



## “LEPTIN AND ADIPONECTIN AS PREDICTING BIOMARKERS IN PREECLAMPSIA.”

Shubhangidevi H. Gawade<sup>1\*</sup>, Dr. Pooja N.Joshi<sup>2</sup>, Dr. G.A.Gulavani<sup>3</sup>, Dr Somnath Salgar<sup>4</sup>

<sup>1\*</sup>(P.hD Student) Tutor, Department of Biochemistry, SKNMC& GH, Pune.

<sup>2</sup>(P.hD guide), Department of Biochemistry, Lecturer, BJMC, Pune

<sup>3</sup>Professor and head, Dept. of Biochemistry, SKNMCGH, Pune

<sup>4</sup>Professor and HOD Department of Biochemistry BJGMC, Pune

**\*Corresponding Author: Shubhangidevi H. Gawade**

\*(P.hD Student) Tutor, Department of Biochemistry, SKNMC& GH, Pune

### Introduction:

Preeclampsia is a pregnancy related disorder involving multiple organs like liver, brain and symptoms resolve after termination pregnancy. HELLP syndrome is a complication of preeclampsia characterized by hemolysis, elevated liver enzymes and low platelets.

Normal fetal growth depends on complex interactions between maternal, placental, and fetal environments. Pre-eclampsia (PE) is a manifestation of dysregulation in this normally finely tuned balance. Even though the clinical features of PE first become apparent in the second half of pregnancy, major pathogenic changes occur early on at the time of trophoblast invasion and remodeling of the spiral arteries [10].

Placental leptin is important cytokine for both mother and foetus. It is involved in reproduction angiogenesis and implantation and comes from the adipose tissue. Many studies show increased levels of leptin in pregnancy than non-pregnant states. During pregnancy leptin comes from the placenta. (9)

Adiponectin plays important role in endocrine function, immune function, inflammation, reproduction and angiogenesis. (8)

Recent workup in the use of these adipokines have demonstrated dysregulation exists in PE. Insulin resistance and its metabolic and vascular consequences are linked with adiponectin levels and PE.

### Aims and objectives:

The purpose of this study was to estimate Leptin and Adiponectin levels in preeclampsia and normotensive pregnancy and their correlation.

### Methods:

The study population 60 cases selected from pregnant women with prior consent attending the Obstetrics and Gynecology Department/ANC OPD at BJMC& GH was collected taking into consideration inclusion and exclusion criteria. The 60 non-obese pregnant women is the control group with matching BP, BMI, with gestational age 20 -28 weeks. Serum concentrations of leptin and adiponectin were determined by ELISA.

A detail history was taken BMI, SBP, DBP of the study group was taken. Venous blood 5ml was collected for Adiponectin and Leptin measurement. During each visit, the patients were monitored for any new signs and symptoms.

### Maternal Characteristics:

During first visit, women reported following

Gravida/para smoking history, para history, Pre-pregnancy BMI. Women’s job and education defined socio-economic status.

### Duration:

This study was done in Department of Biochemistry during July 2021 to December 2022 after getting ethical clearance from institutional ethical committee.

### Statistical Analysis:

A detail was presented on Microsoft excel sheet. Qualitative data was expressed as chi square test. Quantitative data was expressed as t-test.

Baseline characteristics like age, BMI, smoking socio-economic status were compared between all cases and controls.

### Observation and Results:

The mean Leptin levels in normotensive pregnancy was  $25.19 \pm 5.44$  ng/ml...

The mean Leptin levels in Preeclampsia was  $40.42 \pm 4.93$  ng/ml

The mean Adiponectin levels in normotensive pregnancy was  $8.02 \pm 0.87$  ug /ml ...

