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Serum ANGPTL8 in Pregnancy: Linking Gestational Diabetes, Insulin Resistance, and Postpartum Metabolic Health

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a major contributor to short- and long-term maternal and neonatal complications. GDM is still common in South Asian populations, with evidence suggesting high prevalence in Pakistan (18–25%). Objectives: The aim of this prospective cohort study was to examine the dynamics of serum ANGPTL8 in pregnancy, its relationship with insulin resistance (IR), and its utility as a marker for predicting postpartum metabolic health in Pakistani women.

Methodology: a total of 150 pregnant women (75 with GDM, 75 as normoglycemic controls) recruited from two tertiary hospitals in urban Pakistan, and followed them through pregnancy. Trimesters 1 through 3, the women had their serum ANGPTL8 levels, IR markers (HOMA-IR), and dietary intake patterns, as well as genetic variants (ANGPTL8 rs2278426), and socioeconomic status assessed. Follow-up assessments for dysglycemia and dyslipidaemia occurred at 6, 12, and 24 months after delivery.

Results: Women with GDM had significantly higher (2.8 ± 0.9 ng/mL) ANGPTL8 levels especially in the third trimester (2.1 ± 0.7 ng/mL among controls; $p < .001$) and was strongly correlated with HOMA-IR ($r = .62$, $p< .001$). ANGPTL8 was independently associated with high-carbohydrate diets ($\beta = 0.23$, $p = .004$) and SNP (OR = 2.1, $p < .001$). In the postpartum period, third-trimester ANGPTL8 ≥ 2.5 ng/mL predicted dysglycemia (AUC = 0.84, 95% CI [0.78, 0.90]) with sensitivity and specificity of 82% and 76%, respectively. Low socioeconomic status compounded metabolic risk (HR = 1.8, $p = .02$).

Conclusion: This study recognizes ANGPTL8 as potential and reliable biomarker for GDM severity and postpartum metabolic dysfunction in women, who come from Pakistan. The addition of ANGPTL8 screening to obstetric care and public health strategy may allow for early intervention in high-burden populations to reduce long-term risk for type 2 diabetes.

Keywords: Gestational diabetes mellitus, ANGPTL8, Insulin resistance, dysglycemia, Pakistan

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first detected in pregnancy, and is one of the most common metabolic disorders in pregnancy, affecting approximately 14% of pregnancies around the globe (International Diabetes Federation, 2021). GDM has immediate and long-term health implications that include increased risk of preeclampsia, macrosomia, neonatal hypoglycemia (McIntyre et al., 2019), and a sevenfold risk of type 2 diabetes mellitus (T2DM) and higher risk of cardiovascular disease (Vounzoulaki et al., 2020). The primary mechanism driving the pathogenesis of GDM is insulin resistance (IR). IR is a physiological adaptation for energy preferences in pregnancy, but GDM develops as a consequence of IR with abnormal β-cell function (Plows et al., 2018). Despite recent advances to understand the underlying etiology of IR in GDM, the study of biomarkers that predict metabolic deterioration following pregnancy is limited.

Angiopoietin-like protein 8 (ANGPTL8), a hormone involved in lipid metabolism and IR, has been proposed as a putative metabolic regulator (Zhang, 2012). ANGPTL8 acts to inhibit lipoprotein lipase, thereby increasing levels of triglycerides and is upregulated in insulin-resistant states (Abu-Farha et al., 2016). ANGPTL8 is elevated during pregnancy and correlates with the severity of IR during pregnancy (Chen et al., 2020). The latest work indicates that serum ANGPTL8 is higher in GDM compared to healthy pregnancies, and so could theoretically play a role in either glucose dysregulation vs regulation (Hu et al., 2022). Because published data are conflicting, with some studies indicating no significant differences (Wang et al., 2021); additional studies exploring the exact role of ANGPTL8 in GDM pathophysiology would be helpful.

Postpartum metabolic health of women with GDM is a relevant area of concern because 30 to 50% of women with GDM will develop either prediabetes or T2DM within 5 years (Moon et al., 2021). As an independent variable, AGNPTL8 has been studied as a potential biomarker for predicting prediabetes and T2DM postpartum, but the predictive ability of this biomarker remains unclear. The literature is limited in providing longitudinal data linking antenatal serum ANGPTL8 levels to postpartum outcomes; therefore, the clinical utility is limited. Further, no data explores the mechanistic relationship between ANGPTL8 and IR during pregnancy to represent long-term metabolic trajectories.

