The Role of Early Pregnancy Serum Adiponectin Level in Predicting Development of Gestational Diabetes Mellitus (GDM)

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Abstract

Background: *Early prediction of GDM by measuring a biomarker at first trimester of pregnancy may prevent maternal and fetal complication. Adiponectin, which modulate insulin sensitivity, is secreted from adipose tissue and decreases blood glucose level. The objective of the study was to evaluate the association of maternal first trimester serum adiponectin with development of GDM.*

Methodology: *This longitudinal study was conducted in the BSMMU, Dhaka from June, 2021 to May, 2022 where pregnant women of first trimester were selected by purposive convenient sampling. At first 94 pregnant women were selected after excluding diabetes or previous history of GDM and their serum adiponectin level was measured. Then the participants were followed up at 24-28 weeks of gestation and OGTT was done to detect GDM. ROC was used to decide the best cut-off point of adiponectin level for detection of GDM. The respondents were divided into 'below cut-off' group and 'above cut-off' group. Differences between two groups were assessed by statistical test.*

Results: *A total 18 respondents developed GDM from both group. In below cut-off' group, out of 26 respondents 13 developed GDM and remaining 13 were euglycemic. Whereas in above cut-off group, out of 62 respondents, majority 57 were euglycemic and only 5 women developed GDM. ROC analysis of adiponectin level for detection of GDM, a AUC value 0.887 (95% confidence interval 0.802-0.972) was found which was statistically significant (p<0.001). A cut off value of ≤10.165 µg/ml showed the highest youden index (0.651) with 83.3% sensitivity and 81.4% specificity, the accuracy was 79.5%. Moreover a cut of value ≤10.165 µg/ml showed PPV and NPV of 50.8% and 92.8% respectively. A significant association was found between development of GDM and adiponectin level (P<0.001). The odds for developing GDM due to low adiponectin are 11.4 [95% CI: 3.45 – 37.64]. About 72.2% GDM patients had below cut-off adiponectin level.*

Conclusion: *Study finding revealed that maternal serum adiponectin level was lower at early pregnancy to those patients who subsequently developed GDM. So a low adiponectin level at early pregnancy may be a new risk factor for GDM.*

Key words: *adiponectin, gestational diabetes mellitus (GDM), pregnancy, insulin resistance.*

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Introduction:

The incidence of gestational diabetes mellitus (GDM) is increasing globally which affects 3-10% of pregnancies worldwide[1] with an increased risk of short and long term ill health for both mother and off spring. In Bangladesh, prevalence of

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GDM is quite high with frequencies around 7 - 14%.[2] Adipose tissue is a highly active endocrine organ and produces a number of adipocytokines like adiponectin, leptin, resistin, vispatin etc. Adiponectin is a physiologically active polypeptide hormone. Insulin is the main regulator of it's secretion from adipocytes. It stimulates glucose uptake and fatty acid oxidation by binding to it's receptor (typically adipoR1 and adipoR2) and activating AMP activated protein kinase (AMPK) and peroxisome proliferator activated receptor α (PPAR-α) in liver and skeletal muscle. It decreases glucose concentration by inhibition of gluconeogenesis. It reduces the use of insulin by stimulator effect in beta oxidation of fatty acid in skeletal muscle.[3] Plasma adiponectin is inversely correlated with body mass index (BMI), intra-abdominal fat and incidences of insulin resistance.

Low concentration of adiponectin has been reported in GDM subject during pregnancy. Some studies reported that risk of GDM is 5-6 times higher in women with low adiponectin level than women with normal or high level.[4] Adiponectin is not expressed nor produced by the placenta. Maternal adipose tissue is the major source of maternal plasma adiponectin, so it can be assessed as an independent biomarker.

If any association between early pregnancy adiponectin level and subsequent development of GDM can be evaluated then serum adiponectin level can be used as predictor of GDM in early pregnancy with subsequent interventions to minimize complications. The objective of this study was to find out the association of early pregnancy serum adiponectin level with development of GDM.

