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ORIGINAL ARTICLE

Changes in Serum Adiponectin and Serum Leptin Levels Can Predict Pre-Eclampsia in Pregnant Women: A Prospective Study

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ABSTRACT

Background: The study aims to investigate maternal adiponectin and leptin levels as prospective markers of preeclampsia, as well as the ratio of maternal adiponectin to leptin levels. Additionally, this research investigated the relationship between these two hormones. In addition to that, the purpose of this study was to analyze the connection that exists between the two hormones.

Materials and Methods: This is a study that looks forward into the foreseeable future. The pregnant women who were willing to take part in the research were split into two groups: the first group, which was referred to as the study group, consisted of fifty women who had been diagnosed with pre-eclampsia, and the second group, which was referred to as the control group, consisted of fifty normotensive women of the same gestational age who did not have proteinuria. The levels of adiponectin, leptin, and their ratio were evaluated in the maternal serum of pre-eclamptic (the study group)and normotensive women(the control group).. The comparison's outcomes were analysed

Results: There was a statistically significant difference in the levels of adiponectin found in the study group compared to the levels found in the control group. When comparing the levels of leptin in the study group with the control group, there was a statistically significant difference ($p< 0.001$) between the two groups. When compared to the control group, the ratio of adiponectin to leptin was considerably lower in the group that participated in the study ($p<<0.001$). When used as predictors of pre-eclampsia, serum leptin and the serum adiponectin/leptin ratio displayed a sensitivity of 90%, a specificity of 87.9%, a positive predictive value of 88.7%, and a negative predictive value of 73%. Additionally, the ratio of serum adiponectin to leptin exhibited a positive predictive value of 86.9 percent. Both the adiponectin/leptin ratio cutoff point and the leptin cutoff point were found to be optimal at 0.161. It was determined that a cutoff criterion of 24.1 ng/ml for serum leptin should be used. Both the adiponectin/leptin ratio and the serum leptin levels were significantly linked with significant degrees of accuracy ($p <0.001$) in the prediction of obesity.

Conclusion: In research on pre-eclampsia, the examination of the maternal leptin level should be included, and a cut-off level of greater than 24.2 ng/ml should be employed as a diagnostic biomarker. This is due to the fact that pre-eclampsia is linked to hyperleptinemia, which is a condition that is characterised by dangerously high blood pressure in the mother. The ratio of adiponectin to leptin should be checked in every instance of preeclampsia, and the diagnostic threshold should be set to less than 0.153. This ratio is a potential biomarker for preeclampsia and should be examined in every case.

Keywords: Leptin, adiponectin, the ratio of adiponectin to leptin, pre-eclampsia, and biomarkers

INTRODUCTION

Pre-eclampsia syndrome is a condition that only manifests itself during pregnancy. It is characterised by the onset of hypertension (defined as a blood pressure that is higher than 140/90 mmHg) in conjunction with proteinuria or the involvement of other organs. Pre-eclampsia syndrome can only be contracted during pregnancy. After 20 weeks of pregnancy, a pregnant woman who was previously normotensive and did not have protein in her urine may experience other organ involvement, such as thrombocytopenia, impaired liver function, new development of renal dysfunction, new onset of cerebral or visual disturbances, or pulmonary edema. These symptoms may occur in a pregnant woman who had no protein in her urine. It has been related to high rates of morbidity and mortality for both the fetus and the mother, and it can have an impact on anywhere from 2% to 8% of pregnancies. Some pregnancies are at higher risk than others. Even though a great number of hypotheses have been put forward to attempt to explain what brings on pre-eclampsia (PE), the precise aetiopathogenesis of this condition has not yet been discovered. Endothelial cell failure, inflammation, and angiogenesis are, nevertheless, the final stages of the same process, and they are characteristics that are shared by all of these ideas. Insulin resistance (IR), polycystic ovarian syndrome (PCOS), diabetes, obesity, and hyperinsulinemia are all connected conditions that can play a role in the progression of polycystic kidney disease (PKD). PCOS is a disorder that affects the female reproductive organs and is caused by a disruption in the endocrine system (PE). Two examples of the bioactive adipokines that are thought to have played a role in the development of polygenic obesity are adiponectin and leptin (PE). This is as a result of the fact that malfunctions in endothelial cells , inflammation, angiogenesis, blood pressure regulation, and insulin resistance are all linked to both of these adipokines. Additionally, the process of angiogenesis is one that leads to the development of new blood vessels in the body. Adipocytes are the key cells in the body that are responsible for the creation of these proteins. Their contribution to the production of these proteins accounts for practically the entire body's supply. In addition, it has been shown that these adipokines have a part in pregnancies that operate frequently as well as those that do not operate consistently. This is something that has been established. It is hypothesized that people who have PE have an abnormality in the regulation of adipokines, and that these adipokines may play a role in both the etiology and the prognosis of the disorder. This hypothesis is based on the observation that people who have PE have higher levels of certain adipokines. The name given to this way of thinking is the dysregulation of adipokine control hypothesis. Alterations in the adiponectin–leptin ratio, which is sometimes referred to as the A/L ratio, have also been explored for their possible significance in the prognosis and diagnosis of peripheral artery disease (PE). This ratio is sometimes referred to as the A/L ratio, which stands for "area to length." In the event that they do play a role, the levels of these adipokines in the mother may differ between pregnancies that are uncomplicated by preeclampsia and those that are complicated by preeclampsia if the levels do differ. Therefore, it is likely that they are prospective biomarkers, and it is also likely that they will play a role in the diagnosis, prognosis, and management of PE in the not too distant future. In addition, it is a distinct possibility that they will play a part in the management of this

