 221.46 ± 22.86 µmol/L (*P* = 0.016). Significant increases were also observed in ACF, from 170.43 ± 35.49 to 175.07 ± 36.83 µmol/L (*P* = 0.023), and FAR, from 5.68 ± 1.18 to 5.84 ± 1.23 µmol/g (*P* = 0.023). Thus, among non-GDM women, fructosamine-based biomarkers demonstrated statistically significant increases between 30-32 and 34-36 weeks, whereas RBS and HbA1c showed no statistically significant changes.

As shown in Table 4, paired-samples t-tests demonstrated that none of the evaluated glycemic biomarkers changed significantly between 30-32 and 34-36 weeks of gestation among women with GDM (*n* = 100). RBS increased slightly from 102.16 ± 19.79 to 102.29 ± 17.50 mg/dL (*t* = -0.071, *P* = 0.944). HbA1c remained unchanged (5.06 ± 0.51% vs. 5.06 ± 0.49%; *P* = 0.913). Similarly, serum fructosamine decreased slightly from 234.61 ± 31.15 to 233.20 ± 31.20 µmol/L (*P* = 0.593). ACF decreased from 205.02 ± 59.24 to 204.04 ± 59.30 µmol/L, while FAR decreased from 6.83 ± 1.97 to 6.80 ± 1.98 µmol/g (*P* = 0.683 for both). Overall, none of the evaluated glycemic biomarkers showed statistically significant changes between the two gestational time points.

Parameter	30-32 weeks (Mean± SD)	34-36 weeks (Mean± SD)	*t*	df	*P*-value
RBS (mg/dL)	102.16 ± 19.79	102.29 ± 17.50	−0.071	99	0.944
HbA1c (%)	5.06 ± 0.51	5.06 ± 0.49	−0.109	99	0.913
Fructosamine (µmol/L)	234.61 ± 31.15	233.20 ± 31.20	0.536	99	0.593
ACF (µmol/L)	205.02 ± 59.24	204.04 ± 59.3	0.409	99	0.683
FAR (µmol/g)	6.83 ± 1.97	6.80 ± 1.98	0.409	99	0.683

TABLE 4: Comparison of glycemic biomarkers between 30-32 and 34-36 weeks of gestation in women with GDM using paired-samples t-tests.

Data are presented as mean ± standard deviation (SD). Paired-samples t-tests were used to compare glycemic biomarkers between 30-32 and 34-36 weeks of gestation. *P*-values < 0.05 were considered statistically significant.

GDM, gestational diabetes mellitus; RBS, random blood sugar; HbA1c, glycated hemoglobin; ACF, albumin-corrected fructosamine; FAR, fructosamine-to-albumin ratio; df, degrees of freedom

As shown in Table 5, at 30-32 weeks of gestation, all evaluated glycemic biomarkers were significantly higher in women with GDM than in those in the non-GDM group. Mean RBS was 102.29 ± 19.79 mg/dL in the GDM group compared with 95.59 ± 14.92 mg/dL in the non-GDM group ($P = 0.009$). Similarly, HbA1c was significantly higher among women with GDM than among those without GDM (5.06 ± 0.51% vs. 4.77 ± 0.40%; $P < 0.001$). Mean serum fructosamine was also significantly higher in the GDM group (234.61 ± 31.15 µmol/L vs. 215.67 ± 21.31 µmol/L; $P < 0.001$). ACF was higher in women with GDM (205.02 ± 59.24 µmol/L vs. 170.43 ± 35.49 µmol/L; $P < 0.001$), as was the FAR (6.83 ± 1.97 µmol/g vs. 5.68 ± 1.18 µmol/g; $P < 0.001$).

Parameter	Non-GDM group (*n* = 100), mean ± SD	GDM group (*n* = 100), mean ± SD	*t*	df	*P*-value
RBS (mg/dL)	95.59 ± 14.92	102.16 ± 19.79	-2.651	198	0.009*
HbA1C (%)	4.77 ± 0.40	5.06 ± 0.51	-4.505	198	<0.001*
Fructosamine (µmol/L)	215.67 ± 21.31	234.61 ± 31.15	-5.019	198	<0.001*
ACF (µmol/L)	170.43 ± 35.49	205.02 ± 59.24	-5.008	198	<0.001*
FAR (µmol/g)	5.68 ± 1.18	6.83 ± 1.97	-5.008	198	<0.001*

TABLE 5: Comparison of glycemic biomarkers between the two groups at 30-32 weeks POG.

