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Relationship of Adiponectin with Metabolic Syndrome Indicators in Pregnancy: A Cross-sectional Study

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ABSTRACT

Introduction: Obesity, hyperglycemia, dyslipidemia and hypertension are indicators of metabolic syndrome (MetS). Low serum adiponectin levels might be able to predict MetS.

Objective/Aim: This study was meant to assess relationship between MetS and adiponectin.

Materials and Methods: In this cross-sectional study,women in their 24-40 weeks of pregnancywere selected.Study consisted of two groups, one group comprised 100 control, healthy pregnant women, while second group comprised 100 pregnant women with known gestational diabetes. Body mass index (BMI), and systolic and diastolic blood pressuresof participants wererecorded. Blood was tested for HbA1c, HDL, triglycerides, and serum adiponectin levels.

Results: BMI of 30% of participants was ≥30 kg/m², and 43% of the participants had HbA1c ≥6.5%. HDL levels were lower than normal in 30% of participants, and serum triglyceridelevels were higher than normal in 78% of participants. SBP was higher than normal in 23% of the participants. Adiponectin level was low in >60% of cases. No statistically significant difference was found between the BMI of both groups. SBP and DBP were within normal limits in both groups. HbA1c levels were higher than normal, and HDL levels and adiponectin levels were lower than normal in the diabetic group. No statistically significant difference was found in TAG levels in both groups, and it was higher than normal in both groups. Regression analysis showed that adiponectin levels could predict diabetes and low HDL levels in our study.

Conclusion: Hypoadiponectinemia could predict MetS indicators like hyperglycemia and low HDL levels.

Key Words: Adiponectin, Metabolic syndrome, BMI, HDL, LDL, Triglycerides, Hypertension

INTRODUCTION

Metabolic syndrome (MetS) was defined by IDF (International Diabetes Federation) in 2005,as a syndrome that had at least three of the following five features: 1) obesity (BMI ≥30 kg/m²), or gender and ethnicity-specific cut-off values for waist circumference, 2) history ofsystolic blood pressure (SBP) ≥130 mm Hg and/or 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 cholesterol-lowering medication, and 5) fasting plasma glucose (>100 mg/dL), or known history of type 2 diabetes.[1]

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

Our study was meant to assess the relationship between adiponectin levels and MetS indicators.

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MATERIAL AND METHODS

The study was conducted over a period of one year, in outpatient departments of gynecology and obstetrics in four public and one private tertiary care hospital of Peshawar, Khyber Pakhtunkhwa, Pakistan. It was a cross-sectional study. Permission for the study was given by IRB committee of Khyber Medical College, Peshawar Pakistan. IRB committee number was 139/PG/KMC. Healthy women, in their 24-40 weeks of pregnancy, witha single fetus, were selected.Only those women were selected who did not have a history of pre-existing or pre-pregnancy diabetes mellitus. The study consisted of two groups, one group comprised 100 control, healthy pregnant women, while the other group comprised 100 pregnant women with known gestational diabetes. The height, weight, and BMI (body mass index) of study participants were recorded. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also recorded for all the participants. Informed consent was taken from each participant and the study was approved by the Ethical Committee of Khyber Medical College, Peshawar. Blood samples were collected from each participant, after 12-14 hours fasting, for measurements of biochemical markers, including HbA1c, serum high-density lipoprotein (HDL), serum triglyceride (TAG) levels, and serum adiponectin levels. Data were analyzed using SPSS version 20.

RESULTS

A total of 200 pregnant females were included in the study. Out of these 100 women were non-diabetic, and the remaining 100 were suffering from gestational diabetes. About 25% of these participants were <19 years of age. About 30% percent of the participants were in their second trimester of pregnancy, and about 70% were in their third trimester of pregnancy (Table 1).

BMI of 30% of the participants was ≥30 kg/m². Only about 43% of the participants had HbA1c ≥6.5%, which was probably due to good control of gestational diabetes by the remaining diabetic patients over last few months. 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 23% 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 1).

