RESEARCH PAPER

FIRST-TRIMESTER SERUM SFRP-4 LEVELS IN RELATION TO BMI AND ORAL GLUCOSE TOLERANCE TEST OUTCOMES IN PREGNANT WOMEN

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ABSTRACT

Objectives: The goal of this study is to evaluate Secreted Frizzled Related Protein 4 as Potential Biomarkers for GDM. Objective is to estimate the levels of SFRP-4 during first trimester of pregnancy. Methods: The study was conducted in the Department of Biochemistry. Total of 100 pregnant women attending their first prenatal examination between 6 and 13 weeks of gestation (1st Screening) at MMMCH Solan Hospital. Serum SFRP-4 levels were measured using Enzyme-Linked Immunosorbent Assay (ELISA). Results: When categorized based on the BMI, 6 participants were having BMI less than 18.5 indicating under-weight, 60 participants had BMI between 18.5 to 24.9 (normal weight), while 27 participants had BMI = 25 – 29.9 indicating overweight and remaining 7 participants had BMI above 30 which signifies obese. The average BMI of the 100 participants was found to be 23.9 ± 4.17, mean SFRP-4 value was 2.50 ± 2.67 ng/ml and mean OGTT was 119.6 ± 24.35 mg/dl. Conclusion: An increase in circulating SFRP-4 across BMI categories. A positive relationship of SFRP-4 with OGTT values and BMI indicates impaired glucose handling.

Keywords: GDM, SFRP-4, BMI, OGTT, Wnt signaling, Insulin resistance, Pregnancy

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INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as Impaired Glucose Tolerance (IGT) with onset or first recognition during pregnancy. Worldwide, one in 10 pregnancies is associated with diabetes, 90% of which are GDM. According to ICMR-INDIAB-24, Indian population have 22.4% of GDM overall [1]. Undiagnosed GDM leads to maternal & fetal complications [2-6]. Several studies have found higher SFRP-4 (Secreted frizzled-related protein 4) levels in women with GDM compared with normoglycemic pregnant controls. SFRP-4 can be reliable biomarker because of its role in Wnt signaling and impaired insulin secretion and glucose intolerance. Research showed higher SFRP-4 values in GDM [4,6-11]. 1st trimester study demonstrated increased values of SFRP-4 and later developed GDM [3]. Studies have also shown association between BMI and SFRP-4 in GDM [5,8]. Maternal BMI is one of the strongest determinants of GDM risk and is often closely linked to adipokine imbalance and insulin resistance [5,7]. This pattern suggests that SFRP-4 may partly reflect adiposity-related metabolic stress rather than provide a completely separate screening signal. This study has focused on uncovering the significance of SFRP-4 as early biomarker of GDM among pregnant women. Goal of this study is Evaluate Secreted Frizzled Related Protein 4 as Potential Biomarkers for GDM. The objective is to estimate the levels of SFRP-4 during first trimester of pregnancy. To compare the levels of SFRP-4 among pregnant women under different BMI categories during first trimester.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry. Total of 100 pregnant women attending their first prenatal examination between 6 and 13 weeks of gestation (1st Screening) at MMMCH Solan Hospital were enrolled in the study. Written informed consent was obtained from all participants prior to inclusion.

Exclusion criteria: patients on extensive medical treatment, those on lipid-lowering drugs, smokers, and alcoholics.

The study protocol was reviewed and approved by the Institutional Ethics Committee of MMMCH Solan (Approval No. MMMCH/IEC/24/958).

Serum SFRP-4 levels were measured using Enzyme-Linked Immunosorbent Assay (ELISA) according to the manufacturer's instructions (BT-LAB). Plasma glucose was measured in Cobas c311 fully automated analyzer.

Statistical analysis: Data were analyzed using statistical software, and results are presented with appropriate measures of significance.

RESULTS

The present study conducted in the Department of Biochemistry in association with the Department of Obstetrics and Gynecology, MMMCH comprising 100 women with 6-13 weeks of gestation. When categorized based on the BMI, 6 participants were having BMI less than 18.5 indicating under-weight, 60 participants had BMI between 18.5 to 24.9 (normal weight), while 27 participants had BMI = 25 – 29.9 indicating overweight and remaining 7 participants had BMI above 30 which signifies obese (Table 1).

