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Research Paper

Impact of obesity on male fertility

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Abstract

Rationale Nowadays, obesity and dyslipidemia are more prevalent , studies had shown that obese men have around 50% higher rate of infertility compared to normal weight men Aim of the work is to study the impact of obesity on male infertility Subjects and methods This study included 90 males aged (25 - 45) years old , divided into three groups . Semen samples to assess semen quality plus a blood sample to measure serum testosterone and leptin levels were collected Results A statistically significant increases of mean BMI in obese fertile and obese infertile groups compared to non-obese infertile group ($p. < 0.0001$) .There was a statistically significant increase of mean serum leptin in obese infertile group compared to obese fertile group ($p. < 0.0001$) and compared to obese fertile group ($p. < 0.0001$). There was a statistically significant increase of mean serum testosterone level in obese fertile group compared to non-obese infertile group ($p < 0.01$) and there was a statistically significant increase of mean sperm motility in obese fertile group compared to obese infertile group Conclusion. BMI & serum leptin levels in obese infertile men were significantly higher than obese fertile men. Serum leptin had significant negative correlation with sperm count, motility and testosterone level. Leptin had significant correlation with the abnormal sperm morphology. Men with high BMIs had a significant decrease in sperm count, and motility as well as increase in the abnormal forms of spermatozoa compared to those with low BMIs.

Keywords: Obesity, Infertility, Semen Quality, Testosterone, Leptin.

1. Introduction

Obesity is a medical condition in which excess body fat or white adipose tissue accumulate in the body to the extent that accumulation of fat might adversely affect health. Individuals can be defined as being overweight if their body mass index (BMI) is 25–30 kg/m² and obese if their BMI above 30 kg/m². Other more accurate methods to assess obesity include energy x-ray absorptiometry, body adipose tissue computed tomography and waist-hip ratio measurements [1]. Over years, studies had shown that overweight and obese men have an up to 50% higher rate of infertility compared to normal weight men [2]. Studies set in infertility clinics have the advantage of investigating obesity trends within populations of unselected healthy infertile populations. These studies enabled evaluation of the association between obesity and infertility. Studies designed to measure sperm parameters for obese men tended to report a negative association between semen parameters and BMI. Sperm concentration/total sperm count seems most likely to be negatively associated with BMI above 25 kg/m² with reduced normal sperm morphology and motility less consistent across studies [3]. Nowadays, obesity and dyslipidemia are more prevalent because of increasing sedentary lifestyles and diets higher in saturated fats [4]. Obesity was established as an underlying factor in erectile dysfunction after comparing erectile capabilities and the findings of penile duplex between obese and non-obese groups [5]. Leptin is an adipocyte-secreted protein that participates in the regulation of energy homeostasis. Leptin 0riginally thought to act as satiety factor. Deficiencies in leptin signaling or functioning contribute to develop obesity [6]. Since its discovery leptin's biological function has been expanded from anti-obesity to broad effects on reproduction, hematopoiesis, angiogenesis, blood pressure, and bone mass, and T-lymphocyte systems [7]. Leptin has been implicated in the regulation of reproductive function in both experimental animals and humans emerging as a metabolic link between

nutrition and fertility. Its role in male reproduction is poorly investigated [8] It has been shown that leptin secretion by the adipocyte is regulated by other hormones, such as insulin, cortisol and sex steroids mainly testosterone [9]. Leptin was demonstrated to stimulate gonadotrophin releasing hormone secretion with indirect effects on the gonads [10]. The influence of BMI on leptin is a significant factor throughout the pre-pubertal and pubertal years of both sexes suggesting that leptin may have a facilitatory role in human pubertal development. In pre-pubertal boys serum leptin was shown to increase slowly with age and body fat mass obese men usually express a characteristic hormonal profile described as hyperestrogenic hypogonadism. Both total and free blood testosterone levels are decreased in obese men. This may lead to hypogonadal obesity cycle and increased adipose tissue and significant reduction in circulating testosterone leading to subfertility [11].

2. Aim of the work

The aim of this work is to study the impact of obesity on male infertility.

3. Subjects and methods

This study was conducted during the period from March 2013 to June 2013.The study includes 90 male aged from 25 to 45 years old. They were divided into three groups: First group included thirty infertile obese patients. Second group included thirty infertile non-obese patients and third group: thirty obese fertile persons.

Patients having history of chronic diseases, operation or drug intake that may affect his fertility or sexual function, exposure to chemotherapy or radiotherapy, patients who underwent vasectomy. Patients with mental retardation, spinal cord injury, Endocrine disease or Psychiatric problems were excluded.

