Adipokine levels and their association with insulin resistance and fetal outcomes among the newborns of Indian gestational diabetic mothers

Balachandiran Manoharan, MSc, Zachariah Bobby, PhD, Gowri Dorairajan, MD, Vickneshwaran Vinayagam, MSc, Rajaa Muthu Packirisamy, MSc.

ABSTRACT

Objectives: To investigate the cord blood levels of adipokine and to assess their association with the fetal insulin resistance and fetal outcomes in newborns of gestational diabetic women (GDM).

Methods: This cross-sectional study was performed in 40 GDM women and 40 healthy pregnant women (HPW) in the Department of Obstetrics and Gynecology at Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) hospital in Puducherry, India, during the period from May 2016 to December 2017. Cord blood samples were collected at delivery from GDM and HPW groups. Cord plasma biochemical parameters such as insulin, C-peptide, adiponectin, leptin, resistin, and visfatin concentrations were measured. Leptin/adiponectin ratio (L/A), homeostasis model assessment of insulin resistance (HOMA2-IR), insulin sensitivity (HOMA2-%S) and beta cell function (HOMA2-%B) were calculated. The pregnancy outcomes such as birth weight (BW), Ponderal index and Apgar scores of the baby were measured.

Results: The BW and Ponderal index of the baby were found to be significantly higher in GDM newborns compared to HPW newborns. Cord plasma insulin, C-peptide, HOMA2 –IR, visfatin, leptin, and L/A ratio were significantly higher whereas adiponectin level was lower in GDM compared to HPW. A significant positive correlation was observed between L/A ratio and fetal HOMA2-IR.

Conclusion: Altered adipokine levels with increased L/A ratio was observed among the new-borns of Indian gestational diabetic mothers. There was an association between increased L/A ratio, insulin resistance and increased Ponderal index among the new-borns.
Gestational diabetes mellitus (GDM) is characterized by any degree of maternal glucose intolerance developed or first detected during pregnancy. The prevalence of GDM among Indian pregnant women is around 17% in comparison with other populations which is around 4%. Gestational diabetes mellitus is associated with adverse maternal and fetal complications such as shoulder dystocia, respiratory distress, neonatal hypoglycemia, hyperbilirubinemia, and macrosomia. Furthermore, GDM mothers and their offspring are at an increased risk of developing type 2 diabetes mellitus (T2DM), metabolic syndrome (MetS) and cardiovascular complications later in their life. Children of Indian GDM mothers are associated with obesity, insulin resistance and cardiovascular complications. The prevalence of T2DM has significantly increased in India showing as high as 13%. This indicates that the increased cases of GDM may account for the higher prevalence of T2DM in India. However, the underlying mechanisms of transmission of metabolic diseases to offspring in GDM are unknown. The intrauterine environment of GDM women can have adverse effects on their newborns. Maternal hyperglycemia translates into fetal hyperglycemia and hyperinsulinemia which lead to excess fat deposition in adipose tissue of the fetus resulting in adiposity. However, maternal hyperglycemia causes excessive oxidative stress in growing fetus resulting in congenital anomalies and fetal priming for future metabolic diseases in GDM newborns. A recent study in Chinese GDM newborns has shown higher fetal insulin resistance and is correlated with maternal insulin resistance. However, so far no studies were carried out in Indian GDM women regarding the level of fetal insulin resistance in their newborns. Adipokines are secreted by adipose tissue with paracrine and endocrine properties. Adipokines such as leptin, adiponectin, resistin, and visfatin are involved in body weight regulation, insulin resistance, lipid metabolism, and adiposity. Leptin and adiponectin are involved in the pathogenesis of metabolic diseases such as obesity, T2DM, and GDM. Studies have shown that increased maternal leptin and decreased adiponectin levels in GDM women are involved in the development of insulin resistance. Recent studies have shown that there is altered maternal visfatin and resistin levels in GDM women but their role in the pathogenesis of GDM remains unclear. However, the role of adipokines in the development of insulin resistance in newborns of GDM mothers is not yet fully explored. There are only limited studies reported on the levels of these adipokines in the newborns of GDM women with conflicting results. Furthermore, there are no studies carried out among the newborns of GDM women from India on the relationship between adipokine levels and the pathogenesis of GDM. That is quite significant considering India as the diabetic capital of the world. No studies have been carried out so far on the levels of adipokine in the cord blood of Indian GDM newborns. Thus, we hypothesized that there is an altered adipokine level in newborns of GDM women. Further, this could be involved in the development of fetal insulin resistance and fetal adiposity. The present study aimed to investigate the cord blood levels of adipokine and to assess their relationship with insulin resistance, beta cell function, and fetal outcomes in newborns of Indian pregnant women with GDM.

