

Serum Lipid and Leptin Concentrations in Patients with Sheehan Syndrome

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Abstract

Background: Sheehan syndrome (SS) refers to the occurrence of hypopituitarism after parturition. Hypopituitary adults with growth hormone (GH) deficiency have abnormal body composition with increased fat mass. As leptin is secreted almost exclusively by fat cells and the circulating leptin level is proportional to total fat mass, it is expected that abnormal elevations of leptin concentrations are found in GH deficient hypopituitary patients. The present study was undertaken to evaluate the anthropometric, lipid and leptin levels in patients with SS. **Materials and Methods:** Thirty patients with SS and 30 age and body mass index (BMI) matched controls were part in this study. All patients were stable on conventional replacement therapy for at least 6 months before the study. The subjects underwent detail clinical, biochemical, and hormone analysis. **Results:** Patients with SS on conventional replacement therapy showed significantly higher mean triglyceride, total cholesterol, low density lipoprotein cholesterol and lower high density cholesterol concentrations. The leptin levels were significantly raised in the patients with SS on standard replacement therapy compared with controls. The difference was more marked in obese cases versus obese controls than in lean cases and controls ($P = 0.001$). **Conclusion:** SS, a cause of GH deficiency. Our study demonstrated that patients with SS have an abnormal lipid profile, and raised leptin levels as compared to age and BMI matched controls.

Keywords: Leptin, lipid profile, Sheehan syndrome

INTRODUCTION

Sheehan syndrome (SS) refers to the occurrence of varying degrees of hypopituitarism after parturition.^[1] Some degree of hypopituitarism has been reported in 32% of women with severe postpartum hemorrhage.^[2,3] Hypopituitary adults with growth hormone (GH) deficiency have abnormal body composition with increased fat mass.^[4] Patients with hypopituitarism (particularly women) receiving conventional replacement therapy have higher cardiovascular mortality and morbidity than the general population, although this has not been extensively studied in patients with SS.^[5] The exact mechanism of increased vascular disease in hypopituitarism and the causal relationship to GH deficiency is still unclear.^[6] However, changes in carbohydrate and lipid metabolism and body composition may likely play a major role.^[7] Leptin, a hormone secreted exclusively by fat cells is proportional to total fat mass and increased leptin level has been found in GH deficient hypopituitary patients.^[8] Apart from fat mass and gender, many hormones influence circulating leptin levels like

testosterone, GH, glucocorticoids, insulin, and estrogens.^[9-13] In GH deficient hypopituitary adults, GH therapy after 52 weeks of treatment, caused significant decrease in the percentage of fat and leptin.^[14-17] Based on this background, the present study was conducted to evaluate the lipid and leptin levels in patients with SS.

MATERIALS AND METHODS

Over a period of 2 years, 30 SS patients who attended endocrine clinic of internal medicine department were enrolled in the present study. These patients were on follow-up and were on treatment for more than 6 months. In addition, 30 age and BMI matched controls were recruited from hospital staff and friends. A written well-informed consent was obtained from all

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patients and controls and the study was performed according to the Declaration of Helsinki, 1975. The diagnosis of SS was based on history of postpartum hemorrhage and/or failure of lactation and/or amenorrhea following last child birth, more than one anterior pituitary hormone deficiency and empty sella on MR imaging.^[18] Fasting early morning (08:30 am) blood samples were collected for glucose, follicle-stimulating hormone (FSH), luteinizing hormone (LH), cortisol, thyroid stimulating hormone (TSH), total T4, prolactin (PRL), and GH. In addition, samples were also collected in separate vacutainers for biochemical assays like liver function tests and lipid profile.

Statistical analysis

Statistical analysis was done using SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean \pm SD, median, and interquartile range. categorical variables were summarized as percentages. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data were presented by bar and pie diagrams. *P* value of less than 0.05 was considered statistically significant.

RESULTS

The mean age of patients and controls was 47.7 ± 4.47 years and 47.3 ± 4.34 years, respectively. The duration of treatment in cases ranged from 6 months to 8 years. Of the 30 SS subjects, 16 (53.33%) had a BMI in the normal range, that is, (18.5–22.9), 10 patients (33.33%) were overweight (BMI 23–24.9), and only 4 (13.3%) were obese (BMI of >25). The detail of the clinical profile is given in Table 1. At least one hormone deficiency was present in all of the patients and more than one hormone deficiency in 88.7% of patients. The details of the hormone profile in SS patients are given in Table 2. All patients had corticotrophin deficiency and were treated with prednisolone and hydrocortisone. The average dose of hydrocortisone equivalent was 20 mg with mean of 18 ± 4.1 mg. All patients had thyrotroph deficiency and were treated with thyroxine; the average dose was 88 ± 25.1 μ g/day. Twenty-two (73.33%) of 30 cases had blood glucose less than 100 mg/dl, 7 (23.33%) had levels between 100 and 126 mg/dl, and only 1 (3.33%) patient had blood glucose level of >126 mg/dl. The details of the biochemical profile in these subjects are given in Table 3. Patients median T4 was 1.5 μ g/dl (IQR 1.16–3.9), cortisol stimulated was 4.12 μ g/dl (IQR 2.4–7.9). The leptin level in cases was in the range of 11.2–42.8 ng/ml. Statistically, significant difference of leptin level was observed in obese cases versus obese controls (33.15 ± 5.98 vs 28.06 ± 2.99 , *P* = 0.0001). Obese patients also had higher leptin levels than nonobese patients (*P* < 0.001). Similar findings were observed for obese versus nonobese controls (*P* 0.050).