Methodology:

This prospective cohort study was conducted in outpatient department of both Feto-maternal Medicine and general Obs & Gynae, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka over a period of 1 year from June, 2021 to May, 2022. The study population included pregnant women at first trimester who were found non-diabetic (FPG < 7 mmo/L, 2 hour OGTT <11.1 mmol/L according to WHO criteria) and singleton pregnancy. A total 94 pregnant women were selected by purposive sampling who fulfilled the inclusion and exclusion criteria. Inclusion criteria was pregnant women who were non-diabetic (FPG <7 mmo/L, 2 hour OGTT <11.1 mmol/L according to WHO criteria) at their first trimester of pregnancy. Exclusion criteria were multiple pregnancy, pre-existing diabetes mellitus, diagnosed case of cardiovascular disease, chronic hypertension, previous history of pre-eclampsia, eclampsia or SLE. Data regarding demographic profile (e.g. age, BMI, educational status), previous history of GDM, family history were recorded in a semi structured questionnaire. Obstetrics history like gravidity, parity, gestational weeks, past history of any other medical disorders was documented. Then a physical examination was carried out by researcher including height, weight, BMI, BP etc. Written consent along with particulars of the participants was taken after explaining the procedure. Blood sample was collected on the same day at study place and sent to the microbiology laboratory of BSMMU for serum adiponectin assay by ELISA method. The participants were followed up between 24-28 weeks by doing OGTT to detect GDM according to WHO criteria. Six (6) patients were failed to follow up and 88 patients were finally selected for the study.

Data analysis:

Data was analyzed by SPSS statistical software. ROC analysis was used to detect the best cut-off point of adiponectin level for detection of GDM. Youden index was used to find out the accuracy and best threshold value for adiponectin as a marker. Normal distribution of the continuous variables was checked first before comparing the means between below and above cut off value of adiponectin patients and between GDM and normal patients. Then according to the result parametric and non-parametric test (Mann Whitney test) were selected for comparing means of the two groups.

Results :

ROC analysis of adiponectin level for detection of GDM among pregnant women found an AUC value of 0.887 (95% CI 0.802-0.972) which was statistically significant (P <0.001) (Figure:1 and Table I).

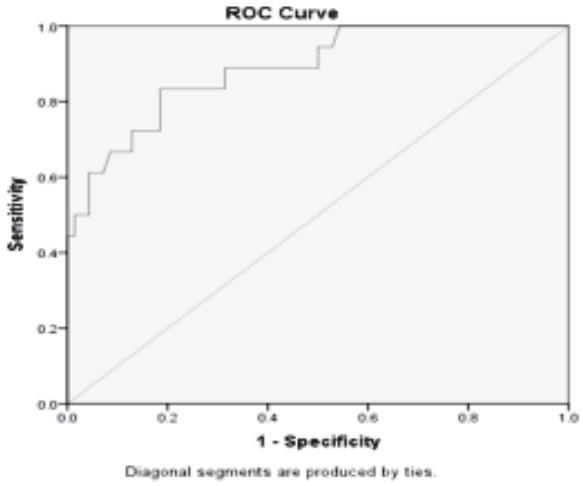

Figure 1: *ROC curve for first trimester serum adiponectin level*

Table II shows a cut-off value of ≤10.165 showed the highest Youden index (0.651) with 83.3% sensitivity and 81.4% specificity. In addition, the accuracy was 79.5%. Moreover, A cut-off value of ≤10.165 showed, PPV and NPV of 50.8% and 92.8%.

A significant association was found between development of GDM and adiponectin level (P<0.001). The odds for developing GDM due to low adiponectin are 11.4 [95% CI: 3.45 – 37.64]. About 72.2% GDM patients had below cut-off adiponectin level. However, only 18.6% normal patients had low adiponectin level (Table-IV).