**Methods.** This was a cross-sectional study carried out in the Department of Biochemistry and Obstetrics & Gynecology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) Hospital, Puducherry, India after obtaining approval from JIPMER Scientific Advisory Committee (Approval no: JSAC 32/6/2016) and the Institute Ethics Committee (Approval no: JIP/IEC/2016/25/825). The study was conducted between May 2016 and Dec 2017 on a South Indian Tamil population recruited from the Department of Obstetrics and Gynecology according to the ethical guidelines of Indian Council of Medical Research for Biomedical research on human participants.

A total of 80 primi pregnant women were recruited for this cross-sectional study. All consecutive GDM patients on insulin therapy were recruited for this study. Women with GDM were diagnosed based on the International Association of Diabetes and Pregnancy Study Groups criteria. Primi gravidae pregnant women with GDM on insulin therapy (n=40) and healthy pregnant women (HPW) without any complications (n=40) in the age group of 18-30 years were included in the present study. We calculated the sample size using the Open Epi program 9 (Open Source Epidemiology statistics for Public Health, version 3.03). The calculation was based on a confidence interval of 95%, power as 90 and ratio of sample size as 1. Women with gestational diabetes mellitus on medical nutrition therapy, hypothyroidism, pre-existing glucose intolerance, pregnancy-induced hypertension, polycystic ovarian syndrome, major vascular complications, known infections in current

**Disclosure.** Authors have no conflict of interests, and the work was not supported or funded by any drug company.
Adipokine levels of GDM newborns... Manoharan et al

pregnancy and autoimmune disorders were excluded from the study.

**Data and blood sample collection.** Five milliliters of umbilical cord blood was collected immediately after delivery from all study subjects. Plasma was separated by centrifugation at 3500 rpm for 10 min and stored immediately at -40°C until further analysis. Maternal characteristics such as age, pre-pregnancy body mass index (BMI) and maternal weight gain were recorded. Fetal outcomes such as gestational age at the time of delivery, birth weight, and length were documented. Apgar scores were also noted soon after delivery at one minute and at 5 minutes. Newborns appearance, pulse, grimace response, activity (muscle tone) and respiratory rate have been considered for Apgar score and was recorded on a scale of 0 to 2. Ponderal Index (PI) was calculated by the formula: PI= birth weight (g)/birth length (3 cm) x 100.

**Measurement of biochemical parameters.** Biochemical parameters such as cord plasma glucose and lipid profile were estimated using enzymatic kits with Olympus AU400 fully automated Clinical Chemistry Analyser (Beckman Coulter, USA). Cord plasma insulin (Diasource Immunoasays S.A, Belgium, with sensitivity 0.17 μIU/ml, intra-assay CV 4.8-6.0% and inter-assay CV 8.1-9.0%) C-peptide (Sigma diagnostics, Livonia, USA, with assay sensitivity 0.2 ng/ml), leprin (DBC Inc, Canada, with sensitivity 0.50 ng/ml, intra-assay CV 3.7 - 5% and inter-assay CV 5.8%), adiponectin (Assaypro, St. Charles, MO, with sensitivity 0.3 ng/ml, intra-assay CV 4.4% and inter-assay CV 9.9%), resistin (Raybiotech, Suite 100 Norcross, GA, with sensitivity 2pg/ml, intra-assay CV <10% and inter-assay CV <12%) and visfatin (Raybiotech, Suite 100 Norcross, GA, with sensitivity 0.778 ng/ml, intra-assay CV <10% and inter-assay CV <15%) were measured by above mentioned ELISA kits.

