

Plasma adipokine concentrations in overweight/obese pregnant women: A longitudinal study

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Abstract

Purpose The purpose of this study was to investigate the differences in plasma concentrations of adipokines in pregnant women with varying body mass indices (BMIs) with every trimester.

Materials and Method In this study, 89 pregnant women were recruited. These women were divided into lean, normal, and overweight/obese groups. Serum levels of adiponectin, resistin, leptin, and visfatin were measured in the first, second, and third trimesters.

Results

In the overweight/obese group, adiponectin, resistin, and visfatin concentrations were not significantly affected by advanced gestational age. Leptin concentrations in the third trimester were significantly higher than those in the first and second trimesters.

Adiponectin concentrations in the overweight/obese group were significantly lower than those in the lean group in the first and second trimesters. Visfatin concentrations in the overweight/obese group were significantly lower than those in the normal group in the first trimester. Leptin concentrations in the overweight/obese group were significantly higher than those in the lean and normal groups in all trimesters.

Conclusion In the first trimester, the largest differences were observed between the overweight/obese group compared to the lean and normal group. The changes in adipokines in overweight/obese groups is different from those in lean and normal groups.

Keyword: adipokine, visfatin, adiponectin, pregnancy, overweight/obesity

Introduction

It has been established that adipose tissue is the largest endocrine organ in the body[1]

Adipokines such as leptin, adiponectin, resistin and visfatin are cytokines secreted by the adipose tissue and are closely involved in metabolic syndromes such as arteriosclerosis, hypertension, and insulin resistance.

Pregnancy is potentially a diabetogenic state. It is well known that insulin resistance is increased during pregnancy; however, this mechanism is not completely understood.

Obesity is the excessive growth of adipose tissue depots as a result of chronic consumption of calories in excess of the energy needs of the individual. In humans, the expansion of adipose depots results from hyperplasia and hypertrophy of adipocytes in a depot-dependent fashion[2]. Obesity most commonly occurs with metabolic syndromes [3].

During pregnancy, obesity and overweight result in a high-risk pregnancy due to the increased risk of conditions such as pregnancy induced hypertension, preeclampsia, and gestational diabetes mellitus.

The purpose of this study was to investigate the differences in the plasma concentrations of adipokines in lean, normal, and overweight/obese pregnant women in every trimester.

Materials and method

In this longitudinal study, 89 pregnant women were recruited from the outpatient clinic of Tokushima University Hospital. Subjects with a history of diabetes mellitus and gestational diabetes mellitus, multiple fetal pregnancy, history of endocrine, renal or liver illness, hypertension or pregnancy induced hypertension and subjects receiving glucocorticoid treatment at an early stage of pregnancy were excluded from the study. The included patients were divided into lean, normal, and overweight/obese groups based on BMI <18.5, 18.5–24.9, and ≥ 25 kg/m², respectively, based on the weight and height before pregnancy. Fasting serum levels of adiponectine, resistin, leptin, and visfatin were measured in the first, second, and third trimesters. Informed consent was obtained from each participant. The ethics committee of Tokushima University Hospital approved the study.

Collection of blood samples

Fasting blood samples were obtained in all women in the first trimester (10–14 weeks of gestation), second trimester (24–28 weeks of gestation), and third trimester (34–36 weeks of gestation). The serum was immediately separated after blood collection and promptly frozen at -80°C until the time of tests. The measurements were performed simultaneously in all samples at the end of the study.

Measurement of concentrations of adipokines

We measured serum levels of leptin (inter- and intra-assay CVs 3.0-6.2%, CV 3.4-8.3%) with a radioimmuno assay (RIA) (Millipore Corporation) and those of adiponectin(inter- and intra-assay CVs <10%, CVs <10%), resistin(inter- and intra-assay CVs 5.1-6.9%, CV 2.8-3.4%), and visfatin(inter- and intra-assay CVs <10%, CVs<8%) using enzyme-linked immunosorbent assays (ELISAs) (Chemicon International, BioVender Laboratory Medicine, Inc. and Wuhan Huamei Biotech, respectively).

