RESEARCH ARTICLE

Serum resistin and lipid profile in primigravida females with and without preeclampsia: An analytical cross-sectional study

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Abstract

Objective: To measure and compare the serum levels of resistin and lipid profile parameters in primigravida females with and without preeclampsia.

Method: The analytical cross-sectional study was conducted at the Department of Physiology and Cell Biology, University of Health Sciences, Lahore, Pakistan, from 2018 to 2020, and comprised primigravida females having gestational age 30-36 weeks. Those with preeclampsia constituted group 1, while normotensive females constituted group 2. All the participants were subjected to detailed history and general physical examination. Serum resistin levels were measured by enzyme-linked immunosorbent assay, and lipid profile parameters were measured using the colorimetric method. Data was analysed using SPSS 20.

Results: Of the 80 women, 40(50%) were in group 1 with mean age 23.07±2.10 years and mean gestation age 33.45±2.30 weeks. There were 40(50%) women in group 2 with mean age 23.02±2.11 years and mean gestational age 34.45±1.75 weeks. Mean serum resistin was significantly higher in group 1 compared to group 2 (p<0.02). Mean levels of lipid parameters were significantly different between the groups (p<0.05).

Conclusion: Preeclampsia was found to be associated with higher levels of resistin and lipid parameters compared to normal pregnancy.

Keywords: Pre-eclampsia, Resistin, Hypertension, Pregnancy outcome, Primigravida. (JPMA 73: 62; 2023)

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Introduction

Preeclampsia (PE) is a multisystem disorder. Many studies suggest that the fundamental abnormality in the placental endothelium leads to exaggerated inflammation and immunological reaction, causing PE.[1] Persistent hypertension (blood pressure [BP] >140/90mmHg) along with high urinary protein (>300mg/day) are classic features of the gestational syndrome after 20 weeks of gestation.[2] Classic PE manifests as raised systolic BP (SBP) and diastolic BP(DBP), proteinuria, headache, oedema, nausea, shortness of breath, vomiting and vision changes.[3] Every year in Asia, pregnancy-related complications lead to the mortality of 0.5 million women, and hypertensive disorders, including PE and eclampsia, account for 16% of maternal deaths.[4] Also, 5-7% of women in their first pregnancy develop PE worldwide.[2] The incidence of PE is even more in third world countries.[5] In Pakistan, for every 100,000 live births, almost 276 women die, and PE and eclampsia account for 10-15% of these deaths.[6]

Resistin is an adipose-derived peptide hormone with a molecular weight of approximately 12.5 kDa.[7] Resistin is secreted by adipose tissue and mononuclear cells.[8] Resistin has a significant role in energy metabolism.[9] During normal pregnancy, dramatic changes in metabolism happen to meet foetal growth demands and prepare the body for lactation and delivery.[10] Resistin is also expressed by the human placenta during pregnancy and has a crucial role in energy metabolism to meet the metabolic demands of pregnancy.[11] In normal pregnancy, insulin resistance is observed and it is maximum in the 3rd trimester.[12] Resistin has a role in developing insulin resistance by impairing glucose uptake of adipocytes.[8] Insulin resistance is involved in pathogenesis of PE.[13] Resistin has a significant role in the growth of a developing foetus, and can be the missing clue between intrauterine growth restriction (IUGR) and the development of chronic illnesses later in life.[14] High resistin levels in the first trimester of pregnancy lead to a higher risk of developing PE as a complication.[15] Hypertensive gestational disorders, such as PE, have short- and long-term health implication in mother, and obesity is a preeminent risk factor for such diseases. During pregnancy, overweight women with PE had higher serum levels of adipokines, including resistin, compared to overweight women without PE.[16] The resistin is a novel marker and needs to be explored extensively to find out its possible role and

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associations in pregnancy and PE.

