Commentary

Can maternal leptin level at early gestation be used as a predictor of postpartum weight retention?

The protein product of the \textit{ob} gene, called leptin, mainly but not exclusively produced by white adipose tissue, is thought to suppress appetite and regulate energy homeostasis\textsuperscript{1,2}. Extremely obese individuals have high leptin levels, which is likely to reflect a state of leptin resistance, suggesting that they have reduced sensitivity to its anorectic and metabolic effects\textsuperscript{1}.

Under normal conditions of eating cycles, leptin reflects the proportion of adipose tissue, therefore its concentration rises with increasing adiposity\textsuperscript{3}. However, there are gender differences in leptin regulation between males and females at the same level of adiposity\textsuperscript{4}. Women have significantly higher leptin concentrations than men\textsuperscript{4} and these gender differences seem to be present already at birth (measured by leptin levels in the umbilical cord plasma), when no remarkable differences in body composition or hormonal values between genders exist\textsuperscript{5}. Interestingly, pregnant women bearing female foetuses have significantly higher increase in leptin concentration compared to pregnant women bearing males foetuses\textsuperscript{6}. These evidences indicate a differential resistance to the action of leptin that might have adaptive importance for reproduction.

Women naturally gain weight during pregnancy and many gradually lose it afterwards. However, for some women it is difficult to lose the pregnancy-related weight during postpartum and there is concern that pregnancy can significantly alter the future weight gain trajectory and that might be a health risk to the women and to the infant\textsuperscript{7}. Obesity in pregnancy includes women who are obese before becoming pregnant and women who become obese from excess weight gain during gestation and postpartum weight retention.

The mechanisms by which maternal weight are regulated during pregnancy are still poorly understood. It is known that leptin levels are correlated with BMI in non pregnant women. Since women experience a pronounced increase in plasma leptin concentrations during pregnancy, it raises an attractive hypothesis that leptin may act as a regulator of gestational weight gain and postpartum weight retention. Maternal plasma leptin concentrations increase as pregnancy advances, reaching peak values during the 3\textsuperscript{rd} trimester, and return to pregravid levels in the hours before and after delivery. Subsequently, maternal leptin levels increase during postpartum with normalization at 6 month postpartum onwards\textsuperscript{8,9}. Yet, whether leptin concentrations at entry into prenatal care can predict an increased risk of subsequent overweight/obesity is uncertain.

It is unlikely that increased leptin levels in pregnant women would impose reduction in energy intake as pregnancy progresses because during this period it is crucial to maintain a positive energy balance to sustain the energy demands of foetal development, promote energy storage in preparation for high metabolic demands of late pregnancy and lactation and preserve maternal health\textsuperscript{8,10}. On the contrary, it is speculated that increased leptin levels may enhance maternal fat depots and fat mobilization to increase availability and to support transplacental transfer of lipids substrates to the foetus, particularly after the second trimester of gestation\textsuperscript{11}. Therefore, pregnancy is an example of temporary leptin resistance, which is analogous to that of obese individuals\textsuperscript{8,12}.

Although some studies have assessed the relationship between leptin concentrations during pregnancy and maternal anthropometry\textsuperscript{9,10,13,14}, a few studies have examined precisely the association of leptin levels at early stages of pregnancy with postpartum weight retention\textsuperscript{15,16}. Kim \textit{et al}\textsuperscript{15} tried to answer the question whether plasma leptin level at
early gestation could be viewed as a biomarker of postpartum weight retention. The authors investigated 75 Korean women, selected by a convenience sampling method, throughout pregnancy and at 6 wk and 6 months postpartum. It was observed that plasma leptin levels at 1st trimester differed significantly across initial BMI groups. Women classified as underweight (5.0 ± 1.6 ng/ml) and normal weight (9.9 ± 4.2 ng/ml) according to ethnic-specific recommendations based on BMI at 1st prenatal visit, had significantly lower levels of leptin compared with women classified as overweight (17.8 ± 9.9 ng/ml; < 0.05). In accordance with previous literature, leptin levels at 3rd trimester of gestation and 6 weeks postpartum were unrelated to initial BMI.

In addition, Kim et al investigated plasma leptin levels at early gestation positively correlated with initial BMI, body weight at term and BMI at term, but surprisingly were not significantly correlated with postpartum weight retention neither at 6 wk nor at 6 months after birth. There were no significant correlations between plasma leptin levels in late gestation and any body weight variable. The authors concluded that plasma leptin level at early gestation was a predictor of maternal weight at term. However, leptin level at first prenatal visit could not predict postpartum weight. Therefore, maternal leptin level at early gestation might not be useful in identifying women at risk of subsequent obesity. This finding is in disagreement with results described by Stein et al.

Stein et al investigated 103 American women of low-income and found that leptin at prenatal entry significantly predicted gestational weight gain and retained weight at 6 months postpartum even after adjustment for potential confounders. They concluded that high concentration of leptin at entry might predict an increased risk of overweight or obesity in vulnerable women.

It remains controversial whether findings of Stein et al can be generalized to other populations. Ethnic differences in leptin levels have been observed for similar degrees of adiposity, implying that this finding might not be directly applied to Korean and other Asian women. Apart from that, the population characteristics regarding age range, mean weight and BMI, smoking status, parity and diet differed considerably between the two studies. Even though all these factors are related to leptin levels and might explain the discrepancies in the results, the study conducted by Kim et al should be followed by others exploring in more detail the role of leptin on weight changes during and after pregnancy in Asian women.

Nevertheless it is postulated that the striking rise in leptin levels from 0 to 6 month postpartum may increase the set-point of the hypothalamic leptin receptor. Thus, the normalization in leptin levels after 6 month postpartum would be interpreted as a net reduction in leptin, inducing an increase in appetite and a decrease in energy expenditure. According to Lage et al, “this is an unproved, but attractive hypothesis for explaining the postpartum weight retention or the postpartum weight increase” experienced by some women. In this circumstance, changes in leptin levels from delivery to late postpartum could better explain postpartum weight retention and postpartum weight increase rather than levels at early gestation.

Although putative actions of leptin during pregnancy are vast and promising, before advocating the inclusion or exclusion of leptin from key biological pathways, a number of well-designed studies including larger sample sizes and involving populations of diverse ethnicity and socio-economic background should be carried out to replicate the previous findings.

There is lack of understanding of the processes that underlie the adaptations of leptin homeostasis related to pregnancy. Studies to clarify the relationship between leptin and insulin and other hormones of pregnancy should continue in order to elucidate the reason why leptin levels are elevated during normal human pregnancy, and whether excess leptin levels are detrimental to the mother and child health.

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References


