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Original Research Article

Correlation of serum leptin levels with clinical and biochemical parameters in obese children

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ABSTRACT

Background: Leptin plays a crucial role in the regulation of appetite, glucose homeostasis and body fat. Authors described various clinical and biochemical parameters of obese children aged 6 to 18 years visiting to outpatient department in a tertiary care hospital followed by their correlation with serum leptin levels. It was a prospective observational study.
Methods: Obese children with Body Mass Index >2 standard deviation according to WHO chart were included. Endocrinological and syndromic obese children were excluded. Authors first compared leptin level of obese children with age and sex matched nonobese children. Followed by correlation of serum leptin levels with various clinical and laboratory parameters in obese children. Pearson's correlation coefficient was used to compute the strength of relationship of leptin with various quantitative parameters. Mann-Whitney Test was also used when standard deviation was high, to calculate statistical significance.
Results: Leptin concentration was significantly higher in obese children than non-obese. No significant difference in sex distribution was found. Serum leptin levels showed positive correlation with BMI, skin fold thickness and abdominal circumference, and blood pressure. No statistical correlation of leptin with biochemical parameters such as dyslipidemia, fasting blood glucose and insulin resistance was seen.
Conclusions: In this study though serum leptin levels had a positive correlation with various clinical parameters, but no statistically significant correlation was seen with biochemical parameters. There is need for further investigation with a larger sample size on the role of leptin in childhood obesity.

Keywords: Body mass index, Dyslipidemia, Insulin resistance, Leptin, Obesity

INTRODUCTION

Leptin is a 167 amino acid, 16-kDa peptide product of ob gene.[1] It is secreted by the adipose tissue.[2] Plays a crucial role in the regulation of appetite, glucose homeostasis and body fat. Leptin regulates the expression of hypothalamic neuropeptides involved in the regulation of feeding and neuroendocrine functions.[3] Leptin correlates most significantly with BMI and body fat.[4] Leptin levels reflect the amount of adipose tissue especially of subcutaneous fat.[5] Leptin levels have been found to correlate with clinical and biochemical parameters of obesity.[6]

Defects in leptin production or function are associated with obesity in animal models and humans. Several studies have confirmed that serum leptin levels decrease following weight reduction.[7,8] Though increased leptin levels have been demonstrated in obesity implicating leptin resistance in human obesity, there is a paucity of data regarding mutations in leptin and leptin receptor genes.[9-11]

There have been limited studies in Indian children with obesity and serum leptin levels and its association with various metabolic disorders. Hence this study is done to demonstrate clinical and biochemical profile of obese children and their correlation with serum leptin levels.

METHODS

Study was conducted at Kanchi Kamakoti Childs Trust Hospital, a tertiary care centre. Period of study was September 2012 to September 2013. Study design was descriptive study.

Inclusion criteria

- Children between 6 to18 years with BMI >2 SD (standard deviation) according to WHO growth chart are included.

Exclusion criteria

- Obesity secondary to endocrinological causes and Syndromic obesity

Children with obesity (body mass index, BMI >2SD of WHO Chart for age and gender presenting to the Pediatric outpatient department were included in the study as cases.

Age and gender matched children without obesity (BMI in normal range for age and gender according to WHO chart), attending outpatient department for minor illnesses were included as controls.

Anthropometric measurements including weight, height, BMI, waist and hip circumference, waist / hip ratio were recorded. Skin fold thickness was measured using HERBEDENS caliper (triceps and sub scapular). Blood pressure was recorded; hepatomegaly and clinical evidence of insulin resistance such as acanthosis nigricans were looked for.

Anthropometry: Body weight was measured to the nearest 0.1 kg with a balance scale and height was measured to the nearest 0.1 cm with stadiometer with subjects lightly dressed and without shoes.

BMI was calculated by standard formula:

Weight in kilograms / (height in meters)^2

Waist Circumference (WC) was measured midway between the lateral lower rib margin and the uppermost lateral border of iliac crest, and hip circumference was measured at the widest point over the great trochanters. Both circumferences were measured in the standing position and at the end of gentle expiration. The Waist-to-Hip Ratio (WHR) was calculated. A non-elastic flexible tape was employed to measure the waist circumference with the subject in the standing position. All measurements were taken 3 times at each site, and the mean of 3 values was used. Children were plotted over centile groups based on abdominal circumference reference values and analyzed. Skin fold thickness was measured at triceps and sub scapular region by the same person to avoid interpersonal variations using HERBEDENS caliper.[12]

Blood pressure >95th centile was considered to be hypertension.

