Serum Leptin Levels in Pregnant Pakistani Females: Relationship with Body Mass Index and Placental Weight

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Abstract

Objective: To determine the serum leptin levels in Pakistani pregnant subjects at the time of delivery and to ascertain the relationship between serum leptin levels and related variables (weight, body mass index, placental weight, gestational age, parity) at delivery.
Setting: Lady Dufferin Hospital, and Ziauddin Hospital Karachi.
Methods: Leptin concentration was measured in 110 subjects from venous samples, using Active Human ELISA Kit (DSL-10-23100). Samples were selected according to the availability.
Results: Mean maternal weight, body mass index and placental weight were 64.3 ± 13.8 kg, 27.1± 5.8 kg/m2 and 523.5 ± 90 gm, respectively. Gestational age was 36 - 41 weeks and maternal age was 18 - 35 years. Mean serum leptin level was 27.9 ± 18.1 ng/ml. Serum leptin levels were found to he positively correlated with body weight (r = 0.73, p<0,01), body mass index (r = 0.80, p<0.01) and placental weight (r = 0.34, p
Conclusion: Our results suggest that leptin does play role in body weight and energy regulation during pregnancy. The significant positive correlation between leptin and placental weight suggests that placenta may he the site of synthesis and/or secretion of leptin during pregnancy UPN1A 51:32; 2001).

The ob-gene product leptin, a 16 kd protein, is regarded as a postulated feed back regulator of adiposity leading to appetite suppression and catabolic effects[1,2]. It is now known to act through interaction with receptors in hypothalamus to induce a complex response involving fat mass regulation and energy homeostasis[3-4]. Leptin is thought to be a communicating link between fatty tissues and the brain; by playing a major role in controlling body fat stores through co-ordinated regulation of feeding behaviour, metabolism, autonomic nervous system and body energy balance in rodents, primates and humans[5]. Mutation of ob-gene results in hyperphagia and gross obesity in ob/ob mice (mice deficient in leptin) and leptin administration to these mice causes normalization of body weight and decrease in fat stores. In contrast, the development of obesity in another line of mice (db/db) is secondary to a mutation of the leptin receptors. In these mice, leptin levels are markedly increased due to the resistance to the effect of leptin[6]. This phenomena is observed in most obese hurnans[7,8].
Apart from its role in the pathophysiology and physiology of body weight regulation, role of leptin in haematology, puberty, neonatal physiology and reproduction has been addressed in recent years[9-13]. Rise in leptin at the onset of puberty[12-14] and fall in postmenopausal women[15,16], suggested that leptin levels may be associated with normal reproductive events. There is evidence that body fat plays a role in sex steroid metabolism[17] and relationship of leptin with gestational hormones in pregnancy have been suggested[10]. Factors other than the fat, for regulation of expression of ob-gene for leptin have been reported[18]. Pregnancy is associated with increased appetite. fat mass, body weight and metabolism as well as characterised by dramatic rise in levels of reproductive hormones, which decline

after delivery. It is noW knwon that low leptin levels disrupt the reproductive system, as ovulation stops in starving women and testosterone levels fall in men[19,20], and these changes have been accounted by the drop in the leptin production[21,22]. Although a ftw studies have documented an increase in circulatory leptin levels during pregnancy[23-25], bitt sources and stimuli are unclear. Further, the hypotheses that high eptin levels could represent an important feedback modulator of substrate supply and subsequently adipose tissue status during late gestation[25], remain to be confirmed. The mechanism underlying maternal weight and fat mass regulation particularly during the third trimester are poorly understood. Information of leptin in relation to pregnancy or any other variable in Pakistani subjects is completely lacking. Therefore, serum leptin levels were measured in pregnant Pakistani females in order to ascertain its relationship with maternal physical obstetrical parameters at delivery and to determine its corelation with maternal weight, body mass index, placental 80 weight and parity.

Subjects and Methods

Subjects

One hundred and ten full term normal pregnant females froni Lady Dufferin Hospital and Ziauddin Hospital. Karachi were included. All subjects gave their consent to participate in this study. Pregnancies less than 36 weeks and those with diabetes or any other illness were excluded. Body mass index (BMI)26 was measured by the formula kg/m^2. The weight of placenta was taken just after delivery. lnforrnations about each subject were recorded on an standardized structured performa.