ailment at some point in the foreseeable future. The hormone of satiety is called leptin, and it has a molecular weight of 16 kDa. This is due to the fact that it raises metabolic rate while simultaneously reducing feelings of hunger. It has been shown that the levels of protein and messenger RNA of leptin in the placentae of pre-eclamptic women are significantly higher than normal. Prior to the disease's clinical presentation, those who have PE have been found to have higher levels of the hormone leptin in their bodies than those who do not have PE. A protein with a molecular weight of 30 kDa, adiponectin is nearly entirely produced by adipocytes and circulates in the blood at a rather high quantity (g/ml). Adipocytes are responsible for practically all of the production of adiponectin. A considerable part of the responsibility for the expression of genes in adipocytes lies with the adipocytes themselves. Multiple researches have come to the conclusion that people who have PE have much higher amounts of the hormone adiponectin in their bodies. It is becoming increasingly common awareness that the ratio of adiponectin to leptin, also referred to as the A/L ratio, is a useful predictor of dysfunction in adipose tissue. There are a few other names for this ratio, including the A/L ratio and the AL ratio. Both chronic low-grade inflammation and a high body mass index have been shown to have a negative link with this component, as has been shown in numerous studies. In recent years, a great number of studies have been carried out with the purpose of determining whether or not this ratio is helpful as a biomarker for PE.

MATERIALS AND METHODS

This study project with an eye toward the future is being carried out in the Obstetrics and Gynecology Department of the Hayat Memorial Teaching Hospital in Lahore. In order to be eligible for participation in this study, female participants need to be at least 18 years old and have a body mass index that falls between 19 and 23. The study did not include any participants who had a history of numerous pregnancies, hypertension either before or during pregnancy, diabetes, or renal disease. The pregnant women who were willing to take part in the study were separated into three groups: the first group, which was given the name of the study group and consisted of fifty participants, was made up of women who had been diagnosed with pre-eclampsia; the second group, which was given the name of the control group and consisted of fifty normotensive pregnant women who did not have proteinuria; and the third group, which was given the name of the comparison group and consisted of fifty pregnant women who were pregnant We were provided with a significant amount of information concerning the history. The participants' blood pressure, height, weight, and body mass index were all assessed, as was their body mass index. Also measured was the participants' body mass index. In addition, five milliliters of venous blood and five milliliters of urine were taken from each person so that the levels of adiponectin and leptin could be measured in nanograms per milliliter. This was done so that the results could be compared. The delivery was one of the things that was properly planned and organized. At each and every meeting, participants were particularly questioned about the appearance of any new symptoms or a worsening of their existing disease. This was done in order to collect as much data as possible regarding the health of the patients. The women who participated in the study were considered to be at an increased risk for developing preeclampsia, whereas the women who participated in the control group were considered to have normal blood pressure. In addition to determining a confidence interval and comparing the quantities and ratios of adiponectin and leptin in the maternal serum of both of the groups, a comparison was also made between the two groups. The analysis of the qualitative data was performed using the Chi-square test and the Fisher exact test, while the analysis of the quantitative data was performed using the T test. If the p-value was less than 0.05, then we came to the conclusion that the data revealed a trend that was statistically significant.

