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# Relationship of Metabolic Syndrome Indicators in Gestational Diabetes with Adiponectin Levels

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## ABSTRACT

**OBJECTIVE:** To assess the relationship between MetS in gestational diabetes with adiponectin.
**METHODOLOGY:** This analytical cross-sectional study was carried out from February 2015 - January 2016 at Gynecology and Obstetrics OPDs in four public and one private tertiary care hospital in Peshawar, Khyber Pakhtunkhwa, Pakistan. Purposive sampling was done. Group one comprised 100 healthy pregnant women, while the second group included 100 pregnant women with known gestational diabetes. Women in the third trimester, with a single fetus, and who did not have pre-existing diabetes mellitus were Included. Women in the first or second trimester, with twin (or more fetuses) pregnancies, and pre-existing diabetes were excluded. BMI and systolic and diastolic blood pressure of participants were recorded. Blood was tested for serum lipids, HbA1c, and serum adiponectin levels.
**RESULTS:** Thirty percent of participants had a BMI ≥30 kg/m². Forty-three percent of participants had HbA1c ≥6.5%. HDL levels were below normal in 30% of participants, and triglyceride levels were higher than average in about 80% of participants. SBP was elevated in 23% of participants. Adiponectin level was low in >60% of cases. BMI was not statistically different between both groups. HDL levels and adiponectin levels were lower than normal in the diabetic group. Triglyceride levels were high in both groups. Regression analysis showed that adiponectin levels were affected by HbA1c and low HDL levels, and vice versa. Data were analyzed by SPSS version 20.
**CONCLUSION:** Low adiponectin levels could predict two MetS indicators in gestational diabetes and vice versa.


**KEYWORDS:** Adiponectin, metabolic syndrome, HDL, triglycerides, hypertension, systolic BP, diastolic BP

## INTRODUCTION

Metabolic syndrome (MetS) was defined by IDF (International Diabetes Federation) as a syndrome in 2005[1]. The syndrome had at least three of the following five: 1) obesity (BMI ≥30 kg/m²) or gender and ethnicity-specific cut-off values for waist circumference (WC). 2) History of systolic blood pressure (SBP) ≥130 mm Hg and diastolic blood pressure (DBP) ≥85 mm Hg or use of antihypertensive medication. 3) TG ≥150 mg/dL, 4) HDL level <50 mg/dL for women or patients with hypercholesterolemia using the cholesterol-lowering medication, and 5) fasting plasma glucose (>100 mg/dL) or known history of type 2 diabetes.

MetS are thought to be a predictor of chronic diseases like type 2 diabetes mellitus and hypertension. The syndrome is mainly comprised of obesity according to IDF 2005 definition, and adiposity is related to low levels of serum adiponectin[1,2]. Hence, the researchers expected that low adiponectin levels could predict MetS and vice versa.

This study was carried out to find a simple way to predict MetS in pregnancy with help of a single biochemical marker i.e. adiponectin level, hence preventing the patients to go through multiple clinical and biochemical examinations

## METHODOLOGY

The study was conducted from February 2015 - January 2016 in Gynecology and Obstetrics OPDs in four public and one private tertiary care hospital in Peshawar, Khyber Pakhtunkhwa, Pakistan. It was an analytical cross-sectional study. The study was done after permission was given by the IRB committee letter number 139/PG/KMC of Khyber Medical College, Peshawar, Pakistan. Purposive sampling was done. Healthy women in their third trimester of pregnancy were selected. Inclusion criteria were women with a single fetus who did not have pre-existing diabetes mellitus. Exclusion criteria were twin (or more fetuses) pregnancy and pre-existing diabetes (i.e. diabetic before gestation). One group comprised 100 controls, healthy pregnant women, while the other group comprised 100 pregnant women with known gestational diabetes. BMI (body mass index) of study participants was calculated and recorded. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also recorded for all the participants. Informed consent was taken from each participant. Blood samples were collected from each participant after 12 to 14 hours of fasting for measurements of biochemical markers. HbA1c, serum high-density lipoprotein (HDL), serum triglyceride (TAG) levels, and serum adiponectin levels were measured. Data were analyzed in SPSS version 20.