Leptin assays

Blood samples were taken from peripheral vein at delivery ‘when the subject was in active labor. After centrifugation serum was obtained and frozen till further analyses. Serum leptin were measured by Active Human

Statistical analyses

SPSS software program (standard version 8.0) was used for statistical analyses of data that entailed student’s test and linear regression. Statistical significance was set at $p< 0.05$.

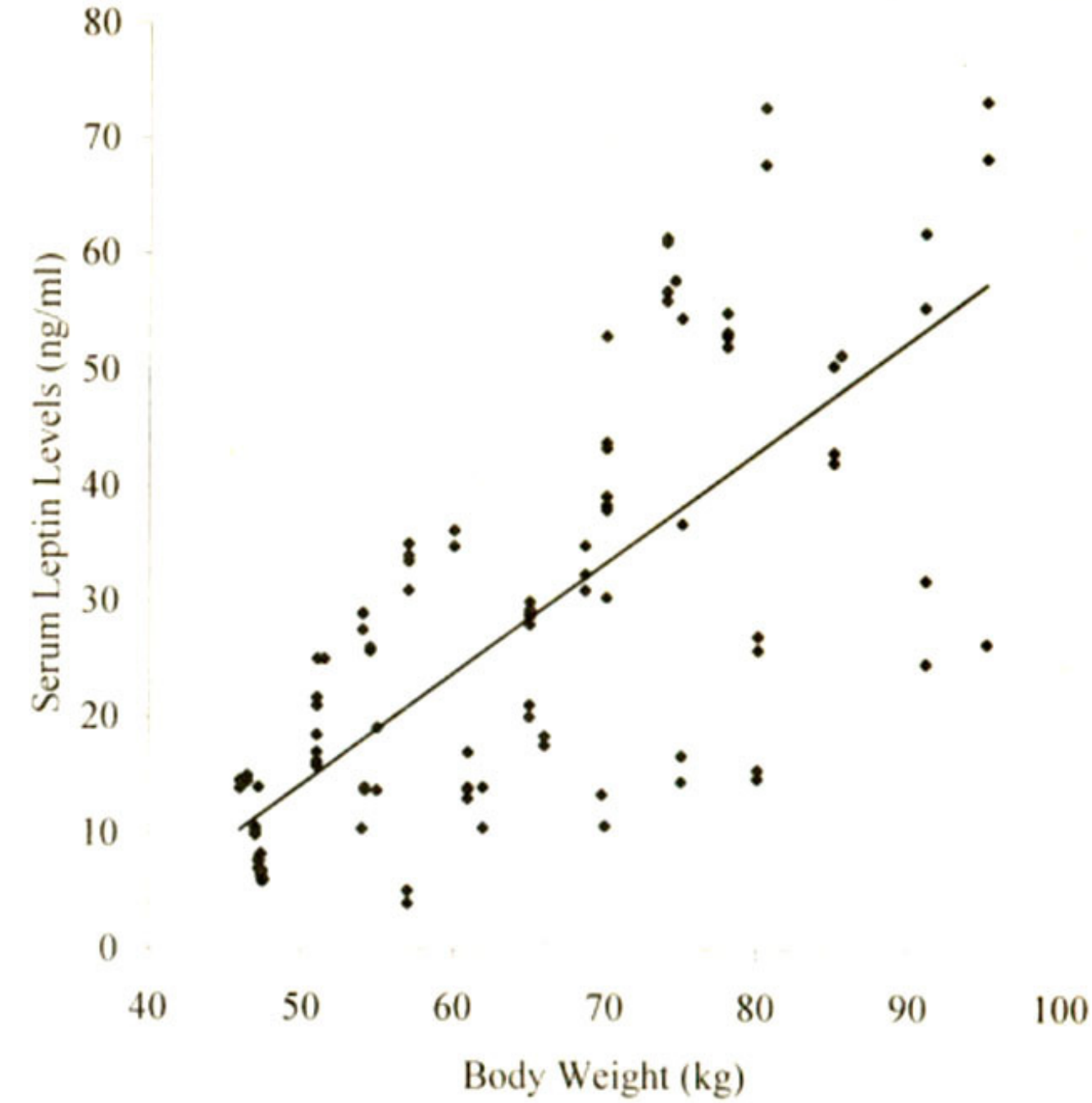
Results

The physical parameters are shown in Table.

Table. Physical Variables and serum leptin levels in pregnant women at delivery.

