WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 9, 86-94. Research Article ISSN 2277– 7105

ASSOCIATION OF MATERNAL OBESITY AT BIRTH WITH INCREASED OFFSPRING BODY SIZE AND SERUM LEPTIN

***Neveen Helmy Abou El-Soud[1], Nahla Abdel Moniem Barakat[2], Mai Mahmoud Youssef[3], Manal Abdel Moniem Mohsen[3], Gamila Mohamed El-Saeed[4]**

[1]Complementary Medicine Department; [2]Pediatric Department; [3] Child Health Department; [4]Biochemistry Department. National Research Centre- El-Behouth Street, Dokki, 12311 Cairo, Egypt.

Article Received on
26 June 2015,

Revised on 16 July 2015,
Accepted on 10 Aug 2015

***Correspondence For Author**
Prof. Dr. Neveen Helmy Abou El-Soud
Complementary Medicine Department, Medical Researches Division, National Research Center, El-Behouth Street,Dokki, 12311 Cairo, Egypt.

ABSTRACT

Background: Maternal obesity and weight gain during pregnancy are risk factors for child obesity. There is a potential role of leptin in the regulation of body weight, energy expenditure and therefore fetal growth and development. The aim of this study was to examine the association of maternal obesity at birth with offspring body size and serum leptin. **Subjects and methods:** Two hundred mothers at delivery with their term healthy human newborns were enrolled in this study. One hundred mothers of them were obese (body mass index (BMI) $\geq$ 30 kg/m^2) and one hundred act as control (BMI between 20 - 24.9 kg/m^2) . Neonatal weight, length, head circumference and ponderal index were determined. Leptin concentrations in venous cord blood were measured using specific enzyme –linked immunosorbent assay (ELISA) method. **Results:** Neonates of obese mothers had significantly higher levels of leptin (21.17±16.7 vs 11.33±10.55 ng/ml, p <0.001) , birth weight (3.64±0.32 vs 3.2±0.67 kg, p < 0.05), ponderal index (3.24±0.38 vs 2.77±0.65 gm/cm^3 , p < 0.05) when compared to non-obese group. Cord serum leptin was found to correlate with maternal BMI (r =0.46 , p < 0.05) and neonatal body measurements; weight (r =0.50 , p < 0.01) , length (r =0.59 , p < 0.001) , head circumference (r =0.56 , p < 0.01) and ponderal index (r = 0.40 , p < 0.05). **Conclusion:** Maternal obesity at delivery is associated with increased neonatal serum leptin and body size with high risk of children obesity later in life.

KEYWARDS: Maternal obesity ; neonatal birth size ; leptin.

INTRODUCTION

Obesity and overweight in children is associated with a wide spectrum of adverse conditions and can negatively affect every organ in the body. Consequences can be insulin resistance, hypertension, dyslipidemia and fatty liver disease.[1] Recent evidence has linked childhood obesity with liver cancer in adulthood.[2]

In addition, overweight and obese children might experience psychological and social problems.[3] Obesity in childhood usually continues into adulthood.[4] A number of epidemiological studies have shown a link between birth weight and BMI in childhood and adulthood,[5,6] and thus potentially creating a life-long condition.

Maternal obesity and gestational weight gain, resulting in over-nutrition of the fetus, are major contributors to obesity and metabolic disturbances in the offspring.[7,8]

Leptin is an adipocyte-derived hormone which is involved in the regulation of food intake and body weight.[9] Through stimulation of sympathetic nerve activity, it leads to a significant increase in energy expenditure.[10] The biologic actions of leptin are thought to be mediated through the activation of leptin receptor in the hypothalamus.[11] Numerous studies have found that plasma leptin concentrations are elevated in several models of animal and human obesity in proportion to the degree of adiposity.[12,13]

This study aimed to investigate the association of maternal obesity at birth with offspring body size and serum leptin.

SUBJECTS AND METHODS

This study was a case control study conducted from Mars 2013 to September 2014. It was observational cross sectional one consisting of three components: a maternal body mass index before delivery, umbilical cord blood collection at the time of delivery to measure serum leptin, and neonatal anthropometric measurements at birth. The study protocol was approved by the ethical committee of the National Research Centre and Obstetric Department of El-Azhar University. Participants gave informed, written consent for themselves and their newborns to enrol into this study.

SUBJECTS

Two hundred healthy pregnant women carrying singleton pregnancies, aged 18-40 years between week 37 and 40 of gestation were recruited in this study. They were attending the Obstetric Department, El-Azhar University for labour. None of them was taking any medication, except for vitamins and iron supplementation.