**Assessment of insulin resistance, insulin sensitivity, and beta cell function.** A computer-based programme called HOMA calculator version 2.2.2 (University of Oxford) was used to calculate the homeostasis model assessment of insulin resistance (HOMA2-IR), insulin sensitivity (HOMA2-%S) and beta cell function (HOMA2-%B) from the values of cord plasma glucose and insulin levels.²¹,²²

**Statistical analysis.** The data were analyzed using the Statistical Package of Social Service (Version 19, SPSS Inc., Chicago, IL, USA). Descriptive data were shown as mean ± standard deviation (SD). Kolmogorov-Smirnov test was used to see the normal distribution of parameters studied. Comparison between the means of 2 groups was analyzed by unpaired Student’s t-test. The differences in percentages of categorical variables were carried out by using a Chi-square test. Pearson’s correlation was applied to assess the correlation between anthropometric and biochemical parameters. A p-value less than 0.05 was considered as statistically significant.

**Results.** **Maternal and neonatal characteristics.** Table 1 shows maternal and neonatal characteristics of all pregnant women involved in this study. There was no significant difference found in the mean age, pre-pregnancy BMI, Apgar scores between the groups. However, birth weight (2.87 ± 0.44 versus 3.18 ± 0.46) and PI of the babies (2.71 ± 0.37 versus 3.04 ± 0.47) were significantly higher (p<0.05) among GDM newborns in comparison with HPW newborns.

**Fetal insulin resistance, insulin sensitivity and beta cell function of HPW and GDM newborns.** Table 2 presents parameters of fetal HOMA2-IR, HOMA2-%S and HOMA2-%B of HPW and GDM newborns. No significant differences were noted for cord plasma glucose levels among HPW and GDM newborns. Cord plasma insulin, C-peptide, and HOMA2-IR levels were significantly higher (p<0.05) whereas HOMA-%S level was significantly lower (p<0.05) in GDM newborns when compared with HPW newborns.

**Cord plasma lipid profile and adipokine levels of HPW and GDM newborns.** Table 3 shows the cord plasma lipid profile and adipokine levels of healthy pregnant and GDM newborns. No significant changes were noted for cord plasma total cholesterol, LDL cholesterol, HDL cholesterol and resistin levels among HPW and GDM newborns. Cord plasma TG, VLDL

---

### Table 1 - Maternal and neonatal characteristics of the study groups.

| Characteristics                  | HPW (n=40) | GDM (n=40) | P-value |
|----------------------------------|------------|------------|---------|
| Age (years)                      | 24.26 ± 2.17 | 24.14 ± 2.46 | 0.124   |
| Prepregnancy BMI (kg/m²)         | 22.19 ± 1.00 | 22.14 ± 2.58 | 0.342   |
| Maternal weight gain (kg)        | 9.95 ± 0.97 | 10.38 ± 0.86 | 0.176   |
| Gestational age at delivery (weeks) | 39.36 ± 1.05 | 38.52 ± 1.06 | 0.082   |
| Caesarean section (n (%))        | 11 (27.5%) | 13 (32.5%) | 0.348   |
| Birth weight (kg)                | 2.87 ± 0.44 | 3.18 ± 0.46* | 0.009   |
| Ponderal index (g/cm³)           | 2.71 ± 0.37 | 3.04 ± 0.47* | 0.003   |
| Apgar 1’ score                   | 8.11 ± 0.32 | 7.90 ± 0.54  | 0.149   |
| Apgar 5’ score                   | 9.11 ± 0.32 | 8.95 ± 0.38  | 0.118   |
| LGA newborn (n (%))              | 02 (5.0%)  | 07 (17.5%)  | 0.077   |
| Neonatal hypoglycemia (n (%))    | 01 (2.5%)  | 05 (12.5%)  | 0.090   |

BMI - body mass index, HPW - healthy pregnant women,
GDM - insulin controlled gestational diabetes mellitus, LGA - large for gestational age, *p<0.05 is considered statistically significant, descriptive data were expressed as mean ± S.D and categorical data expressed as numbers and percentage.

