

## ORIGINAL ARTICLE

**Association of Serum Leptin with Gestational Diabetes Mellitus**SHAIMA SULTANA MEMON<sup>1</sup>, FIZZAH ALI<sup>2</sup>, SOHA HAQUE<sup>3</sup>, SAADIA SAAD<sup>4</sup>, ZAFAR IQBAL<sup>5</sup>, UZMA IFTIKHAR<sup>6</sup><sup>1</sup>Assistant Professor, Department of Pathology, Dow Medical College, Dow University of Health Sciences, Karachi<sup>2</sup>Assistant Professor, Department of Pharmacology, Liaquat National Medical and Dental College, Karachi.<sup>3</sup>Lecturer, Department of Pharmacology, Ziauddin Medical College, Ziauddin University, Karachi<sup>4</sup>BDS, M.Phil scholar, Department of Oral Biology, Baqai Dental College, Baqai University, Karachi.<sup>5</sup>Assistant Professor, Department of Preventive and Community Dentistry, Bhattai Dental and Medical College, Mirpurkhas<sup>6</sup>Professor, Department of Physiology, United Medical and Dental College, KarachiCorresponding author: Shaima Sultana Memon, Email: [Shaimanabeel@yahoo.com](mailto:Shaimanabeel@yahoo.com)**ABSTRACT**

**Background:** It has been stated that leptin has a role in glucose regulation as it decreases the insulin resistance and regulates the insulin mediated glucose metabolism. As the body need more glucose, more secretion of insulin which stimulates adipose tissues to secrete more leptin which causes the release of cytokines which decreases insulin sensitivity and develop insulin resistance. The aim of the current study was to find out the association of serum leptin with gestational diabetes mellitus in current setting.

**Methods:** A case control study was conducted at the Gynecology department of Abbasi Shaheed Hospital Karachi during April to September 2022. A self-designed proforma was used, consisting of 4 parts consisting of demographic variables, general physical examination and laboratory findings. Blood sample was collected during 24<sup>th</sup> to 28<sup>th</sup> week of gestation for testing fasting blood sugar, OGTT and then ELISA was done. Statistical Package for Social Science (SPSS) version-20 was used to analyze the data. p-value  $\leq 0.05$  was considered as significant.

**Results:** The mean age of the study participants was  $27.42 \pm 0.39$  and  $24.96 \pm 0.51$  in cases and controls respectively. The basal metabolic index (BMI) was higher among the cases of gestational diabetes as compared to normal controls. Likewise, oral glucose tolerance test results showed higher levels of blood glucose than the normal controls during all steps of the test. The comparison of serum insulin and serum leptin during pregnancy and after delivery in cases of gestational diabetes showed a decrease in both serum insulin and serum leptin levels with significant p-value (p-value  $\leq 0.05$ ).

**Conclusion:** Leptin is the contributory factor of insulin resistance and leads to gestational diabetes mellitus. Both serum insulin and serum leptin levels were having strong significant association with gestational diabetes mellitus.

**Keywords:** Gestational diabetes mellitus, Serum Leptin, Hyperinsulinemia

**INTRODUCTION**

There is a list of pregnancy induced physiological changes including increased appetite, fat accumulation in the body and gradually developing insulin resistance (1). In the first trimester of pregnancy, the metabolic rate suddenly increases so the cells need more glucose and more insulin for glucose entry into the cell. The body compensate it by increasing the secretion of insulin on the other hand, fat cells in the mother body also increases with time resulting in developing insulin resistance progressively. From the start of second trimester insulin resistance develop markedly, just to maintain normal blood glucose level body needs to secrete insulin double of normal. If there is any abnormality in this normal physiological process, the compensatory mechanism fails to develop resulting in gestational diabetes (2). Underlying pathology of gestational diabetes include either the body is producing little insulin and can't fulfil the demand or the body cells are developing resistance against insulin (3).

