ORIGINAL ARTICLE

RELATIONSHIP OF SERUM ADIPONECTIN LEVELS WITH GLYCAEMIC STATUS IN PREGNANT WOMEN

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Background: Adiponectin plays an important role in glucose metabolism and released in response to insulin. It helps to decrease glucose levels and insulin resistance; however, this relation is not been studied in pregnant ladies. Objective was to determine serum adiponectin level and glycaemic status in pregnant women belonging to Peshawar, Khyber Pakhtunkhwa (KPK) and to find any possible relationship between them. **Methods:** Hundred pregnant women with gestational diabetes mellitus (GDM) and 100 healthy pregnant women without GDM were randomly selected in a cross-sectional study. After an overnight fast, their blood samples were taken for determination of serum adiponectin, glycosylated haemoglobin (HbA1c) and fasting blood glucose (FBG). The relationship of adiponectin with glycaemic status was determined with Pearson Correlations coefficient (r). **Results:** Pregnant women with GDM when compared to healthy pregnant women showed significantly low levels of serum adiponectin (µg/mL) (2.2±0.2 vs. 11.25±4.8, $p<0.05$) and significantly high level of FBG (mg/dl) (182.7±64.2 vs. 93.6±5.9, $p<0.05$) and HbA1c (%) (7.4±0.1 vs. 5.4±0.1, $p<0.05$). Serum adiponectin level showed a statistically significant negative correlation with FBG (r = -0.203, $p=0.042$) and HbA1c (r = -0.744, $p=0.000$) in pregnant women with GDM. **Conclusion:** Serum adiponectin concentration is markedly decreased in pregnant women with GDM which concludes that Hypoadiponectinemia is related with deranged (elevated) glycaemic status in pregnancy. Moreover, adiponectin is associated negatively with FBG and HbA1c in the studied population.

Keywords: Adiponectin; Gestational Diabetes Mellitus; Glycosylated Haemoglobin; HbA1c

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INTRODUCTION

Adiponectin is one of the most important adipocytokine (adipokine) secreted mainly the by adipose tissue. Adipokines act like hormones and that's why adipose tissue is said to be an active endocrine gland.[1–3] Skeletal muscle, pancreatic, smooth muscle and endothelial cells are other major sites where adiponectin is produced in high amount.[4,5] Adiponectin is protein in nature containing 244 amino acids. Structurally it consists of four domains; an N-terminal signal peptide, variable region, collagenous region and a C-terminal globular domain.[6–9] Its normal blood level ranges between 5–30 µg/mL, more in women than men. Although produced in and released from fat tissue, the levels tend to decrease in increasing adiposity and obesity.[9,10] Serum adiponectin concentrations are also decreased in complications related to obesity e.g., diabetes mellitus[11], cardiovascular diseases[12,13], non-alcoholic hepatic steatosis[14] and in pregnancy.[15] Apart from many other known functions, Adiponectin plays important role in carbohydrate metabolism.[16] It is released in response to Insulin thereby increasing its sensitivity.[17] Insulin is the hormone which stimulates cells to absorb and metabolize glucose. Thus, adiponectin helps to decrease blood glucose level and it counteracts insulin resistance.[18] The important biochemical effect of serum adiponectin is the regulation of insulin sensitivity among pregnant women, which makes them prone to gestational diabetes. Low serum adiponectin levels are associated with risk of developing diabetes mellitus and gestational diabetes mellitus (GDM).[16]

Glycaemic status of an individual is best determined with the help of glycosylated haemoglobin or HBA1c. Under physiologic conditions, HbA is slowly and non-enzymically glycosylated, the extent of glycosylation being dependent on the prevailing plasma concentration of glucose. It has glucose residues attached predominantly to the NH_2 groups of the N-terminal valines of the β-globin chains. Increased concentration of HbA1c is found in RBCs of patients with diabetes mellitus because their HbA has contact with higher glucose concentrations during the 120-day lifetime of these cells.[19] The relationship of serum adiponectin level with HbA1c and FBG in women with GDM has been

described in various regions and racial groups. However; limited data is available on relationship of serum adiponectin levels with the glycaemic control in GDM women of Khyber Pakhtunkhwa, Pakistan. Therefore, the aim of this study is to determine the association of adiponectin with glycaemic control in GDM.

