ORIGINAL ARTICLE

MATERNAL SERUM VISFATIN LEVEL IN PRE-ECLAMPSIA AND LATE PREGNANCY AND ITS EFFECTS ON BIOCHEMICAL PARAMETERS

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ABSTRACT

Objective: To determines and evaluate the quantitative variations in the circulating visfatin in conditions like pre-eclampsia and to compare with the normal pregnant subjects.

Material and Methods: This study conducted in three tertiary care hospitals (Hayatabad Medical Complex, Lady Reading Hospital, Khyber Teaching Hospital, Peshawar) from May 2014 to February 2015. It included a total of 160 pregnant women. 86 comprising of PE and while 74 were normal healthy pregnant women with gestational age of more than 20 weeks. Serum visfatin level was determined by enzyme linked immunoassay whereas lipid profile was determined by enzymatic colorimetric methods. Data was analyzed using SPSS version 19.

Results: Among the pre-eclampsia patients seventy five (46.90%) were suffering from severe pre-eclampsia and 6.90% were with mild pre-eclampsia. Serum visfatin was noted to be 4.81±3.11 and 5.48±2.74 ng/mL and were highly significant ($p<0.000$) when compared with controls. Similar trends in results were observed for urinary albumin, serum creatinine and blood urea respectively.

Conclusions: Significant difference in the serum visfatin levels of the pre-eclampsia compared to healthy pregnant women was observed.

Key Words: Pre-eclampsia, Circulating Visfatin, low birth weight, babies.

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INTRODUCTION

Adipose tissue in the last several decades, in the human body has been found as the most active and largest endocrine organ that via the production and secretion of adipokines can express its pleiotropic effects[1]. Moreover in the pathophysiology of obesity[2], insulin resistance[1], dysregulation of adipokines has been implicated. Consistent withthese findings, adipokines have been implicated in metabolic adaptations to normal gestation[1-3], other complications are pregnancy[4], SGA[5] and pre-eclampsia[6]. Life-threatening condition that occurs during pregnancy is pre-eclampsia (PE), which is characterized by maternal proteinuria, hypertension and damage of multiple organ[7-8]. It occurs worldwide in 2 to 8%of pregnant women[9]. Worldwide the rate of pre-eclampsiahas increased especially in developed countries due to an increase in number of multiple births and older mothers and, conditions known to increase its risk by 40% between 1990 and 1999[10]. It contributes significantly to maternal and fetal mortalityand morbidity where in Pakistan 1 in 89 women dies of maternal causes with PEand eclampsia as one of the major causes[11]. Redistribution of adipose tissue occurs during the period of pregnancy. The adipose tissues are not just storage depots but are metabolically active tissues. They produce adipocytokines exerting endo-paracrine effects[12]. Adipocytokines including leptin and adiponectin take part in homeostasis of energy and in resistance due to insulin; therefore, changes contribute to

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metabolic conditions[13]. Despite extensive research the cause of pre-eclampsia remains unknown. One of the newly discovered adipocytokines is serum visfatin also known as pre-B cell colony-enhancing factor (PBEF) on the long arm of chromosome 7 (7q22.2) the gene for visfatin is located. Visfatin is 52 kDa adipokine, has been occupied in ruling of Type-2 diabetes mellitus[14]. In fact, high circulating concentrations of visfatin are associated withhyperglycemia[15] and gestational diabetes mellitus (GDM)[5].

Based on the existing data on the effects of changes in the serum levels of adiponectin, leptin and resistin along with the literature-based notions indicating that alteration in the circulating visfatin levels have been coincidental with insulin resistance associated diseases such as type-2 DM, gestational diabetes and obesity[13]. Considering the physiological activity and characteristics of circulating visfatin[16], we arrived at the hypothesis that the circulating visfatin level is altered in females with PE. In order to test and verify this hypothesis, we conducted this study in order to evaluate the quantitative variations in the serum level of visfatin in conditions like mild PE to severe PE and to compare these values with those of the normal pregnant women.

