DOI: https://doi.org/10.3329/jacedb.v4i20.84922

Intestinal Alkaline Phosphatase: A Novel Enteric Biomarker and Potential Mediator in the Pathogenesis of Gestational Diabetes Mellitus

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Abstract

Background: Gestational diabetes mellitus (GDM) represents a complex condition where the interplay between insulin resistance and β-cell dysfunction is central to its pathophysiology. Emerging evidence implicates, intestinal alkaline phosphatase (IAP), a crucial gut barrier enzyme that detoxifies bacterial lipopolysaccharides (LPS), has a key contribution to insulin resistance. However, its role in the unique metabolic milieu of pregnancy and GDM remains largely unexplored.

Objective: This study aims to determine the frequency of intestinal alkaline phosphatase deficiency in pregnancy and its association with abnormal glucose tolerance, and to evaluate the predictive utility of fecal IAP for GDM.

Method: This observational cross-sectional study involved 198 pregnant women, comprising 55 with GDM and 143 with normal glucose tolerance (NGT), diagnosed according to WHO 2013 criteria by a 75g OGTT. Stool sample collection was done, and IAP assay was performed using a pNPP/DEA protocol with L-phenylalanine inhibition to ensure isoform specificity. Logistic regression was used to identify independent predictors of GDM, and the ROC curve analysis was performed to assess the diagnostic utility of IAP.

Result: Women with GDM demonstrated significantly reduced median stool IAP levels compared to controls (23.59 vs 46.48 U/g, $p < 0.001$). Severe IAPD (≤18 U/g) was nearly twice as prevalent in GDM cases (43.6% vs 24.5%, $p<0.001$). After adjustment for BMI and previous history of GDM, a 10 U/g decrease in stool IAP corresponds to about 22% higher odds of having GDM ($p<0.001$). ROC analysis revealed a diagnostic threshold of 29.19 U/g with 61.8% sensitivity, 65.7% specificity, and a remarkable 81.7% negative predictive value.

Conclusion: Fecal IAP emerges as a non-invasive biomarker for risk stratification besides OGTT, rather than replace it. The high negative predictive value suggests particular utility for ruling out GDM risk, while the mechanistic link through bacterial endotoxin detoxification opens promising preventive and therapeutic avenues. *[J Assoc Clin Endocrinol Diabetol Bangladesh, 2025;4(Suppl 1): S36]*

Keywords: Gestational diabetes mellitus, Insulin resistance, Intestinal alkaline phosphatase

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