Our study group was divided into diabetic and non-diabetic groups. Mean values of all MetS indicators, as well as adiponectin levels, were compared between both groups. Although no statistically significant difference was found between the BMI of both groups, it was >30 in the non-diabetic group only, but close to 30 kg/m² in diabetic group. SBP and DBP were not different in both groups and were within normal limits as well. HbA1c levels were higher than normal, and HDL levels and adiponectin levels were lower than normal in the diabetic group. No statistically significant difference was found in TAG levels in both groups, and it was higher than normal in both groups (Table 2).

Binary regression analysis showed that HbA1c negatively predicted the adiponectin levels, and HDL levels positively predicted adiponectin levels, after adjusting with age, gestational age, BMI, SBP, DBP, and TAG levels (Table 3). Adiponectin levels could predict diabetes in pregnancy in our study, after adjusting with age and gestational age (Table 3). Its levels could also predict low HDL levels (Table 3).

DISCUSSION

Metabolic syndrome (MetS) was defined in different ways by many institutions including WHO and IDF. Although there were many other definitions, they were very similar. According to IDF 2005, it was defined 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/or 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] As MetS is considered to be a predictor of chronic diseases like type 2 DM and hypertension, its identification in all populations is important.

Our study population comprised pregnant females. Fifty percent of these females were known diabetics (gestational diabetes only) by history. HbA1c was done to confirm diabetes.[4] Hence, mean HbA1c levels of the diabetic group were higher than normal, and those of non-diabetics were within normal limits (Table 2), but only about 43% of the participants had HbA1c ≥6.5%, which showed good control of diabetes by the remaining diabetic patients.

BMI of about 80% of the study participants was above 25kg/m² (Table 1), which is not beyond expectation as gestational weight gain (GWG) significantly changes the BMI even if this gain is within the recommended range.[5,6] But 30% of the study population had a BMI ≥30 (Table 1), showing that this weight gain was excessive, and could be related to MetS, because even if the gestational weight gain was within normal range, it showed that pre-pregnancy weight of these participants was still high. Whether this BMI was high before pregnancy or increased during pregnancy, it showed presence of one indicator of MetS in at least 30% participants of this study group. However, the BMI of both diabetic and non-diabetic groups was not significantly different, and the

mean BMI of the non-diabetic group was higher than 30 kg/m² (Table 2).

Both systolic and diastolic blood pressures of both groups were within normal levels (Table 2), but serum TAG levels of both groups were higher than normal cut-off values. HDL levels were lower than normal in the diabetic group only. Although hyperlipidemia is a normal physiological phenomenon during pregnancy, mechanisms which regulate this hyperlipidemia might malfunction and result in adverse pregnancy outcomes like gestational diabetes or pre-eclampsia. Abnormal lipid profile might includeraised TAG levels, and decreased HDL levels.[7] TAG levels during 24 to 28 weeks of pregnancy were found to be significantly increased in GDM as compared to healthy pregnant women in many studies.[7] Some studies showed low HDL levels pattern in women with gestational diabetes, but other studies showed no change in HDL levels even in patients with GDM[7], but our study showed significantly decreased levels of HDL in diabetic group (Table 2).

Adiponectin levels decrease in conditions associated with insulin resistance, like T2DM, gestational diabetes and obesity.[8,9,10] Adiponectin has been found to reduce oxidative stress, 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 well. In our study, serum adiponectin levels were found to be low in the diabetic group, as expected.[11]

MetS is mainly comprised of obesity according to IDF 2005, whichin turn is related to low levels of serum adiponectin.[2,12,13] It was expected that serum adiponectin levels were low in obese (≥30 kg/m²), but it could not be proved in this study.

Adiponectin can promote the storage of TAG in adipocytes, and it reduces the accumulation of triglycerides in the liver. Hence, it induces a decrease in circulating lipid levels, and its low levels are expected to cause a rise in TAG levels.[8,14] 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 2). TAG levels were unable to predict serum adiponectin levels (Table 3).