## RESULTS

Two hundred pregnant females were included in the study. Out of these, 100 women were non-diabetic, and the remaining 100 had gestational diabetes. About 1/4$^{th}$ of these participants were <19 years of age. The BMI of 30% of the participants was ≥30 kg/m² (obese category). Only about 43% of the participants had HbA1c ≥6.5%, probably due to good control of diabetes. HDL levels were lower than normal limits in 30% of the participants, and serum triglyceride (TAG) levels were higher than normal in 78% of participants. SBP was higher than normal in about 25% of the participants, but DBP was higher than normal in only 4% of patients. Adiponectin level was low in more than 60% of cases (**Table I**).

Our study group was divided into diabetic and non-diabetic groups. Mean values of all MetS indicators and adiponectin levels were compared between both groups. No statistically significant difference was found between the BMI of both groups. However, BMI was >30 in the non-diabetic group only but near 30 kg/m² in the diabetic group. SBP and DBP were normal and similar in both groups. HbA1c levels were higher than normal in the diabetic group, as expected. HDL levels and adiponectin levels were lower than normal in the diabetic group. No statistically significant difference in TAG levels was found to be higher than normal in both groups (**Table II**).

Binary regression analysis showed that HbA1c predicted the adiponectin levels negatively. HDL levels predicted adiponectin levels positively after adjusting with age, gestational age, BMI, systolic and diastolic blood pressures, and TAG levels (**Table III**). Adiponectin levels could predict diabetes in pregnancy in our study after adjusting with age and gestational age, and its levels could also indicate low HDL levels (**Table III**).

## DISCUSSION

Metabolic syndrome (MetS) was defined differently by many institutions, including WHO and IDF. According to IDF 2005, it was described as a syndrome that had at least three of the following five features:
1) obesity (BMI ≥30 kg/m²), or waist circumference > cut-off values according to gender and ethnicity, 2) SBP ≥130 mm Hg and DBP ≥85 mm Hg, or use of antihypertensive medicines, 3) TG ≥150 mg/dL, 4) HDL level <50 mg/dL for females, or patients using cholesterol-lowering medicines, and 5) fasting plasma glucose (>100 mg/dL), or known history of type 2 DM [1,3]. MetS are considered a predictor of chronic diseases like type 2 DM and hypertension, so it is essential to identify it in all populations.

**TABLE I: CHARACTERISTICS OF THE GROUP**

| Variable | Categories | Frequency | Percentage |
|---|---|---|---|
| Age | =<19 years | 49 | 24.5 |
| | >19 years | 151 | 75.5 |
| Status of diabetes: | Non-diabetic | 100 | 50.0 |
| | Diabetic | 100 | 50.0 |
| Gestational age | <28 weeks | 59 | 29.5 |
| | =>28 weeks | 141 | 70.5 |
| BMI[1] | >18.4<24.9 | 19.5 | 19.5 |
| | >24.9<30 | 101 | 50.5 |
| | ≥30 | 60 | 30.0 |
| HbA1c (%) | <6.5 | 115 | 57.5 |
| | ≥6.5 | 85 | 42.5 |
| HDL[2] (mg/dL) | <50 | 59 | 29.5 |
| | ≥50 | 141 | 70.5 |
| TAG[3] (mg/dL) | <150 | 45 | 22.5 |
| | ≥150 | 155 | 77.5 |
| Systolic BP[4] (mm Hg) | <130 | 154 | 77.0 |
| | ≥130 | 46 | 23.0 |
| Diastolic BP (mm Hg) | <85 | 192 | 96.0 |
| | ≥85 | 8 | 4.0 |
| Adiponectin level (µg/mL) | <5 | 123 | 61.5 |
| | ≥5 | 77 | 38.5 |

[1]BMI=Body mass index, [2]HDL=High-density lipoprotein, [3]TAG= Triglycerides, [4]BP=Blood pressure

Our study population comprised pregnant females. Fifty percent of these females had gestational diabetes. HbA1c was done to confirm diabetes [4,5]. The HbA1c levels of the diabetic group were higher than normal, as expected, and those of non-diabetics were within normal limits (**Table II**). Still, only about 43% of the participants had HbA1c ≥6.5%, which showed reasonable control of diabetes by these patients.