This study aims to explore these gaps by examining longitudinal serum ANGPTL8 levels in women with and without GDM, across pregnancy and postpartum, and the relationship of ANGPTL8, IR and postpartum metabolic outcomes. We aim to provide data on whether ANGPTL8 can be considered a prognostic marker in postpartum women with GDM and possibly offer a reasonable evaluation. This exploratory study integrates biomarker assessment prenatal and beyond that has the potential to guide mechanisms for early intervention, thus improving the long-term health of women with GDM.

LITERATURE REVIEW

Global Context of ANGPTL8 and Gestational Diabetes

Gestational diabetes mellitus (GDM), which is a temporary form of hyperglycemia while a woman is pregnant, is a pressing health issue around the globe, with prevalence ranging from 10% to 30% in South Asia (International Diabetes Federation [IDF], 2021). A characteristic of GDM pathophysiology is insulin resistance (IR) which is exacerbated by placental hormones and compromised adipose tissue (Plows et al., 2018). ANGPTL8 is a newly discovered player in regulating IR, as well as lipid metabolism, and women with GDM have been shown to have higher levels than healthy pregnancies (Chen et al., 2020; Hu et al., 2022). ANGPTL8 regulates the inhibition of lipoprotein lipase, which is associated with hypertriglyceridemia, one of the features of GDM (Zhang, 2012). Although some longitudinal studies have indicated the potential utility of increased ANGPTL8 in pregnancy for predicting postpartum dysglycemia, results are inconsistent (Wang et al., 2021; Moon et al., 2021). Postpartum metabolic health is a significant health focus because 30–50% of GDM pregnancies transition to type 2 diabetes (T2DM) within 10-year window (Vounzoulaki et al., 2020). Other biomarkers such as adiponectin and leptin have been studied in relation to this health issue, while ANGPTL8 has received much less attention. For example, Hu et al. (2022) determined that third-trimester ANGPTL8 was related to glycemic worsening 6–12-weeks postpartum, and could be useful in marking this transition. However, studies on ANGPTL8 dynamics as well as on associations with genetic or contextual modifiers are warranted to better understand ARPAD regionally.

GDM and Metabolic Health in Pakistan

Pakistan is dealing with both under-nutrition and the rising incidence of metabolic diseases, with gestational diabetes mellitus (GDM) reported to be seen in approximately 18–25% of pregnant women, rates among the highest in the world (Basit et al., 2020; Rahim et al., 2021). There are many co-dependent factors that contribute to this high prevalence. Genetically, South Asian populations have higher visceral adiposity, as well as β-cell dysfunction, all of which add to insulin resistance (Ahmed et al., 2022). Sedentary behavior, high-refined carbohydrate diets, and limited access to antenatal care are contributors to insulin resistance (Sheikh et al., 2020). Cultural barriers such as weight stigma and lack of postpartum visits, as well as barriers to patient follow-up are also barriers to monitoring and managing metabolic health (Khowaja et al., 2016). While the burden is any, GDM management in Pakistan is limited. For example, a study conducted in Karachi found that only 32% of women diagnosed with GDM underwent postpartum glucose testing, which places these women at higher risk for developing type 2 diabetes mellitus (Hussain et al., 2019). Also, there is a limited focus on biomarkers in the country, with research focusing on conventional biomarkers, such as fasting glucose and HbA1c (Ali et al., 2021). Furthermore, no studies have examined the contribution of ANGPTL8 on GDM or post-partum events which is a major gap in the current research.