**P*-values < 0.05 were considered statistically significant.

POG, period of gestation; GDM, gestational diabetes mellitus; SD, standard deviation; df, degrees of freedom; RBS, random blood sugar; HbA1C, glycated hemoglobin; ACF, albumin-corrected fructosamine; FAR, fructosamine-to-albumin ratio

As shown in Table 6, at 34-36 weeks of gestation, HbA1c, serum fructosamine, ACF, and FAR remained significantly higher in the GDM group than in the non-GDM group ($P < 0.05$). However, the difference in RBS between the groups was not statistically significant (102.29 ± 17.50 vs. 99.40 ± 16.53 mg/dL; $P = 0.231$). These findings indicate that HbA1c and fructosamine-based biomarkers continued to show significant between-group differences during late pregnancy, whereas RBS did not differ significantly between the groups at this assessment.

Parameter	Non-GDM group (*n* = 100), mean ± SD	GDM group (*n* = 100), mean ± SD	*t*	df	*P*-value
RBS (mg/dL)	99.4 ± 16.53	102.29 ± 17.50	-1.201	198	0.231
HbA1C (%)	4.82 ± 0.43	5.06 ± 0.49	-3.751	198	<0.001*
Fructosamine (µmol/L)	221.46 ± 22.86	233.20 ± 31.20	-3.035	198	0.0028*
ACF (µmol/L)	175.07 ± 36.83	204.04 ± 59.30	-4.150	198	<0.001*
FAR (µmol/g)	5.84 ± 1.23	6.80 ± 1.98	-4.150	198	<0.001*

TABLE 6: Comparison of glycemic biomarkers between the two groups at 34-36 weeks POG.

**P*-values < 0.05 were considered statistically significant.

POG, period of gestation; GDM, gestational diabetes mellitus; SD, standard deviation; df, degrees of freedom; RBS, random blood sugar; HbA1C, glycated hemoglobin; ACF, albumin-corrected fructosamine; FAR, fructosamine-to-albumin ratio

As shown in Table 7, maternal outcomes differed significantly between the groups. The rate of normal vaginal delivery was significantly lower in the GDM group than in the non-GDM group (59% vs. 77%; $P = 0.01$). Induction of labor was more common among women with GDM (88% vs. 61%; $P = 0.0001$), and the rate of cesarean section was significantly higher in the GDM group (41% vs. 23%; $P = 0.01$).

Maternal outcome	Groups	*n*	*n* (%)	*P*-value
Normal vaginal delivery (NVD)	Non-GDM	100	77 (77%)	0.01*
	GDM	100	59 (59%)	
Induction of labor (IOL)	Non-GDM	100	61 (61%)	0.0001*
	GDM	100	88 (88%)	
Cesarean section (CS)	Non-GDM	100	23 (23%)	0.01*
	GDM	100	41 (41%)	

TABLE 7: Distribution of maternal outcomes among the non-GDM and GDM groups.

**P*-values < 0.05 were considered significant.

GDM, gestational diabetes mellitus

Table 8 shows that neonatal outcomes also differed significantly between the groups. The mean Apgar score at 1 minute was lower in the GDM group (8.05 ± 0.38 vs. 8.37 ± 0.52, $P < 0.001$), although the Apgar score at 5 minutes did not differ significantly (9.00 ± 0.20 vs. 9.03 ± 0.22, $P = 0.319$). Mean birth weight was comparable between neonates born to mothers with GDM and those born to mothers without GDM (2997.39 ± 387.63 g vs. 2994.19 ± 392.00 g, respectively; $t = -0.058$, $P = 0.954$). No statistically significant difference in birth weight was observed between the two groups.