Table I

Area Under the Curve

Test Result Variable(s): adiponectin

Area	Std. Error[a]	P value	95% Confidence Interval	
			Lower Bound	Upper Bound
0.887	0.043	<0.001	0.802	0.972

Table II

Determination of cut off value with youden index

Cutoff value	Sensitivity	Specificity	PPV	NPV	Accuracy	youden index (j=sen+spe-1)
10.115	0.722	0.814	0.486	0.889	0.784	0.541
10.165	0.833	0.814	0.508	0.916	0.795	0.651
10.230	0.833	0.801	0.474	0.928	0.772	0.632

Table III

Cross tabulation of GDM with adiponectin level based on derived cut-off value

Adiponectin (µgm/ml)	GDM	Non-GDM	Total
≤10.165	True positive	False positive	26 (TP+FP)
	13	13	
>10.165	False negative	True negative	62 (FN+TN)
	5	57	
	All patients with GDM (TP+FN)	All patients without GDM (FP+TN)	88 (TP+FN+FP+TN)
	18	70	
	All patients with GDM (TP+FN)	All patients without GDM (FP+TN)	88 (TP+FN+FP+TN)
	18	70	

Table IV

Association of GDM with low adiponectin.

		GDM		OR	P value
		Yes	No		
Adiponectin(ig/ml)	below cut-off (≤10.165)	13 (72.2%)	13 (18.6%)	11.4	<0.001
	above cut-off (>10.165)	05 (27.8%)	57 (81.4%)		
Total		18	70		

Here, P value obtained from chi square test.

Discussion:

This prospective longitudinal study was carried out among 88 women with singleton pregnancy at their first trimester of pregnancy, having no evidence of GDM. The responders were divided into two groups. One group with below cut-off of adiponectin (≤10.165 igm/ml) and another group with above cut-off of adiponectin level (>10.165 μgm/ml). Among them, 26 women (29%) were in below cut-off of adiponectin group and 62 (71%) women were in above cut-off of adiponectin group. During follow up 18(20.5%) women developed GDM and 70 (79.5%) were diagnosed as non GDM.

ROC analysis of adiponectin level for detection of GDM among pregnant women found an AUC value of 0.887 (95% CI 0.802-0.972) which was statistically significant (P <0.001). A cut-off value of ≤10.165 igm/ml showed the highest Youden index (0.651) with 83.3% sensitivity and 81.4% specificity. In addition, the accuracy was 79.5%. Moreover, A cut-off value of ≤10.165 μgm/ml showed, PPV and NPV of 50.8% and 92.8%. In a study by Madhu et al (2019), ROC curve revealed a cut-off value of adiponectin was 9.1 μgm/ml in the first trimester with 100% sensitivity and 95.6% specificity in prediciting GDM.[5]

In this study, the levels of serum adiponectin were significantly lower in GDM subjects (8.24±2.31) μgm/ml than healthy pregnant women (11.83±1.76) μgm/ml and related adversely to blood glucose level. Moreover, a significant association was found between development of GDM and adiponectin level (P<0.001). The odds for developing GDM in below cut-off of adiponectin group were 11.4 [95% CI: 3.45 – 37.64]. About 72.2% GDM patients had below cut-off of adiponectin level. However, only 18.6% normal patients had below cut-off of adiponectin level. Saini et al (2015) showed that adiponectin concentration was lower in pregnant women with GDM and found an inverse relationship between adiponectin level and fasting blood sugar.[6] Results of the study by Pala et al (2005) were similar to this study; adiponectin levels were significantly lower than the control group.[7] Tsai et al (2005) reported that the concentration of serum adiponectin was lower in GDM group.[8] A systematic review and meta-analysis have demonstrated a significant decline in adiponectin levels in GDM group vs. control group.[9]

Conclusion:

In this longitudinal study, the level of adiponectin in early pregnancy was evaluated. The results of this study show that adiponectin has the potential to be used as an important screening biomarker for the early pregnancy which strongly predicts GDM in Bangladesh women. Apart from diagnosis, adiponectin levels can help in stratifying pregnant women so that measures to prevent GDM can be instituted in the early pregnancy to the at-risk patients. In country with growing burden of GDM and inadequate resources, such information can significantly improve maternal and fetal outcomes in women at risk for GDM.

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