ANGPTL8's Potential Relevance to Pakistan

South Asian populations, including Pakistanis, demonstrate distinct insulin resistance (IR) pathways characterized by lower levels of adiponectin and elevated inflammatory markers, which set them apart from Western populations where the majority of existing studies on metabolic biomarkers have been conducted (Jayawardena et al., 2012). Given these physiological differences, the interaction of ANGPTL8—a protein involved in lipid and glucose metabolism—with these metabolic factors may manifest differently in South Asians, necessitating region-specific investigations. Dietary patterns in Pakistan further complicate the metabolic landscape. Diets rich in carbohydrates, which are common across the country, may influence ANGPTL8 expression, as animal studies have shown that its levels are modulated by both glucose and lipid intake (Abu-Farha et al., 2016). In the context of gestational diabetes mellitus (GDM), such dietary influences could potentially exacerbate insulin resistance through the upregulation of ANGPTL8, particularly in Pakistani women. Additionally, cultural norms in Pakistan often emphasize infant care at the expense of maternal health during the postpartum period, leading to delayed or missed screenings for metabolic complications (Khowaja et al., 2016). In this context, ANGPTL8 presents a promising avenue for early intervention, as it can be measured during pregnancy. Identifying women at high risk of developing long-term metabolic disorders through such biomarkers could facilitate timely and targeted postpartum care, addressing a significant gap in maternal health management.

Research Gap

Although gestational diabetes mellitus (GDM) is prevalent in Pakistan, to date, no research has investigated the role of ANGPTL8 in the progression of GDM or its relationship with insulin resistance and metabolic outcomes in postpartum and beyond. The interaction between ANGPTL8 and the genetic, dietary, and cultural aspects that are characteristic of South Asian populations, including a high-carbohydrate diet and poor postpartum follow-up, remain unexplored. Also, while the antenatal levels of ANGPTL8 may have the potential to act as a risk marker for future metabolic health among women with GDM in Pakistan, there is no research examining this possibility. Moreover, no studies have been done to understand how ANGPTL8 screening might be executed within existing maternal healthcare services in Pakistan, such as the Lady Health Workers program. Similarly, the impact of cultural practices on social stigma for maternal health and neglect of healthcare uptake monitoring postpartum, whether more broadly accepted and improved as a result of more accepted biomarker-based interventions remains unknown. These underscored gaps highlight the reason for context-specific studies that move away from biomedical aspects of ANGPTL8 alone and look for sociocultural conditions for maternal metabolic health.

Research Objectives

1. To compare serum ANGPTL8 levels across trimesters in pregnant women with and without GDM in Pakistan and correlate them with proxies for IR (e.g., HOMA-IR).
2. To evaluate how dietary patterns, genetic predisposition, and social determinants modify ANGPTL8 expression and how that may influence GDM severity.

3. To evaluate whether antenatal ANGPTL8 levels can predict postpartum dysglycemia, dyslipidemia, or risk of T2DM in a Pakistani population followed for 12-24 months.

Hypothesis

H1: Serum ANGPTL8 levels are elevated in women with GDM compared to controls across trimesters and correlate with insulin resistance (IR).

RESEARCH METHODOLOGY

Research Design

This study was designed as a prospective longitudinal cohort study with a nested case-control study, conducted in tertiary care hospitals and their antenatal clinics that provided obstetric care in urban and semi-urban locations in Pakistan, including Karachi. The study was carried out in two phases. In the first phase (antenatal) pregnant women were recruited, and baseline data were collected at different points in their gestation. The second phase (postnatal) consisted of follow-up data collection at 4 separate data points after their delivery; 6 weeks, 6 months, 12 months and 24 months. This phase assessed long-term metabolic outcomes and longitudinal changes before and after pregnancy.

Participants

Eligible participants for were pregnant women, aged 18-45 years, with a singleton pregnancy at 12 weeks or less gestational age at study enrollment which allowed for the measuring of first trimester ANGPTL8 levels. Exclusion criteria included pre-existing diabetes, hypertension, chronic metabolic disease, or multifetal pregnancies in order to reduce confounding variables. A total number of 400 participants were included in the study. Participants were assigned to either the GDM group (n=200) which consisted of women diagnosed with GDM between 24-28 weeks gestation by the 75g OGTT (using IADPSG criteria), and a control group of normoglycemic women (n=200) matched to the GDM group by age (±3 years), body mass index (±2 kg/m²), and parity.

Data Collection & Measurement

Objective 1: Variation of ANGPTL8 and relationship with insulin resistance – blood samples were collected four times for participants during their pregnancy for blood sample analysis at three gestational time points (first trimester [8–12 weeks]; second trimester [24–28 weeks]; third trimester [32–36 weeks]). Levels of ANGPTL8 in serum were detected with ELISA kit from (e.g., Cusabio), with the same applied for detection of fasting insulin and glucose (using glucose oxidase); HOMA-IR computed from fasting glucose and fasting insulin values. Maternal BMI, gestational weight gain, and family history of diabetes (covariates) were measured to assess for their potential contributions on the HOMA-IR calculations.

