ORIGINAL ARTICLE

Study to Compare Serum Visfatin Concentration in Different Trimesters of Pregnancy

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ABSTRACT

Aim: To compare serum visfatin level in different trimesters of pregnancy and to explore the use of serum visfatin as a predictor of insulin resistance and hence gestational diabetes mellitus.
Study design: A cross sectional comparative study
Study duration: from April 2010 to September 2012
Place: This study was carried out in the department of Physiology BMSI- JPMC in collaboration with Abbasi Shaheed Hospital Karachi.
Patients and methods: 88 women were included in the study, divided into four groups. All women underwent anthropometric variables, metabolic parameters and serum visfatin evaluation. Homeostasis mathetical model assessment (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI).
Results: Maternal serum visfatin concentration gradually increased during pregnancy as compared to non pregnant normal weight control women. We also observed a progressive increase in insulin resistance and decrease of insulin sensitivity during pregnancy. Maternal weight, BMI and body fat percentage also increased gradually.
Conclusion: It was concluded that insulin resistance in normal pregnancy seems to increase throughout 2nd and 3rd trimesters. Adipose tissue derived visfatin increases in pregnancy to compensate for insulin resistance by its insulin mimetic properties.
Keywords: Serum visfatin evaluation, pregnancy, insulin sensitivity

INTRODUCTION

Adipose tissue has shown to be an active metabolic organ secreting adipocytokines. Adipocytokines are involved in the energy homeostasis, regulation of glucose and lipid metabolism, immunity, neuroendocrine and cardiovascular functions[1]. Visfatin is an adipocytokine also known as nicotinamide phosphoribosyl transferase (Nampt) and pre B-cell colony enhancing factor (PBEF).It consists of 491 amino acids with a molecular mass of 52 kilodaltons. It is a protein that is preferentially produced in visceral adipose tissue and both its tissue expression and secreted plasma levels increase in parallel with obesity. It is also found in skeletal muscles, liver, bone marrow and lymphocytes. It has multiple biological functions including an insulin-mimetic effect in culture cells by binding to and activating insulin receptor[2,3,4]. Pregnancy is a unique condition characterized by transient physiologic insulin resistance which progresses with advancing gestation[5]. Pregnancy is associated with alterations in the regulation of glucose metabolism caused by the actions of human placental growth hormone, prolactin, cortisol and progesterone; these hormones antagonize the action of insulin, particularly during the 2nd and 3rd trimesters, leading to a state of relative insulin resistances as pregnancy progress[6].

In pregnancy, the decreased insulin sensitivity is best characterized as a post receptor defect resulting in the decreased ability of insulin to bring about GLUT4 mobilization from the interior of the cell to the cell surface[7]. In pregnancy, there is evidence that insulin receptor and IRS-1(insulin receptors substrate 1) tyrosine phosphorylation are impaired, and serine phosphorylation is increased in late gestation in skeletal tissue[8]. It was suggested that visfatin improves insulin sensitivity. Visfatin effects the insulin signal transduction pathway by inducing tyrosine phosphorylation of insulin receptor and IRS-1 and 2 (insulin receptors substrate 1 and 2) in the liver and muscle[9].

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MATERIAL AND METHODS

This cross sectional study was conducted in Department of Physiology, Basic Medical Sciences Institute (BMSI), in collaboration with the Department of Gynecology and Obstetrics at Abbasi Shaheed Hospital, Karachi. Eighty eight women between 18 – 29 years of age, non obese and non diabetics were included in the study. Subjects were divided into four groups "A" non-pregnant women, "B" 1st trimester pregnant women, "C" 2nd trimester pregnant women and "D" 3rd trimester pregnant women. Multi gravid, precious pregnancy, women with gestational diabetes mellitus and women with preeclampsia were excluded from the study.

Physical parameters included age (years), Weight (Kg), Height (m) and Body fat percentage (%). Biochemical parameters included Serum Visfatin by C Terminal Human ELISA Kit, Serum insulin by Immunenzymatic assay and Blood glucose by enzymatic method.

The blood samples of those subjects who fulfilled the inclusion criteria were collected after an overnight fasting of 8-10 hours. About 7ml of blood was drawn from anticubital vein after all aseptic measures while the subjects were sitting in upright position. Strictly pre-defined protocol were used for sample preparation. 5ml of blood was collected in gel barrier silicon coated tubes from BD, UK. 2ml of blood was collected in NaF vacutainer from BD, UK. The gel tubes were kept under room temperature until clotting was completed. Samples were centrifuged at 3000 rpm for 10 minutes within 1 hour after collection. Serum was separated and stored in alliquotes in deep freezer at -80ºC until assayed. Each aliquot was labeled with patient's name and identification number.