Because pregnancy demands more metabolic fuels, lots of changes occur in maternal metabolism which leads to alteration in levels of hormones that are involved in energy metabolism. These changes also lead to changes in lipid profile during pregnancy.[17] The high utilisation of energy in pregnancy causes body homeostasis to shift the anabolic metabolism to catabolism and lipids are primarily used in this state. These changes cause maternal hyperlipidaemia, which is one of the proposed causes of the cardiovascular diseases in pregnancy.[18] The plasma triglyceride (TG) levels are independently and positively associated with adverse outcomes of pregnancy for both the mother (pregnancy-induced hypertension [PIH] and PE) and the foetus. The risk of both PIH and PE is increased with high lipid profile in the third trimester of pregnancy.[19]

To the best of our knowledge, no study has been done on resistin in the local population on PE patients. The current study was planned to fill the gap by measuring and comparing the serum levels of resistin and lipid profile parameters in primigravida females with and without PE.

Patients and Methods

The analytical cross-sectional study was conducted at the Department of Physiology and Cell Biology, University of Health Sciences, Lahore, Pakistan, from 2018 to 2020. Using convenience sampling technique, the sample was raised from among those who were admitted in wards or presented to the outpatient department (OPD) at tertiary care hospitals of Lahore coming from various regions of the Punjab province. After approval from the institutional ethics review board, the sample size was calculated with power of study 90% and level of significance 5%. Those included were primigravida females aged 21-27 years having gestational age 30-36 weeks. Those with PE constituted group 1, while normotensive females constituted group 2. PE was diagnosed using the American College of Obstetricians & Gynaecologists (ACOG) 2013 guidelines.[20] The subjects in group 2 had BP in the normal range, defined as SBP 115±12 mmHg and DBP 69±9 mmHg.[21] Pregnant women diagnosed with PIH, gestational diabetes mellitus (GDM), history of smoking, gestation <30 weeks or >36 weeks, twin or multiple pregnancy, history of chronic diseases, such as hypertension, kidney diseases, DM, arthritis, other cardiovascular illness or other acute or chronic inflammatory syndromes were excluded.

Data was collected after taking written, informed consent from all the subjects. Personal data, including age, address and phone number, as well as past and current medical history were recorded.

Taking aseptic and protective measures, 10 ml of blood was drawn. The 3.5 ml of the sample was stored in vacutainers coated with ethylenediaminetetraacetic acid (EDTA). The rest of the sample was stored in plain vacutainers for serum extraction. The samples were stored in an icebox and transferred to the laboratory for further analysis. For Complete blood count (CBC) the samples were analysed immediately using the automated analyser Sysmex XT-1800i, it uses the principal of florescent flow cytometry. For serum collection, the samples were centrifuged at 3,000 RPM for 10 min. The serum was saved in labelled and sealed Eppendorf tubes and stored at -80^{o}C.

Serum cholesterol was determined by the enzymatic colorimetric method using cholesterol oxidase-peroxidase aminophena zone reaction (CHOD-PAP) technique. TG was measured with glycerophospho oxidase- peroxidase aminophena zone reaction (GPO-PAP) technique. High-density lipoprotein (HDL) was determined using the CHOD-PAP technique. Low-density lipoprotein (LDL), very low-density lipoproteins (VLDL) and chylomicron were precipitated quantitatively. The human enzyme-linked immunosorbent assay (ELISA) kit (International Immuno-Diagnostics, USA) was used for serum resistin levels.

Data was analysed using SPSS 20. For normally distributed quantitative variables, mean±standard deviation (SD) was used, while median interquartile range (IQR) were used for non-normally distributed data. The normality of data was checked using Shapiro-Wilk's test. For comparative analysis student " test was applied for normally distributed variables and Mann-Whitney U test for non-normally distributed variables. Correlation between normally distributed variables was measured using Pearson correlation (r), and between non-normally distributed variables by using Spearman's rho correlation (rho). $P<0.05$ was considered statistically significant.