Statistical analysis

Data are described as mean±standard deviation (SD). The changes in the levels of the adipokines during pregnancy were tested using one-way repeated analysis of variance (ANOVA) test for normally distributed variables. The associations between variables were tested using one-way ANOVA test. P values less than 0.05 were considered to be statistically significant.

Results

This study included 89 pregnant women with 15, 56, and 18 in the lean, normal, and overweight/obese groups. The characteristics of these subjects are shown in Table 1. Neither were any statistically significant differences observed between the gravidity, heights, gestational weeks at the time of blood sampling in all the trimesters, the gain in body weight at delivery, the gain in the body weight from pre-pregnancy to first, second, and third trimesters and the birth weights of the neonates between the three trimester groups based on BMI. (Table 1).

Changes in the levels of adipokines between each BMI group (Fig1)

In the first trimester, adiponectin levels in women in the overweight/obese group were significantly lower ($p<0.05$) than those in women in the lean group. Visfatin

levels in women in the overweight/obese group were significantly lower ($p<0.05$) than those in women in the normal group. Leptin levels in women in the overweight/obese group were significantly higher ($p<0.001$) than those in women in the lean and normal BMI groups.

In the second trimester, adiponectin levels in women in the overweight/obese group were significantly lower ($p<0.05$) than those in women in the lean group. Leptin levels in women in the overweight/obese group were significantly higher ($p<0.001$) than those in women in the lean and normal BMI groups.

In the third trimester, levels of leptin were significantly higher (<0.001) in women in the overweight/obese group than those in women in the lean and normal BMI groups.

Changes in the levels of adipokines between each trimester (Fig. 2)

In lean group of women, adiponectin levels in the third trimester were significantly lower ($p<0.05$) than those in the first and second trimesters.

In normal group of women, adiponectin levels in the second trimester were significantly lower ($p<0.05$) than those in the first trimester and those in the third trimester were significantly lower ($p<0.001$) than those in the first trimester. Visfatin levels in the second trimester were significantly lower ($p<0.05$) than those in the first

trimester. Leptin levels in the third trimester were significantly higher ($p < 0.01$) than those in the first trimester.

In overweight/obese group of women, adiponectin, resistin, and visfatin levels were not significantly different based on advanced gestational age. Leptin levels in the third trimester were significantly higher ($p < 0.01$) than those in the first trimester, and those in the third trimester were significantly higher ($p < 0.001$) than those in the second trimester.

Discussion

- The effect of different BMIs group

Leptin is produced and secreted by white adipose tissue as well as the placenta[4]. Obesity is associated with increased concentrations of circulating free leptin[5]. This increase is positively correlated with BMI and fat mass [6]. In our data, leptin levels in women in the overweight/obese group were significantly higher ($p < 0.001$) than those in women in the lean and normal BMI groups with positively correlated with BMI.

In the first trimester, adiponectin concentrations in the overweight/obese weight group were significantly lower than those in the lean weight group. Visfatin concentrations in the overweight/obese group were significantly higher than those in the normal group.

To the best of our knowledge, no previous studies have reported the differences in the levels of adipokines between lean, normal weight, and overweight/obese pregnant women in the first trimester.

Berndt J reported that visfatin concentration correlates positively with the BMI [7]. In the overweight/obese group, decreased adiponectin and increased visfatin concentrations suggest that the insulin resistance was higher in comparison with the lean and normal groups in the first trimester. In the third trimester, adiponectin and visfatin concentrations were not significantly different between the lean, normal, and overweight/obese groups in this study. Hendler I et al. observed no differences in adiponectin or resistin levels before labor among normal weight, overweight, and obese groups [8]. Vernini MJ et al. reported that adiponectin and resistin concentrations at 37–38 weeks of gestation were not significant different in normal, overweight and obese pregnant women [9]. Our results are in agreement with those of above studies in that adiponectin and resistin concentrations in the third trimester were not significantly different in lean, normal and overweight/obese pregnant women.