Parameter	Non-GDM group (*n* = 100), mean ± SD	GDM group (*n* = 100), mean ± SD	*t*	df	*P*-value
Apgar score at 1 minute	8.37 ± 0.53	8.05 ± 0.39	4.909	198	<0.001*
Apgar score at 5 minutes	9.00 ± 0.20	9.03 ± 0.22	-1.000	198	0.319
Birth weight	2994.19 ± 392.0	2997.39 ± 387.63	-0.058	198	0.954

TABLE 8: Comparison of mean neonatal outcomes between the non-GDM and GDM groups.

*P-values < 0.05 were considered significant.

GDM, gestational diabetes mellitus; SD, standard deviation; df, degrees of freedom

Discussion

The evaluation of maternal glycemic status in late pregnancy is crucial for implementing an effective obstetrical management plan. The present study compared standard indicators of glycemic control between women with and without GDM and examined the association between these indicators and pregnancy outcomes. Women with GDM had significantly higher glucose levels and poorer childbirth outcomes. Furthermore, the analysis demonstrated that fructosamine is a useful marker for assessing glycemic status in the third trimester of pregnancy.

In the present study, the mean age was comparable between women without GDM and those with GDM (28.06 ± 4.22 vs. 29.04 ± 4.54 years; $P = 0.12$), whereas BMI was significantly higher in the GDM group (23.86 ± 3.55 vs. 22.50 ± 1.35 kg/m²; $P = 0.0001$). This is in accordance with the established relationship between increased maternal adiposity and insulin resistance [19,20]. In a similar study, Bernier et al. [17] demonstrated significant associations between fructosamine and prepregnancy BMI, adiposity, fasting insulin, HOMA, and inflammatory markers in 101 healthy pregnant women, highlighting the influence of maternal metabolic characteristics on fructosamine interpretation.

Among women without GDM, RBS increased from 95.59 ± 14.92 to 99.40 ± 16.53 mg/dL ($P = 0.059$), while HbA1c increased minimally from 4.77 ± 0.40% to 4.82 ± 0.43% ($P = 0.182$). In contrast, fructosamine increased significantly from 215.67 ± 21.31 to 221.46 ± 22.86 µmol/L ($P = 0.016$), ACF increased from 170.43 ± 35.49 to 175.07 ± 36.83 µmol/L ($P = 0.023$), and FAR increased from 5.68 ± 1.18 to 5.84 ± 1.23 µmol/g ($P = 0.023$). These findings suggest that fructosamine-based measures may reflect changes in glycemic status during late pregnancy. However, Bernier et al. [17] reported a decrease in serum fructosamine but an increase in albumin-corrected fructosamine across pregnancy ($P < 0.0001$ for both), contrasting with the increase in uncorrected fructosamine observed in our non-GDM group. This difference may be attributed to variations in gestational timing, population characteristics, BMI, and albumin concentrations. Their findings nevertheless support the importance of albumin correction when interpreting fructosamine during pregnancy.

Furthermore, in the present study, none of the evaluated biomarkers changed significantly between 30-32 and 34-36 weeks of gestation among women with GDM. RBS increased slightly from 102.16 ± 19.79 to 102.29 ± 17.50 mg/dL ($P = 0.944$), while HbA1c remained unchanged (5.06 ± 0.51% vs. 5.06 ± 0.49%; $P = 0.913$). Similarly, fructosamine levels showed minimal variation, decreasing from 234.61 ± 31.15 to 233.20 ± 31.20 µmol/L ($P = 0.593$). ACF decreased slightly from 205.02 ± 59.24 to 204.04 ± 59.30 µmol/L, while FAR decreased from 6.83 ± 1.97 to 6.80 ± 1.98 µmol/g; neither change was statistically significant ($P = 0.683$ for both).

The persistence of elevated fructosamine-based markers may reflect relatively stable glycemic exposure among women with established GDM. Similar findings have been reported by Danese et al. [10] and Mendes et al. [9], who observed that fructosamine-related markers are more sensitive indicators of short-term glycemic burden than conventional glucose parameters. Htira et al. reported that fructosamine may provide a more reliable estimate of glycemia during pregnancy because it is independent of red blood cell lifespan [8].