Women were excluded from this study if they had preeclampsia, chronic hypertension and pregravid type 1 or type 2 diabetes. At delivery, participants were excluded if delivery was caesarean, newborns were born preterm (< 37 weeks of gestation), small for gestational age (SGA) or with severe birth asphyxia (5-min Apgar score <6 or cord blood pH < 7), congenital metabolic or endocrine disease, with major malformations, CNS deficit, congenital infections, or disorders known to affect growth.

The studied women and their offspring were divided into two groups according to maternal BMI: obese group (BMI ≥ 30 kg/m^2) ; control group with normal body mass index (BMI: 20-24.9 kg/m^2).

METHODS

All pregnant women were evaluated by history, clinical examination, and routine investigations. Newborns gestational age, sex and mode of delivery were recorded. Apgar scores at 1,5 minutes were recorded , each determined as the sum of scores (0,1 or 2) related to five neonatal vital signs (heart rate, respiratory rate, muscle tone, excitability and skin colour).

Measurements of anthropometric parameters

Maternal weight and height were measured before delivery. Maternal body mass index was assessed as weight in kg/height in meters ^{2}. Neonatal weight , height and head circumference were determined. Ponderal index (in kg/m3) was calculated as body weight in grams/ length^3 in centimetres X 100. Anthropometric data were assessed as originally described by Cameron.[14]

Biochemical analysis

Umbilical cord blood was collected at delivery and cord serum was separated by centrifugation and stored at −20 °C until analysis. Serum leptin was determined using specific enzyme –linked immunosorbent assay (ELISA) method using commercial kit

(Medizyme leptin from Medipan Diagnostica, Germany.) according to manufacture instructions. For each sample 100 µl of serum per tube was used for duplicate. The limit of detection of lipid assay was 0.45 ng/ml. The intra-assay and interassay coefficient of variation were 8% and 10.8% respectively.

Statistical analysis

Data was analysed using SPSS version 17 and expressed as mean ±SD. Data was divided into two groups according to maternal BMI with the cutoff point 30 kg/m^2 . Data of the two groups were compared using t-test for independent variables. When dividing the offspring data according to sex no significant differences were detected. Pearson correlation coefficient was used to determine the relation between continuous variables. Values of p <0.05 were considered significant.

RESULTS

Mothers mean age was 29.1±5.53 years with range 19-40 years and of weight 65.63±8.7 kg with range 60-86 kg. Their offspring mean birth weight was 3.39± 0.49 kg with range 2.6-4.0 kg and gestational age was 38.6 ± 1.29 weeks with range 37-40 weeks.

The mean cord serum leptin was 16.17 ±12.4 ng/ml with rage 1-50 ng/ml. There was no leptin sex differences (16.9 ±10.2 ng/ml for males vs 18.71±11.4 ng/ml for females). When comparing the two groups based on maternal BMI at delivery; obese (BMI ≥ 30 kg/m^2) and control (BMI: 20- 24.9 kg/m^2) , it was found that neonates of obese mothers had significantly higher levels of leptin (21.17±16.7 vs 11.33±10.55 ng/ml, p <0.001) , neonatal birth weight (3.64±0.32 vs 3.2±0.67 kg, p < 0.05), ponderal index (3.24±0.38 vs 2.77±0.65 gm/cm^3 , p < 0.05) (Table 1).

Table 1. Characteristics of study participants

Mother data	**Obese group (n=100) BMI ≥ 30 kg/m^2**	**Control group (n=100) BMI : (20- 24.9 kg/m^2)**	***P* value**
Age (years)	28.73±3.69	28.53±6.92	NS
Parity	2.07± 0.88	2.46±1.40	NS
Height (meter)	158.66± 4.08	159.26±5.31	NS
Weight (kg)	80.13± 4.36	68.66±4.8	<0.001
BMI (Kg/m^2)	32.05±3.21	26.76±2.4	<0.01
Neonatal data			

G.A (weeks)	38.66±1.04	38.93±1.28	NS
Weight (Kg)	3.64±0.32	3.20±0.52	<0.05
Length (cm)	49.00±1.46	48.60±0.82	NS
H.C (cm)	33.86±0.91	34.40±1.18	NS
P.I (cm)	3.24±0.38	2.77±0.67	<0.05
Leptin (ng/ml)	21.17±16.70	11.33±10.55	<0.001
H.C:Head circumference ; P.I :Ponderal index; NS: Non- significant			

Cord serum leptin was found to correlate with birth weight (r =0.50 , p < 0.01) , length (r =0.59 , p < 0.001) , head circumference (r =0.56 , p < 0.01) ,ponderal index (r =0.40 , p < 0.05) and maternal BMI (r =0.46 , p < 0.05) (Table 2).

Table 2. Correlation of cord serum leptin with maternal body mass index and neonatal anthropometric measurements.