The mean Adiponectin levels in Preeclampsia was  $4.85 \pm 1.00$  ug /ml

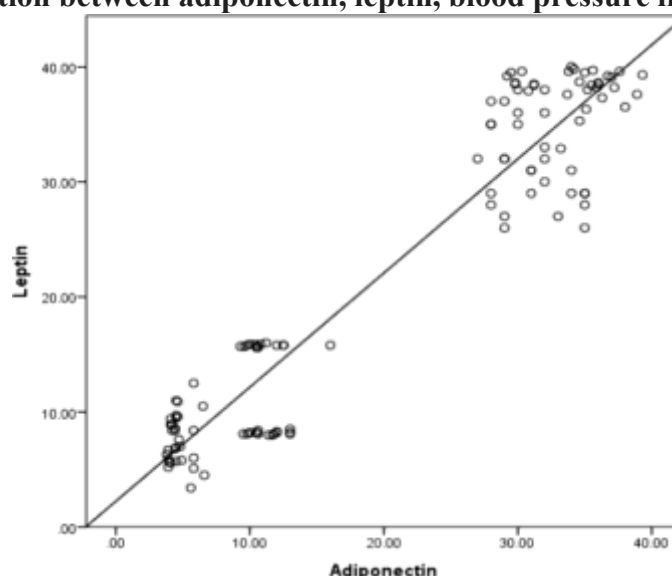
**Table no. 1 Baseline characteristics**

Baseline characteristics	Cases	Controls	P value
Age ( years )	$27.1 \pm 4.2$	$26.9 \pm 2.6$	NS
Parity	$1.9 \pm 1.0$	$1.8 \pm 1.1$	NS
BMI ( $\text{kg}/\text{m}^2$ )	$35.1 \pm 2.4$	$34.6 \pm 1.5$	NS

**Table no. 2 : comparison between cases and controls**

Variable	Preeclampsia (Mean $\pm$ SD)	Control (Mean $\pm$ SD)	t-test statistic	p-value
Leptin ng /ml	$40.42 \pm 4.93$	$25.19 \pm 5.44$	21.0646	< 0.0001
Adiponectin ug /ml	$4.85 \pm 1.00$	$8.02 \pm 0.87$	-24.2059	< 0.0001

**Fig. 1 Correlation between adiponectin, leptin, blood pressure in preeclampsia.**



### **Leptin**

Leptin, an adipocytokine predominantly secreted by adipose tissue and the placenta during pregnancy, was found to be significantly elevated in the preeclamptic group ( $40.42 \pm 4.93$  ng/ml) compared to the normotensive control group ( $25.19 \pm 5.44$  ng/ml), (with a t-statistic of 21.0646 and p value < 0.0001). This increase in leptin is believed to contribute to the proinflammatory state and endothelial dysfunction characteristic of preeclampsia. (7) Leptin can activate sympathetic nervous activity, increase oxidative stress, and impair vasodilation by disrupting nitric oxide bioavailability. Elevated leptin levels in early pregnancy have also been associated with an increased risk of developing preeclampsia, making it a potential early biomarker for disease prediction and risk stratification. (6)

### **Adiponectin**

Adiponectin levels were significantly lower in women with preeclampsia ( $4.85 \pm 1.00$  µg/ml) than in the control group ( $8.02 \pm 0.87$  µg/ml), (with a t statistic of -24.2059 and p-value < 0.0001). Adiponectin is known for its anti-inflammatory, insulin-sensitizing, and vasodilatory effects. Its reduced levels suggest the presence of systemic metabolic dysregulation and increased vascular resistance in preeclampsia. (5) The deficiency of adiponectin may also impair placental vascular remodeling and contribute to poor trophoblast invasion, both of which are crucial in the pathogenesis of preeclampsia. (4)

### **Discussion:**

The results of the current investigation revealed a significant elevation of leptin and significant decrease in adiponectin in pregnant women with PE compared with normotensive pregnant women which is in accordance with many other reports.

Ning et al. showed increase in leptin concentration is associated with a 30% increase in PE risk. Also, it has been found that higher leptin levels inhibit the proliferation of cytotrophoblasts. As was detected previously, the first abnormalities linked to PE are decreased cytotrophoblast migration and invasion of the uterus.(11)

Masuzaki H et.al. found that leptin play a important role in pregnancy complications. Recent study showed that leptin has vital role in its biologic effect on neuroendocrine and reproductive function. Leptin is responsible for inflammatory response through the proinflammatory cytokine induction in placenta and adipose tissue. Leptin also induced lipid peroxidation in human endothelial cell culture, so therefore leptin is thought to facilitate atherogenesis in preeclampsia. (14)

Ramsay et al. (10) reported an elevation of plasma adiponectin concentration in women with PE compared with controls and suggested that adiponectin released during pregnancy could be a physiological response to minimize fat accumulation and also to decrease endothelial damage. Many previous studies have shown that the low-grade inflammation typical of preeclamptic women is correlated with obesity and to insulin resistance. (4,5,6,7)

All these studies may lead to use of these adipokine biomarkers (adiponectin and leptin), as early predictive markers which should guard the adverse outcomes linked to late presentation of PE.