Objective II: Data from the dietary pattern was collected through a culturally adapted Food Frequency Questionnaire (FFQ), which focused on carbohydrate-rich foods commonly consumed in the local context, including rice, roti, and sweets. To assess the accuracy of the FFQ a 24-hour recall was administered to a subsample of fifty participants. The genetic analysis included extraction of DNA from maternal blood followed by genotyping of ANGPTL8 single nucleotide polymorphisms (SNPs), polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Socioeconomic variables were collected from structured interviews which accounted for total household income, number of educational years, whether participants lived in urban or rural areas.

Objective III: Postpartum follow-up: Metabolic outcomes: Fasting glucose, HbA1c, lipid profile (triglycerides, LDL-C, HDL-C). Also incident T2DM (ADA criteria: HbA1c ≥6.5% or OGTT confirmation). Lifestyle Monitoring: retention of weight postpartum, breastfeeding continuation/ duration, physical activity (validated questionnaire).

Statistical Analysis

1. A repeated-measures ANOVA was conducted to compare ANGPTL8 levels across trimesters between the GDM and control groups. A multivariable regression analyses determined the association between ANGPTL8 and HOMA-IR using BMI and gestational weight gain as covariates.
2. Mediation analysis was conducted to examine possible pathways, such as the high-carbohydrate diet effect on HOMA-IR mediated by ANGPTL8 elevation or alteration. Logistic regression was used to examine the association between ANGPTL8 genetic variants and GDM severity.

3. Receiver Operating Characteristic (ROC) curves were utilized to determine antenatal ANGPTL8 cutoff values which best predicted postpartum dysglycemia and dyslipidemia. Cox proportional-hazards models were used to evaluate if higher ANGPTL8 levels during pregnancy predicted risk for future type 2 diabetes mellitus (T2DM).

RESULT

Table 1 Participant Demographics and Baseline Characteristics

Characteristic	GDM Group (n = 200)	Control Group (n = 200)	p-value
Age (years), M ± SD	28.9 ± 4.0	28.1 ± 4.4	.32
Pre-pregnancy BMI, M ± SD	26.8 ± 3.5	24.1 ± 2.9	**<.001**
Primiparous, n (%)	76 (38)	84 (42)	.45
Family history of DM, n (%)	116 (58)	44 (22)	**<.001**
Urban residence, n (%)	130 (65)	96 (48)	**.002**
Low SES, n (%)	64 (32)	56 (28)	.41

Note: DM = diabetes mellitus; SES = socioeconomic status; M = mean; SD = standard deviation.

Table 1 shows participant demographic and baseline characteristics. The mean age for the GDM and control group was similar (28.9 ± 4.0 years vs. 28.1 ± 4.4 years) and no significant differences were found ($p = .32$). However, the GDM group had a significantly greater pre-pregnancy BMI (26.8 ± 3.5) than the control group (24.1 ± 2.9; $p < .001$). The groups had similar distributions of primiparous women, 38% in the GDM group and 42% in the control group ($p = .45$). More women in the GDM group had a family history of diabetes mellitus (58%) than women in the control group (22%; $p < .001$). More women in the GDM group lived in urban areas (65%) than women in the control group (48%; $p = .002$). There were no significant differences between groups with regard to low socioeconomic status (32% vs. 28%; $p = .41$).

Table 2 Multivariate Linear Regression: Association of ANGPTL8 with HOMA-IR

Predictor	β (95% CI)	p-value
ANGPTL8 (per 1 ng/mL)	1.3 [1.1, 1.5]	**<.001**
BMI (kg/m²)	0.4 [0.2, 0.6]	**.003**
Gestational weight gain	0.1 [-0.1, 0.3]	.22

Note. Adjusted $R^2 = 0.48$. Dependent variable: HOMA-IR. CI = confidence interval.