Laboratory investigations including fasting glucose, lipid profile, insulin levels, Blood samples were taken after an overnight fast. Glucose, Total Cholesterol (TC), TGL (triglycerides) measurements were performed using enzymatic assays, HDL-C (High density lipoprotein - cholesterol) was measured by a direct enzymatic assay without precipitation. Low Density Lipoprotein Cholesterol (LDL-C) was estimated by Friedewald formula.[13] Insulin measurement was done by using solid phase chemiluminescence immunoassay.

Fasting glucose =100-125 mg/dl was considered as prediabetic range and >126 mg/dl was considered as diabetic range.14Homeostasis model assessment for insulin resistance (HOMAIR) was estimated by = FI (fasting insulin) × FG (fasting glucose) /22.5. 15

A HOMA-IR cut-off of 2.5 provided the maximum sensitivity and specificity in diagnosing MS in both genders as per ATP III and IDF criteria. Hence HOMAIR >2.5 was defined for insulin resistance.

Lipid profile:

- Cholesterol (CHL) >200 mg/dl
- LDL cholesterol >130 mg/dl
- HDL cholesterol >40 mg/dl
- Triglycerides >100 mg/dl in <15 years age and >125 mg/dl in >15 years age considered as abnormal

Authors correlated clinical and biochemical parameters in obese children with leptin.

Data was recorded on a predesigned proforma and managed on an Excel spreadsheet. SPSS (statistical package for social sciences) for windows statistical software version 17 was used for data analysis. p value less than 0.05 was considered significant. Pearson's correlation coefficient was used to compute the strength of relationship of leptin with various quantitative parameters in cases. Mann-Whitney Test was also used when standard deviation was high, to calculate statistical significance.

RESULTS

Authors have included 107 obese children in this study of which 7 children were excluded of which 3 children had hypothyroidism, 2 had Cushing's syndrome, 1 with

Prader willi syndrome and 1 with Bordet beidl syndrome. 100 obese children with simple obesity were included as cases. 50 children without obesity as controls.

Table 1: Leptin comparison.

Variables	Cases	Controls
Leptin mean values	52.66 ng/ml	4.35 ng/ml

Serum leptin levels measured in 100 obese children chosen as cases and 50 age and sex matched children with normal body mass index who were chosen as controls.

Leptin values were significantly higher in obese children. Serum leptin levels in controls were in lower range. Mean serum leptin levels in obese children were significantly higher than controls (Table 1).

Table 2: Leptin mean values in obese children.

Variable	Male	Female
Leptin (mean values)	52.97 ng/ml	52.24 ng/ml

Among 100 obese children 58 were male and 48 were female. Authors compared serum leptin levels in both sex in obese group as hormones can influence serum leptin levels.

Serum leptin levels though had a wide range in both sexes. Mean values of leptin in both male and female children were almost same and no difference was observed (Table 2).

Table 3: Statistical correlation between serum leptin and clinical parameters in obese.

Variables	Mean±sd	R	p value
BMI	25.6±3.7	0.412	0.001
TFT	12.61±3.9	0.79	0.001
SFT	9.4±4.1	0.75	0.001
AC	66.49±7.3	0.48	0.001
SBP	114.44±6	0.56	0.001
DBP	77.8±4.6	0.63	0.001
Leptin	52.66±27.99	-	-

Leptin correlates well with BMI and was statistically significant (r =0.412) (Table 3).

Leptin showed significant correlation with other anthropometric parameters such as Triceps skin Fold Thickness (TFT), subscapular Skin Fold Thickness (SFT), Abdominal Circumference (AC) in obese children. (Table 3).

Leptin was found to correlate significantly with mean systolic and diastolic blood pressures (Table 3).

Leptin was also correlated with above variables with ANOVA (analysis of variance) between various centile groups in obese children which showed statistically significant correlation.

Correlation coefficients r (Pearson test) between fasting leptin concentrations and physical characteristics are shown. $p<0.05$ values were considered significant correlation. Leptin correlating with clinical parameters. (Table 3).

Table 4: Statistical correlation between serum leptin and biochemical variables in obese.