Another pregnancy induced physiological change in the body is increased appetite and increased food intake resulting in increased production of leptin, as there is insulin resistance so leptin fails to stimulate satiety center in hypothalamus. If there is leptin deficiency or the body produce resistance against leptin, there will be increased food uptake which leads to obesity (4). As the fat cells increasing so producing more leptin besides that additional leptin is produced by the placenta as well. It has been observed that the serum leptin level is highest at 28<sup>th</sup> week of pregnancy then it decreases gradually and returns to normal soon after delivery because of the removal of placenta from the body (5). It has been stated that leptin has a role in glucose regulation as it decreases the insulin resistance and regulates the insulin mediated glucose metabolism and also regulates the gluconeogenesis in in the liver (6, 7).

Literature revealed that during pregnancy, the mRNA receptors of leptin decreases resulting in developing leptin resistance in the body. During first trimester of pregnancy, the marked increase in serum leptin level, is a predictor of gestational diabetes in the second trimester of pregnancy (8). It is a vicious cycle, as the body need more glucose, more secretion of insulin

which stimulates adipose tissues to secrete more leptin which causes the release of cytokines including interleukin-6 and tumor necrosis factor-alpha (TNF-  $\alpha$ ), resulting in inflammation which further stimulates the secretion of leptin. On the other hand, the interleukin-6 and tumor necrosis factor-alpha (TNF-  $\alpha$ ) also decrease insulin sensitivity and develop insulin resistance so increased level of insulin in blood increases leptin level (9). Very few of the studies has been done in Pakistan to find out the association between serum leptin and gestational diabetes mellitus. So the aim of the current study was to find out the association of serum leptin with gestational diabetes mellitus in current setting.

**MATERIAL AND METHODS**

A case control study was conducted at the Gynecology department of Abbasi Shaheed Hospital Karachi during April to September 2022. Study got ethical approval from the concerned institute. Sample size was calculated by using the OpenEpi calculator and was 50 cases with gestational diabetes mellitus and 50 normal controls (case to control ratio 1:1). The inclusion criteria for the cases was the pregnant women with age group between 18-40 years, diagnosed case of gestational diabetes mellitus within 24<sup>th</sup> to 28<sup>th</sup> week of gestation. Oral glucose tolerance test (OGTT) was used to confirm the gestational diabetes mellitus. The control group included normal pregnant women with no gestational diabetes mellitus. The exclusion criteria were known case of metabolic disorders, previously diagnosed case of diabetes mellitus, pre-eclampsia or any other pregnancy related complication. Both the cases and controls were followed for four weeks postpartum.

A self-designed proforma was used, consisting of 4 parts. The first part was of demographic variables like age, period of gestation, past history of gestational diabetes mellitus, family history of diabetes mellitus, past medical and surgical history and drug history. Second part consisted of general physical examination in which weight, height, body mass index and blood pressure was noted. Third part consisted of laboratory reports of oral glucose tolerance test (OGTT) and enzyme linked

immunosorbent assay (ELISA). Blood sample was collected during 24<sup>th</sup> to 28<sup>th</sup> week of gestation for testing fasting blood sugar and then OGTT was performed for the confirmation of gestational diabetes mellitus. After that ELISA was done to measure serum insulin and serum leptin levels.

Statistical Package for Social Science (SPSS) version-20 was used to analyze the data. All the numerical variables were calculated as mean with standard deviation. Paired t-test was used to find out the association of serum insulin and serum leptin during pregnancy and after delivery. p-value less than 0.05 was considered as significant.

## RESULTS

The mean age of the study participants was  $27.42 \pm 0.39$  and  $24.96 \pm 0.51$  in cases and controls respectively. The basal metabolic index (BMI) was higher among the cases of gestational diabetes as compared to normal controls. Likewise, oral glucose tolerance test results showed higher levels of blood glucose than the normal controls during all steps of the test including fasting glucose level, after 1 hour of giving glucose and after 2 hours. Serum insulin and serum leptin levels in gestational diabetes cases were  $25.97 \pm 0.52$  mIU/L and  $29.77 \pm 0.82$  ng/ml respectively which were comparatively higher than control group as mentioned in Table 1.