All groups were subjected to complete medical history and General examination .Semen samples were obtained from all subjects, collected by masturbation into sterile plastic jars, after 3-5 days of sexual abstinence. They were allowed to liquefy for 30 min at room temperature (22ºC) and were then evaluated according to World Health Organization (WHO) guidelines [12]. Also 5 ml of venous blood was collected in the early morning divided into two samples for assessing serum testosterone and leptin level using a solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle [13].

Ethical consideration:

The whole research process was explained to all the participants and a written consent was obtained from all the them. This study was approval by the ethical committee of Fayoum universityStatistical Analysis: Analysis of data was performed using SPSS V16 (Statistical Package for Scientific Studies) Description of quantitative variables was in the form of mean, standard deviation, minimum and maximum. Description of qualitative variables was in the form of numbers (No.) and percentages (%). Comparison between quantitative variables was carried out by student T-test of two independent samples. Repeated measures Analysis of Variance (ANOVA) test and T- test were used when comparing between more than two groups of independent variables. Results were expressed in the form of P-values. Binary correlation was carried out by Pearson correlation test. Results were expressed in the form of correlation coefficient (R) and P-values. P-value ≤ 0.05 was considered to be significant.

4. Results

This study included 90 male patients the results of the study parameters are shown in table -1.

Table 1: Study Parameters of All Cases (N=90).

	Non-obese infertile Mean ±SD	Obese fertile Mean ±SD	Obese infertile Mean ±SD
Age (years)	30.5±2.91	29.50±3.205	32.96±5.37
BMI (Kg/ m^2)	19.34±0.99	31.82±1.077	34.08±2.69
Duration (years)	4.00±1.61	0	9.40±4.73
Leptin (ng/ml)	26.46±5.34	10.81±3.12	22.92±6.00
Sperm density(million/ml)	20.86±10.96	71.26±24.44	24.35±11.38
Sperm motility grade	1.81±0.75	3.70±0.48	1.63±0.66
Sperm viability (%)	30.27±10.91	73.80±11.18	31.73±13.54
Testosterone (ng/ml)	4.53±1.52	8.16±2.74	3.75±1.140

There was statistically highly significant increases of mean BMI in obese fertile group (31.82+1.07 kg/m²) and obese infertile group (34.08+2.09 kg/m²) compared to non-obese infertile group (26.68+0.99 kg/m²) (p.< 0.0001) (Fig-1).

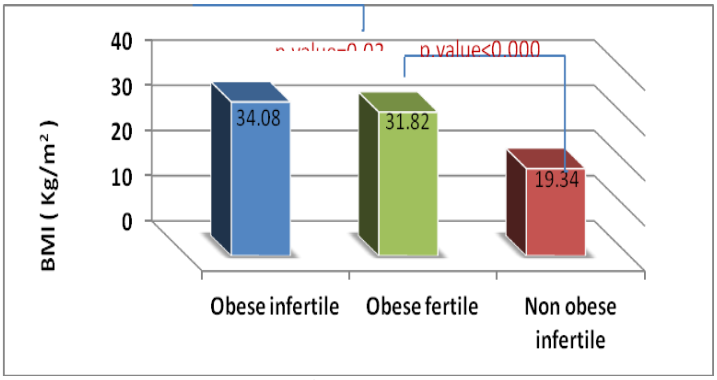


Fig. 1: Comparison of Mean BMI in the Study Groups

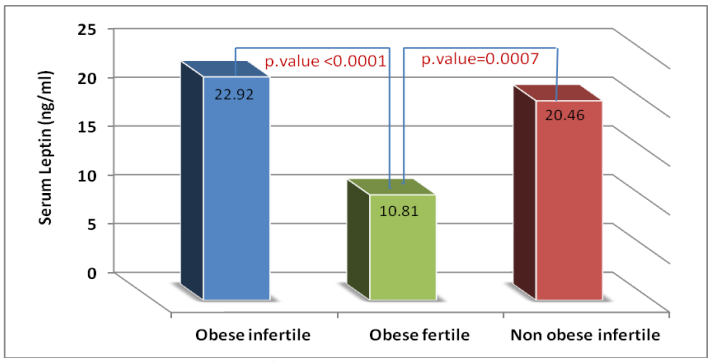


Fig. 2: Comparison of Mean Serum Leptin in the Study Groups

Mean serum leptin was higher in obese infertile group (22.92±6.00) compared to obese fertile group (10.81±3.12). And compared to obese fertile group (10.81±3.12) and the differences were highly significant (p. < 0.0001) (Fig 2)
The mean serum testosterone was significantly higher in obese fertile group (8.16±2.74) compared to non-obese infertile group (4.53±1.52) and compared to obese infertile group (3.75±1.140) (p. < 0.01) (Fig 3) (Table-1).