### **Conclusion:**

The study has found that adiponectin levels were more likely to be lower in pregnant women with preeclampsia than in the normotensive pregnancies, and leptin levels were more likely to be significantly higher in pregnant womenwith preeclampsia than in the normotensive pregnancies.

Moderate bias as well as small number of cases are the limitations of this study and large group of patients should be considered to validate these results.

### **Conflict of Interest**

No conflict of interest to disclose.

### **Funding**

No funding is required.

## References

1. Wang T, Zhou R, Gao L, et al. (2014). Elevation of urinary adipsin in preeclampsia: correlation with urine protein concentration and the potential use for a rapid diagnostic test. *Hypertension*, 64: 846–851.
2. Martinez-Fierro ML, Garza-Veloz I, Carrillo-Sanchez K, et al. (2014). Expression levels of seven candidate genes in human peripheral blood mononuclear cells and their association with preeclampsia. *Hypertens Pregnancy*, 33: 191–203.
3. Khosrowbeygi A, Ahmadvand H. (2013). Leptin to adiponectin ratio in preeclampsia. *Bangladesh Med Res Counc Bull*, 39: 18–21.
4. Machado JS, Cavalli RC, Sandrim VC, et al. (2012). PP002. Study of polymorphisms of the adiponectin gene in women with gestational hypertension and preeclampsia. *Pregnancy Hypertens*, 2(3): 241
5. Eleuterio NM, Palei AC, Rangel Machado JS, Tanus-Santos JE, Cavalli RC, Sandrim VC. (2015). Positive correlations between circulating adiponectin and MMP2 in preeclampsia pregnant. *Pregnancy Hypertens*, 5: 205–208.
6. Sudjai D. Association of pre-pregnancy body mass index with early- and late-onset severe preeclampsia. *Eur J Obstet Gynecol Reprod Biol X* 2023; 19: 100223.
7. Miller GJ. Dietary fatty acids and blood coagulation. *Prostaglandins Leukot Essent Fatty Acids* 1997; 57: 389-394.
8. Dusse LM, Rios DRA, Pinheiro MB, Cooper AJ, Waleed BA. Preeclampsia: relationship between coagulation, fibrinolysis and inflammation. *Clin Chim Acta* 2011; 412: 17-21.
9. Schwingshackl L, Hoffmann G. Monounsaturated fatty acids and risk of cardiovascular disease: synopsis of the evidence available from systematic reviews and meta-analyses. *Nutrients* 2012; 4: 1989-2007.
10. Thagaard IN, Hedley PL, Holm JC, Lange T, Larsen T, Krebs L, Christiansen M. Leptin and Adiponectin as markers for preeclampsia in obese pregnant women, a cohort study. *Pregnancy Hypertens* 2019; 15: 78-83.
11. Robinson NJ, Minchell LJ, Mys JE, Hubel CA, Crocker IP. A potential role for free fatty acids in the pathogenesis of preeclampsia. *J Hypertens* 2009; 27: 1293-1302.
12. Herlambang H, Puspasari A, Maharani C, Enis RN, Tarawifa S, Fitri AD, Harahap H, Harahap AH, Kusdiyah E, Syamsunarno MRAA. Comprehensive fatty acid fractionation profiling in preeclampsia: a case control study with multivariable analysis. *BMC Pregnancy Childbirth* 2022; 22: 8.
13. Zorena K, Jachimowicz-Duda O, Ślęzak D, Robakowska M, Mrugacz M. Adipokines and Obesity. Potential Link to Metabolic Disorders and Chronic Complications. *Int J Mol Sci* 2020; 21: 3570.
14. Masuzaki H, Ogawa Y, Sagawa N, Hosoda K, Matsumoto T, et al. (1997) Nonadipose tissue production of leptin: leptin as a novel placenta-derived hormone in humans. *Nat Med* 3: 1029-1033