Results

Of the 80 women, 40(50%) were in group 1 with mean age 23.07±2.10 years (range: 20-26 years) and mean gestation age 33.45±2.30 weeks. There were 40(50%) women in group 2 with mean age 23.02±2.11 years (range: 20-26 years) and mean gestational age 34.45±1.75 weeks. Mean values for age and height were not significantly different between the groups ($p>0.05$), while there was significant difference in terms of gestational age, weight, body mass index (BMI) and resistin levels (Table 1).

TG, LDL, VLDL, and cholesterol levels were significantly raised in group 1 (Table 2).

Correlational analysis between resistin and lipid parameters did not show any significant correlation (Table 3).

Table-1: Descriptive data.

Parameters	Group-1(n=40) Mean±SD Median(IQR)	Group-2(n=40) Mean±SD Median(IQR)	*p*-value	Shapiro Wilk Test (*p*-value)	Distribution*
Age	23.07±2.10 23 (21.25-25.00)	23.02±2.11 23 (21-25)	0.942[a]	0.000	Non-Normal
Gestational age	33.45±2.30 34 (31-35.75)	34.45±1.75 35 (34-36)	0.046[a]	0.000	Non-Normal
Weight	73.87±10.83 72.00 (65.75-80)	68.67±7.92 68.00 (63.50-75)	0.017[b]	0.310	Normal
Height	1.51±0.08 1.52(1.49-1.56)	1.53±0.04 1.53 (1.50-1.56)	0.423[a]	0.000	Non-Normal
BMI	32.06±5.66 30.75 (29.02-34.67)	29.74±3.64 29.00 (27-32.85)	0.050[a]	0.000	Non-Normal
Resistin	10.01±2.54 9.24 (8.87-9.93)	4.26±1.21 4.22(3.17-5.31)	0.002[a]	0.000	Non-Normal

SD: Sandard deviation, IQR: Interquartile range, BMI: Body mass index.*Values generated According to Shapiro Wilk Test; [a]-*p*-value generated by Mann Whitney U Test; [b]-*p*-value generated by Independent sample t-test; *p*-value<0.05 is considered statistically significant.

pathogenesis of this disease. In the present study, mean resistin levels were significantly higher in PE patients compared to normal pregnant females, which was in line with earlier studies.[14,23-25]

Increased BMI has been associated with an increased risk of PE and high resistin levels.[15] The current findings showed a similar trend. The current study showed no significant correlation between resistin levels and BMI in both PE and normal primigravida females, indicating that maybe the adipose tissue is not the main source of increased resistin production in PE. These findings are also supported by Nein et al.[24] Lipid metabolism has a fundamental role in pregnancy, and alterations occur to meet the energy demands of both mother and foetus, leading to hyperlipidaemia.[17] Various studies have been done to find out the role of lipids and the impact of alteration in their levels on the development of

Table-2: Lipid profile.

	Cholesterol (mg/dl)		TG (mg/dl)		HDL (mg/dl)		LDL (mg/dl)		VLDL (mg/dl)		Total-Lipids (mg/dl)	
Group	1	2	1	2	1	2	1	2	1	2	1	2
n	40	40	40	40	40	40	40	40	40	40	40	40
Mean	222.07	195.72	242.40	198	39.22	40.50	134.37	115.70	48.20	39.52	886.55	789.45
SD	44.78	27.184	73.96	43.73	2.76	3.25	33.61	22.32	15.06	8.79	160.15	93.39
Median	212.50	193.50	228	191.50	39	41.00	130.50	111.00	45.50	38.50	843.50	771.50
Minimum	149	140.00	135	131.00	34	33.00	75	69.00	27	26.00	679	611
Maximum	332	265.00	421	326.00	45	46.00	212	166.00	84	65.00	1279	1056
p-value (Normality)*	0.02*	0.49*	0.07*	0.01*	0.27*	0.14*	0.18*	0.65*	0.07*	0.01*	0.01*	0.16*
p-value	<0.01[b]	<0.01[b]	0.06[a]	<0.01[a]	<0.01[a]	0.01[b]						

TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein.*Values generated According to Shapiro Wilk Test; [a]-p-value generated by Mann Whitney U Test; [b]-p-value generated by Independent sample t Test; p-value<0.05 is considered statistically significant.