The BMI of 78% of the study participants was above 25kg/m² (**Table I**); this was not beyond expectation as gestational weight gain (GWG) significantly changes the BMI even if this gain is within the recommended range [6]. However, 30% of the study population had a BMI ≥30 (**Table I**), and this weight gain was excessive. It could be related to MetS because even if these patients had gained weight within the normal range, it reflected that the pre-pregnancy weight of these participants was high. In any case, it showed the presence of one indicator of MetS in at least 30% of the participants of this study group. The BMI of both diabetic and non-diabetic groups was not significantly different (**Table II**).

Both groups' systolic and diastolic blood pressures were within normal levels (**Table II**). However, serum TAG levels of both groups were higher than normal, and HDL levels were lower than normal in the diabetic group only. Hyperlipidemia is a normal physiological phenomenon during pregnancy. But mechanisms that regulate this hyperlipidemia might not function well and result in adverse pregnancy outcomes like gestational diabetes or pre-eclampsia.

**TABLE II: DIFFERENCES IN METS INDICATORS BETWEEN GROUPS**

| Variables | Group | N | Mean | SD | P-value |
|---|---|---|---|---|---|
| BMI[1] | Non-diabetic | 100 | 30.43 | 6.58 | -- |
| | Diabetic | 100 | 28.88 | 5.84 | |
| Systolic Blood Pressure (mmHg) | Non-diabetic | 100 | 117.60 | 7.67 | -- |
| | Diabetic | 100 | 119.10 | 8.53 | |
| Diastolic Blood Pressure (mmHg) | Non-diabetic | 100 | 75.00 | 5.55 | -- |
| | Diabetic | 100 | 74.55 | 6.70 | |
| HbA1c (%) | Non-diabetic | 100 | 5.38 | 0.85 | 0.000 |
| | Diabetic | 100 | 7.35 | 1.13 | |
| HDL[2] (mg/dL) | Non-diabetic | 100 | 63.58 | 10.27 | 0.000 |
| | Diabetic | 100 | 49.66 | 6.25 | |
| TAG[3] (mg/dL) | Non-diabetic | 100 | 215.61 | 93.56 | -- |
| | Diabetic | 100 | 224.94 | 97.31 | |
| Adiponectin (µg/mL) | Non-diabetic | 100 | 9.93 | 4.81 | 0.000 |
| | Diabetic | 100 | 2.17 | 1.84 | |

[1]BMI=Body mass index, [2]HDL=High-density lipoprotein, [3]TAG= Triglycerides

Abnormal lipid profiles can include raised TAG levels and decreased HDL levels [7]. TAG levels during the second trimester of pregnancy were significantly increased in GDM compared to healthy pregnant females in many studies [7]. Some studies showed low HDL level patterns in women with gestational diabetes, but other studies could not show changes in HDL levels even in patients with GDM [7]. However, our study showed significantly decreased HDL levels in the diabetic group (**Table II**).

Adiponectin levels decrease in conditions associated with insulin resistance, like obesity, T2DM, and gestational diabetes [8,9]. Adiponectin reduces oxidative stress, hence leading to the reduction of insulin resistance. Adiponectin increases the use of glucose and fatty acids by skeletal muscles and reduces hepatic gluconeogenesis and glycogenolysis. As expected, our study found that serum adiponectin levels were low in the diabetic group[10].

MetS are mainly comprised of obesity, according to IDF 2005, which is related to low levels of serum adiponectin [11,12]. It was expected that serum adiponectin levels would be low in obese (≥30 kg/m²), but this study could not show it.

Adiponectin promotes TAG storage in adipocytes and reduces the accumulation of triglycerides in the liver. Hence, it induces a decrease in circulating lipid levels, and its low levels could cause a rise in TAG levels [13]. However, adiponectin levels were found to be low only in the diabetic group, but TAG levels were high and not significantly different in both groups (**Table II**). In our study, TAG levels could not predict serum adiponectin levels (**Table III**).

