Serum Leptin Levels In Infertile Males.

LOVIE BENETA T MERWIN
Department of Physiology,
MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract:
Background. The incidence of obesity is on the rise and infertility among men is also a growing problem in the recent years. Leptin, an adipocyte derived protein hormone, has emerged as a metabolic link between nutrition and fertility by its involvement in regulation of reproductive function in both experimental animals and humans. Several studies support the role of serum leptin in the regulation of gonadal functions in men indirectly via the central neuroendocrine system and directly via peripheral tissue membrane receptors. Establishment of such a link may provide a new insight into the causes of infertility and may lead to better treatment modalities in infertile men. In this study we aim to compare the serum leptin levels among a group of normospermic and oligospermic men and correlate leptin levels with Body Mass Index (BMI).

Materials and Methods. A cross sectional case-control study was conducted among 60 men at the age group of 25 to 40 years attending an infertility clinic. 30 men diagnosed as infertile were grouped as cases. 30 men with normospermia were selected as controls. The height, weight, and BMI were calculated. 5 ml of blood was collected and serum leptin levels were analysed using the leptin ELISA kit. The data obtained was analysed using SPSS software version 7.5. Independent student t test was employed. p value less than 0.05 was taken as significant. Results. Oligospermic males had a significantly higher BMI than that of the controls. The mean serum leptin levels of the oligospermic males was found to be significantly higher than that of the controls. A strong positive correlation was observed between the BMI and leptin levels of both the study groups. Conclusion. Increased BMI and serum leptin levels in oligospermic males suggest that obesity is associated with infertility in men and a possible link between the
adipocyte derived hormone, leptin and male gonadal dysfunction.

**Keyword**: 'Leptin', 'BMI', 'Oligospermic', 'Normospermic', 'infertility'.

**Materials and Methods:**
The study was conducted among 60 men at the age group of 25 to 40 years attending an infertility clinic.

**Inclusion criteria**
30 men diagnosed as oligospermic as per WHO criteria (less than 15 million sperm/ml, consistent with the 5th percentile for fertile men) selected from an infertility clinic were grouped as cases. 30 men with normospermia were selected as controls.

**Exclusion criteria**
Men with obstructive azoospermia, varicocele, chronic disease like diabetes, hypertension, liver or renal diseases were excluded from the study. After obtaining informed consent, the height and weight of all men were recorded and BMI was calculated. 5 ml of blood was collected from all men and serum was separated and stored at -20°C and serum leptin levels were analysed using the leptin ELISA kit.

**Serum Leptin Levels In Infertile Males.**

**Introduction:**
The incidence of obesity continues to be on the rise owing to reduction in physical activity, an increase in the accessibility of, and overindulgence in energy-dense foods, combined with genetic, social and economic factors.1 Infertility among men is also a growing problem in the recent years. Leptin, an adipocyte derived protein hormone of 167 amino acids, which enables the body to maintain energy homeostasis, has emerged as a metabolic link between nutrition and fertility by its involvement in regulation of reproductive function in both experimental animals and humans. Leptin receptors are present in testicular tissue.2 It is expressed mainly on the spermatocytes in the seminiferous tubules and its expression increases with spermatogenic dysfunction. Several studies support the role of serum leptin in the regulation of gonadal functions in men indirectly via the central neuroendocrine system and directly via peripheral tissue membrane receptors. Predominant stimulatory effects, primarily at the hypothalamus, are observed at physiological leptin levels above a minimal threshold and direct inhibitory actions at the testicular level may take place in the presence of a significantly elevated leptin concentration, as detected in obesity.4 Establishment of such a link may provide new insight into the causes of infertility and may lead to better treatment modalities in infertile men. In this study we aim to compare the serum leptin levels among a group of normospermic and oligospermic men and correlate leptin levels with Body Mass Index (BMI).

**Results:**
The data obtained was analysed using SPSS (Statistical Package for the Social Sciences) software version 7.5. Independent student t test was employed. p value <0.05 was taken as significant.

The mean age among the controls was 33.2±4.09 as against 34.03±4.72 among the oligospermic males. The difference was not statistically significant. The mean BMI of the oligospermic males was found to be 28.04±4.72 among the oligospermic males. The difference was not statistically significant. The mean BMI of the oligospermic males was found to be 25.95±3.04. The mean serum leptin levels of the oligospermic males was found to be 11.13±4.78 which was
higher than that of the controls 7.16±4.85 and was highly significant.

**Table 1**

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>GROUPS</th>
<th>MEAN±SD</th>
<th>p VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in Years</td>
<td>Controls</td>
<td>33.2±4.08</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Cases</td>
<td>34.0±4.72</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>25.6±3.04</td>
<td></td>
</tr>
<tr>
<td>Serum Leptin (ng/ml)</td>
<td>Controls</td>
<td>11.3±4.78</td>
<td>0.00**</td>
</tr>
<tr>
<td></td>
<td>Cases</td>
<td>4.0±3.34</td>
<td></td>
</tr>
</tbody>
</table>

* - Significant ** - Highly Significant.

**Graph1** Comparison Of BMI Among The Study Groups:

**Graph2** Comparison Of Serum Leptin Levels Among The Study Groups

The BMI and leptin levels of both the study groups showed a strong positive correlation which was found to be highly significant.

**Discussion**:

From this study we could find that the serum leptin levels was significantly higher in the infertile oligospermic men compared to the normospermic men. This was in accordance to earlier studies by Steinman et al. (2001), Hanafy et al 2007, and Von Sobbe et al.(2003). BMI was higher in oligospermic males similar to earlier studies by Sallmén et al., (2005);Ruby et al., (2007). There was a strong positive correlation of serum leptin levels and BMI in both the groups as reported by Considine RVet al8 and Ostlund RE et al (1996).
Leptin release per gram adipose tissue is two times greater in obese because fat cell size is usually enlarged 2–4 times in the obese. As the fat mass is the main regulator of leptin levels, an increased number of fat cells, in extreme obesity, contributes to increases in serum leptin levels.\(^{10}\) Leptin acts indirectly to regulate gonadotropin secretion in the hypothalamus by modulating kisspeptins in the arcuate nucleus. The KiSS1 neurons are decreased in the hypothalamus of \(ob/ob\) leptin deficient mice, indicating that leptin regulates KiSS1 neurons, and indirectly gonadotropin release. Increased leptin level in overweight might disrupt hypothalamic pituitary gonadal axis, leading to reproductive dysfunctions, including infertility.\(^{11}\)

Leptin possibly has a direct inhibitory effect on testosterone production by binding to Leydig cells and it appears to act as a direct inhibitory signal for testicular steroidogenesis. It has been observed in obese men that the peripheral leptin receptors in the testis are directly exposed to high-leptin concentrations with possible negative effects on gonadal functions. Overweight and obese men report an inverse relationship between serum levels of leptin and testosterone.\(^{12}\)

**Conclusion:**

The results of the study suggest that obesity is associated with infertility in men and a possible link between the adipocyte derived hormone, leptin and male gonadal dysfunction. Further studies are required to establish the possible link of leptin and serum testosterone levels and spermatogenesis.

**References:**