---

www.smj.org.sa  Saudi Med J 2019; Vol. 40 (4) 355
Adipokine levels of GDM newborns... Manoharan et al

cholsterol and adiponectin levels were significantly lower ($p<0.05$) whereas cord serum leptin, L/A ratio and visfatin levels were significantly higher ($p<0.05$) in GDM newborns when compared with HPW newborns.

Correlations between fetal insulin resistance and various metabolic parameters in newborns of GDM women. In the GDM newborns, PI of babies was positively correlated to cord blood insulin, C-peptide, HOMA-IR, leptin and L/A ratio and negatively correlated to HOMA-%S (Table 4). In the GDM newborns L/A ratio was positively correlated with HOMA-IR levels ($r=0.438$, $p<0.05$) (Figure 1) and negatively correlated with HOMA-%S ($r=-0.438$, $p<0.05$). No correlations were found between visfatin and fetal insulin resistance. However, there was a negative correlation between visfatin levels with total cholesterol ($r=-0.335$), LDL cholesterol ($r=-0.414$), and TG levels ($r=-0.465$, $p<0.05$) in GDM newborns.

Table 2 - Fetal insulin resistance, insulin sensitivity and beta cell function of healthy pregnant and GDM newborns.

| Parameters          | HPW (n=40) | GDM (n=40) | P-value |
|---------------------|------------|------------|---------|
| Glucose (mg/dl)     | 89.13 ± 24.46 | 79.25 ± 22.95 | 0.180   |
| Insulin (µIU/ml)    | 11.34 ± 4.13  | 19.73 ± 6.17* | 0.000   |
| C-Peptide (ng/ml)   | 1.42 ± 0.49   | 2.91 ± 0.97* | 0.011   |
| HOMA2-%B            | 123.04 ± 39.92 | 149.40 ± 43.72 | 0.087   |
| HOMA2-%S            | 139.73 ± 41.30 | 90.38 ± 32.59* | 0.003   |
| HOMA2-IR            | 0.66 ± 0.25   | 1.48 ± 0.34* | 0.000   |

*HOMA2-IR - homeostasis model assessment of insulin resistance, HOMA2-%S - insulin sensitivity, HOMA2-%B - beta cell function. *$p<0.05$ is considered statistically significant, GDM - insulin controlled gestational diabetes mellitus, data were expressed as mean ± SD

Table 3 - Cord plasma lipid profile and adipokine levels of healthy pregnant and GDM newborns.

| Parameters          | HPW (n=40) | GDM (n=40) | P-value |
|---------------------|------------|------------|---------|
| TG (mg/dl)          | 68.80 ± 22.19 | 44.00 ± 19.79* | 0.008   |
| TC (mg/dl)          | 76.64 ± 18.58 | 79.81 ± 32.48 | 0.367   |
| LDL-C (mg/dl)       | 35.30 ± 12.27 | 37.50 ± 18.46 | 0.866   |
| HDL-C (mg/dl)       | 28.66 ± 7.78  | 27.93 ± 6.15 | 0.611   |
| VLDL-C (mg/dl)      | 13.76 ± 4.63  | 8.80 ± 4.25* | 0.008   |
| Adiponectin (µg/ml) | 33.39 ± 12.92 | 22.20 ± 10.65* | 0.024   |
| Leptin (ng/ml)      | 54.72 ± 22.81 | 88.74 ± 28.48* | 0.006   |
| Leptin/adiponectin  | 1.48 ± 0.48   | 3.72 ± 0.64* | 0.000   |
| Resistant (ng/ml)   | 12.67 ± 5.30  | 7.19 ± 4.28* | 0.608   |
| Visfatin (ng/ml)    | 7.78 ± 3.83   | 10.51 ± 4.28* | 0.005   |