**TABLE III: REGRESSION ANALYSIS**

| Variables | p-value | OR | 95% Confidence interval | |
|---|---|---|---|---|
| | | | Lower | Upper |
| ***Model 1: Adiponectin with MetS indicators*** | ***p= 0.000*** | | | |
| HbA1c | 0.002 | 0.002 | 0.00 | 1.02 |
| HDL[1] | 0.000 | 1.56 | 1.22 | 1.96 |
| Age | 0.590 | -- | -- | -- |
| Gestational age | 0.205 | -- | -- | -- |
| BMI[2] | 0.255 | -- | -- | -- |
| SBP[3] | 0.685 | -- | -- | -- |
| DBP[4] | 0.311 | -- | -- | -- |
| TAG[5] | 0.197 | -- | -- | -- |
| ***Model 2: HbA1c with Adiponectin levels*** | ***p= 0.000*** | | | |
| Age | 0.893 | -- | -- | -- |
| Gestational age | 0.665 | -- | -- | -- |
| Adiponectin levels | 0.000 | 0.006 | 0.00 | 0.04 |
| ***Model 3: HDL with Adiponectin levels*** | ***p= 0.000*** | | | |
| Age | 0.534 | -- | -- | -- |
| Gestational age | 0.097 | -- | -- | -- |
| Adiponectin levels | 0.000 | 3.19 | 1.86 | 5.47 |

[1]HDL=High-density lipoprotein, [2]BMI=Body mass index, [3]SBP= Systolic blood pressure, [4]DBP= Diastolic BP, [5]TAG= Triglycerides

Adiponectin increases HDL levels, and its low levels could be related to low HDL levels [14]. Our study showed low HDL levels in the diabetic group (**Table II**). HDL levels also significantly affected adiponectin levels and vice versa (**Table III**).

Adiponectin suppresses angiotensin II to decrease blood pressure, and adiponectin possibly regulates blood pressure[15]. In pregnant women, low serum adiponectin levels were found to be related to pre-eclampsia. It was found that adiponectin levels fall physiologically as pregnancy advances, and it was also found that low adiponectin level is present in obese preeclamptic women [16]. But in our study, despite low serum adiponectin levels in the diabetic group, both the systolic and diastolic blood pressures were normal in both groups (**Table II**).

According to this study, at least 30% of the study population was obese, about 30% of the study participants had HDL levels <50 mg/dL and about 80% of participants had TAG levels >150 mg/dL. 23% of the participants also had SBP ≥130 mm Hg. According to these findings, at least 23% of our study population fulfilled the criteria of MetS, i.e. obesity plus at least two components (according to IDF, 2005)[1]. More than 60% of our study population had low adiponectin levels (**Table I**). Adiponectin levels were significantly low in the diabetic group (**Table II**). According to the literature, low adiponectin levels could predict diabetes[8], obesity[17], high TAG and low HDL levels[14], and high blood pressure[15]. But in our study, adiponectin levels could predict blood glucose levels[18] and low HDL levels[7], but it could not predict BMI, TAG levels, or blood pressure.

Pregnancy could cause a decline in adiponectin levels due to gestational weight gain and normal hormonal changes leading to insulin resistance[19]. Low HDL and high TAG levels could also be a part of normal physiological changes in pregnancy[7]. But as the adiponectin levels were found to be low in the diabetic group alone, and HbA1c and HDL levels showed their effect on adiponectin levels, we could assume that pregnancy alone was not a predictor of adiponectin levels. MetS probably played a definite role in our study group's decline in adiponectin levels.

One limitation of the study was that pregnancy acted as a confounder for MetS. Also, as the study was confined to pregnant women, it could not be generalized to both genders.

## CONCLUSION

Low adiponectin levels could predict indicators of MetS like hyperglycemia and low HDL levels in gestational diabetes, and vice versa.

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**Data Sharing Statement:** The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## AUTHOR CONTRIBUTIONS

Akhtar Y: Concept and design, drafting, final approval
Khan MA: Design, critical revision, final approval
Malik MK: Analysis, critical revision, final approval
Kashif S: Interpretation, drafting, final approval
Rehman G: Interpretation, drafting, final approval

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