Variable	Mean±sd	R	p value
CHL	171.21±82.86	0.02	0.80
TGL	128.57±96.99	0.20	0.092
LDL	102.74±69.67	0.09	0.36
HDL	43.03±12.89	0.038	0.70
FBS	89.25±12.94	0.093	0.35
Insulin	21.27±15.72	0.04	0.67
IR	4.69±3.53	0.01	0.89
Leptin	52.66±27.99	-	-

Serum leptin values compared with mean values various biochemical parameters (Table 4).

Leptin did not show statistically significant correlation with serum cholesterol, low density lipoproteins, high density lipoproteins and triglyceride levels (Table 4).

When compared with fasting blood glucose levels no statistically significant correlation was observed (Table 4).

Insulin resistance of obese children also did not show any statistically correlation with serum leptin levels (Table 4). Leptin not correlating with bio-chemical parameters (Table 4).

DISCUSSION

Leptin correlation with anthropometric and clinical parameters

Leptin concentration in this study is significantly higher in obese children than non-obese.

In this study, all obese children had high serum leptin levels suggesting a role of leptin resistance in the pathogenesis of obesity. In addition, it also suggests that resistance to the effects of leptin may start in early childhood.[16,17]

Leptin levels are higher in obese subjects, a finding confirmed in this study.[18,19] The present study reaffirms previously reported studies done by Nageswar Rao et al, and Dubey et al.[6,20] Serum Leptin level did not show much difference between males and females.

Earlier studies of Nageswar Rao et al, and Dubey et al, have shown higher serum leptin levels in females compared to males.[6,20]

However, this difference could be explained by a study of effects of gender, body composition and fat distribution done by Tim R et al.[21]

He arrived at a conclusion that serum leptin concentrations in children are highly correlated with measures of body fat, and that gender differences in serum leptin concentrations may be due to differences in body composition and body fat distribution.[21]

Leptin levels in this study showed statistically significant positive correlation with BMI which was consistent with earlier studies done by Nageswar Rao et al, and Dubey et al.[6,20] The available information suggests that BMI is the main determinant for the variations of leptin levels and these data is in agreement with that reported by others.[6,20]

Despite good correlation of leptin and BMI, authors observed significant variability in leptin levels in subjects with similar BMI. This may be related to differences in body composition and fat distribution.

Maffie et al, described significant heterogeneity in leptin concentration in subjects with similar BMI.[22] It is possible that subjects with appropriate leptin levels are able to keep their weight stable, whereas those with lower levels are prone to weight gain. Another possibility could be the differential sensitivity of individuals to leptin.

Authors observed significant positive correlation of serum leptin levels with waist circumference consistent with previous studies done by Nageswar Rao et al, and Dubey et al.[6,20] No correlation was seen between leptin and waist hip ratio which was not consistent with previous studies done by Nageswar Rao et al, and Dubey et al.[6,20]

However previous studies have shown relationship of leptin with abdominal circumference will be affected by various factors including hyperinsulinemia.[23] WHR values were not correlated with leptin concentrations in a previous study done by Minocci et al, a finding which is similar to this study.[24]

Leptin showed statistically significant correlation with skin fold thickness which is similar to a previous study done by Pilcova et al.[25] Leptin showed significant correlation with systolic and diastolic blood pressure in this study.

Similar to other studies done by Valle et al, and Nishina et al, authors found that hypertension is related to high levels of leptin.[26,27]

This phenomenon may be due to potential vasoconstrictive effects of leptin as a result of increased sympathetic activity.[27]

In addition, leptin may act through indirect pathways such as rennin, aldosterone, and angiotensinogen. Despite these suggestions, the mechanisms underlying the relationship between leptin and blood pressure are still unclear.[28]

Leptin correlation with biochemical parameters

No correlation of leptin with fasting blood glucose levels was observed in this study which was similar to previous study done by Dubey et al.[6]

Previous studies however have reported mixed results concerning the association between serum leptin and fasting blood glucose levels.

Some studies have observed higher glucose levels in obese and overweight individuals and reported positive correlation between leptin and blood glucose levels.[29]

However, other studies have found no correlation of leptin with fasting blood glucose levels in obese children was observed.[6] Leptin did not show statistically significant correlation with insulin resistance.