Table 1: Participants under various BMI categories

BMI	**BMI <18.5**	**BMI 18.5 – 24.9**	**BMI 25– 29.9**	**BMI above 30**
No. of participants	6	60	27	7

The average BMI of the 100 participants was found to be 23.9 ± 4.17, mean SFRP-4 value was 2.50 ± 2.67 ng/ml and mean OGTT was 119.6 ± 24.35 mg/dl (Table 2).

Table 2: Levels of BMI, SFRP-4 and OGTT of the participants

Sample	**BMI (Mean ± SD)**	**SFRP-4 (ng/ml) (Mean ± SD)**	**OGTT (mg/dl) (Mean ± SD)**
100	23.9 ± 4.17	2.50 ± 2.67	119.6 ± 24.35
	t = 0.0000	t = -0.0000	t = 0.0000
	p-values = 0.500	*p* = 0.500	*p* = 0.500

significance level (p= 0.05)

Seven (07) participants out of 100 had 2-hour plasma glucose values 140 mg/dl and above while 46 participants had 2-hour plasma glucose values between 120 – 140 mg/dl.

The levels of BMI, SFRP-4 and OGTT among the participants were consistent and statically significant variation was not observed (Table 2).

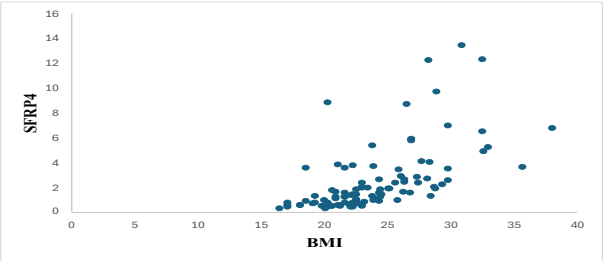

Figure 1. Scatter plot showing the correlation between serum SFRP-4 levels (ng/ml) and BMI (kg/m²) among study participants (r = 0.5979, p < 0.001)

Table 3 shows levels of SFRP-4 and OGTT of the participants categorized under different BMI group. The Lowest levels of SFRP-4 and OGTT was seen among the participants having BMI less than 18.5 and higher levels of those parameters were noted among the participants having BMI above 30. But these variations in the levels under different BMI were not statistically significant.

Table 3: OGTT and SFRP-4 values on Different categories of BMI

	BMI <18.5	BMI 18.5 – 24.9	BMI 25– 29.9	BMI above 30
SFRP-4 (ng/ml)	0.55±0.15	1.53±1.43	3.75±2.78	7.58±3.80
OGTT (mg/dl)	114.83±15.75	112.89±23.83	132.24±24.17	132.37±9.09

At the 0.05 significance level, we reject the null hypothesis of no correlation. The relationship between the two variables is unlikely to be due to chance alone.

Table 4: Pearson's correlation of OGTT and SFRP-4 with BMI

SN	Parameter		*r* value	Significance (*p*)
		BMI		
1	SFRP-4		r = 0.5979	p = 0.000000
2	OGTT		r = 0.3738	p = 0.000128

significance level (p= 0.05)

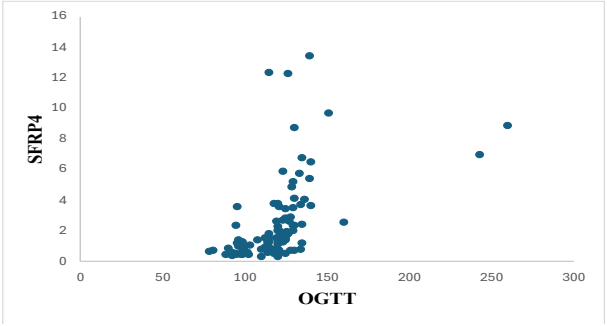

Figure 2. Scatter plot showing the correlation between OGTT values (mg/dl) and BMI (kg/m²) among study participants (r = 0.3738, p = 0.000128).

The correlation coefficient (r) indicates a strong positive relationship of SFRP-4 and OGTT with BMI (Tabel 4).