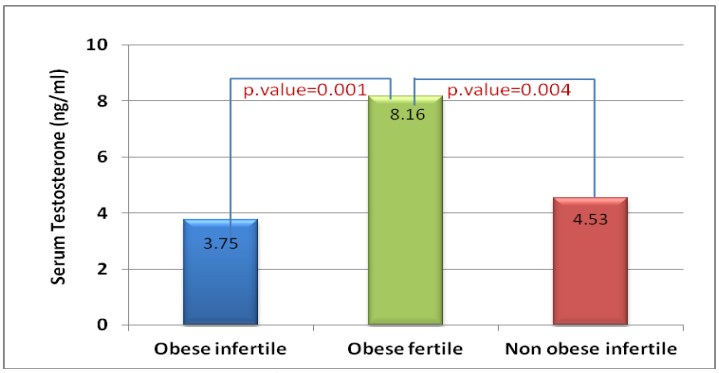


Fig. 3: Comparison of Serum Testosterone in the Study Groups

There was statistically significant increase of mean infertility duration in obese infertile group (9.40±4.73 years) compared to non-obese group (4.00±1.61) (p. <0.0014) (Fig-4.).

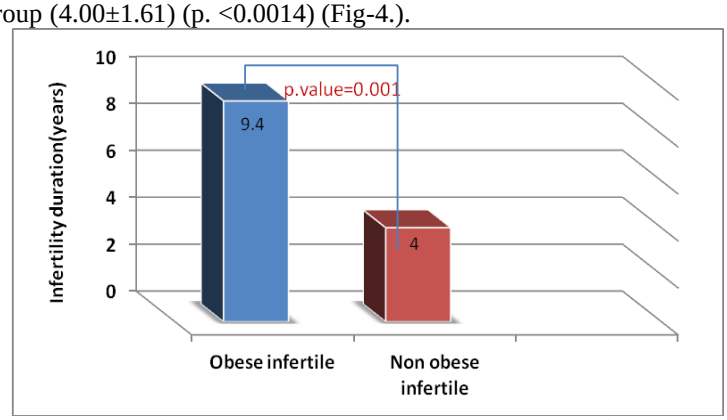


Fig. 4: Mean Infertility Duration Between Obese and Non-Obese Infertile Group

Table 2: Comparison between Obese Infertile Group and Obese Fertile Group by (N=60).

	Obese fertile (n=30) Mean ±SD	Obese infertile(n=30) Mean±SD	P.value
Age	29.50±3.2	32.96±5.372	0.1373
BMI (kg/ m^2)	31.82±1.07	34.08±2.69	0.0218
Leptin (ng/ml)	10.81±3.12	22.92±6.00	<0.0001
Sperm density(million/ml)	71.26±24.44	24.35±11.38	<0.0001
Sperm motility	3.70±0.48	1.63±0.66	<0.0001
Sperm viability (%)	73.80±11.18	31.73±13.54	0.002
Testosterone (ng/ml)	8.16±2.74	3.75±1.140	0.001

The mean sperm density and mobility were more in obese fertile group compared to obese infertile group (p.< 0.0001) (Table-2) There was statistically significant increase of mean sperm viability and testosterone level in obese fertile group compared to obese infertile group (p.< 0.05) (Table-2 In obese fertile group serum testosterone is higher and leptin is lower compared to the obese fertile group and the differences were statistically significant ($p < 0.001$, $p < 0.0001$ respectively) (Fig -5).

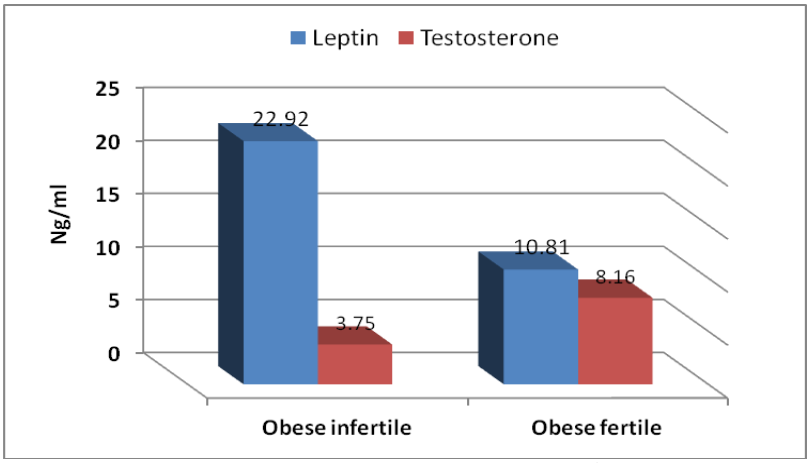


Fig. 5: Leptin and Testosterone in Obese Fertile Obese Infertile Groups

Table 3: Pearson Correlation "R" between Different Variables Among All Cases (N=90).