*TG - triglycerides, TC - total cholesterol, LDL-C - low-density lipoprotein - cholesterol, HDL-C - high-density lipoprotein - cholesterol, VLDL-C - very low-density lipoprotein – cholesterol, *$p<0.05$ is considered statistically significant, data were expressed as mean ± SD

Table 4 - Correlations between the Ponderal index and fetal metabolic parameters in newborns of GDM group.

| Neonatal Ponderal index |      |      |
|-------------------------|------|------|
| Parameter               | $r$  | $P$-value |
| Insulin                 | 0.397 | 0.028 |
| C-peptide               | 0.445 | 0.032 |
| HOMA2-IR                | 0.408 | 0.011 |
| HOMA2-%S                | -0.408 | 0.020 |
| Leptin                  | 0.428 | 0.022 |
| Leptin/adiponectin ratio| 0.594 | 0.001 |

$r$ - Pearson’s coefficient, *$p<0.05$ considered as statistically significant, HOMA2-IR - homeostasis model assessment of insulin resistance and HOMA2-%B - beta cell function.

Discussion. The most significant findings of this study were higher fetal insulin resistance and lower insulin sensitivity among the newborns of Indian GDM pregnant women when compared to HPW newborns. Further, increased cord plasma leptin, L/A ratio, visfatin levels and PI were observed in GDM newborns. A decreased cord plasma adiponectin was observed in GDM newborns and the L/A ratio positively correlated with fetal insulin resistance. These observations suggest that newborns of Indian GDM mother with higher insulin resistance and altered adipokine levels are associated with fetal adiposity.

The rapid increase in the prevalence of T2DM and metabolic syndrome in the general population has become a worldwide problem in all countries. India is the diabetic capital of the world with 72 million diabetic patients and this is expected to double by 2025. The prevalence of T2DM among Indians is 13% and GDM is 17%.3,11 Besides the lifestyle, GDM has an impact on the development of T2DM and obesity. Children of Indian GDM mothers are associated with adiposity, insulin resistance and cardiovascular complications.10 It is clear that the offspring of GDM women are more prone to develop T2DM and obesity later in their adult life. However, the underlying mechanism of fetal priming of metabolic diseases in GDM newborns is unknown. Recent studies reveal that adverse intrauterine milieu such as hyperglycemia and heightened oxidative stress can affect the fetal growth and are involved in fetal programming for future disease.23

Adipokines such as leptin, adiponectin, resistin, and visfatin are secreted from maternal adipose tissue and placenta. They are involved in the regulation of body weight, insulin resistance, lipid metabolism, adipogenesis, and inflammation. Several studies have shown the altered levels of adipokine and its association with insulin resistance in pregnant women.
Adipokine levels of GDM newborns... Manoharan et al

with GDM. Adiponectin is an anti-inflammatory adipokine involved in glucose and lipid metabolism and enhances insulin sensitivity through increased fatty acid oxidation and inhibition of hepatic glucose production. It has been shown that adiponectin improves insulin resistance and reduces fasting glucose level through activating AMP-kinase and PPAR-α. A decreased level of adiponectin was reported in GDM women and is an independent negative predictor of gestational diabetes mellitus. Leptin is a pro-inflammatory adipokine involved in body weight regulation and glucose metabolism by regulating food intake. Moreover, leptin suppresses the secretion of insulin from pancreatic β cells. Studies reported that homozygous mutations in the leptin or leptin receptor (OB-R) genes create obese, insulin resistant and diabetic mice. Increase or unaltered leptin levels were reported in GDM women. Leptin levels are positively associated with increased body weight, insulin resistance, and inflammation. Leptin/adiponectin ratio (L/A ratio) is a potential parameter used to evaluate insulin resistance in patients with metabolic syndrome, T2DM and in GDM. Although leptin or adiponectin levels are independently associated with risk for the development of MetS and T2DM, the risk association is stronger with L/A ratio. Maternal visfatin and resistin levels were reported in GDM with conflicting results. Visfatin has insulin-mimetic effects by binding to the insulin receptor. It is associated with markers of obesity, insulin resistance, and metabolic syndrome. The role of resistin in the pathogenesis of GDM is unknown. This suggests that adipokines play a major role in the pathogenesis of GDM by modulating the insulin secretion, insulin sensitivity, and insulin resistance. However, only limited studies reported the cord blood levels of adipokine in newborns of GDM women and its association with the fetal insulin resistance, beta cell function, and fetal adiposity. The present study aimed to investigate the cord blood levels of adipokine and to assess their relationship with insulin resistance, beta cell function and fetal outcomes in newborns of Indian pregnant women with GDM.