MATERIAL AND METHODS

The participants of the instant cross sectional study were 160 pregnant women with the age ranges from 18 to 45 years and with gestational age of > 20 weeks. They were randomly selected from, three major tertiary care hospitals i.e., Hayatabad Medical Complex (HMC), Khyber Teaching Hospital (KTH) and Lady Reading Hospital (LRH), Peshawar, KPK, Pakistan from May 2014 to February 2015. Eighty-six women were diagnosed with pre-eclampsia. Seventy-four normal healthy pregnant women matched for body mass index (BMI), age, and socioeconomic status who served as controls. Before conducting the study approval was taken from the Ethical Review Board of Khyber Medical University, Peshawar. A structured proforma was developed with all requisite information. Inclusion criteria for the participants of the instant study was gestational age >20 weeks with persistent high blood pressures (140/90 mm Hg or greater), gross proteinuria and with or without edema. The participants with the present and past history of liver diseases, renal diseases, hypertension, diabetes mellitus and any drug effecting adipokines were excluded from the study. BMI was calculated by the formula [MI= Weight (Kg)/Heights (meter^2)][17]. Approximately 4 mL of blood was taken under aseptic techniques and collected in a gel tube for further analysis. The samples were isolated with proper labeling and stored at -80^{o}C. Lipid profile was determined by enzymatic colorimetric methods[18]. According to the instructions of the manufacturer's, serum visfatin levels (ng/mL) were determined by ELIZA kit procured from Biovision Research Products-CA94043, USA19 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

Distribution and frequency of study population is depicted in Table 1. A total of 160 subjects were recruited in the instant study out of which eighty six were known pre-eclampsia patients and seventy four were normotensive pregnant women who served as control group. Out of 86 pre-eclampsia patients seventy five (46.90%) were suffering from severe pre-eclampsia and eleven (6.90%) were presented with mild pre-eclampsia.

Table 2 represents general and biochemical parameters of the study subjects. There was no significant change in the age of pre-eclampsia patients when compared with control subjects. Systolic blood pressure in severe and mild pre-eclampsia women was 160.93±24.44 and 151.82±20.889 mm Hg and in normotensive pregnant women it was 106.89±11.33 mm Hg and were significantly higher ($p<0.000$) when compare with controls. Similar result was observed for diastolic blood pressure. Serum visfatin was noted to be 4.81±3.11 and 5.48±2.74 ng/mL and were highly significant ($p<0.000$) when compare with controls. Similar trends in results ($p<0.000$) were observed for urinary albumin, serum creatinine and blood urea respectively.

Table 3 summarizes the level of serum visfatin (ng/mL) vs. different parameters in the overall study participants and its comparison with normotensive pregnant women who served as controls. As it is evident from the table serum visfatin of pre-eclampsia patients in the age group 21-30 and 31-40 were significantly higher ($p<0.000$) when compared with controls. Similar results were obtained for the age at time of marriage and no of children (parity n < 5). The results were insignificant ($p>0.05$) for both the systolic and diastolic blood

Table 1: Distribution and frequency of Pre-eclampsia patients and Normotensive pregnant women (controls)

Groups		Frequency and percentages
Pre-eclampsia (Group-A)	Mild	75 (46.90)
	Severe	11 (6.90)
Controls (Group-B)		74 (46.20)
Total		160 (100.0)

Table 2: General and biochemical parameters of Pre-eclampsia patients and Normotensive pregnant women (controls)