DISCUSSION

GDM develops from early pregnancy metabolic disorder. SFRP-4 is probable early diagnostic tool as it is associated with adipose tissue, pancreatic beta-cell function and Wnt signaling, all causing insulin resistance and glucose intolerance [12,13].

An increase in circulating SFRP-4 across BMI categories (mean SFRP-4: 0.55, 1.53, 3.75, 7.58 ng/ml for BMI <18.5, 18.5–24.9, 25–29.9 and >30 respectively) and a strong positive correlation between SFRP-4 and BMI (r = 0.5979, p < 0.000001) is observed in our study. Elevated first trimester BMI is a well established risk factor for development of GDM and for adverse maternal–fetal outcomes, so the association of higher SFRP-4 with BMI suggests SFRP-4 may be linked to the metabolic milieu present early in pregnancy that predisposes to GDM. [14,15,16]

We also found a positive relationship between OGTT values and BMI (r = 0.3738, p = 0.000128), indicating that higher BMI in our cohort paralleled impaired glucose handling- an axis relevant when considering early pregnancy screening for abnormal glucose tolerance [15,16].

SFRP-4 is a secreted Wnt antagonist that correlates with prediabetic stages and may predict future progression to type 2 diabetes, supporting that higher SFRP-4 reflects systemic metabolic stress. Because pregnancy induces major metabolic adaptations from the first trimester onward, circulating SFRP-4 elevations in overweight/obese pregnant women could reflect early insulin resistance or adipose derived inflammatory signaling that predisposes to later GDM, making it a plausible early biomarker candidate [15,17,19].

The metabolic association we observed aligns with a 2024 study showing SFRP-4 correlates positively an early predictor of diabetes risk, indicating that elevated serum SFRP-4 reflects systemic metabolic stress. This supports the interpretation that higher SFRP-4 in overweight and obese individuals could be a consequence of adipose- or liver-derived secretion in response to insulin resistance or low-grade inflammation, as proposed in metabolic studies of SFRP-4[16]. SFRP-4 could be evaluated as an additive biomarker within multivariable first trimester prediction models (combined with other established markers) to test whether it improves early detection of women who will develop GDM by standard 24-28 week criteria [16,18,22-25].

Limitations: absence of longitudinal follow up to confirm which participants progress to GDM, and potential confounding by sex /age related or inflammatory mediators not measured here (e.g., CRP, adipokines). For clinical relevance in obstetrics, prospective first trimester cohort studies should (1) measure SFRP-4 at a defined early gestational window, (2) record insulin resistance indices [16,18,22-27]. Clinically, if validated, an early pregnancy SFRP-4 measurement used together with maternal characteristics could allow monitoring in high risk women and potentially reduce GDM related complications by earlier intervention [20-27].

However, the evidence is not fully consistent for immediate clinical use. First-trimester screening studies

show only moderate predictive performance when biomarkers are added to maternal characteristics, meaning SFRP-4 alone is unlikely to be sufficient as a stand-alone test.

CONCLUSION:

GDM indicated as Impaired Glucose Tolerance (IGT) with onset or first recognition during pregnancy. The standard diagnostic test is OGTT, but it is usually performed in mid-pregnancy. This delay has created interest in first-trimester biomarkers that may identify high-risk women earlier. SFRP-4 is involved in Wnt signaling and is linked to impaired insulin secretion and glucose intolerance. Higher SFRP-4 levels in women suggests a possible role in the pathogenesis of pregnancy-related hyperglycemia. The current study also shows increased SFRP-4 level and impaired OGTT result among higher BMI pregnant women. SFRP-4 could be evaluated as an additive biomarker within multivariable first trimester prediction of GDM.

Conflict of Interest: The authors declare no conflict of interest related to this study.

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Author's Contributions

Miss Samiksha (PhD Scholar) contributed to the initial drafting of the manuscript, literature review, sample collection, sample analysis and data analysis. Dr. Monika Jindal participated in data collection and result interpretation and literature review.

Dr. Bharti Kwatra supported data validation, helped refine the study design, and provided critical revisions to improve the manuscript. The overall study supervision at all stages of data analysis and interpretation was under Dr. Bharti Kwatra. All authors reviewed and approved the final version of the manuscript.

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