In the first trimester, the differences in circulating level of visfatin, leptin, and adiponectin between the overweight/obese group compared to the lean and normal group may be related to BMI and insulin resistance.

- The effect of gestational age

Mastorakos et al. observed that maternal serum concentrations of visfatin increased during pregnancy. The gradually increasing insulin resistance during pregnancy may be compensated by the sustained increase of visfatin[10]. Mazaki-Tovi et al. reported that the median maternal plasma concentration of visfatin peaks between 19–26 weeks of gestation and has a nadir between 27–34 weeks of gestation. This discrepancy could be explained by the different time points of sampling in the studies in addition to different methodologies [11]. However, in our data, visfatin concentrations in the second trimester were significantly lower than those in the first trimester in women with normal BMI. It is very difficult to explain this discrepancy based only on the differences in insulin resistance according to advanced gestation. Kim et al. reported that central visfatin improved glucose homeostasis by increasing insulin secretion and insulin sensitivity in euglycemia through the hypothalamus in a model of diabetic rats, and it has also been observed that plasma visfatin concentrations are lower in patients with gestational diabetes mellitus. It can, therefore, be hypothesized that visfatin might act as a positive modulator of glucose homeostasis by delivering the hypothalamic signals to the peripheries [12].

Fuglsang J et al. reported that adiponectin levels changed significantly during pregnancy and observed increasing levels in the first trimester, followed by declining levels throughout pregnancy from maximum levels at mid-gestation in their longitudinal study [13]. In the present study, the circulating levels of adiponectin decreased with advancing gestational age in the lean and the normal weight groups. Our results are in agreement with those of the aforementioned study. The decrease in serum adiponectin concentrations may occur with increasing maternal weight and insulin resistance according to advancements in the age of gestation. However, in the overweight/obese group, no statistically significant change in adiponectin concentrations was observed in the overweight/obese group. A possible explanation for this alleged inconsistency may be an alteration in the adiponectin regulation during gestation. Adiponectin expression and secretion have been shown to be regulated by numerous factors, some of which are possibly affected by the unique hormonal milieu of pregnancy in women who are overweight/obese.

In our study, leptin concentrations in the overweight/obese group were significantly higher than those in the lean and normal groups in all trimesters. Higher leptin concentration is positively correlated with BMI and fat mass[6]. We believe that leptin

concentration increased with BMI and total body fat mass in the overweight/obese weight group from the first trimester.

Conversely, visfatin is also predominantly produced by the visceral fat depots of adipose tissue. Insulin resistance dramatically increases with the period of gestation regardless of body composition. However, in this study, adiponectin and visfatin concentrations were not significantly changed. Adiponectin and visfatin are cytokines secreted by the maternal adipose tissue, especially visceral adipose tissue[14,15].

Overweight/obese women had greater total body fat and abdominal subcutaneous fat than did normal weight women, while there was no difference in the abdominal visceral fat [16]. This suggests that adiponectin and visfatin concentrations did not change according to the weight-class in these pregnant women.

In conclusion, in the first trimester, the differences in circulating level of visfatin, leptin, and adiponectin between the different weight groups were more pronounced than later in pregnancy. The largest differences were observed between the overweight/obese group compared to the lean and normal group. By advancing gestational week, the changes in adipokines such as visfatin, leptin and adiponectin concentration in overweight/obese group is different from those in lean and normal group.

Disclosure

The authors declare no conflict of interest.