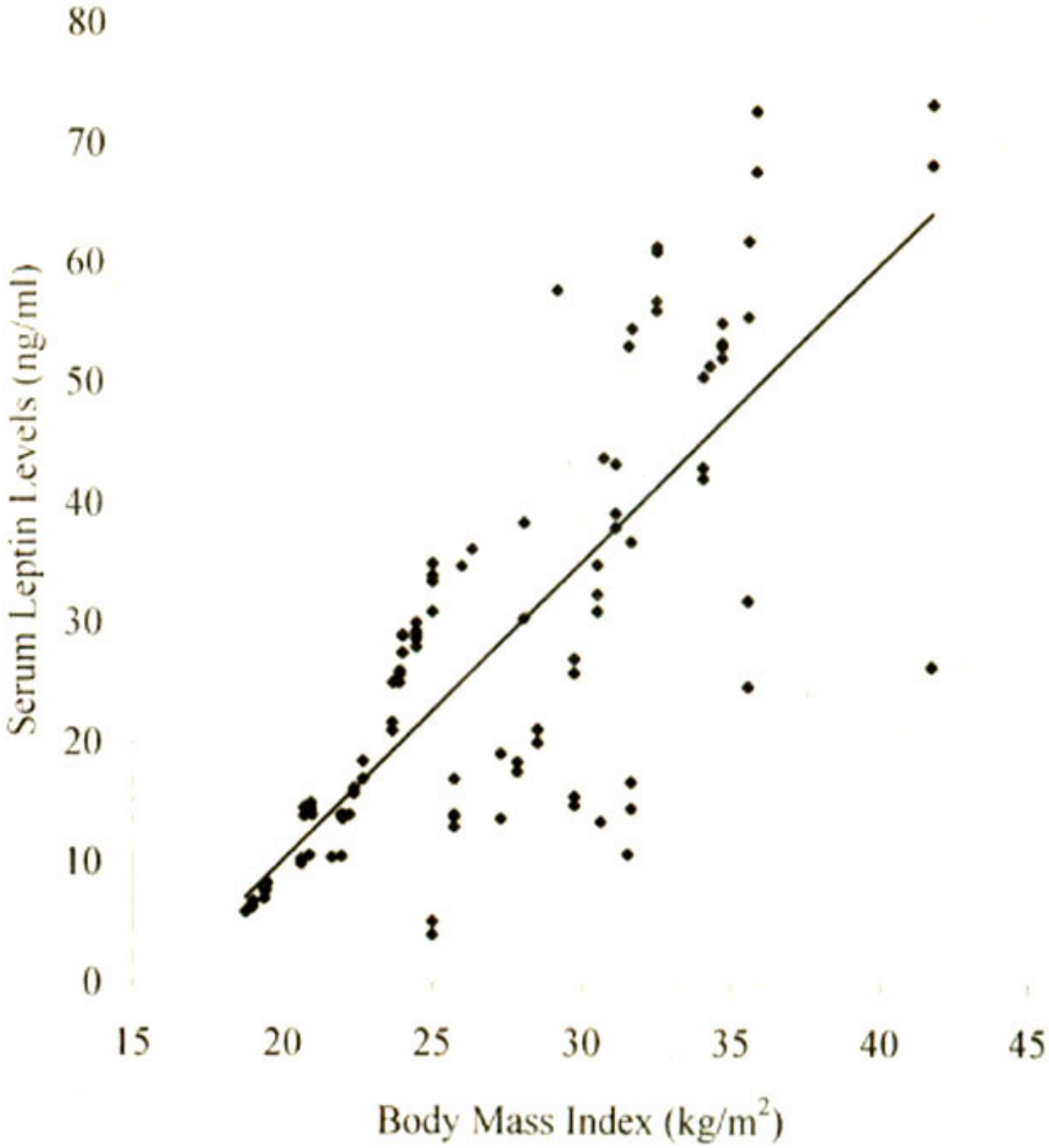
	Mean ± S.D.	95% Confidence Interval	Range
n = 110			
Age (yrs)	24.7 ± 4.5	23.9, 25.5	18-35
Height (cm)	154 ± 10	153.1, 155.2	142-168
Body weight (kg)	64.3 ± 13.8	61.7, 66.9	46-95.0
BMI (kg/m2)	27.1 ± 5.8	26.0, 28.2	18.8-41.7
Placental Weight (gm)	523.5 ± 90.0	506.5, 540.5	300-750
Serum Leptin Levels (ng/ml)	27.9 ± 18.1	24.5, 31.4	4.0-73.4