Statistical software SPSS version 11.0 was used for data feeding and analysis. The results were given in the text as mean and standard error of mean (SEM) for continuous/qualitative variables (age, height, weight, BMI, etc.). Statistical comparisons were performed by using student t-test, or one-way analysis of variance (ANOVA) with multiple comparisons. In all statistical analysis only p-value <0.05 was considered significant.

RESULTS

Table 1 shows the comparison of anthropometric variables among all groups. Mean ages of all four groups were comparable on average, as samples were collected from age matched women. Non significant changes were observed in the height among all groups, but weight in group D was significantly more (P<0.05) as compared to control (61.4±1.99, 52.9±1.41 respectively). Body mass index (BMI) was significantly more in group C and group D as compared to controls (23.1±0.62, 25.4±0.64, 20.1±0.64 respectively), (P<0.05). Body fat % was also significantly more in group C and group D as compared to control (29.3±2410.83, 29.9±0.83, 24.3±0.64 respectively) (P<0.05).

Table 2 shows the comparison of metabolic parameters among all groups. Serum insulin was significantly higher in group D as compared to control (10±2.88 and 3.1±0.66 respectively). HOMA-IR was also significantly more in group B and group D subjects as compared to controls (0.3±0.07, 3±1.07 and 0.7±0.14 respectively). While QUICKI was significantly more in group B (0.56±0.03) subjects as compared to controls (0.47±0.02). However, non significant changes were observed in plasma glucose levels.

Table 3 shows comparison of serum visfatin among all groups. Serum visfatin was significantly increased in group C (13.1±0.77) and group D (22.3±0.82) as compared to controls (5.4±1.06).

Table 4 shows comparison of anthropometric variables during pregnancy. Gestational age was significantly increased in group C (24.3±0.20) and group D (34.9±0.21) as compared to group B (12.9±0.16). Gestational age was also significantly increased in group D (34.9±0.21) as compared to group C (24.3±0.20). Weight was significantly increased in group D (61.4±1.99) as compared to group B (53±1.64). Body mass index (BMI) was significantly increased in group C (23.1±0.62) as compared to group B (20.9±0.51). BMI was also significantly increased in group D (25.4±0.64) when compared to group C (23.1±0.62). Body fat percentage was significantly increased in group C (29.3±0.83) and group D (29.9±0.83) as compared to group B (25±0.65). Non significant changes were observed in age and height of all groups.

Table 5 shows comparison of metabolic parameters during pregnancy. Serum insulin was significantly increased in group D (10±2.88) when compared to group B (1.4±0.28). HOMA-IR was significantly increased in group D (3±1.07) when compared to group B (0.3±0.07). QUICKI was significantly decreased in group C (0.44±0.02) and group D (0.39±0.04) as compared to group B (0.56±0.03). Non significant changes were observed in fasting plasma glucose level.

Table 6 shows comparison of serum visfatin during pregnancy. Serum visfatin was significantly increased in group C (13.1±0.77) and group D (22.3±0.82) as compared to group B (5.8±0.69). Serum visfatin was also significantly increased in group D (22.3±0.82) when compared to group C (13.1±0.77)

Table 1: comparison of anthropometric variables among all groups

Variables	Group A (n=22)	Group B (n=22)	Group C (n=22)	Group D(n=22)
	Controls	1st trimester	2nd trimester	3rd trimester
	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
Age (Years)	23.8±0.32	22.9±0.63	22.5±0.63	23.0±0.64
Weight (Kg)	52.9±1.41	53.0±1.64	56.7±1.43	61.4*±1.99
Height (m)	1.62±0.01	1.59±0.01	1.57±0.01	1.55±0.01
BMI (Kg/m^2)	20.1±0.64	20.9±0.51	23.1*±0.62	25.4*±0.64
Body Fat (%)	24.3±0.64	25.0±0.65	29.3*±0.83	29.9*±0.83

*Difference was statistically significant as compared to controls P<0.

Table 2: comparison of metabolic parameters among all groups

Variables	Group A (n=22)	Group B (n=22)	Group C (n=22)	Group D (n=22)
	Controls	1st trimester	2nd trimester	3rd trimester
	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
Fasting plasma glucose (mg/dl)	85±2.74	83±1.98	89±2.62	94±6.29
Serum insulin (µIU/ml)	3.1±0.66	1.4±0.28	5.7±1.56	10.0*±2.88
HOMA - IR	0.7±0.14	0.3*±0.07	1.4±0.41	3.0*±1.07
QUICKI	0.47±0.02	0.56*±0.03	0.44±0.02	0.39±0.04

*Difference was statistically significant as compared to controls P<0.05.

Table 3: comparison of visfatin among all groups

Variables	Group A (n=22)	Group B (n=22)	Group C (n=22)	Group D (n=22)
	Controls	1st trimester	2nd trimester	3rd trimester
	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
Serum visfatin (ng/ml)	5.4±1.06	5.8±0.69	13.1*±0.77	22.3*±0.82

*Difference was statistically significant as compared to controls P<0.05.

