ORIGINAL ARTICLE

CIRCULATING VISFATIN LEVEL AND ITS ASSOCIATION WITH LIPID BIOMARKERS IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Background: Hypertensive disorder in pregnancy is a major disorder that affects the fetal and maternal prognosis. A newer adipokine, visfatin has been related in the pathogenesis of pregnancy induced hypertension. The aim of this study was to evaluate and compare the serum visfatin and lipid profile in women with pregnancy induced hypertension and normotensive pregnant women.

Materials & Methods: This cross sectional study was done at Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, from January to September, 2015. The patients included were 160 pregnant women with gestational age more than 20 weeks comprising of cases of pregnancy induced hypertension and controls consisting of 74 normal pregnant woman. ELISA method was used to determine serum visfatin level whereas lipid profile was determined by enzymatic colorimetric methods. Data was analyzed using SPSS version19.0.

Results: Statistically significant ($p<0.001$) serum visfatin levels was found in patients group when compared with controls. When compared with normotensive pregnant women in patients group, the association between serum visfatin level and triglyceride (TG) were significantly higher ($p<0.001$). A similar trend in results was found between circulating visfatin level and HDL-C and LDL-C in patients upon comparison with controls ($p<0.001$). The mean difference of the ratio of TC:HDL-C ratio and LDL-C:HDL-C ratio between the patients, and control was statistically significant.

Conclusion: Elevated circulating visfatin level is associated with pregnancy induced hypertension and dyslipidemia in pregnancy.

KEY WORDS: Visfatin; Hypertension; Pregnancy; Dyslipidemia; Cholesterol.

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INTRODUCTION

A recently recognized adipo-cytokine, visfatin is also identified as PBEF (Pre-B cell colony-enhancing factor). For early-stage B cells PBEF is a growth factor. Visfatin is produced largely by the visceral adipose tissue and is present in peripheral lymphocytes as well as in the muscles, liver, lungs, bone marrow, placenta, heart and kidneys.[1] In-vivo and in-vitro studies have revealed that visfatin is related with insulin resistance, inflammation, type 2 diabetes mellitus and endothelial dysfunction.[2] However, there are a limited number of studies on visfatin levels in pregnancy induced hypertension and lipid profile.

Preeclampsia is a disorder of pregnancy, characterized by new onset hypertension (BP ≥140/90 mm Hg, at least 6 hours apart on two occasions) and proteinuria, urine collection or a dipstick of ≥2+). These symptoms usually develop in previously normotensive women after 20 weeks of gestation.[3,4] Some other symptoms e.g. disturbance of hemostasis, edema, liver or renal failure and the hemolysis, high liver enzymes and low platelet counts (HELLP syndrome) depending on the system involved also complicate the clinical presentation.[5] Its cause is still unclear, but it is believed to be likely multi factorial. Part of this maternal predisposition could be ex-

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plained by abnormal lipid metabolism. During pregnancy-induced hypertension (PIH) the serum lipids increase significantly.[6] The prevalence of eclampsia in developing countries varies widely from 1 in 100 to 1 in 1700.[7] In Pakistan the eclampsia prevalence reported in different parts range from 1.6% to 3.1% while the maternal death from this condition is 9 to 16.9.[8] The etiology of preeclampsia remains unclear despite extensive research. A variety of adipokines secreted by adipose tissue have been incriminated like leptin, adiponectin, resistin and the latest discovered visfatin.[9] Visfatin, a 52 KDa protein originally identified as pre-B cell colony enhancing factor (PBEF) also showed nicotinamide phosphoribosyl transferase activity (NAMPT).[1,10] The expression of NAMPT is found in human heart, brain, placenta, lungs, liver, skeletal muscles, and kidneys. Visfatin expression has also been noted in lipid loaded macrophages in the atherosclerotic lesions particularly in plaques of symptomatic patients.[9,11]

The development of pregnancy induced hypertension may be correlated to visfatin. The association of visfatin to the essential hypertension is well documented. Different studies have reported maternal visfatin concentration along gestation. Others reports suggest that the variation of lipid profile are important in hypertension. Lipoprotein metabolism disorders are an essential cause of endothelial dysfunction that fallout in proteinuria, and hypertension and clinical hallmarks of pregnancy-induced hypertension.[12] Increased triglyceride levels in PIH is probable to be storage in the vessels, such as uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL-C.[13]

The aim of this study was to evaluate and compare the serum visfatin and lipid levels among women with pregnancy induced hypertension and in normotensive pregnant women.