Parameters	Pre-eclampsia (PE)		Controls	p-value
	Severe PE	Mild PE		
Age (Years)	32.63±8.16	29.82±6.969	30.99±7.54	0.318
Age at Marriage (Years)	15.63±2.43	17.00±1.612	15.50±2.21	0.130
Gestational Age (Weeks)	34.15±3.28	37.00±1.673	35.68±3.88	0.006
Parity (N)	2.99+2.52	2.36±2.014	1.82±1.07	0.002
Systolic BP (mmHg)	160.93±24.44	151.82±20.889	106.89±11.33	0.000
Diastolic BP (mmHg)	108.00±15.68	106.36±9.244	68.51±9.60	0.000
BMI (kg/m2)	28.47±5.33	29.65±4.57	30.72±6.26	0.060
S. Visfatin (ng/mL)	4.81±3.11	5.48±2.74	2.23±1.57	0.000
U. Albumin (mg/L)	2.57±.550	1.00±.000	0.09±0.443	0.000
S. Creatinine (μ mol/L)	0.99±0.97	0.851±0.37	0.51±0.17	0.000
Urea (mg/dL)	32.88±14.42	28.82±10.400	9.77±4.08	0.000

Table–3: Means+SD Serum Visfatin Vs Different Parameters in Overall Population

Parameters	Means±SD Serum Visfatin (ng/mL)						p-values
	Pre-eclampsia (PE)				Controls		
Age Group (Years)	Severe Pre-eclampsia		Mild Pre-eclampsia				
	N	Means±SD	N	Means±SD	N	Means±SD	
<20	6	4.78±3.34	2	5.26±4.40	4	3.51±2.13	0.763
21-30	25	4.16±3.00	3	6.32±3.42	35	2.00±1.28	0.000
31-40	30	5.50±3.31	6	5.13±2.42	27	2.35+1.87	0.000
41-50	14	4.53±2.75	—	—	8	2.18±1.22	0.034
Age at Marriage (Year)							
< 15	23	4.60±3.70	—	—	23	1.62±1.15	0.000
> 15	52	4.91±2.84	11	4.84±2.74	51	2.51±1.66	0.000
Parity (N)							
< 5	64	4.51±3.04	10	5.78±2.69	74	2.23±1.57	0.000
> 5	11	6.57±3.06	1	2.50±0.09	—	—	0.231
Systolic BP (mm Hg)							
< 120	4	3.55±3.69	2	4.03±3.49	72	2.26±1.57	0.147
> 120	71	4.89±3.08	9	5.80±2.68	2	1.06±0.70	0.140
Diastolic BP (mm Hg)							
< 80	1	2.17	--	--	70	2.25±1.57	0.959
> 80	74	4.85±3.11	11	5.48±2.74	4	1.95±1.66	0.134
Body Mass Index (Kg/m2)							
Normal	26	4.54±3.27	2	7.44±1.32	14	2.57±1.60	0.029
Overweight	19	4.89±3.13	3	4.27±4.20	22	2.17±1.34	0.003
Obese	30	5.01±3.03	6	5.43±2.28	38	2.14±1.70	0.000

Table 4: Frequency of Low Birth Weight Babies (LBWB) among the Pre-eclampsia Patents and Controls.

LBWB	Pre-eclampsia (PE)		Controls	P-value
	Severe Pre-eclampsia	Mild Pre-eclampsia		
No	41(54.70%)	02(18.20%)	66(89.20%)	<0.0001
Yes	34(45.30%)	09(81.80%)	08(10.80%)	
Total	75 (100.00%)	11 (100%)	74 (100%)	

Table 5: Serum Visfatinlevel in Low Birth Weight Babies (LBWB) due to the Pre-eclampsia Patents and its comparison with Controls.

LBWB	Means±SD Serum Visfatin (ng/mL)						p-value
	Pre-eclampsia (PE)				Controls		
	Severe Pre-eclampsia		Mild Pre-eclampsia				
No	41	4.67±2.92	2	8.54±0.24	66	2.33±1.60	0.000
Yes	34	4.99±3.35	9	4.80±2.55	8	1.39±0.87	0.012

pressure of severe and mild pre-eclampsia patients when compared with controls. The serum visfatin in severe and mild pre-eclampsia patients in overweight and obese categories were found to be 4.89±3.13, 4.27±4.20 ng/mL and 5.01±3.03 and 5.43±2.28 ng/mL respectively and were significantly higher ($p<0.003$ and 0.000) when compare with controls.