DISCUSSION

SS classically refers to postpartum hypopituitarism due to pituitary necrosis occurring secondary to massive bleeding at or just after delivery.^[1] Pituitary insufficiency in SS may manifest

Table 1: Clinical profile of patients with Sheehan syndrome

Parameters	Cases (n=30)	
	No.	%
History of postpartum hemorrhage	27	90
Failure of lactation	25	83.33
H/o blood transfusions	12	40
Secondary amenorrhea	30	100
Empty sella on MRI	30	100
Hyponatremia	14	46.67

Table 2: Basal thyroid and pituitary hormonal parameters

Hormone (plasma)	Units	Values	Normal values
T ₃	ng/ml	<.5	0.7-2.5
T ₄	μ g/dl	<3	5.5-13.5
TSH	μ IU/ml	4.33	0.5-6.5
LH	IU/L	2.13	3-12
FSH	IU/L	5.53	2-6.6
Prolactin*	μ g/L	4.47	>2
GH*	μ g/L	0.50	>3
Cortisol*	μ g/dl	7.35	>20

T₃, tri-iodothyronine; T₄, thyroxine; TSH, thyroid stimulating hormone; FSH, follicle stimulating hormone; LH, luteinizing hormone; GH, growth hormone. *Peak values after insulin tolerance test. Hormone assays performed with specific radioimmunoassay

Table 3: Biochemical profile in patients with Sheehan syndrome

Parameters	Cases	Controls	<i>P</i>
TG (mg/dl)	234.37 \pm 90.86	160.37 \pm 54.82	<0.001
HDL (mg/dl)	45.73 \pm 9.23	57.33 \pm 6.82	0.001
Cholesterol (mg/dl)	208.83 \pm 47.96	183.10 \pm 39.08	0.026
LDL (mg/dl)	122.03 \pm 53.31	87.27 \pm 12.54	0.002

in the form of partial or complete hormone insufficiency.^[19] Severe GH deficiency is an established feature of SS and GH deficiency is associated with abnormal body composition, altered lipid profile, reduced quality of life, and osteoporosis. Replacement with recombinant GH results in significant improvement in most of these altered parameters. Although severe GH deficiency is a well-established feature of SS, the effects of GH deficiency in these patients has not been extensively investigated. Our study also revealed that the SS patients on conventional replacement therapy had significantly higher mean triglyceride (234 vs 160 mg/dl; *P* < 0.001), total cholesterol (208 vs 183 mg/dl; *P* = 0.026), and LDL cholesterol (122 vs 87 mg/dl; *P* = 0.002) and lower HDL cholesterol concentrations (45 vs 57.3 mg/dl; *P* = 0.026). These findings were consistent with Bhat *et al.*^[20] who found total cholesterol (5.21 ± 0.98 mg/dl vs 4.57 ± 0.88 mg/dl, *P* < 0.001), LDL-cholesterol (3.15 ± 0.90 mg/dl vs 2.67 ± 0.75 mg/dl; *P* = 0.02), and triglycerides (2.14 ± 1.00 mg/dl vs 1.43 ± 0.45 mg/dl; *P* = 0.00) were significantly higher in patients with SS. Ozbeyet *et al.*^[21]

studied serum lipid and leptin concentrations in hypopituitary patients with GH deficiency. Hypopituitary patients with GH deficiency on conventional replacement therapy showed significantly higher TG, LDL cholesterol, and lower HDL cholesterol concentrations. Bohdanowicz-Pawlak *et al.*^[22] also observed that the HDL cholesterol level was lower and TG level higher in hypopituitary patients than in controls. Serum concentrations of total cholesterol in both GH deficient patients and controls were not significantly different. The level of LDL cholesterol was significantly higher in GH deficient women, whereas in men the difference was not statistically significant. Similar findings were reported by Hagmar *et al.*^[23] who reported that in untreated GH-deficient adults, levels of total cholesterol, LDL cholesterol, triglycerides, and apolipoprotein B were increased, and HDL-cholesterol level was reduced compared with those in healthy adults. Tanriverdi *et al.*^[24] also reported that at baseline, mean total cholesterol, LDL-cholesterol, and triglyceride levels were higher than the normal reference ranges but HDL-cholesterol levels were within the lower normal range. In the present study, it was observed that the leptin levels were significantly higher in the cases with a mean \pm of 24.7 ± 7.46 ng/ml compared to controls (14.9 ± 3.76 ng/ml). This difference was statistically significant ($P \leq 0.001$). The difference was more marked in obese cases versus obese controls than in lean cases and controls. Obese patients also had higher leptin levels than nonobese patients. Similar findings were observed for obese versus nonobese controls. Ozbey *et al.*^[21] also found significantly higher leptin concentrations in patients with hypopituitarism compared with healthy controls with similar body fat content ($23.5 + 11.8$ ng/ml vs $11.7 + 6.9$ ng/ml, $P = 0.01$). This difference remained significant even when leptin values were expressed in relation to fat mass percentage.

CONCLUSION

Patients with SS have an abnormal lipid profile, and raised leptin levels as compared to age and BMI matched controls. Whether this is a result of the adverse effects of GH deficiency on body composition needs to be elucidated.

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Conflicts of interest

There are no conflicts of interest.

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