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Figure legends

In the first trimester in the three groups

Adiponectin levels in women in the overweight/obese group were significantly lower ($p < 0.05$) than those in women in the lean group. Visfatin levels in women in the overweight/obese group were significantly lower ($p < 0.05$) than those in women in the normal group. Leptin levels in women in the overweight/obese group were significantly higher ($p < 0.001$) than those in women in the lean and normal groups. L: lean; N: normal; O: overweight/obese groups.

In the second trimester in the three groups

Adiponectin levels in women in the overweight/obese group were significantly lower ($p < 0.05$) than those in women in the lean group. Leptin levels in women in the overweight/obese group were significantly higher ($p < 0.001$) than those in women in the lean and normal groups.

In the third trimester in the three groups

Leptin levels in women in the overweight/obese group were significantly higher ($p < 0.001$) than those in women in the lean and normal groups.

Figure 2

* Statistically significant change from first trimester and second trimester are as follows.

In overweight/obese group of women, adiponectin, leptin levels in the third trimester and in lean group of women, adiponectin levels in the third trimester.

** Statistically significant change from first trimester are as follows

In normal group of women, adiponectin levels in the second trimester and the third trimester, visfatin levels in the second trimester and leptin levels in the third trimester.

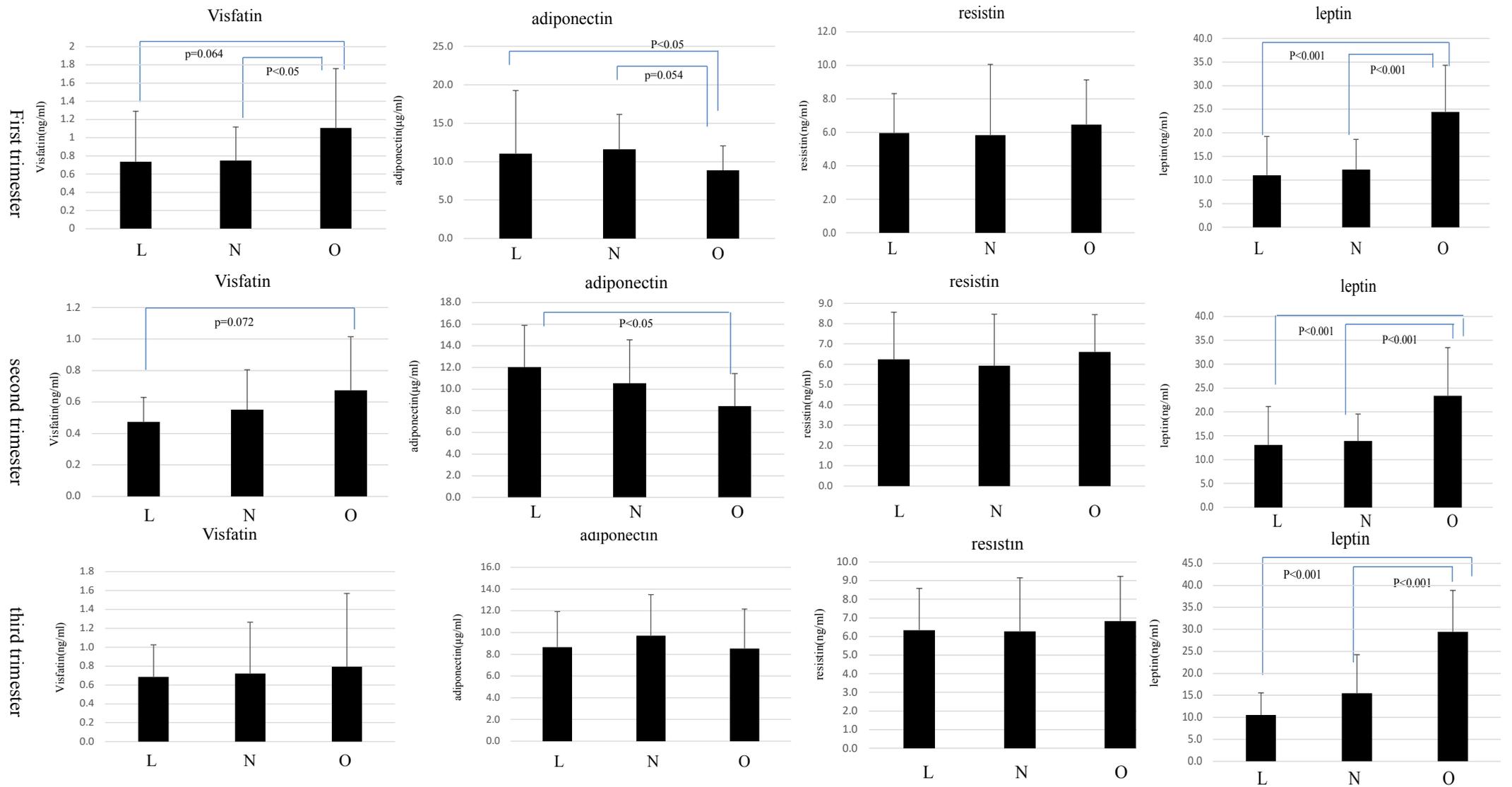
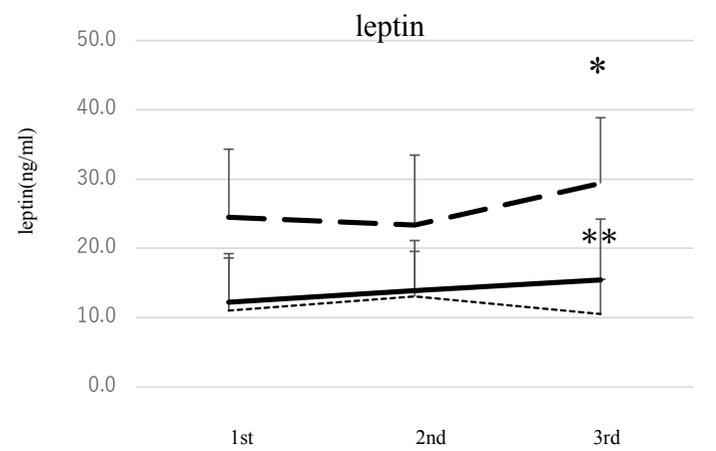
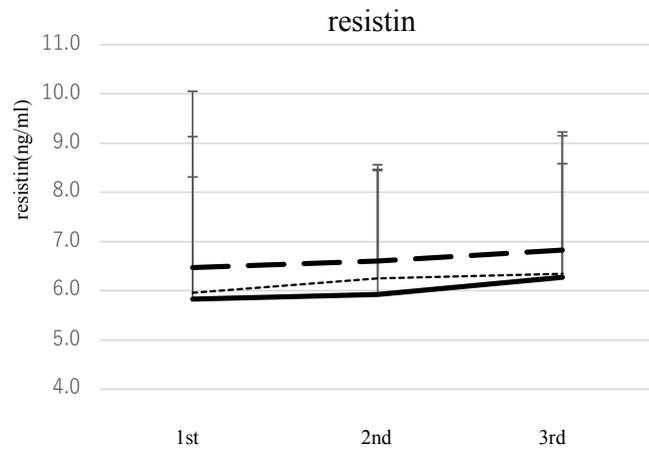
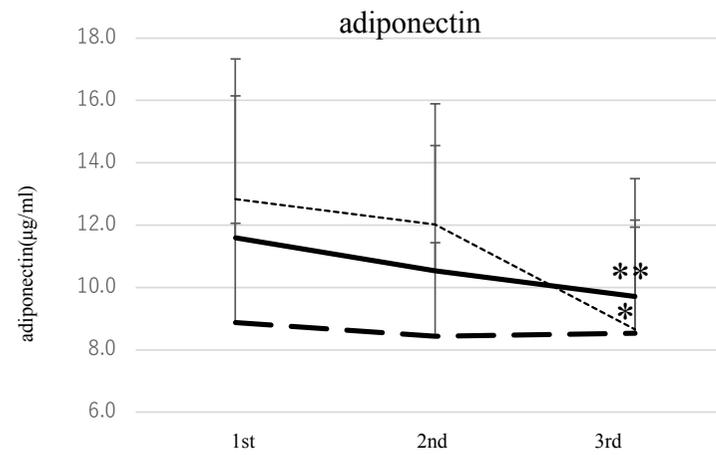
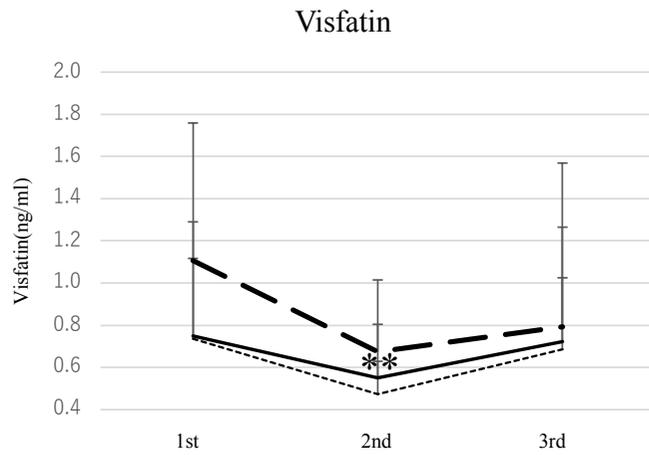