Table 4: comparison of anthropometric variables during pregnancy

Variables	Group B (n=22)	Group C (n=22)	Group D (n=22)
	1st trimester	2nd trimester	3rd trimester
	Mean±SEM	Mean±SEM	Mean±SEM
Gestational age (Weeks)	12.9±0.16	24.3*±0.20	34.9*ɔ±0.21
Age (Years)	22.9±0.46	22.5±0.63	23.0±0.64
Weight (Kg)	53.0±1.64	56.7±1.43	61.4*±1.99
Height (m)	1.59±0.01	1.57±0.01	1.55±0.01
BMI (Kg/m^2)	20.9±0.51	23.1*±0.62	25.4*ɔ±0.64
Body fat (%)	25.0±0.65	29.3*±0.83	29.9*±0.83

**Difference was statistically significant compared to group B P<0.05.*
ɔDifference was statistically significant compared to group C P<0.05.

Table 5: comparison of metabolic parameters during pregnancy

Variables	Group B (n=22)	Group C (n=22)	Group D (n=22)
	1st trimester	2nd trimester	3rd trimester
	Mean±SEM	Mean±SEM	Mean±SEM
Fasting plasma glucose (mg/dl)	83±1.98	89±2.62	94±6.29
Serum insulin (µIU/ml)	1.4±0.28	5.7±1.56	10.0*±2.88
HOMA - IR	0.3±0.07	1.4±0.41	3.0*±1.07
QUICKI	0.56±0.03	0.44*±0.02	0.39*±0.04

*Difference was statistically significant compared to group B P<0.05.
ɔDifference was statistically significant compared to group C P<0.05.

Table 6: comparison of visfatin during pregnancy

Variables	Group B (n=22)	Group C (n=22)	Group D (n=22)
	1st trimester	2nd trimester	3rd trimester
	Mean±SEM	Mean±SEM	Mean±SEM
Serum visfatin (ng/ml)	5.8±0.69	13.1*±0.77	22.3*ɔ±0.82

*Difference was statistically significant compared to group B P<0.05.
ɔDifference was statistically significant compared to group C P<0.05.

DISCUSSION

Our study results showed that maternal weight, BMI and percentage body fat increased gradually but significantly from 1st to 2nd and 3rd trimesters of pregnancy, these findings are in accordance with Chamberlain [10] and Baker[11] who also stated increase in maternal weight during pregnancy due to enlarge uterus, placenta and growing fetus.

In this study we used mathematically derived formula. HOMA-IR[12] and QUICKI[13] for the assessment of insulin resistance and insulin sensitivity respectively in normal pregnancy. We observed a significant progressive increase of insulin resistance and decrease of insulin sensitivity from 1st to the 3rd trimester. These finding of our study are in agreement with study done by Mastorakos et al[14] who also found the same result**.**

In prospective longitudinal studies done by Catalano et al[15]it is shown that women with normal glucose tolerance have a 50-60% decrease in insulin sensitivity during the course of gestation. These findings are comparable with our study.

In the conducted study maternal serum visfatin concentration gradually increased during pregnancy from 1st trimester to 3rd trimester. These finding are in agreement with study done by Mastorakos et al[14] who found a gradual increase in serum visfatin concentration from 1st to 3rd trimester during normal pregnancy to compensate the insulin resistance by its insulin-mimetic properties.

Mazakitovi et al[16] also reported high visfatin concentration during 1st and 2nd trimesters of normal pregnancy of normal weight women but decrease in 3rd trimesters as compared to 2nd trimester this may be due to use of groups with wide range of gestational age.

Morgan[17,]Jacek[18] and Zhou and Seidel[19] also reported elevated levels of serum visfatin in pregnancy. They stated that parous state is accompanied by increase in visfatin, since visfatin possesses insulin-mimetic properties it seems plausible to suggest that increase in visfatin seen in pregnancy may be a compensatory change in intermediary metabolism to ameliorate the insulin resistance which so often accompanies pregnancy. Our results suggest that visfatin compensates for the impairement of insulin action especially during the early stages of development of insulin resistance.

We realize from our study Visfatin concentration during the first and early second trimester may be a predictor of second trimester insulin sensitivity. Visfatin and insulin sensitivity did not change in a similar way during all three trimesters. The loss of close association of visfatin with insulin sensitivity after the second trimester may be attributable to an increase in visfatin production by an additional source other than adipose tissue namely the placenta. These findings are also collaborated by the findings of Mastorakos et al[14].

CONCLUSION

Serum visfatin concentration increases gradually during pregnancy to compensate the insulin resistance by its insulin-mimetic properties. During normal pregnancy in non obese women, increased adipose tissue is a forerunner of significant progressive increase of insulin resistance. The 1st and 2nd trimester concentrations of adipose tissue derived visfatin, an insulin-mimetic adipocytokine, may predict insulin sensitivity during the 2nd trimester.

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