Table 4 depicts the frequency of low birth weight babies among the study population. It was found that thirty four (45.30%) low birth weight babies were born to women with severe pre-eclampsia, nine (81.80%) to mild pre-eclampsia patients and only eight (10.80%) to normotensive pregnant women and these findings were highly significant ($p<0.0001$) when compared with controls.

Table 5 represents the frequency serum visfatin in study population with low birth weight babies. It was observed that level visfatin in severe and mild pre-eclampsia with low birth weight babies were 4.99±3.35 and 4.80±2.55 ng/mL and the change was only significant ($p<0.01$) when compared with the control subjects.

DISCUSSION

Visfatin, was initially known as a growth factor for early B cell also recognized as PBEF; (Pre-B cell colony-enhancing factor)[20]. Consequently, which is created by the visceral fat depot it was known as a novel adipokine. PBEF (Visfatin) has been concerned in the ruling of glucose homeostasis. In fact, in vitro, adipocytes secrete visfatin in response to treatment with glucose[15] and insulin-resembling effects can apply this protein[21]. In vivo, visfatin lacking mice have weakened tolerance for glucose metabolism[22] and in the human visfatin gene accelerator polymorphism is related with a susceptibility to type–2 DM. Moreover, elevated circulating concentrations of this adipokine characterize patients with insulin resistance[23]. In addition to its pro-inflammatory properties, adipokine (visfatin) has metabolic effects. In vitro, visfatin synergizes with interleukin (IL)–7 and stem cell factors to promote the growth of B-cell precursors and treatment of human monocytes with visfatin results in an elevated secretion of IL-6, tumor necrosis factor-a and IL-1b in a dose-dependent manner[24]. An elevated level of circulating visfatin in a rheumatoid arthritis[25] patients with inflammatory bowel disease[24] and have been reported than the normal subjects.

We in the present study found an association between the visfatin levels and the systolic and diastolic blood pressures in pre-eclamptic patients. This outcome is consistent with earlier studies on normal individuals[26] and type–2 DM patients[14]. From the normal population in a study with 500 subjects investigating the association between visfatin levels and the anthropometric measurements and metabolic syndrome criteria, visfatin level was establish to be negatively interrelated with BMI[26]. In the present study, no association was found between visfatin level and BMI, in pre-eclampsia and thus is in agreement with the above cited studies. We also did not find any correlation between the visfatin levels and the gestational age (gestational age in weeks).

In human pregnancy the visfatin concentrations rests on the relationship between alteration between adipokines concentrations and adaptations to gestation[27], moreover with pregnancy complications such as pre-eclampsia[28], intra-amniotic infection/inflammation29, preterm labor, macrosomia[30], delivery of an SGA neonate[31], and pyelonephritis[32] gestational diabetes mellitus (GDM)[30]. In addition, visfatin is expressed in the placenta, foetal mem-

branes[33] and the myometrium[34]. Normal pregnancy is associated with elevated maternal circulating visfatin concentrations[35]. Moreover this adipokine, GDM is characterized by changes in maternal visfatin concentrations[35,1]. We found that intra-amniotic infection is related with visfatin higher amniotic fluid concentrations than in the nonappearance of disease[29], and that preterm labor is characterized by high maternal level of this adipokine[30].

A serious limitation of the present study was the relatively small sample size. Also, as a prospective source of bias, the cross sectional design could not reveal the causality between the parameters.

CONCLUSION

Significant difference in the serum visfatin levels of the pre-eclampsia compared to normotensive healthy pregnant women was observed.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Shaheen A: Contributed to concept design acquisition of data final approval
Ahmed Z: Data analysis
Khan I: Proof reading
Nazli R: Drafting of manuscript
Khattak S: Bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.