Variable	Leptin	
	r	***p***
Maternal BMI	0.46	<0.05
Weight	0.50	<0.01
Length	0.59	<0.001
H.C	0.56	<0.01
P.I	0.40	<0.05
H.C:Head circumference ; P.I :Ponderal index; r: Pearson correlation coefficient.		

DISCUSSION

Increasing overweight influence the health of pregnant women, and also possess critical risk complications to maternal and Feto-Neonatal healthcare.[15]

The impact of maternal obesity on the fetus has been investigated in several populations, and a range of adverse outcomes such as: Large for Gestational Age (LGA, birth weight > 90th percentile of gestational age- and sex-specific references) and macrosomia (birth weight ≥ 4500g), shoulder dystocia , birth defects , preterm delivery , stillbirth and early neonatal death have consistently been reported.[16,17,18,19]

Results from the large Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study has provided strong evidence of an association between maternal obesity and birth weight.[20] A recent meta-analysis estimated that maternal obesity increases the risk of LGA, high birth weight (> 4000g) and macrosomia, with odds ratios of 2.08, 2.00 and 3.06, respectively.[21]

Our data show that offspring of obese mothers have significantly higher body weight and body size. Interestingly, it was reported that the increased birth weight in offspring of obese mothers seems to be the result of increased fat mass, rather than lean mass.[22,23] suggesting that the in utero metabolic environment affects primarily growth of fat mass, not lean mass.[24]

Leptin, the product of the obesity (ob) gene, is a hormone of 16 kDa comprising 167 amino acids.[25] The central source of leptin is the adipose tissue (white and brown), both maternal and fetal adipose tissues although it can be also produced in other sites, including the placenta.[26] While its receptors are expressed in the uterine endometrium and trophoblast and the fetus.[27]

Although leptin, which has a molecular weight of 16,000 probably does not cross the placenta, there was a significant correlation in leptin concentrations between maternal serum and cord serum.[28] This could be explained by the production of cord serum leptin by neonatal adipose tissue, placenta or both.[29] In the present study cord serum leptin was correlated with maternal BMI before delivery, in agreement with previous studies.[28,30]

Leptin have an essential role in regulation energy homeostasis and consequently body weight. [26] The presence of leptin in human cord blood and its relation to birth weight has been reported [31] We observed significant positive association of cord leptin with neonatal birth weight, in agreement with the results of other investigators. [32,33] Mastuda et al [33] reported correlation of serum leptin with body weight (r= 0.55; p <0.001). A similar correlation (r= 0.57; p <0.001) was reported by Schubring et al.[28] , who observed in addition a positive association between cord serum leptin and placental weight (r= 0.50; p <0.01), suggesting the positive relation between leptin synthesis and release in circulation with birth weight and fetal fat mass during gestation. However, other investigators denied this association.[34] Leptin levels have been widely accepted as a marker for neonatal fat mass, and leptin receptors are expressed in several tissues including fetal cartilage, bone, lung, kidney, and hypothalami, suggesting that leptin may exert biological functions in the fetus and/or early in life.[35]

CONCLUSION

Maternal obesity at delivery is associated with increased neonatal serum leptin and body size with high risk of children obesity later in life.

REFERENCES

1. Daniels SR. Complications of obesity in children and adolescents. Int J Obes (Lond)., 2009; 33(1): S60-5
2. Berentzen, TL, Gamborg M, Holst C, Sørensen TI, Baker JL.Body Mass Index in Childhood and Adult Risk of Primary Liver Cancer. J Hepatol., 2014; 60(2): 325-30.
3. Pitrou I, Shojaei T, Wazana A, Gilbert F, Kovess-Masféty V. Child overweight, associated psychopathology, and social functioning: a French school-based survey in 6- to 11-year-old children.Obesity (Silver Spring)., 2010; 18(4): 809-17.
4. Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obes Rev., 2008; 9(5): 474-88.
5. Parsons TJ, Power C, Manor O. Fetal and early life growth and body mass index from birth to early adulthood in 1958 British cohort: longitudinal study. BMJ., 2001; 323(7325): 1331-5.
6. Schellong K, Schulz S, Harder T, Plagemann A. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. PLoS One., 2012; 7(10): e47776.
7. Drake AJ, Reynolds RM. Impact of maternal obesity on offspring obesity and cardiometabolic disease risk. Reproduction., 2010; 140(3): 387-98.
8. Tie HT, Xia YY, Zeng YS, Zhang Y, Dai CL, Guo JJ, Zhao Y. Risk of childhood overweight or obesity associated with excessive weight gain during pregnancy: a meta-analysis. Arch Gynecol Obstet., 2014; 289(2): 247-57.
9. 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.
10. Tartaglia, LA, Dembski M, Weng X, Deng N, Culpepper J, Devos R, Richards GJ, Campfield LA. Identification and expression cloning of a leptin receptor, OB-R. Cell., 1995; 83:1263–1271.
11. Fei H, Okano HJ, Li C, Lee GH, Zhao C, Darnell R, Friedman JM. Anatomic localization of alternatively spliced leptin receptors (Ob-R) in mouse brain and other tissues. Proc. Natl. Acad. Sci.USA., 1997; 94: 7001–7005.
12. Maffei, M., Halaas J, Ravussin E, Pratley RE, Lee GH, Zhang Y, Fei H, Kim S, Lallone R, Ranganathan S. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. *Nat.Med*., 1995; 1: 1155–1161.

13. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, Ohannesian JP, Marco CC, McKee LJ, Bauer TL. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N. Engl. J. Med*., 1996; 334: 292–295.
14. Cameron N. Methods of auxological anthropometry. In human growth, post natal growth. Vol.2.Falkner F and Tanner J(eds).Casselle Ltd.Plenum Press.London.New York: 1978, pp. 35-42.
15. Awan S, Bibi S, Makhdoom A, Farooq S, Tahir SM, Qazi RA. Adverse fetomaternal outcome among pregnant overweight women. Pak J Med Sci., 2015; 31(2): 383-387.
16. Catalano PM, Ehrenberg HM. The short- and long-term implications of maternal obesity on the mother and her offspring. BJOG., 2006; 113(10): 1126-1133.
17. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, Regan L, Robinson S. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. Int J Obes Relat Metab Disord., 2001; 25(8): 1175-82.
18. Cedergren MI. Maternal morbid obesity and the risk of adverse pregnancy outcome. Obstet Gynecol., 2004; 103(2): 219-24.
19. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. JAMA., 2009; 301(6): 636-50.
20. Group HSCR. Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study: associations with maternal body mass index. BJOG, 2010; 117(5): 575-84.
21. Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. PLoS One., 2013; 8(4): e61627.
22. Sewell M.F, Huston-Presley L, Super DM, Catalano P. Increased neonatal fat mass, not lean body mass, is associated with maternal obesity. Am J Obstet Gynecol., 2006; 195(4): 1100-3.
23. Waters TP, Huston-Presley L, Catalano PM. Neonatal body composition according to the revised institute of medicine recommendations for maternal weight gain. J Clin Endocrinol Metab., 2012; 97(10): 3648-54.
24. Tanvig M. Offspring body size and metabolic profile – Effects of lifestyle intervention in obese pregnant women. Dan Med J., 2014; 61(7): B4893.
25. 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.

26. Christou H, Serdy S, Mantzoros CS. Leptin in relation to growth and developmental processes in the fetus. Semin Reprod Med., 2002; 20: 123–130.
27. Henson MC, Castracane VD. Leptin in pregnancy: an update. Biol Reprod., 2006; 74: 218–229.
28. Schubring C1, Kiess W, Englaro P, Rascher W, Dötsch J, Hanitsch S, Attanasio A, Blum WF. Levels of leptin in maternal serum, amniotic fluid, and arterial and venous cord blood: relation to neonatal and placental weight. J Clin Endocrinol Metab., 1997; 82(5): 1480-3.
29. Hoggard N, Hunter L, Duncan JS, Williams LM, Trayhurn P, Mercer JG. Leptin and leptin receptor mRNA and protein expression in the murine fetus and placenta. Proc Natl Acad Sci U S A., 1997; 94(20): 11073–11078.
30. Butte NF, Hopkinson JM, Nicolson MA. Leptin in human reproduction: serum leptin levels in pregnant and lactating women. J Clin Endocrinol Metab., 1997; 82(2): 585-9.
31. Marchini G, Fried G, Ostlund E, Hagenäs L. Plasma leptin in infants: relations to birth weight and weight loss. Pediatrics., 1998; 101(3 Pt 1): 429-32.
32. Señarís R, Garcia-Caballero T, Casabiell X, Gallego R, Castro R, Considine RV, Dieguez C, Casanueva FF. Synthesis of leptin in human placenta. Endocrinology., 1997; 138(10): 4501-4.
33. Matsuda J, Yokota I, Iida M, Murakami T, Naito E, Ito M . Serum leptin concentration in cord blood: Relationship to birth weight and gender. J Clin Endocrinol Metab., 1997; 82: 1642–4.
34. Ertl T, Funke S, Sárkány I, Szabó I, Rascher W, Blum WF, Sulyok E. Postnatal changes of leptin levels in full-term and preterm neonates: their relation to intrauterine growth, gender and testosterone. Biol Neonate., 1999; 75(3): 167-76.
35. Teague AM, Fields DA, Aston CE, Short KR, Lyons TJ, Chernausek SD. Cord blood adipokines, neonatal anthropometrics and postnatal growth in offspring of Hispanic and Native American women with diabetes mellitus. Reproductive Biology and Endocrinology., 2015; 13(68): 1-9.