RESULT

There was a statistically significant difference in the levels of adiponectin found in the study group compared to the levels found in the control group. When comparing the levels of leptin in the study group with the control group, there was a statistically significant difference (p 0.001) between the two groups. When compared to the control group, the ratio of adiponectin to leptin was considerably lower in the group that participated in the study (p<0.001). When used as predictors of pre-eclampsia, serum leptin and the serum adiponectin/leptin ratio displayed a sensitivity of 90%, a specificity of 87.9%, a positive predictive value of 88.7%, and a negative predictive value of 73%. Additionally, the ratio of serum adiponectin to leptin exhibited a positive predictive value of 86.9 percent. Both the adiponectin/leptin ratio cutoff point and the leptin cutoff point were found to be optimal at 0.161. It was determined that a cutoff criterion of 24.1 ng/ml for serum leptin should be used. Both the adiponectin/leptin ratio and the serum leptin levels were significantly linked with significant degrees of accuracy (p< 0.001) in the prediction of obesity.

Table 1 Systolic and diastolic blood pressure, adiponectin, leptin, and the ratio of adiponectin to leptin were measured in the study and control groups.

Parameter	Study group (n=50)	Control group (n=50)	p value
SBP (mm hg)	146.32 ± 8.91	108.98 ± 5.76	< 0.0001
DBP	97.88 ± 7.94	73.01 ± 7.99	< 0.0001
Adiponectin (µg/ml)	9.46 ± 15.01	8.67 ± 7.02	0.088
Leptin (ng/ml)	67.31 ± 43.95	13.01 ± 15.42	< 0.0001
Adiponectin–leptin ratio	0.23 ± 0.36	0.79 ± 39.1	< 0.0001

Table 2 Adiponectin and leptin levels and A/L ratio in mild and severe pre-eclampsia

Parameter	Mild (n = 41)	Severe (n = 9)	p value
1.Adiponectin(µg/ml)	5.84 ± 5.62	31.04 ± 23.27	< 0.0001
1.Leptin(ng/ml)	67.31 ±45.01	71.09 ±43.77	0.652
A/L ratio	0.14 ± 0.24	0.59 ± 0.7	0.0001

DISCUSSION

This survey found that the average maternal age of the population under consideration was 27.91 years, with the majority of women lying within the age range of 24–29. Comparable to the control group in terms of maternal age, with a mean of 26.934.36 years, with the majority of women (46.66%) falling between the ages of 24 and 29. In terms of parity, educational status, occupational status, and body mass index, the two groups did not differ significantly. In contrast, the study group had a statistically significant higher proportion of women living in rural areas than the control group (p = 0.021).

At the initial visit, women in the study group had significantly higher systolic and diastolic blood pressure than women in the control group, with p values less than 0.00001 for both measurements. The ladies in the study group also had considerably higher systolic blood pressure than those in the control group. The study group had a mean systolic blood pressure of 146.32 ± 8.91 and a mean diastolic blood pressure of 97.88 ± 7.94 when compared to the control group. In contrast, the mean systolic blood pressure of the control group was 108.98 ± 5.76 and the mean diastolic blood pressure was 73.01 ± 7.99. Two separate studies, one conducted on the Iranian population and the other on the Ghanaian population, have yielded comparable results. During this investigation, it was determined that the levels of adiponectin in the study group were significantly higher than those in the control group. The concentrations in the study group ranged from 0.13 to 84.2 ug/ml, with a mean value of 9.46 ± 15.01ug/ml. In the control group, results varied from 0.08 to 27.50 ug/ml, with an overall mean concentration of 8.67 ± 7.02 ug/ml.

It has been established that the pre-eclampsia syndrome is linked to insulin resistance, an elevated inflammatory response

everywhere throughout the body, and a condition that is anti-angiogenic. Lower levels of adiponectin are associated with the above listed factors, which are all depicted in PE. This is because adiponectin possesses anti-diabetic, anti-inflammatory, and angiogenesis capabilities. Angiogenesis is another process that can be encouraged by adiponectin.

PE is characterised by increased quantities of the hormone angiotensin II, which finally presents clinically as hypertension. Hypertension is the clinical manifestation of PE. There is a good chance that hyperadiponectinemia is a protective feedback mechanism that restricts synthesis of angiotensin II and helps to keep blood pressure stable. This is because adiponectin blocks the formation of angiotensin II, which is the reason for this effect. A rise in adiponectin levels may offer some protection against the proteinuria that is linked with ES, according to a theory that has been put up. [There is a need for citations] Patients suffering from PE may have an easier time returning to normal endothelium function if they take use of adiponectin's anti-inflammatory properties. Patients diagnosed with PE have been shown to have lower levels of this protein, according to the research. The authors are of the opinion that raising adiponectin levels can help prevent the pathological deterioration of PE, and this perspective is supported by their findings.