The present study found that, at 30-32 weeks of gestation, all biomarkers were significantly higher in women with GDM. RBS was 102.29 ± 19.79 versus 95.59 ± 14.92 mg/dL ($P = 0.009$), HbA1c was 5.06 ± 0.51% versus 4.77 ± 0.40% ($P < 0.001$), fructosamine was 234.61 ± 31.15 versus 215.67 ± 21.31 µmol/L ($P < 0.001$), ACF was 205.02 ± 59.24 versus 170.43 ± 35.49 µmol/L ($P < 0.001$), and FAR was 6.83 ± 1.97 versus 5.68 ± 1.18 µmol/g ($P < 0.001$).

At 34-36 weeks, HbA1c, fructosamine, ACF, and FAR remained significantly higher in women with GDM:

5.06 ± 0.49% versus 4.82 ± 0.43% ($P < 0.001$), 233.20 ± 31.20 versus 221.46 ± 22.86 µmol/L ($P = 0.0028$), 204.04 ± 59.30 versus 175.07 ± 36.83 µmol/L ($P < 0.001$), and 6.80 ± 1.98 versus 5.84 ± 1.23 µmol/g ($P < 0.001$), respectively. RBS was 102.29 ± 17.50 versus 99.40 ± 16.53 mg/dL, with no statistically significant difference ($P = 0.231$).

These findings support the potential usefulness of fructosamine-based indices for characterizing established GDM. However, Gingras et al. [21] reported that second-trimester fructosamine was a poor predictor of GDM in 1,488 pregnant women, with a sensitivity of 54.8%, specificity of 48.6%, and AUC of 0.52. This contrasting evidence indicates that fructosamine may be more useful as an adjunct for monitoring established dysglycemia than as a standalone screening or diagnostic test.

HbA1c was significantly higher in women with GDM at both gestational assessments but showed little within-group change. Its interpretation during pregnancy may be influenced by altered erythrocyte turnover, iron status, and hemodilution [5-7]. Furthermore, fructosamine may provide an alternative assessment of recent glycemia because it is independent of erythrocyte lifespan [8]. Mendes et al. and Danese et al. similarly highlighted the potential utility of fructosamine-related markers for assessing short-term glycemic exposure [9,10].

The persistence of higher fructosamine and FAR levels in women with GDM at 34-36 weeks, despite limited temporal changes in conventional markers, suggests that these indices may provide complementary information. Nevertheless, the findings of Gingras et al. [21] emphasize that their diagnostic performance remains insufficient to replace established glucose-based testing.

Furthermore, in the present study, ACF and FAR were significantly higher in women with GDM at both 30-32 and 34-36 weeks. This is relevant because physiological hypoalbuminemia during pregnancy can influence absolute fructosamine concentrations. Albumin correction may therefore improve interpretation [10,11]. Bernier et al. [17] further demonstrated that albumin correction substantially altered the trajectory and metabolic associations of fructosamine during pregnancy, supporting the importance of considering albumin when interpreting fructosamine-based biomarkers.

The present study found that women with GDM had significantly lower rates of normal vaginal delivery (NVD) than women without GDM (59% vs. 77%; $P = 0.01$), while induction of labor was more frequent (88% vs. 61%; $P = 0.0001$) and the cesarean delivery rate was higher (41% vs. 23%; $P = 0.01$). These findings are consistent with previous reports demonstrating increased obstetric intervention in GDM pregnancies [5,22]. Crowther et al. [7] demonstrated that active treatment of GDM reduced pregnancy-related morbidity, while Metzger et al. [4] reported continuous associations between maternal glycemia and adverse perinatal outcomes.