In this study, we found significantly higher levels of cord plasma insulin, C-peptide, and HOMA2-IR and lower levels of HOMA2-%S in GDM newborns. These findings suggest that newborns of Indian GDM mother and more prone to develop insulin resistance. These observations are in agreement with previous reports from other populations. There was no impairment in the beta cell function among the newborns of GDM mothers as supported by other studies. These results reveal that the newborns of GDM mothers are at increased of insulin resistance than beta cell dysfunction.

In our study, we found an increased cord plasma leptin and decreased adiponectin levels in newborns of GDM when compared to HPW newborns. Similar results have been reported with newborns of GDM mothers with higher leptin concentrations and decreased adiponectin levels. Cord plasma leptin levels were reported to be positively correlated with fetal adiposity. In our study, we found a positive correlation of leptin levels with a PI of the babies. We also found an increased L/A ratio in the GDM newborns and it had a strong positive correlation with fetal HOMA2-IR. These observations suggest that altered levels of leptin and adiponectin affect the fetal insulin resistance which favors fetal adiposity in newborns of GDM mothers.

The levels of fetal resistin were reported to be either not altered or elevated in GDM newborns as compared to HPW newborns. We found no differences in fetal resistin levels between GDM and HPW groups. Further studies are needed to explain the role of resistin in fetal metabolism. Decreased cord plasma visfatin levels have been reported in GDM. However, we found that visfatin was significantly increased in GDM newborns when compared to HPW newborns. This finding is supported by the fact that the circulating visfatin concentrations have been shown to increase in parallel with glucose administration. No correlations were found between visfatin and insulin resistance. However, it showed a negative correlation with total cholesterol, LDL-cholesterol and TG levels among the GDM newborns. In the GDM group, we found a decreased TG and VLDL-cholesterol levels in

![Figure 1 - Correlation of fetal HOMA - IR with fetal L/A ratio. L/A ratio - leptin / adiponectin ratio, Pearson correlation test, p<0.001.](image-url)
the cord blood. Similar results were reported in other studies.\textsuperscript{49,50} Studies have shown that cord blood TG levels were negatively correlated with birth weight, resulting in significantly higher TG levels in SGA newborns compared with AGA or LGA infants of GDM pregnancy.\textsuperscript{51} This shows that visfatin plays a role in fetal lipid metabolism and adiposity.

**Study Limitations.** We recruited only primi pregnant women to avoid the impact of metabolic changes caused by previous pregnancies. We excluded GDM mothers with co-morbidities such as hypothyroidism and hypertension, and so forth which may influence our results. The main limitation of the present study is the smaller sample size. Further GDM mothers were on insulin therapy would have influenced our results.

In conclusion, altered adipokine levels with increased L/A ratio was observed among the newborns of Indian gestational diabetic mothers. There was an association between increased L/A ratio, insulin resistance, and increased PI among the newborns.

We recommend future studies with a larger sample size to clarify the exact role of these adipokines in the development of fetal insulin resistance and fetal adiposity. Further studies are needed to use these adipokines as a predictor of future development of T2DM and other metabolic diseases in GDM offsprings.