It was discovered that the levels of leptin that were present in the pre-eclamptic patients in the study group were much higher than those that were present in the control group (normotensive). The participants in the study had leptin levels that varied from 43.95 to 67.31 ng/ml, with a standard deviation of 43.95 ng/ml. The average leptin level was 67.31 ng/ml. The control group had leptin levels that ranged from 13.01 ng/ml on average to 15.42 ng/ml on average, with a standard deviation of 15.42 ng/ml. The levels of leptin found among the participants in the study ranged from 3.5 to 197.2 ng/ml. There was a difference in the amounts that were discovered between the two groups, and this difference had the potential to be considered statistically significant (p value less than 0.0001). It is consistent with previous research carried out in India, as well as research carried out in Ghana, Pakistan, Iran, and China that this study observed a significant rise in leptin levels in the study group. In contrast, the findings of the study that was carried out in the United States showed that there was not a discernible difference in the levels of leptin that were present in either of the two groups. There are a number of potential explanations for why pre-eclampsia is linked to increased leptin levels, and any one of these explanations could be the root cause of this connection. Even in healthy pregnancies, the placenta secretes leptin, which is surprisingly comparable to the leptin generated by adipose tissue in terms of size and immunoreactivity, and hence contributes to high levels. Placental stress, which is common in preeclamptic pregnancies, may have been caused in part by hypoxia, which is typical of the placenta in these pregnancies. This may have led to an increase in levels. A lack of oxygen in the blood is a hallmark of the condition known as hypoxia. Because of the significant angiogenic action of leptin, its levels may be elevated in PE in order to improve the placental blood supply through the process of neovascularization. In order to prevent placental hypoxia, this procedure is carried out. Because of the effect that leptin has on the transport of food across the placenta, increased leptin levels in PE may be the result of a compensatory reaction that is designed to promote the transfer of nutrients to the under perfused placenta that is present in PE. Leptin is responsible for controlling the transport of nutrients, so this is made feasible. The fact that the levels of leptin in PE have increased is evidence that demonstrates this point.

The ratio of adiponectin to leptin, denoted as "A/L.": According to the results of this research, the ratio of adiponectin to leptin, which is also referred to as the A/L ratio, was significantly lower in the group that took part in the study in comparison to the group that served as the control. On the other hand, the findings of a research study that was carried out in found that pre-eclamptic women had an A/L ratio that was significantly higher than the normotensive controls who participated in the study. In contrast, the levels of adiponectin that were measured and analyzed for this study were taken during the first trimester of pregnancy, which is the first stage of pregnancy. According to the findings of a research project carried out in Denmark, there is not enough data to back up the contention that there is a connection between the A/L ratio and the development of PE. Since can be seen, there is an issue with the regulation of adipokines in PE, as the A/L ratio was much lower in the group that was analysed in comparison to the group that served as the control. It is quite likely that the decreased A/L ratio in the preeclamptic group is a reflection of the increased insulin resistance and inflammation that are known to be prevalent in preeclampsia.

As a consequence of this, a shift in the A/L ratio during pregnancy may be a biomarker of PE and the attendant adipose tissue malfunction; hence, its measurement may be included in the diagnostic investigations for PE. This is because pregnancy has been shown to change the proportion of adiponectin to lipoprotein in the body. For the purpose of predicting PE, an A/L ratio cutoff of 0.153 has been shown to have a sensitivity of 67.8%, a specificity of 89% ($p< 0.001$), a positive predictive value of 86.8, and a negative predictive value of 73. These data are offered in addition to the positive predictive value of 87.2 and the negative predictive value of 73 that are presented earlier.

CONCLUSION

There was a statistically significant correlation between the presence of pre-eclampsia and the high amounts of leptin that were found in the mother. When compared to moderate pre-eclampsia, severe pre-eclampsia is related with dramatically elevated levels of the hormone adiponectin. This is in contrast to moderate pre-eclampsia, which is associated with normal levels. On the other hand, pre-eclampsia that is just mildly severe is related with levels that are normal. It was shown that pre-eclamptic women had a much decreased ratio of adiponectin to leptin in their bodies. However, when it came to severe pre-eclampsia, the ratio of adiponectin to leptin was significantly higher than when it came to moderate pre-eclampsia.