This was similar to a previous study done by Valerio et al, who found no correlation of leptin with insulin resistance.[30] In this study no correlation was seen between serum leptin with total cholesterol, triglycerides LDL and HDL-cholesterol which was in contrast with previous studies done by Nageswar Rao et al, and Dubey et al.[6,20]

Dubey et al, noted good correlation of leptin with total cholesterol, triglycerides and LDL cholesterol and no correlation was seen with HDL cholesterol.[6]

Previous studies have reported mixed results concerning the association between serum leptin and lipid profile. Few studies have shown no significant relationship between leptin and lipids, whereas in other lipids showed significant correlation with leptin levels.[6,19,31,32]

The relationship between serum leptin and lipids remains unclear. Although 15% of the obese children in this study had evidence of metabolic Syndrome no significant correlation with leptin was observed.

Leptin levels are shown to predict the development of the metabolic syndrome independent of baseline obesity in one study.[33]

In another study leptin did not appear to have a major role in metabolic syndrome, even though it was strongly associated with obesity parameters.[34]

CONCLUSION

Serum leptin levels correlate with BMI, skin fold thickness and abdominal circumference, blood pressure.

No statistical correlation of leptin with biochemical parameters of obesity was seen.

There is a need for further investigation with a larger sample size on the role of leptin in childhood obesity and its correlation with various clinical and biochemical parameters.

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REFERENCES

1. 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 Dec 1;372(6505):425-32.
2. Klein S, Coppack SW, Mohamed-Ali V, Landt M. Adipose tissue leptin production and plasma leptin kinetics in humans. Diabetes. 1996 Jul 1;45(7):984-7.
3. Ahima RS, Saper CB, Flier JS, Elmquist JK. Leptin regulation of neuroendocrine systems. Front Neuroendocrinol. 2000 Jul 1;21(3):263-307.
4. Argente J, Barrios V, Chowen JA, Sinha MK, Considine RV. Leptin plasma levels in healthy Spanish children and adolescents, children with obesity, and adolescents with anorexia nervosa and bulimia nervosa. J Pediatr. 1997 Dec 1;131(6):833-8.
5. Lahlou N, Landais P, De Boissieu D, Bougneres PF. Circulating leptin in normal children and during the dynamic phase of juvenile obesity: relation to body fatness, energy metabolism, caloric intake, and sexual dimorphism. Diabetes. 1997 Jun 1;46(6):989-93.
6. Dubey S, Kabra M, Bajpai A, Pandey RM, Hasan M, Gautam RK, et al. Lead Article. Ind Pediatr. 2007;44:257-62.
7. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. New Eng J Med. 1996 Feb 1;334(5):292-5.
8. Reiterer EE, Sudi KM, Mayer A, Limbert-Zinterl C, Stalzer-Brunner C, Füger G, et al. Changes in leptin, insulin, and body composition in obese children during a weight reduction program. J Pediatr Endocrinol Metab. 1999;12(6):853-62.
9. Lönnqvist F, Arner P, Nordfors L, Schalling M. Overexpression of the obese (ob) gene in adipose tissue of human obese subjects. Nature Ned. 1995 Sep;1(9):950-3.
10. Montague CT, Farooqi IS, Whitehead JP, Soos MA, Rau H, Wareham NJ, et al. Congenital leptin deficiency is associated with severe early-onset obesity in humans. Nature. 1997 Jun;387(6636):903-8.
11. Strobel A, Issad T, Camoin L, Ozata M, Strosberg AD. A leptin missense mutation associated with hypogonadism and morbid obesity. Nature Gene. 1998 Mar;18(3):213-5.
12. Owen GM. Measurement, recording, and assessment of skinfold thickness in childhood and adolescence: report of a small meeting. Am J Clin Nutri. 1982;35:629-38.
13. Alberty RR, Albertyová D. Serum lipid growth curves for children and adolescents in predicting adult dyslipidemia (Data from the Slovak Lipid Community Study). Advan Biol Chem. 2013 Oct 10;2013.
14. Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care 2006; 29 (Suppl 1):S43-8.
15. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentration in man. Diabetol. 1985;28:412-4.
16. Sudi K, Gallistl S, Tröbinger M, Reiterer E, Payerl D, Aigner R, et al. Insulin and insulin resistance index are not independent determinants for the variation in leptin in obese children and adolescents. J Pediatr Endocrinol Metab. 2000;13(7):923-32.
17. Zimmet P, Hodge A, Nicolson M, Staten M, De Courten M, Moore J, et al. Serum leptin concentration, obesity, and insulin resistance in Western Samoans: cross sectional study. Bmj. 1996 Oct 19;313(7063):965-9.
18. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. New Eng J Med. 1996 Feb 1;334(5):292-5.
19. Ostlund Jr RE, Yang JW, Klein S, Gingerich R. Relation between plasma leptin concentration and body fat, gender, diet, age, and metabolic covariates. J Clin Endocrinol Metab. 1996 Nov 1;81(11):3909-13.
20. Rao GSN, Gurumurthy P, Gururajan P, Arumugam SB, Kirthivasan SV, Cherian KM, et al. Clinical and Biochemical Parameters in Relation to Serum Leptin Levels in South Indian Children and Adolescents. Ind J Pediatr. 2010;77:555-9.
21. Nagy TR, Gower BA, Trowbridge CA, Dezenberg C, Shewchuk RM, Goran MI. Effects of gender, ethnicity, body composition, and fat distribution on serum leptin concentrations in children. J Clin Endocrinol Metab. 1997 Jul 1;82(7):2148-52.
22. Maffei Á, Halaas J, Ravussin E, Pratley RE, Lee GH, Zhang Y, et al. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nature Med. 1995 Nov;1(11):1155-61.
23. Al-Daghri NM, Al-Attas OS, Al-Rubeaan K, Mohieldin M, Al-Katari M, Jones AF, et al. Serum leptin and its relation to anthropometric measures of