Mean body weight was 64.3 ±13.8 kg. BMI was 27.1 ± 5.8 kem^2 and placental weight was 523.5±90.0 gm. Mean gestational age was 38.3±1,4 weeks. Thirty-six subjects were primigravida whereas seventy-four were multigravida in our study. Serum leptin levels in mothers was 27.9+ 18.1mg/ml. Significant positive correlation exist between serum leptin levels and body weight ($r=0.73$, $p<0.01$), BMI (r 0.80, p< 0.0!) and placental weight (r 0.34, p< 0.05) as shown in Figures 1-3.



$r^2 = 0.54$, $r = 0.73$, $p<0.01$

Figure 1 Relationship between Serum Leptin Levels and Body Weight of Mothers at Delivery



$r^2 = 0.64$, $r = 0.80$, $p<0.01$

Figure 2. Relationship between Serum Leptin Levels and Body Mass Index of Mothers at Delivery

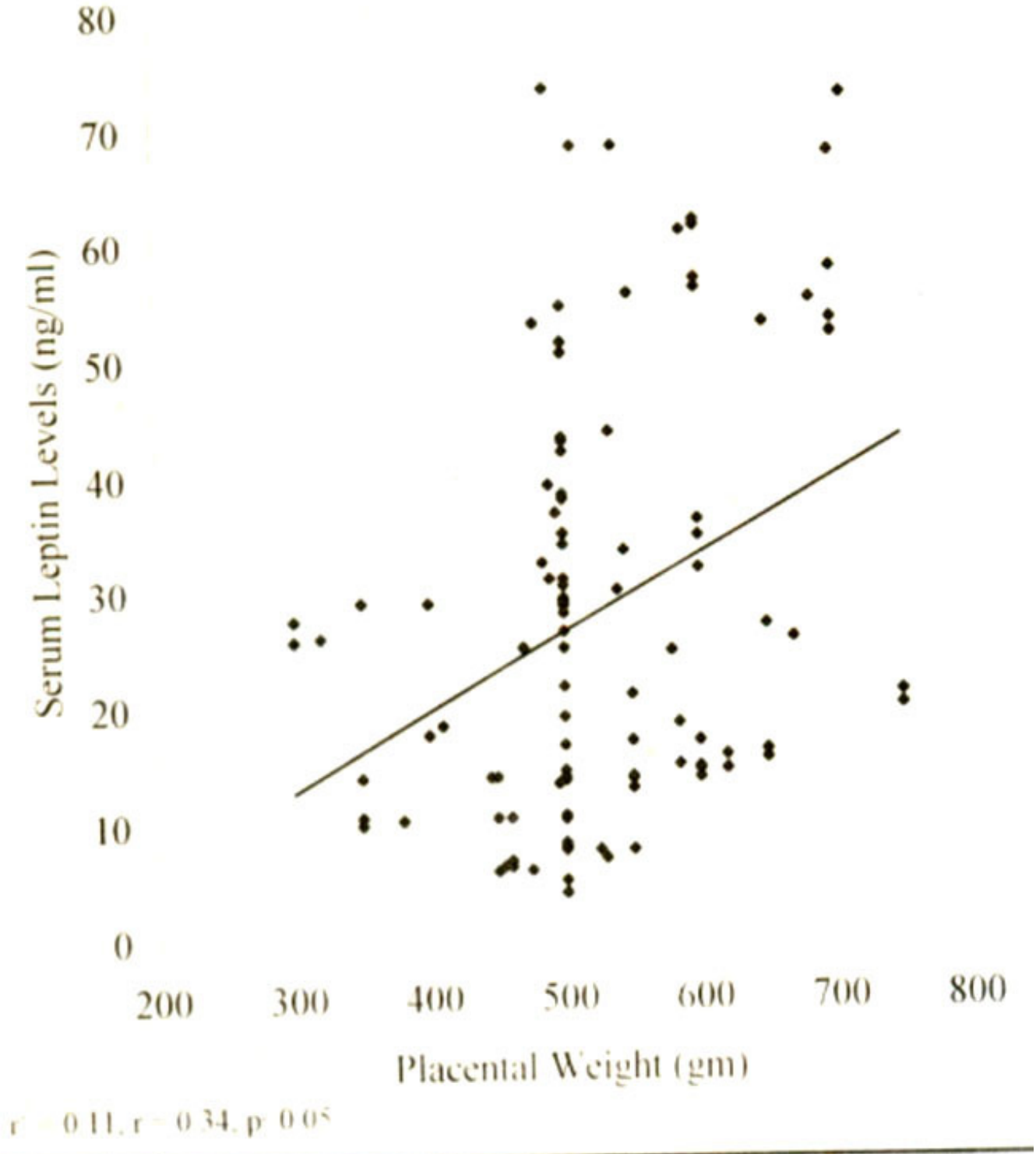


Figure 3 Relationship between Serum Leptin Levels of Mothers at Delivery and Placental Weight

Primigravida had significantly ($p< 0.01$) lower leptin levels (23.1 ± 18.9) than multigravida subjects (30.2 ± 17.5). However, when it was controlled for BMI this effect was not seen.

Discussion

Serum leptin is considered to reflect the state of nutriton, energy reserve and serves as a metabolic gate

to the reproduction[11] . Its levels and potential role in pregnancy Body Mass Index (kg/m) have been reported[11,23,25]. but its source and functional significance in maternal physiology remains unclear. The present report describes leptin ‘s relationship with BMI and placental weight. Our data provides evidence that leptin levels are present in maternal serum and correlate positively with maternal BMI. Leptin levels increase with increase in weight and body mass index and that 54% and 66% of increase in leptin can be explained on the basis of increase in the body weight (r 0.54) and BMI (r2 = 0.66), respectively. Similar findings were reported in other populations[10,13,14]. These results suggest that at delivery the regulation of leptin is not different from that in non-pregnant females in whom leptin levels are also correlated positively with BMI[7]. In another study, leptin concentration was increased progressively during the first two trimesters with peak at 28 week and levels are correlated significantly with maternal weight and BMI[27]. As expected energy expenditure increased during pregnancy because of additional maternal and fetal tissues and decreased postpartum in accordance with weight loss. Leptin not only decreased food intake, but also normalised elevated levels of appetite - stimulating hypothalamic peptide, neuropeptide Y (arcuate nucleus) in genetically obese mice and rats[28]. Leptin’s role in suppressing appetite, as well as, accelerating