MATERIAL AND METHODS

The study was conducted for a period of one year, in four selected public and one private tertiary care hospital of Peshawar, Khyber Pakhtunkhwa. This was a cross-sectional analytical study conducted on randomly selected otherwise healthy women, primi- or multigravida, in their 24–40 weeks of gestation with normal singleton foetus and no history of pre-existing or pre-pregnancy diabetes mellitus attending the outpatient department of the three hospitals for routine antenatal visit. The study consisted of two groups: Group A comprised of 100 control healthy pregnant women, while Group B comprised of 100 pregnant women with GDM. Detailed medical history of each woman was taken and physical examination parameters like blood pressure, height, weight and BMI were recorded on a well-designed proforma/ questionnaire. Informed written consent was taken from each woman and the study was approved by the Ethical Committee of Khyber Medical College, Peshawar. A blood sample of 5 ml was collected from each woman included in the study after 12 hours of overnight fast. Fasting blood glucose and glycosylated haemoglobin were measured on 2 ml of the fresh samples transferred to EDTA tube. The remaining 3 ml of the collected blood sample was centrifuged at 3000 rpm to obtain serum which was stored at -70°C for later analysis of adiponectin. FBG was measured colorimetrically using kit provided by Elitech-Sees, France. Glycosylated haemoglobin was measured colorimetrically using kit provided by Human Diagnostics, Germany. Serum adiponectin level was measured on Metrolab by enzyme linked immunosorbent assay (ELISA) method using Human adiponectin ELISA kit provided by Biovendor, Germany.

Data was analyzed using SPSS version 20. Results were expressed as Mean±SD. *p*-value less than 0.05 was considered significant. Comparison of parameters between the two groups was done by independent sample t-test. The correlation of adiponectin with glycaemic status in the form of HbA1c was found using Pearson correlation.

RESULTS

Mean and standard deviation of the demographic, clinical and biochemical parameters of the studied population are summarized in Table-1. Group A consisted of 100 normal healthy pregnant women without GDM having a mean age of 21.9±2.7 years and group B consisted of 100 pregnant women with GDM having a mean age of 21.4±2.9 years. No significant difference across both the groups was detected. In the same way the inter group comparison for BMI (kg/m^2), Systolic Blood Pressure (SBP) (mmHg) and Diastolic Blood Pressure (DBP) (mmHg) was not significant. The comparison of variables between the two groups showed significantly high levels of FBG (mg/dl) (182.7±64.2 vs 93.6±5.9, p=0.003) and HbA1c (7.4±0.1 vs 5.4±0.1, p=0.007) in the GDM group than the normal control group. Serum adiponectin level (ug/mL) was significantly lower in women with GDM with 2.2±0.2 vs. 11.25±4.8 in normal healthy pregnant women without GDM (p-value <0.05) (Table-1).

Bivariate correlation analysis among women without GDM (Group A) indicated that serum adiponectin had a strong inverse relationship with HbA1c (r = -0.744, p=0.000) and also fasting blood sugar (r = -0.203, p=0.042). Relationship of adiponectin with age, BMI, SBP and DBP was not significant (Table 2) in women without GDM. The bivariate correlation analysis, for the Group B, women with GDM showed significant association between adiponectin and HbA1c (r = -0.548, p=0.0001). Moreover, a strong positive association was observed among serum adiponectin level and gestational age (r = 0.199, p=0.047) and DBP (r = 0.238, p=0.017) in women with GDM (Table-2).

Table-1: Comparison of basic parameters among women with GDM (Group B) and women without GDM (Group A)

Parameters	Group A	Group B	*p*-value*
Age (yr.)	21.9±2.7	21.4±2.9	0.164
Body Mass Index (kg/m^2)	30.4±6.6	28.9±5.8	0.080
Systolic Blood Pressure (mmHg)	117.6±7.7	119.1±8.5	0.193
Diastolic Blood Pressure (mmHg)	75.0±5.6	74.6±6.7	0.606
Fasting Blood Glucose (mg/dL)	93.6±5.9	182.7±64.2	0.003
Glycosylated haemoglobin (HbA1c %)	5.4±0.1	7.4±0.1	0.007
Adiponectin (ug/mL)	11.25±4.8	2.2±0.2	0.001

*p-value < 0.05 considered significant

Table-2: Bivariate correlation of Adiponectin with different parameters among women with (Group B) and without GDM (Group A)