**Acknowledgment.** We are grateful to Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India for providing research grant for Ph.D. scholar (Grant sanction order No. JIP/Red/Intra-PhD/PhD1/0112016-17, dated 09 Sep 2016). Also, we thank the Department of Biotechnology (DBT), India for providing financial support for the conduct of this study.

**References**

1. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003; 26: 55-520.
2. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2004; 27: 588-590.
3. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. J Assoc Physicians India 2004; 52: 707-711.
4. Yue DK, Molyneaux LM, Ross GP, Constantino MI, Child AG, Turtle JR. Why does ethnicity affect prevalence of gestational diabetes? The underwater volcano theory. Diabet Med 1996; 13: 748-752.
5. Beischer NA, Wein P, Sheedy MT, Steffen B. Identification and treatment of women with hyperglycaemia diagnosed during pregnancy can significantly reduce perinatal mortality rates. Aust NZ J Obstet Gynaecol 1996; 36: 239-247.
6. HAPO Study Cooperative Research Group. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycaemia and adverse pregnancy outcomes. N Engl J Med 2008; 358: 1991-2002.
7. Metzger BE. Long-term outcomes in mothers diagnosed with gestational diabetes mellitus and their offspring. Clin Obstet Gynecol 2007; 50: 972-979.
8. Catalano PM, Kirwan JP, Haugel-de Mouzon S, King J. Gestational diabetes and insulin resistance: role in short- and long-term implications for mother and fetus. J Nutr 2003; 133: S1674-S1683.
9. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009; 373: 1773-1779.
10. Krishnaveni GV, Veena SR, Hill JC, Kehoe S, Karat SC, Fall CH. Intrauterine exposure to maternal diabetes is associated with higher adiposity and insulin resistance and clustering of cardiovascular risk markers in Indian children. Diabetes Care 2010; 33: 402-404.
11. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol 2017; 5: 585-596.
12. Pedersen J. Weight and length at birth of infants of diabetic mothers. Acta Endocrinol (Copenh) 1954; 16: 330-342.
13. Eriksson UJ. Congenital anomalies in diabetic pregnancy. Semin Fetal Neonatal Med 2009; 14: 85-93.
14. Wang Q, Huang R, Yu B, Cao F, Wang H, Zhang M, et al. Higher fetal insulin resistance in Chinese pregnant women with gestational diabetes mellitus and correlation with maternal insulin resistance. PLoS One 2013; 8: e59845.
15. Cseh K, Baranyi E, Melczer Z, Csákány GM, Speer G, Kovács M, et al. The pathophysiological influence of leptin and the tumor necrosis factor system on maternal insulin resistance: negative correlation with anthropometric parameters of neonates in gestational diabetes. Gynecol Endocrinol 2002; 16: 453-460.
16. Yamauchi T, Kamon J, Minokoshi Y, Ito Y, Waki H, Uchida S, et al. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. Nat Med 2002; 8: 1288-1295.
17. Liang Z, Wu Y, Xu J, Fang Q, Chen D. Correlations of serum visfatin and metabolisms of glucose and lipid in women with gestational diabetes mellitus. J Diabetes Investig 2016; 7: 247-252.
18. Bao W, Baekker A, Song Y, Kiely M, Liu S, Zhang C. Adipokine levels during the first or early second trimester of pregnancy and subsequent risk of gestational diabetes mellitus: A systematic review. Metabolism 2015; 64: 756-764.
19. Li JI, Rifa-Shiman SL, Aris IM, Young JG, Mantzoros C, Hivert MF, et al. Associations of maternal and cord blood adipokines with offspring adiposity in Project Viva: is there an interaction with child age? Int J Obes 2018; 42: 608-617.
20. Weinert LS. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycaemia in pregnancy: comment to the International Association of Diabetes and Pregnancy Study Groups Consensus Panel. Diabetes Care 2010; 33: e97.
21. Kumar H, Mishra M, Bajpai S, Pokhria D, Arya AK, Singh RK, et al. Correlation of insulin resistance, beta cell function and insulin sensitivity with serum sFas and sFasL in newly diagnosed type 2 diabetes. Acta Diabetol 2013; 50: 511-518.
22. Mojjiminiyi OA, Abdella NA. Effect of homeostasis model assessment computational method on the definition and associations of insulin resistance. Clin Chem Lab Med 2010; 48: 1629-1634.
Adipokine levels of GDM newborns... Manoharan et al