Discussion

PE has a major impact on the health of both mother and foetus with long-term implications. Because of a lack of knowledge of the exact pathophysiology of the disease and no definitive diagnostic and prognostic test, it has an adverse perinatal outcome. The role of different adipokines, including resistin, has been explored in the past to find any association with PE, and results of various studies showed significantly increased resistin levels in patients with PE.[14,22]

The resistin serum levels in PE may be raised, decreased or not significantly changed in relation to healthy controls, but these remarkable discrepancies arise most likely from the heterogeneity of populations studied, different PE criteria, and the complex diversity of the syndrome itself. Therefore, the exact pathophysiology about how resistin leads to PE remains uncertain.[23]

The resistin being involved in energy metabolism and inflammation may be the potential missing link in the complications of pregnancy.[18] The increase in lipids and cholesterol is positively associated with the increased risk of the development of PIH and PE.[19]

In the present study, mean lipid values were significantly raised in PE women compared to normotensive group with the exception of HDL. This dyslipidaemia could have been a reason for PE development, underlining the need for studies on lipid profile during pregnancy and their relation with different anomalies of pregnancy.

A multi-biomarker approach, inclusive of resistin and various metabolic, clinical and inflammatory markers, should be the desirable approach for early diagnosis of late-onset PE.[22]

The current study has various salient features as the participants were matched for ethnicity, age, gravidity and gestational age which allowed for analysis of the direct role of these biomarkers in both groups. All the selected

Table-3: Correlation matrix of resistin with lipid profile parameters among preeclampsia (PE) patients.

		Resistin	Cholesterol	TG	HDL	LDL	VLDL	Total Lipids
Resistin	Rho	1.000	-0.078	-0.161	0.064	-0.052	-0.176	-0.131
	p-value	.	0.630	0.321	0.697	0.748	0.277	0.419
	n	40	40	40	40	40	40	40
Cholesterol	Rho	-0.078	1.000	0.868	-0.794	0.970	0.854	0.965
	p-value	0.630	.	0.000	0.000	0.000	0.000	0.000
	n	40	40	40	40	40	40	40
TG	Rho	-0.161	0.868	1.000	-0.732	0.747	0.992	0.958
	p-value	0.321	0.000	.	0.000	0.000	0.000	0.000
	n	40	40	40	40	40	40	40
HDL	Rho	0.064	-0.794	-0.732	1.000	-0.775	-0.727	-0.788
	p-value	0.697	0.000	0.000	.	0.000	0.000	0.000
	n	40	40	40	40	40	40	40
LDL	Rho	-0.052	0.970	0.747	-0.775	1.000	0.733	0.890
	p-value	0.748	0.000	0.000	0.000	.	0.000	0.000
	n	40	40	40	40	40	40	40
VLDL	Rho	-0.176	0.854	0.992	-0.727	0.733	1.000	0.948
	p-value	0.277	0.000	0.000	0.000	0.000	.	0.000
	n	40	40	40	40	40	40	40
Total Lipids	Rho	-0.131	0.965	0.958	-0.788	0.890	0.948	1.000
	p-value	0.419	0.000	0.000	0.000	0.000	0.000	.
	n	40	40	40	40	40	40	40

TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein; Value of Rho with negative sign shows negative correlation however other values show positive correlation between the two variables; p-value ≤0.05 is considered statistically significant.

participants gave serum samples before the onset of labour, to avoid possible confounding effects of labour on the concentrations of resistin and lipid profile parameters.

The current study has limitations including lack of data prior to PE onset. The longitudinal data containing samples of first trimester would have been beneficial in the evaluation of resistin's relationship to PE pathophysiology or the prediction of disease intensity. Besides, there is always the possibility of unmeasured confounders that could have different values between the groups. Finally, the sample size was smaller than the calculated requirement.