metabolism and selectively suppressing fat synthesis and most recently elucidated a fascinating role in reproduction has been documented[23,29]. in the present study, positive correlation between serum leptin and placental weight may suggest placenta as a site for leptin and/or leptin receptors synthesis/secretion. With the increase in adipose tissues during pregnancy, the placental and/or secretion of leptin may be an additional factor, that contributes to the maternal serum leptin concentration, since mRNA encoding leptin has also been documented[30-32]. In another study[10]. plasma leptin levels of 18 healthy women immediately before delivery and on day 3 after delivery were measured and significant higher leptin concentration before delivery than at day 3 post-delivery were implicated to support the placental syiithesis and/or secretion of leptin. Further, chronic elevation of leptin levels throughout pregnancy suggest that maternal resistance to leptin may occur, which possibly counters appetite satiating and metabolic effects and would therefore faciliatate maternal weight gain[24]. During pregnancy, appetite is increased and low leptin levels would be expected. In fact, the opposite is true and leptin levels in pregnancy are high. It has been argued that pregnancy might represent a leptin-resistance state[33]. Such resistance to endogenous leptin, as has been attributed to defect in leptin transport system or hypothalamic receptors or in the central leptin signaling cascade in obese sub jects[31].

Preliminary findings of raised maternal level at one of the link between the neuroendocrine system and adipose tissue, which expands during pregnancy. Role of neuropeptide Y (NPY), one of the neuroendocrine mediators, has been discussed in the relation of malnutrition, energy expenditure and sexual maturation[36,37]. The effect of leptin on hypothalamic neuropeptide Y gene expression[38] and the presence of leptin receptors in the ovary[39] may be the mechanisms by which leptin could influence the hypothalamic-pituitary-ovarian axis and hence reproductive function in the female. Since leptin affect NPY synthesis in hypothalamus and probably its release, role of leptin in the regulation of reproductive functions and sexual maturation has been hypothesised. Thus, a negative feedback system regulation of food intake. leptin secretion and hypothalamic NPY expression has been documented[40] To ascertain this and the contribution of leptin in maternal blood, if any, has yet to be determined. Further studies are needed to establish this hypothesis of leptin contribution by placenta.

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