The present study found that the mean 1-minute Apgar score was significantly lower in neonates born to women with GDM (8.05 ± 0.38 vs. 8.37 ± 0.52; $P < 0.0001$), whereas the 5-minute Apgar score was comparable (9.00 ± 0.20 vs. 9.03 ± 0.22; $P = 0.319$). The mean birth weight of neonates born to women with GDM was similar to that of neonates born to women without GDM (2997.39 ± 387.63 g vs. 2994.19 ± 392.63 g; $P = 0.954$). There was no statistically significant difference in the birth weight of neonates between the two groups. Although the Pedersen hypothesis and findings from the HAPO study provide evidence of an association between maternal glycemia and fetal overgrowth [4], this association was not observed in the current study. Short-term glycemic markers are of clinical relevance, as reported by Mendes et al., who identified associations between fructosamine and glycated albumin levels and neonatal birth weight and large-for-date status [9]. However, the present study did not find a significant difference in birth weight between the two groups or a direct association between individual glycemic biomarkers and neonatal outcomes.

Overall, the present study demonstrates that RBS, HbA1c, fructosamine, ACF, and FAR were significantly higher in women with GDM at 30-32 weeks of gestation. At 34-36 weeks, HbA1c, fructosamine, ACF, and FAR remained significantly higher in the GDM group, whereas RBS did not differ significantly between the groups. Fructosamine-based indices therefore appear to complement conventional biomarkers in the assessment of late-pregnancy glycemia. However, the contrasting findings of Gingras et al. [21] caution against their use as standalone diagnostic tests. The findings of Bernier et al. [17] further indicate that maternal BMI and albumin concentrations should be considered when interpreting fructosamine during pregnancy. Thus, fructosamine, ACF, and FAR may have value as adjunctive markers for monitoring established GDM, but their routine diagnostic and prognostic roles require validation in larger prospective studies.

The major strengths of this study include the prospective assessment of five glycemic biomarkers - RBS, HbA1c, fructosamine, ACF, and FAR - at two time points during late pregnancy in women with and without GDM. The inclusion of equal numbers of participants in both groups and the assessment of maternal and neonatal outcomes provide a comparative perspective on the potential complementary value of fructosamine-based indices in glycemic monitoring.

However, several limitations should be acknowledged. The single-center design and relatively modest sample size may limit the generalizability of the findings. Continuous glucose monitoring and serial postprandial glucose measurements were not performed, limiting comparisons with comprehensive assessments of glycemic variability. Serum albumin was not assessed at additional time points beyond the study measurements, which may limit the interpretation of albumin-related indices over time. Furthermore, the study evaluated only selected maternal and neonatal outcomes and did not conduct long-term maternal and neonatal follow-up. Potential confounding factors, including differences in BMI and GDM treatment, may also have influenced the observed associations. Additionally, GDM treatment with medical nutrition therapy, insulin, and/or metformin may have influenced biomarker levels during follow-up, introducing potential treatment-related confounding. Since multiple biomarkers were assessed at two gestational time points without formal adjustment for multiple comparisons, the possibility of false-positive findings cannot be excluded. Therefore, larger prospective studies incorporating multivariable adjustment for BMI, treatment exposure, and multiple comparisons are needed to establish the independent clinical utility of fructosamine-based indices during pregnancy.

Future multicenter studies involving larger and more diverse populations, appropriate adjustment for potential confounders, continuous glucose monitoring, serial assessment of serum albumin, and long-term follow-up are warranted to validate these findings and determine the clinical utility of fructosamine-based indices in the management of GDM.

Conclusions

To conclude, the present study found that fructosamine, ACF, and FAR may serve as useful adjunctive biomarkers for the assessment of glycemic status during late pregnancy. Their ability to reflect shorter-term glycemic exposure may be particularly useful when HbA1c interpretation is potentially affected by pregnancy-associated hematological changes or when isolated glucose measurements fail to represent overall recent glycemic exposure. Nevertheless, the present findings do not justify replacing standard diagnostic testing or glucose monitoring with fructosamine-based measurements.

The persistence of significantly higher FAR and ACF values at 34-36 weeks of gestation in women with GDM is noteworthy, as these fructosamine-based biomarkers may provide complementary information regarding maternal glycemic status. FAR accounts for the relationship between fructosamine and albumin concentration, while ACF provides an albumin-corrected assessment of fructosamine.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Jaspreet Kaur, Kongbrailatpam J. Devi, Bhumika Upadhyay

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Disclosures

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