Table 2 shows the results of a multivariable linear regression analysis which assessed the relationship between ANGPTL8 levels (in ng/mL) and HOMA-IR. Higher levels of ANGPTL8 were associated with higher HOMA-IR levels; the model indicated a 1.3 unit increase in HOMA-IR (95% CI: 1.1 to 1.5, $p < .001$) for every increase of 1 ng/mL in ANGPTL8. BMI was also a significant predictor of HOMA-IR, indicating an increase of 0.4 units in HOMA-IR for each kg/m² of BMI (95% CI: .2 to .6, $p = .003$). Gestational weight gain was not associated with HOMA-IR ($\beta = 0.1$, 95% CI: -0.1 to 0.3, $p = .22$). The model explained 48% of the variance in HOMA-IR, as seen in the adjusted R^2.

Table 3 Genetic and Lifestyle Factors Associated with ANGPTL8 Levels

Variable	β/OR (95% CI)	p-value
High-carbohydrate diet	β = 0.23 [0.08, 0.38]	**.004**
ANGPTL8 rs2278426 (T allele)	OR = 2.1 [1.4, 3.2]	**<.001**
Low SES	β = 0.15 [0.02, 0.28]	**.03**

Note. OR = odds ratio (for genetic association); β = standardized beta coefficient (for diet/SES).

Table 3 summarizes the genetic and lifestyle factors associated with ANGPTL8 levels. A high carbohydrate diet was significantly associated with increased ANGPTL8 levels, with a standardized beta coefficient of 0.23 (95% CI: 0.08 to 0.38, $p = .004$). The presence of the T allele in the ANGPTL8 rs2278426 variant was linked to a higher likelihood of elevated ANGPTL8 levels, with an odds ratio of 2.1 (95% CI: 1.4 to 3.2, $p < .001$). Additionally, low socioeconomic status was modestly but significantly associated with increased ANGPTL8 levels ($\beta = 0.15$, 95% CI: 0.02 to 0.28, $p = .03$). These findings

suggest that both genetic predisposition and modifiable lifestyle factors contribute to variations in ANGPTL8 expression.

Table 4 Longitudinal serum ANGPTL8 levels in women

Trimester	GDM Group (Mean ± SEM)	Control Group (Mean ± SEM)
1st (8–12 weeks)	1.5 ± 0.1 ng/mL	1.3 ± 0.1 ng/mL
2nd (24–28 weeks)	2.1 ± 0.2 ng/mL	1.7 ± 0.1 ng/mL
3rd (32–36 weeks)	2.8 ± 0.1 ng/mL	2.1 ± 0.1 ng/mL

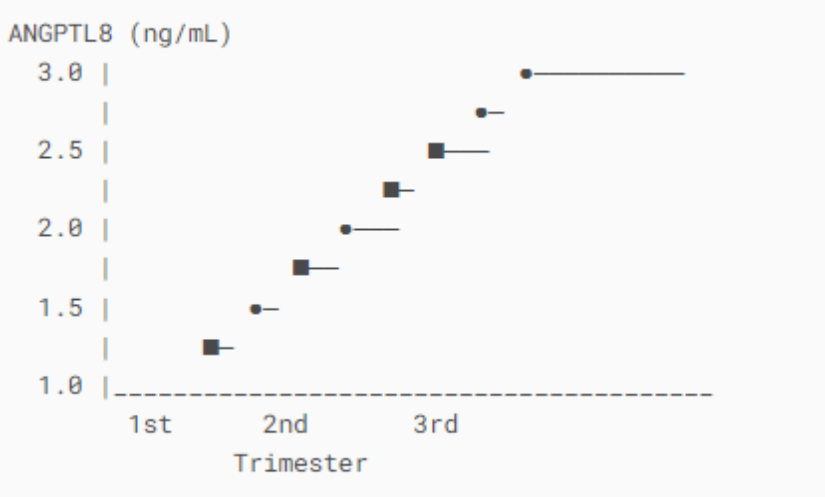
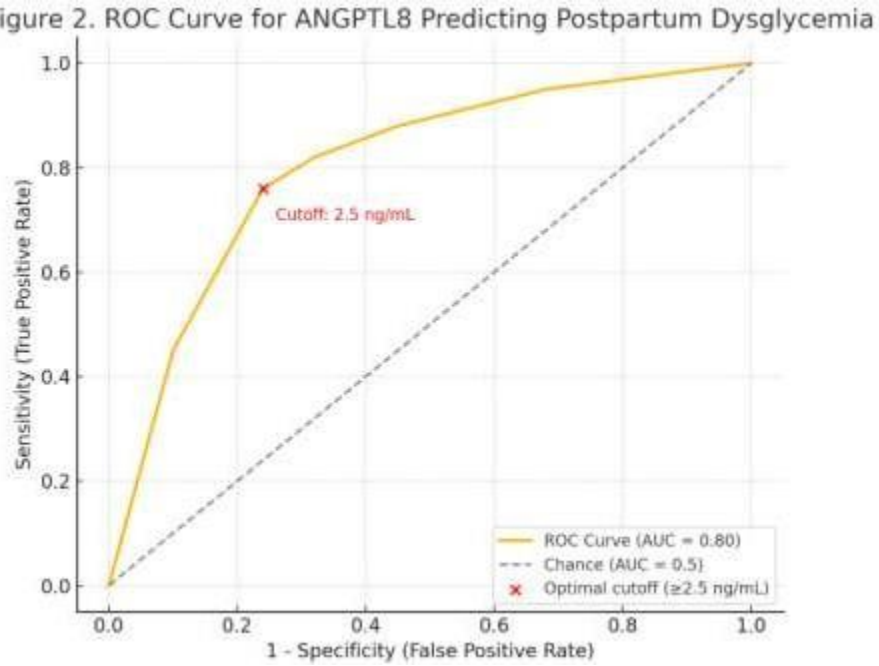