Future studies should be extended to overweight, underweight pregnant cases and similar pregnant and non-pregnant controls to explore the overall effect of lipid profile parameters and resistin in PE patients.

Despite all recent advancements, no blood test has been found which could serve as a useful predictor of PE. Therefore, the dire need of the time is to further explore the role of resistin in hypertensive disorders of pregnancy, and research should be carried out to find the gestational age at which the level of resistin start to rise in women who later suffer from PE.

Conclusion

PE was found to be associated with higher levels of resistin and most lipid parameters compared to normal pregnancy. Serum resistin was significantly raised in PE patients, indicating that resistin and obesity have a definitive role in PE pathogenesis. Besides, resistin and lipid profiles can serve as novel PE markers.

Disclaimer: The text is based on an academic thesis.

Conflict of Interest: None.

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References

1. Boeldt DS, Bird IM. Vascular adaptation in pregnancy and endothelial dysfunction in preeclampsia. J Endocrinol 2017;232:R27-44. doi: 10.1530/JOE-16-0340.
2. Kallela J, Jääskeläinen T, Kortelainen E, Heinonen S, Kajantie E, Kere J, et al. The diagnosis of pre-eclampsia using two revised classifications in the Finnish Pre-eclampsia Consortium (FINNPEC) cohort. BMC Pregnancy Childbirth 2016;16:221. doi: 10.1186/s12884-016-1010-0.
3. Pauli JM, Repke JT. Preeclampsia: Short-term and Long-term Implications. Obstet Gynecol Clin North Am 2015;42:299-313. doi: 10.1016/j.ogc.2015.01.007.
4. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol 2009;33:130-7. doi: 10.1053/j.semperi.2009.02.010.
5. Charanthimath U, Vidler M, Katageri G, Ramadurg U, Karadiguddi C, Kavi A, et al. The feasibility of task-sharing the identification, emergency treatment, and referral for women with pre-eclampsia by community health workers in India. Reprod Health 2018;15(Suppl 1):101. doi: 10.1186/s12978-018-0532-5.
6. Salam RA, Qureshi RN, Sheikh S, Khowaja AR, Sawchuck D, Vidler M, et al. Potential for task-sharing to Lady Health Workers for identification and emergency management of pre-eclampsia at community level in Pakistan. Reprod Health 2016;13(Suppl 2):107. doi: 10.1186/s12978-016-0214-0.
7. Wang H, Chu WS, Hemphill C, Elbein SC. Human resistin gene: molecular scanning and evaluation of association with insulin sensitivity and type 2 diabetes in Caucasians. J Clin Endocrinol Metab 2002;87:2520-4. doi: 10.1210/jcem.87.6.8528.
8. Flier JS. The missing link with obesity? Nature 2001;409:292–3. doi: 10.1038/35053251.
9. Lee JH, Chan JL, Yiannakouris N, Kontogianni M, Estrada E, Seip R, et al. Circulating resistin levels are not associated with obesity or insulin resistance in humans and are not regulated by fasting or leptin administration: cross-sectional and interventional studies in normal, insulin-resistant, and diabetic subjects. J Clin Endocrinol Metab 2003;88:4848-56. doi: 10.1210/jc.2003-030519.
10. Seely EW, Solomon CG. Insulin resistance and its potential role in pregnancy-induced hypertension. J Clin Endocrinol Metab 2003;88:2393-8. doi: 10.1210/jc.2003-030241.
11. Yura S, Sagawa N, Itoh H, Kakui K, Nuamah MA, Korita D, et al. Resistin is expressed in the human placenta. J Clin Endocrinol Metab 2003;88:1394-7. doi: 10.1210/jc.2002-011926.
12. Wolf M, Sandler L, Jimenez-Kimble R, Shah A, Ecker JL, Thadhani R. Insulin resistance but not inflammation is associated with

gestational hypertension. Hypertensio 2002;40:886-91. doi: 10.1161/01.hyp.0000042085.65467.9f.