	Group A: Without GDM		Group B: with GDM	
Parameters	**r-value**	***p*-value**	**r-value**	***p*-value**
Age (yr.)	0.050	0.623	-0.106	0.293
B.M.I (kg/m^2)	0.100	0.321	-0.073	0.468
Systolic Blood Pressure (mmHg)	-0.087	0.392	0.107	0.289
Diastolic Blood Pressure (mmHg)	-0.055	0.587	0.238	0.017
Fasting Blood Sugar (mg/dl)	-0.203	0.042	-0.101	0.317
HbA1C (%)	-0.744	0.000	-0.548	0.000

DISCUSSION

This study showed low levels of serum adiponectin in women with GDM as compared to healthy pregnant women and the levels were inversely related to fasting blood glucose level. A significant negative association of adiponectin with HbA1c was observed in our study. This has been shown by Saini *et al.*[20], where adiponectin levels were lower in pregnant women with gestational diabetes mellitus along with an inverse relationship between adiponectin concentration and fasting blood sugar. Similar findings are observed in several other studies showing significantly lower serum adiponectin level in women with GDM as compared to healthy control groups.[21–25] In a systematic review and meta-analysis by Xu J *et al*, 2014, it was demonstrated that adipokines levels including leptin, adiponectin and tumour necrosis factor-alpha were significantly different in patients with GDM.[26] Williams *et al*.[27] have shown that each µg per mL decrease in serum adiponectin levels of pregnant women increased their risk of developing GDM by more than 15%. They also demonstrated that adiponectin concentration was higher in normal otherwise healthy pregnant women. Tsai *et al*[28] reported extremely lower levels of serum adiponectin in GDM group than the control group which is consistent with results of our study. They also showed a negative correlation between adiponectin concentration and development of GDM. Hypoadiponectinemia is correlated negatively with GDM in one of the studies performed on 180 pregnant women.[29] Lain *et al.* demonstrated that pregnant women with the lowest quartile of serum adiponectin were at an increased risk of GDM.[30] A study performed on 445 pregnant women, which evaluated their adiponectin levels in the first trimester revealed that a subsequent decline in adiponectin levels had a positive correlation with GDM in the mid-trimester.[31] This suggested that serum levels of this particular hormone may be used as a predictor and an indicator for the development of GDM in later trimesters. However, several studies have contradictory results in comparison to our study. Saucedo *et al* demonstrated no difference in adiponectin levels of women with GDM and pregnant normal women without GDM.[18] In another study no significant difference in terms of adiponectin level in non-GDM control and GDM groups were observed.[32] Inconsistencies have been reported previously in order to find an association between low levels of adiponectin and increased risk of GDM. Some studies have shown that low levels of adiponectin are associated with increased risk of GDM, in contrast no association has been reported by others. These discrepancies in the results can be explained due to differences in racial, ethnic demographic, socio-economic background and study design along with number of sample size.

Adiponectin has insulin sensitizing effect by activating "peroxisome proliferator-activated receptors-M" in the liver. It is not clear by which mechanism/s adiponectin exerts its effects on tissues but it is suggested that after binding of adiponectin to its receptors, protein kinase cascade pathway is activated, leading to increased oxidation of fatty acids and inhibition of gluconeogenesis. In GDM, adiponectin level is markedly decreased which led to insulin resistance and hyperglycaemia.[33] In our study, after taking precautions to match for chronological age of expecting mothers, gestational age and other parameters like BMI, we found that women with decreased adiponectin concentration are at increased risk of developing GDM. Strength of our study is the randomized design of the study and that association of serum adiponectin level with the biochemical parameters of glycaemic status has not been studied before in the population of Khyber Pakhtunkhwa. The study has got its limitations which are its small sample size which might have led to non-significant results, and the inclusion of the participants of specific age group.

CONCLUSION

Adiponectin is negatively associated with FBG and HbA1c in women with gestational diabetes mellitus belonging to Peshawar, Khyber Pakhtunkhwa

AUTHORS' CONTRIBUTION

YA: Conception and study design, acquisition of data, drafting the manuscript, critical review, approval of final version to be published. **SN:** Acquisition of data, drafting the manuscript, approval of final version to be published. **MSK:** Analysis and interpretation of data, drafting the manuscript, approval of final version to be published. **SHH:** Study design, Acquisition, analysis and interpretation of data, critical review, and approval of final version to be published. **SF, MOM:** Analysis

and interpretation of data, drafting the manuscript, approval of final version to be published

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