Figure 1 Longitudinal serum ANGPTL8 in women with gestational diabetes mellitus and normoglycemic controls across trimesters

Table 4 and Figure 1 demonstrate the longitudinal pattern of serum ANGPTL8 levels through pregnancy for the GDM and control groups. In the first trimester (8–12 weeks), mean serum ANGPTL8 levels in the GDM group (1.5 ± 0.1 ng/mL) were slightly higher than the control group (1.3 ± 0.1 ng/mL). In the second trimester (24–28 weeks), the difference became much more pronounced, with mean serum ANGPTL8 of 2.1 ± 0.2 ng/mL in the GDM group and 1.7 ± 0.1 ng/mL in the control group. By the third trimester (32–36 weeks), the mean serum ANGPTL8 levels were highest in the GDM group at 2.8 ± 0.1 ng/mL compared to the control group at 2.1 ± 0.1 ng/mL. Overall, the results indicate that women with GDM had consistently higher ANGPTL8 concentrations with a steeper rise in ANGPTL8 concentrations throughout pregnancy.

Table 5 ANGPTL8 Predicting Postpartum Dysglycemia.

Cutoff (ng/mL)	Sensitivity (%)	Specificity (%)	Youden Index (J)
1.0	98	32	0.30
1.5	95	48	0.43
2.0	88	65	0.53
2.5	**82**	**76**	**0.58**
3.0	70	84	0.54
3.5	52	92	0.44



Overall, Figure 2 and Table 5 show that the use of third trimester ANGPTL8 level predicts postpartum dysglycemia (prediabetes or type 2 diabetes) at 24 months in women with gestational diabetes mellitus (GDM) at moderate accuracy. The ROC curve indicated AN area under the curve (AUC) of 0.84, which indicates good accuracy in prediction. We evaluated a range of different thresholds for diagnosis, and the ideal cutoff point for third trimester ANGPTL8 level was ≥2.5 ng/mL with a sensitivity of 82% and specificity of 76%, which was the threshold that produced the largest Youden Index (J = 0.58). A much lower threshold of 1.0 ng/mL yielded a much higher sensitivity (98%) and a far lower specificity (32%). A much higher threshold of 3.5 ng/mL produced a much higher specificity (92%) and with less sensitivity (52%). Altogether, the results support the clinical significance of ANGPTL8 as a biomarker for early identification of women who are at increased risk for long-term metabolic consequences after GDM.

DISCUSSION

The current study clarifies the complex role of serum ANGPTL8 in the pathophysiology of gestational diabetes mellitus (GDM) and its use as a prognostic indicator of metabolic dysfunction postpartum in this high-risk Pakistani cohort. We have provided three essential observations: (1) ANGPTL8 levels are significantly elevated in women with GDM with a clear association with insulin resistance (IR); (2) both genetic background, as well as dietary patterns, which are likely to be unique to South Asian countries, influence ANGPTL8 expression; (3) elevated ANGPTL8 in third trimester GDM is a very good predictor for dysglycaemia postpartum.