Fig1. Adipokine concentrations in the each trimester between three group (Variable expressed as mean ± SD)

L: lean,
N: normal weight
O: overweight/obese



(Variable expressed as mean ± SD)

- - - Lean
 — Normal
 - · - Overweight/obese

Fig2 adipokine concentrations between each trimester

Table 1 Characteristics of women with lean, normal and overweight/obese pregnant women

	lean (n=15)	normal (n=56)	overweight/obese (n=16)	significance
Age(y)	29.1 ± 6.9	31.5 ± 5.2	29.2 ± 4.3	*
Gravidy	0.9 ± 1.1	1.6 ± 1.4	1.4 ± 1.0	N.S.
Parity	0.4 ± 0.6	0.9 ± 0.8	1.0 ± 0.8	**
Pre-pregnancy weight(kg)	43.0 ± 3.2	52.6 ± 4.8	68.4 ± 9.5	p<0.001
Pre-pregnancy BMI	17.7 ± 0.7	21.2 ± 1.7	28.1 ± 3.5	p<0.001
weight at labor(kg)	53.8 ± 4.0	64.0 ± 6.5	78.9 ± 7.0	p<0.001
BMI at labor				
Gestational weeks (wk)				
at blood drawn				
first trimester	12.1 ± 0.6	11.7 ± 5.5	11.6 ± 5.7	N.S.
second trimester	25.0 ± 4.3	25.0 ± 5.3	25.0 ± 4.3	N.S.
third trimester	36.4 ± 1.9	36.3 ± 2.3	36.4 ± 2.3	N.S.
Body weight gain from				

pre-pregnancy				
at delivery	10.9 ± 3.2	11.8 ± 4.4	10.8 ± 4.6	N.S.
first trimester	1.1 ± 1.6	0.9 ± 3.2	0.1 ± 2.9	N.S.
second trimester	6.3 ± 2.7	6.3 ± 5.5	4.6 ± 3.6	N.S.
third trimester	10.5 ± 3.0	10.7 ± 4.4	10.0 ± 4.4	N.S.
Birth weight(g)	2991 ± 290	3069 ± 412	2972 ± 491	N.S.

*: Age in normal weight women was significantly($p < 0.05$) higher than that in lean weight women.

**.: Parity in overweight/obese women was significantly($p < 0.05$) higher than that in lean weight women.