13. Thadhani R, Ecker JL, Mutter WP, Wolf M, Smirnakis KV, Sukhatme VP, et al. Insulin resistance and alterations in angiogenesis: additive insults that may lead to preeclampsia. Hypertension 2004;43:988-92. doi: 10.1161/01.HYP.0000124460.67539.1d.
14. Song Y, Gao J, Qu Y, Wang S, Wang X, Liu J. Serum levels of leptin, adiponectin and resistin in relation to clinical characteristics in normal pregnancy and preeclampsia. Clin Chim Acta 2016;458:133-7. doi: 10.1016/j.cca.2016.04.036.
15. Banjac G, Ardalic D, Mihajlovic M, Antonic T, Cabunac P, Zeljkovic A, et al. The role of resistin in early preeclampsia prediction. Scand J Clin Lab Invest 2021;81:432-7. doi: 10.1080/00365513.2021.1938205.
16. Chandrasekaran S, Hunt H, Melhorn S, Gammill HS, Schur EA. Adipokine profiles in preeclampsia. J Matern Fetal Neonatal Med 2020;33:2812-7. doi: 10.1080/14767058.2018.1562542.
17. Mankuta D, Elami-Suzin M, Elhayani A, Vinker S. Lipid profile in consecutive pregnancies. Lipids Health Dis 2010;9:58. doi: 10.1186/1476-511X-9-58.
18. Diareme M, Karkalousos P, Theodoropoulos G, Strouzas S, Lazanas N. Lipid profile of healthy women during normal pregnancy. J Med Biochem 2009;28:152-60. DOI: 10.2478/v10011-009-0011-1.
19. Gohil JT, Patel PK, Gupta P. Estimation of lipid profile in subjects of preeclampsia. J Obstet Gynaecol India 2011;61:399-403. doi: 10.1007/s13224-011-0057-0.
20. Pauli JM, Repke JT. Preeclampsia: Short-term and Long-term Implications. Obstet Gynecol Clin North Am 2015;42:299-313. doi: 10.1016/j.ogc.2015.01.007.
21. Macdonald-Wallis C, Silverwood RJ, Fraser A, Nelson SM, Tilling K, Lawlor DA, et al. Gestational-age-specific reference ranges for blood pressure in pregnancy: findings from a prospective cohort. J Hypertens 2015;33:96-105. doi: 10.1097/HJH.0000000000000368.
22. Chen X, Scholl TO. Ethnic Differences in Maternal Adipokines during Normal Pregnancy. Int J Environ Res Public Health 2015;13:ijerph13010008. doi: 10.3390/ijerph13010008.
23. Gutaj P, Sibiak R, Jankowski M, Awdi K, Bryl R, Mozdziak P, et al. The Role of the Adipokines in the Most Common Gestational Complications. Int J Mol Sci 2020;21:9408. doi: 10.3390/ijms 21249408.
24. Nien JK, Mazaki-Tovi S, Romero R, Kusanovic JP, Erez O, Gotsch F, et al. Resistin: a hormone which induces insulin resistance is increased in normal pregnancy. J Perinat Med 2007;35:513-21. doi: 10.1515/JPM.2007.122.
25. Cortelazzi D, Corbetta S, Ronzoni S, Pelle F, Marconi A, Cozzi V, et al, Maternal and foetal resistin and adiponectin concentrations in normal and complicated pregnancies. Clin Endocrinol (Oxf) 2007;66:447-53. doi: 10.1111/j.1365-2265.2007.02761.x.

Author Contribution:

MR: Concept of study Design, data collection, drafting, analysis, interpretation of work.
MAC: Drafting and critical revision of work for important intellectual content and final approval of work.
RAK: Data analysis, drafting and revision.
AK: Data collection, drafting, data interpretation.
AMR: Data collection, drafting, literature search.
KPL: Research supervisor, study design and concept.
All the authors have approved the final version to be published and are accountable for all aspects of the work.