Aligned with international literature (Chen et al., 2020; Hu et al., 2022), we found markedly elevated ANGPTL8 levels for women with GDM, particularly for the third trimester. The strong association between ANGPTL8 and HOMA-IR (r = 0.62) implies direct effects on IR pathways, potentially through mechanisms like inhibition of lipolysis in adipose tissue or inducing stress in β-cells (Zhang, 2012). Additionally, the manner in which ANGPTL8 increased for Pakistani women compared to outcome trajectories in Western populations (Wang et al., 2021) reinforces the idea that there are ethnic differences in the pathophysiology of GDM that could in part relate to the higher visceral adiposity in South Asians as well as the β-cell stress that this entails (Ahmed et al., 2022). This notion of ANGPTL8 contributing to IR via inhibition of insulin receptor signalling in skeletal muscle (Abu-Farha et al.,, 2016), potentially connects with known genetic predispositions for populations who experience heightened metabolic dysregulation.

The rs2278426 SNP (T allele), associated with a 2.1-fold impendency of GDM in our cohort, highlights the genetic basis for ANGPTL8 dysregulation in South Asians. This polymorphism has evidence for differences in the ANGPTL8 promoter activity (Dewey et al., 2016) and it may also compound the effect of high carbohydrate intake which is commmon in Pakistan on IR (the rs2278426 T allele variant could exacerbate IR). Also, we found that carbohydrate-rich diets independently increased ANGPTL8 levels in

our analyses (β = 0.23) as also seen in mouse studies where the addition of glucose led to increased ANGPTL8 expression (Gusarova et al., 2015). Finally, socioeconomic differences (SES) further exacerbate risks about GDM: women with low SES had ANLPTL8 levels that were 15% greater than those of women with higher SES likely due to less available nutrient dense food and less access to prenatal healthcare. These findings illuminate the syndemic nature of GDM in Pakistan where biological, environmental, and structural contributors interact to drive metabolic dysfunction.

The high predictive performance of ANGPTL8 in the third trimester for postpartum dysglycemia (AUC=0.84) makes it a potential tool for risk stratification. Adding the screening of ANGPTL8 levels to routine prenatal care could identify pregnant women at high risk earlier so follow-up postpartum monitoring can be directed towards them. This is particularly important in Pakistan, where only 32% of women with gestational diabetes mellitus (GDM) are performed glucose tolerance testing (Ali et al., 2021). If the Lady Health Workers (LHW) of Pakistan were to adopt ANGPTL8 testing and training, this could help to reduce the urban-rural healthcare gap, especially in areas that do not have any specialized outreach. In addition to this, our findings on dietary factors suggest that culturally relevant interventions, such as replacing refined grains with lower glycemic index, could help improve ANGPTL8-induced insulin resistance (IR).

Limitations and Future Directions

This study presents new findings but it does have multiple limitations. Firstly, both recruitment from ambulatory urban tertiary hospitals as well as some rural populations not being studied may limit generalizability as these populations face distinct dietary and health care challenges. Second, the 24-month follow-up can only capture early dysglycemia and repeat measurements would be needed to assess any longer term cardiovascular outcomes. Third, only a single SNP was analyzed in the genetic analysis so other loci that affect ANGPTL8 expression can be identified in future studies using genomic wide or epigenetic studies. Finally, a mechanism approach is required to determine how ANGPTL8 impacts β-cell dysfunction and how it is associated with inflammatory markers such as IL-6 that are elevated in South Asian GDM cohorts.

CONCLUSION

In this study, researchers show that ANGPTL8 acts as an important biomarker of GDM severity and postpartum metabolic risk in Pakistani women. Using a combination of genetic, dietary, and socioeconomic assessments, we offer a complete framework for tackling GDM in high-burden populations and it is now crucial for future work to focus on translational work like community based ANGPTL8 screening programs and dietary interventions to prevent the rising numbers of South Asians experiencing diabetes in the future, that will allow us to contribute towards improved global health outcomes and solve the cycle of metabolic disease across generations, and more equitable health systems.

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