MATERIAL AND METHODS

This cross sectional study was done at Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, from January to September, 2015. The subjects/patients of the present study between the ages of 18-45 years were 234 of pregnant women with gestational age of >20 weeks. They were registered from three major tertiary care hospitals of Peshawar i.e. Khyber Teaching Hospital, Hayatabad Medical Complex and Lady Reading Hospital, Peshawar, Pakistan. One hundred and sixty (n=160) women with pregnancy induced hypertension were selected randomly. Healthy pregnant females, seventy-four (n=74) matched for socioeconomic status, body mass index (BMI) and age, were selected as controls. A structured proforma was prepared with all requisite information. For this study gestational age >20 weeks with persistent high blood pressures (140/90 mmHg or more), gross proteinuria and with or without oedema was inclusion criteria. The subjects with renal diseases, diabetes mellitus, past and present history of hypertension, any drug effecting adipokines, and liver diseases were excluded from the study. BMI was calculated by the formula "BMI= Weight (Kg)/Height (meter^2)".[14] Before collecting data, from all the study group written informed consent was obtained and ethical approval was taken from Ethical Board of Khyber Medical University (KMU).

Under aseptic technique about 5mL of blood was taken and for further process was collected in gel tubes. The samples were isolated with proper labeling and stored at -80° C. Lipid parameters were determined by enzymatic colorimetric methods.[15] According to the instructions of the manufacturer's, serum visfatin levels (ng/mL) were determined by enzyme linked immune sorbent assay procuring kit from Biovision Research Products- CA94043, USA.[16] at IBMS, KMU, Peshawar KPK, Pakistan. SPSS version 19 was used to analyze the data. For calculation of mean differences in study subjects the Student's t-test was applied.

RESULTS

The general and clinical characteristics of the participants groups are summarized in Table 1. Con-

Table 1: Comparison of general and clinical parameters of study population.

Parameters	Pregnancy induced hypertension Patient, (n=160)	Controls (n=74)	p-value
Age (Years)	30.84+8.48	30.99+7.54	0.897
Age at Marriage (Years)	15.42+2.42	15.50+2.21	0.822
BMI (Kg/m2)	29.41+5.61	30.72+6.26	0.110
Systolic BP (mm Hg)	159.38+22.16	106.89+11.33	0.000
Diastolic BP (mm Hg)	106.75+12.91	68.51+9.60	0.000
Monthly Income (PKR)	7578.75+6121.16	11831.08+5235.72	0.000
S. Visfatin (ng/mL)	4.30+2.71	2.23+1.57	0.000

Values are expressed as Means±SD

Table 2: Relationship of serum visfatin level and lipid profile in pregnancy induced hypertension and normotensive pregnant women.

Lipid Parameters	Patients with pregnancy induced hypertension (n=160)	Controls (n=74)	t. test	p-value
Total Cholesterol (mg/dL)	194.25+55.40	180.09+36.76	2.002	0.046
Triglyceride (mg/dL)	195.64+93.45	187.31+84.82	0.652	0.515
HDL-C (mg/dL)	45.31+11.11	54.35+6.87	-6.448	0.000
LDL-C (mg/dL)	109.81+52.04	88.28+39.74	3.158	0.002
TC: HDL-C ratio	4.70+2.42	3.41+1.10	4.364	0.000
LDL: HDL-C ratio	2.74+1.96	1.70+0.99	4.306	0.000
TG: HDL-C ratio	4.80+3.74	3.55+1.90	2.713	0.007
HDL: VLDL C ratio	1.39+0.72	1.78+0.87	-3.527	0.001

Values are expressed as mean $\pm$SD.

Table 3: Relationship of serum visfatin level and various Lipid Parameters (normal/abnormal) in Overall PIH Patients and Its comparison with Normal Healthy Pregnant Women.

Biochemical Parameters		PIH Patients (n=160)	Control (n=74)	p-value
T. Cholesterol (mg/dL)	Abnormal (> 200)	4.02+2.62 (69)	1.94+1.03 (18	0.000
	Normal (< 200)	4.51+2.77 (91)	2.33+1.70 (56)	0.000
TG (mg/dL)	Abnormal (>150)	4.05+2.57 (111)	2.25+1.34 (46)	0.000
	Normal (< 150)	4.84+2.96 (49)	2.20+1.90 (28)	0.000
HDL-C (mg/dL)	Abnormal (< 40)	5.27+3.24 (30)	2.18 (01)	0.357
	Normal (> 40)	4.07+2.53 (130)	2.23+1.58 (73)	0.000
LDL-C (mg/dL)	Abnormal (>150)	4.12+2.89 (32)	1.73+1.18 (08)	0.030
	Normal (< 150)	4.35+2.68 (127)	2.29+1.60 (66)	0.000
VLDL-C (mg/dL)	Abnormal (>40)	3.80+2.30 (52)	1.97+1.13 (26)	0.000
	Normal (< 40)	4.49+2.87 (108)	2.37+1.75 (48)	0.000

Values are expressed as Means+ SD (No in parentheses show the number of participants)

trol subjects and PIH patients do not differ significantly in age, age at marriage, and BMI (p>0.05). Systolic BP, diastolic BP, monthly income and serum visfatin were significantly higher (p<0.001) in PIH patients when compared with the controls respectively.