23. Rodríguez-Rodríguez P, Ramiro-Cortijo D, Reyes-Hernández CG, López de Pablo AL, González MC, Arríbas SM. Implication of Oxidative Stress in Fetal Programming of Cardiovascular Disease. Front Physiol [Internet]. 2018 [cited 2019 Jan 10]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5974045/

24. Fasshauer M, Blüher M, Stumvoll M. Adipokines in gestational diabetes. Lancet Diabetes Endocrinol 2014; 2: 488-499.

25. Bellos I, Fitrou G, Pergialiotis V, Perrea DN, Daskalakis G. Serum levels of adipokines in gestational diabetes: a systematic review. J Endocrinol Invest 2018.

26. Xu J, Zhao YH, Chen YP, Yuan XL, Wang J, Zhu H, et al. Maternal circulating concentrations of tumor necrosis factor-alpha, leptin, and adiponectin in gestational diabetes mellitus: a systematic review and meta-analysis. ScientificWorldJournal 2014; 2014: 926932.

27. Tsuchida A, Yamauchi T, Kadowaki T. Nuclear receptors as targets for drug development: molecular mechanisms for regulation of obesity and insulin resistance by peroxisome proliferator-activated receptor gamma, CREB-binding protein, and adiponectin. J Pharmacol Sci 2005; 97: 164-170.

28. Doruk M, Uğur M, Oruç AS, Demirel N, Yildiz Y. Serum adiponectin in gestational diabetes and its relation to pregnancy outcome. J Obest Gynaecol 2014; 34: 471-475.

29. Bhograj A, Suryanarayana KM, Nayak A, Murthy NS, Tsuchida A, Yamauchi T, Kadowaki T. Maternal lipids as strong determinants of insulin resistance. Minerva Med 2014; 105: 447-453.

30. Ilidromiti S, Sarsarini J, Kelsey TW, Lindsay RS, Sattar N, Nelson SM. Accuracy of circulating adiponectin for predicting gestational diabetes: a systematic review and meta-analysis. Diabetologia 2016; 59: 692-699.

31. Kieffer TJ, Heller RS, Leech CA, Holz GG, Habener JF. Leptin suppression of insulin secretion by the activation of ATP-sensitive K+ channels in pancreatic beta-cells. Diabetes 1997; 46: 1087-1093.

32. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. Nature 1994; 372: 425-432.

33. Tartaglia LA, Dembski M, Wen X, Deng N, Calpepper J, Devos R, et al. Identification and expression cloning of a leptin receptor, OB-R. Cell 1995; 83: 1263-1271.

34. Yang M, Peng S, Li W, Wan Z, Fan L, Du Y. Relationships between plasma leptin levels, leptin G2548A, leptin receptor Glu223Arg polymorphisms and gestational diabetes mellitus in Chinese population. Sci Rep 2016; 6: 23948.

35. Inoue M, Machata E, Yano M, Taniyama M, Suzuki S. Correlation between the adiponectin-leptin ratio and parameters of insulin resistance in patients with type 2 diabetes. Metabolism 2005; 54: 281-286.

36. Finucane FM, Luan J, Wareham NJ, Sharp SJ, O’Rahilly S, Balkau B, et al. Correlation of the leptin:adiponectin ratio with measures of insulin resistance in non-diabetic individuals. Diabetologia 2009; 52: 2345-2349.

37. Rueda-Clausen CF, Lahera V, Calderón J, Bolívar IC, Castillo VR, Gutiérrez M, et al. The presence of abdominal obesity is associated with changes in vascular function independently of other cardiovascular risk factors. Int J Cardiol 2010; 139: 32-41.