REFERENCES

1. Jeyabalan A. Epidemiology of preeclampsia: impact of obesity. Nutr Rev. 2013;71:S18-S25.
2. Sharma A, Satyam A, Sharma JB. Leptin, IL-10 and Inflammatory Markers (TNF-α, IL-6 and IL-8) in Pre-Eclamptic, Normotensive Pregnant and Healthy Non-Pregnant Women. American Journal of Reproductive Immunology. 2007;58:21-30.
3. Ramos-Lobo AM, Donato J Jr. The role of leptin in health and disease. Temperature (Austin). 2017;4(3):258-291.
4. Napso T, Yong HEJ, Lopez-Tello J, Sferruzzi-Perri AN. The Role of Placental Hormones in Mediating Maternal Adaptations to Support Pregnancy and Lactation. Front Physiol. 2018;9:1091.
5. Pérez-Pérez A, Toro A, Vilariño-García T, Maymó J, Guadix P, Dueñas JL et al. Leptin action in normal and pathological pregnancies. J Cell Mol Med. 2018;22(2):716-727.
6. Kelesidis T, Kelesidis I, Chou S, Mantzoros CS. Narrative review: the role of leptin in human physiology: emerging clinical applications. Ann Intern Med. 2010;152(2):93-100.
7. Ajala OM, Ogunro PS, Elusanmi GF, Ogunyemi OE, Bolarinde AA. Changes in serum leptin during phases of menstrual cycle of fertile women: relationship to age groups and fertility. Int J Endocrinol Metab. 2013;11(1):27-33.
8. Sattar N, Greer IA, Pirwani I, Gibson J, Wallace AM. Leptin levels in pregnancy: marker for fat accumulation and mobilization? Acta Obstet Gynecol Scand. 1998;77(3):278-83.
9. Laird SM, Quinton ND, Anstie B, Li TC, Blakemore AI. Leptin and leptin-binding activity in women with recurrent miscarriage: correlation with pregnancy outcome. Hum Reprod. 2001;16(9):2008-13.
10. Challier J, Galtier M, Bintein T, Cortez A, Lepercq J, Hauguel-de Mouzon S. Placental leptin receptor isoforms in normal and pathological pregnancies. Placenta. 2003;24(1):92-9.
11. Lopez-Jaramillo P, Barajas J, Rueda-Quijano SM, Lopez-Lopez C, Felix C. Obesity and Preeclampsia: Common Pathophysiological Mechanisms. Front Physiol. 2018;9:1838.

12. Thagaard IN, Hedley PL, Holm JC, Lange T, Larsen T, Krebs L and Christiansen M: Leptin and adiponectin as markers for preeclampsia in obese pregnant women, a cohort study. Pregnancy Hypertens. 2019;15:78-83.
13. Xiao WQ, He JR, Shen SY, Lu JH, Kuang YS, Wei XL et al. Maternal circulating leptin profile during pregnancy and gestational diabetes mellitus. Diabetes Research and Clinical Practice. 2020;161:108041.
14. Taylor BD, Ness RB, Olsen J, Hougaard DM, Skogstrand K, Roberts JM et al. Serum leptin measured in early pregnancy is higher in women with preeclampsia compared with normotensive pregnant women. Hypertension. 2015;65(3):594-9.
15. Mise H, Sagawa N, Matsumoto T, Yura S, Nanno H, Itoh H et al. Augmented placental production of leptin in preeclampsia: possible involvement of placental hypoxia. J Clin Endocrinol Metab. 1998;83(9):3225-9.
16. Dotsch J, Nusken KD, Knerr I, Kirschbaum M, Repp R, Rascher W. Leptin and neuropeptide Y gene expression in human placenta: ontogeny and evidence for similarities to hypothalamic regulation. The Journal of Clinical Endocrinology & Metabolism. 1999;84(8):2755-8.
17. Giordano R, Cacciatore A, Romano M, La Rosa B, Fonti I, Vigna R. Uterine artery Doppler flow studies in obstetric practice. J Prenat Med. 2010;4(4):59-62.
18. Salimi S, Farajian-Mashhadi F, Naghavi A, Mokhtari M, Shahrakipour M, Saravani M et al. Different profile of serum leptin between early onset and late onset preeclampsia. Disease markers. 2014;2014.
19. Laivuori H, Gallaher MJ, Collura L, Crombleholme WR, Markovic N, Rajakumar A et al. Relationships between maternal plasma leptin, placental leptin mrna and protein in normal pregnancy, pre-eclampsia and intrauterine growth restriction without pre-eclampsia. Mol Hum Reprod. 2006;12:551-556.
20. Bakacak M, Kılınç M, Serin S, Ercan Ö, Köstü B, Avcı F, et al. Changes in Copper, Zinc, and Malondialdehyde Levels and Superoxide Dismutase Activities in Pre-Eclamptic Pregnancies. Medical science monitor: international medical journal of experimental and clinical research. 2015;21:2414.