The association and relationship of serum visfatin levels in various lipid profiles in subjects diagnosed with pregnancy induced hypertension (PIH) and normotensive pregnant women (controls) is depicted in Table-2. It was observed that HDL-C, LDL-C, were significantly higher (p<0.001) in pregnancy induced hypertension patients when compared with control subjects. Similar trends in results were noted for TC: HDL-C ratio, LDL: HDL-C ratio, TG: HDL-C ratio and HDL: VLDL-C ratio respectively. However the changes in triglycerides (TG) were found to be non-significant.

The association and relationship of serum visfatin levels in various lipid profiles in subjects diagnosed with overall PIH patients and normotensive pregnant women (controls) is depicted in Table-3. It was observed that serum total cholesterol, triglycerides (TG), HDL-C, and VLDL-C showed significantly higher changes (p<0.001) in the overall patients when compared with control subjects. Changes in LDL-C were found to be only significant.

DISCUSSION

Our study shows higher serum level of visfatin in pregnancy induced hypertension when compared with normal pregnant women. It has also been depicted by some other study.[1] One more study have revealed the increase in serum lipids during PIH and particularly during pregnancy in general.[17] Some prior studies revealed that most impressive alteration in the lipid profile in healthy pregnancy is serum hyper-triglyceridemia, with an increase of two to three folds in the last trimester above the normal levels in normotensive women.[18] In our study insignificant alteration in triglyceride level was noted in third trimester of pregnancy in PIH subjects when

compared with normotensive pregnant women. In return to increasing and metabolic requirements of fetus and placenta during pregnancy, reorganization of maternal adipose tissue and changes in maternal metabolism occur. During foetal growth, visfatin is altered in endocrine and exocrine tissue. Intracellular NAMPT is highly released by amnion, fetal membranes, myometrium, adipose tissue and placenta. The deciduae and amnion at term contained high levels of PBEF mRNA.[19]

In current study statistically significant ($p<0.05$) increase in TC level was observed in PIH. A study found insignificant increase in serum TG in preeclampsia.[20] Other have similar findings that significant increase was found in serum TC in PIH patients.[13] However some have reported that serum visfatin was negatively correlated with triglycerides.[21] This difference between the two studies can be attributed to the difference in the study design, number of study population, racial as well as socio demographic and geographical distribution of study participants. PIH patients have high lipid profile, with significantly increased HDL and LDL levels and decreased HDL level in preeclampsia only. A study found that visfatin is negatively correlated with LDL-C and positively correlated with HDL-C.[22] However, Chen et al, found no relationship between visfatin and HDL-C.[23] Further study established a positive correlation between visfatin levels and the LDL-C and HDL-C.[24] However Wang and colleagues (2007) reported that visfatin is negatively correlated with triglycerides and positively correlated with HDL-C.[21] In the current study, we observed the significant change in visfatin level, total cholesterol, HDL-C, LDL-C and VLDL-C but did not observe any significant change in TG in PIH patients when compared with controls. We have also calculated the ratios between different lipids like TC:HDL-C, LDL-C:HDL-C, TG:HDL-C and HDL-C:VLDL-C and significant differences were observed in PIH patients as compared to normal pregnant women.

The importance of change ratio of (LDL-C:HDL-C, TC:HDL-C TG:HDL-C and HDL-C:VLDL-C) in pregnancy and PIH is established and its risk in PIH cannot be ignored. The endothelial cells of placenta activated due to dyslipidemia resulting in endothelial disturbing factors including trophoblastic components and lipid peroxides or placental factor combined with lipoproteins having possible contribution in pathogenesis of PIH.[21,23,24] The blood lipid assessment may be important in preventing complication like PIH. However, in the study conducted elsewhere found that LDL-C:HDL-C, TC:HDL-C TG:HDL-C and HDL-C:VLDL-C raised significantly in PIH subjects.[25] The results of present study are in agreement with the above cited study. Though the relevance of these provisions in pregnancy and PIH is yet to be confirmed, the significance of changed TC:HDL-C, TG:HDL-C and HDL-C:VLDL-C ratios cannot be ignored as they point to the additional risks in PIH subjects.

CONCLUSION

Elevated circulating visfatin level is associated with pregnancy induced hypertension and dyslipidemia in pregnancy.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.

AUTHORS' CONTRIBUTION

Conception and Design:	AS, SK,
Data collection, analysis & interpretation:	AS, SK, ZA, MJ, RN,
Manuscript writing:	AS, SK, ZA, RN