Adiponectin can increase HDL levels, and its low levels can be related to low HDL levels.[9,15] Our study showed low levels of HDL in the diabetic group (Table 2), and HDL levels also showed a significant effect on adiponectin levels (Table 3).

Adiponectin was found tosuppress angiotensin II to decrease blood pressure, and adiponectin possibly regulates blood pressure.[16] 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 hypoadiponectinemia is evident in obese preeclamptic women.[16] But in our study, although serum adiponectin level was quite low in the diabetic group, both the systolic and diastolic blood pressures were normal in both groups (Table 2). Both SBP and DBP could not predict low serum adiponectin levels (Table 3).

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 78% participants had TAG levels >150 mg/dL. Study also showed that 23% of the participants had SBP ≥130 mm Hg. According to these findings, we could see that 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 1), and adiponectin levels were significantly low in diabetic group (Table 2). Although, according to literature, low adiponectin levels could predict diabetes[9], obesity[17], high TAG and low HDL levels[15], and high blood pressure[18], adiponectin levels could predict blood glucose levels[19], as well as low HDL levels[7], but it could not predict BMI, TAG levels, or blood pressure in our study.

Apart from the effects of obesity and diabetes on adiponectin levels, pregnancy itself can lead to a decline in adiponectin levels due to gestational weight gain and normal hormonal changes leading to insulin resistance.[2] Similarly, low HDL levels and high TAG levels could be a part of normal physiological changes of pregnancy.[7] But as the adiponectin levels were low only in diabetic group, and HbA1c and HDL levels showed their effect on adiponectin levels, we could assume that merely pregnancy was not a predictor of adiponectin levels, and MetS had definitely played a role in decline of adiponectin levels in our study group.

One limitation of the study was that pregnancyacted as a confounder for MetS indicators, because pregnancy is also a cause of weight gain, insulin resistance, dyslipidemia, and hypoadiponectinemia. As the study was confined to pregnant women, it could not be generalized to both genders.

CONCLUSION

Low adiponectin levels could be used as an indicator of MetS as it could predict various indicators of MetSi.e., hyperglycemia and low HDL levels in gestational diabetes. Hence, we could possibly use low adiponectin levels as sole predictor MetS rather than using all already in use indicators of MetS, but to do this, larger studies need to be done to verify this relationship.

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Authors' Contribution

All authors contributed equally towards the data collection, data analysis & compilations

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Table 1: Characteristics of the study group:

Variable	Categories	Frequency	Percentage
Age	=<19 years	49	24.5
	>19 years	151	75.5
Diabetes status	Non-diabetic	100	50.0
	Diabetic	100	50.0
Gestational age	<28 weeks	59	29.5
	=>28 weeks	141	70.5

Table 1: *(Continued)*

Variable	Categories	Frequency	Percentage
BMI[a] (kg/m²)	>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[b] (mg/dL)	<50	59	29.5
	≥50	141	70.5
TAG[c] (mg/dL)	<150	45	22.5
	≥150	155	77.5
Systolic BP[d] (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

[a]BMI=Body mass index, [b]HDL=High-density lipoprotein, [c]TAG= Triglycerides, [d]BP=Blood pressure

Table 2: Differences between MetS indicators between diabetes-based groups:

Variables:	Group:	N:	Mean:	SD:	p-value:
BMI[a] (kg/m²)	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[b] (mg/dL)	Non-diabetic	100	63.58	10.27	0.000
	Diabetic	100	49.66	6.25	
TAG[c] (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	

[a]BMI=Body mass index, [b]HDL=High-density lipoprotein, [c]TAG= Triglycerides

Table 3: Binary logistic regression analysis:

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

[a]BMI=Body mass index, [b]SBP= Systolic blood pressure, [c]DBP= Diastolic BP, [d]HDL=High-density lipoprotein, [e]TAG= Triglycerides