Table 1: Characteristics of study participants

| Variables                                  | Cases            | Controls         |
|--|------------------|------------------|
| Age (years)                                | $27.42 \pm 0.39$ | $24.96 \pm 0.51$ |
| Basal metabolic index (kg/m <sup>2</sup> ) | $27.12 \pm 0.92$ | $22.49 \pm 0.47$ |
| OGTT fasting (mmol/L)                      | $5.87 \pm 0.34$  | $3.99 \pm 0.10$  |
| OGTT after 1 hour (mmol/L)                 | $14.40 \pm 0.22$ | $9.0 \pm 0.19$   |
| OGTT after 2 hours (mmol/L)                | $11.21 \pm 0.10$ | $7.11 \pm 0.12$  |
| Serum insulin (mIU/L)                      | $25.97 \pm 0.52$ | $15.02 \pm 0.23$ |
| Serum Leptin (ng/ml)                       | $29.77 \pm 0.82$ | $13.19 \pm 0.25$ |

The comparison of serum insulin and serum leptin during pregnancy and after delivery in cases of gestational diabetes, was done and the results found that both serum insulin and serum leptin levels were decreased after delivery and had a significant association as p-value was less than 0.05.

Table 2: Serum insulin and serum leptin levels in cases of gestational diabetes during pregnancy and after delivery

|                       | Cases            |                 | p-value |
|-----------------------|------------------|-----------------|---------|
|                       | During Pregnancy | After Pregnancy |         |
| Serum Insulin (mIU/L) | $24.21 \pm 2.4$  | $17.98 \pm 1.0$ | 0.000   |
| Serum Leptin (ng/ml)  | $34.11 \pm 1.7$  | $15.87 \pm 1.2$ | 0.002   |

## DISCUSSION

Current study found that those females who have gestational diabetes mellitus were having higher level of serum insulin and serum leptin as compared to the control group but during post-partum period the serum leptin level decreases in both cases as well as control group. The most possible reason for the rise of serum leptin level might be the excess adipose tissue and high level of serum insulin due to insulin resistance (11). Some of the hormones are responsible for insulin resistance during pregnancy including human placental lactogen (HPL), prolactin, glucocorticoid and progesterone leading to hyperinsulinemia (12). Adipose tissues are the source of leptin production but during pregnancy placenta becomes an additional source of leptin that is why soon after delivery the leptin level suddenly fall (13).

Current results are favored by many studies like one of the cohort study reported a strong significant association between serum leptin level and gestational diabetes mellitus while BMI and other risk factors were the independent variable (14). Likewise, a case control study was conducted by Saini et.al and found a strong positive association between serum leptin and gestational diabetes mellitus but on the other hand found a negative association of adiponectin with gestational diabetes mellitus (15). Bomba et al

also conducted a case control study in which he took 36 cases of gestational diabetes mellitus and 24 normal controls, results revealed that both serum insulin and serum leptin levels were higher in gestational diabetes mellitus cases and he concluded a positive association between serum insulin and serum insulin in gestational diabetes mellitus (16).

Current study also found that BMI was high in cases of gestational diabetes mellitus as compared to normal controls, the finding is an evident of the fact that accumulation of adipose tissue is an important risk factor for developing resistance in cases of gestational diabetes mellitus. Mazor et.al favored the current finding, he did an experimental study on animal and concluded that obesity is a promoting factor of leptin resistance as it activates matrix metalloproteinase-2 enzyme in hypothalamus thus blocking the peripheral receptors of leptin so reduces the leptin sensitivity (1).

## CONCLUSION

It can be concluded that serum leptin level is increased during pregnancy while the adipose tissues and placenta are the source of leptin production. Leptin is the contributory factor of insulin resistance and leads to gestational diabetes mellitus. Both serum insulin and serum leptin levels were having strong significant association with gestational diabetes mellitus so the serum leptin can be an initial screening tool for the diagnosis of gestational diabetes mellitus.

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