obesity in pre-diabetic Saudis. Cardio Diabetol. 2007 Jul 7;6:18.
24. Minocci A, Savia G, Lucantoni R, Berselli ME, Tagliaferri M, Calo G, et al. Leptin plasma concentrations are dependent on body fat distribution in obese patients. Inter J Obes. 2000 Sep;24(9):1139-44.
25. Pilcova R, Sulcova J, Hill M, Bláha P, Lisá L. Leptin levels in obese children: effects of gender, weight reduction, and androgens. Physiol Res. 2003 Jan 1;52(1):53-60.
26. Valle M, Gascon F, Martos R, Bermudo F, Ceballos P, Suanes A. Relationship between high plasma leptin concentrations and metabolic syndrome in obese pre-pubertal children. Inter J Obes. 2003 Jan;27(1):13-8.
27. Nishina M, Kikuchi T, Yamazaki H, Kameda K, Hiura M, Uchiyama M. Relationship among systolic blood pressure, serum insulin and leptin, and visceral fat accumulation in obese children. Hyperten Res. 2003;26(4):281-8.
28. Chu NF, Wang DJ, Shieh SM. Obesity, leptin and blood pressure among children in Taiwan: the Taipei Children's Heart Study. Am J Hyperten. 2001 Feb 1;14(2):135-40.
29. Chu NF, Chang JB, Shieh SM. Plasma leptin, fatty acids, and tumor necrosis factor-receptor and insulin resistance in children. Obes Res. 2003 Apr;11(4):532-40.
30. Nobili V, Manco M, Ciampalini P, Diciommo V, Devito R, Piemonte F, et al. Leptin, free leptin index, insulin resistance and liver fibrosis in children with non-alcoholic fatty liver disease. Eur J Endocrinol. 2006 Nov 1;155(5):735-43.
31. Misra A, Arora N, Mondal S, Pandey RM, Jailkhani B, Peshin S, et al. Relation between plasma leptin and anthropometric and metabolic covariates in lean and obese diabetic and hyperlipidaemic Asian Northern Indian subjects. Diabe, Nutri Metab. 2001 Feb;14(1):18-26.
32. Tamer L, Ercan B, Unlü A, Sucu N, Pekdemir H, Eskandari G, et al. The relationship between leptin and lipids in atherosclerosis. Ind Heart J. 2002;54(6):692-6.
33. Franks PW, Brage S, Luan JA, Ekelund U, Rahman M, Farooqi IS, et al. Leptin predicts a worsening of the features of the metabolic syndrome independently of obesity. Obe Res. 2005 Aug;13(8):1476-84.
34. Hamidi A, Fakhrzadeh H, Moayyeri A, Heshmat R, Ebrahimpour P, Larjani B. Metabolic syndrome and leptin concentrations in obese children. Ind J Pediatr. 2006 Jul 1;73(7):593-6.

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