		BMI	Leptin	density	motility	viability	Testosterone
BMI	R		0.135	0.135	0.011	0.111	-0.020
	P.value		0.3504	0.3485	0.9383	0.4428	0.8882
Leptin (ng/ml)	R	0.135		-0.373	-0.409	-0.337	-0.380
	P.value	0.3504		0.0077	0.0032	0.0167	0.0065
Sperm density (million/ml)	R	0.135	-0.373		0.567	0.775	0.740
	P.value	0.3485	0.0077		<0.0001	<0.0001	<0.0001
Sperm motility	R	0.011	-0.409	0.567		0.674	0.600
	P.value	0.9383	0.0032	<0.0001		<0.0001	<0.0001
Sperm viability (%)	R	0.111	-0.337	0.775	0.674		0.632
	P.value	0.4428	0.0167	<0.0001	<0.0001		<0.0001
Testosterone (ng/ml)	R	-0.020	-0.380	0.740	0.600	0.632	
	P.value	0.8882	0.0065	<0.0001	<0.0001	<0.0001	

There was a statistically significant negative correlation between serum leptin and testosterone level among all cases (p. < 0.0065) (Fig-6). There was a statistically significant positive correlation between sperm motility and leptin level among all cases (p. < 0.0032) Table-3.

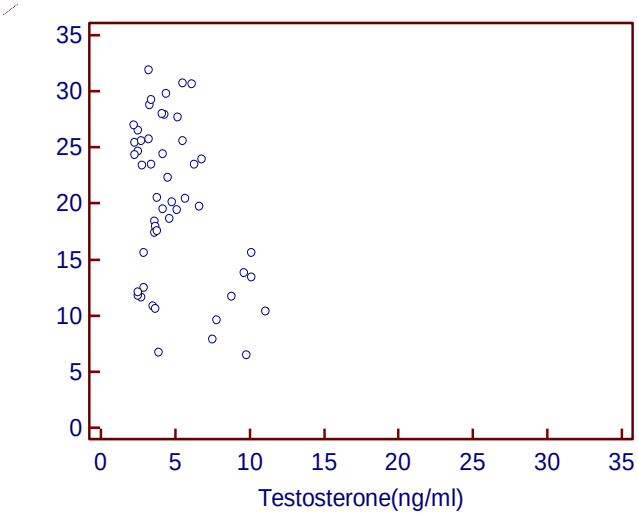


Fig. 6: Correlation between Leptin and Testosterone in All Cases.

5. Discussion

Male factor in infertility plays a role in approximately 50% of infertile couples [12]. Semen analysis is the cornerstone for the evaluation of infertile men. Semen volume and pH level are indices of seminal vesicle and prostate function. Sperm concentration, motility and morphology are largely determined by testicular function. Although fertile men have higher mean sperm parameters (concentration, motility and morphology) than infertile men, there is a significant overlap between both groups. Leptin plays a central role in regulating the balance of fuel stores and energy expenditure. Also leptin has a role in reproductive functions [14]. and antigenic activity Increased infertility associated with diet induced obesity or central leptin resistance is likely mediated through Gonadotrophin Releasing Hormone (GnRH).Furthermore, Leptin regulates reproductive functions by altering the sensitivity of the pituitary gland to GnRH homeostasis and neuroendocrine function [15]. This study aimed to detect the impact of obesity on male infertility and investigate serum testosterone and leptin levels and their Impact on seminal parameters this study showed that the mean BMI was inversely correlated with sperm concentration, sperm motility and sperm morphology. Similar to our results Kort (2006), [3].found that BMI correlated negatively with the total number of normal spermatozoa. He did not report on sperm count or morphology. Furthermore, he found no clear effects of BMI on both hormonal profile and semen quality. This study showed that BMI positively correlated with serum leptin levels and negatively to testosterone level and this was similar to Al-Harithy and Abualnaja (2006) [16] and Zohdy et al., (2007) [17]. Who showed that the accumulation of fatty tissue in men was associated with decreased total Testosterone? Zorn (2007), [18]. Demonstrated a link between leptin and testicular function possibly involving Testosterone and Sex Hormone Binding Globulin (SHBG} through a regulation of Leydig cell function. Ishikawa and co-workers in 2007 [19]. Illustrated the presence of a leptin receptor on intact sperm plasma membrane, suggesting that it might have an impact on the gonadal function indirectly by the central neuroendocrine system and directly through the peripheral tissue membrane receptors. Also Aquila et al., in 2007 [20]. Showed that spermatogenic dysfunction is associated with increased leptin and leptin receptor expression in the testis, demonstrating that leptin increases phosphor-inositol -3 kinase (PI3K) activity in incapacitated spermatozoa [20]. Serum leptin in obese infertile patients was significantly higher than in obese fertile subjects and was positively correlated with patient's age, correlated with sperm density, sperm motility, sperm viability, and serum Testosterone. leptin acts as a direct inhibitory signal for testicular steroid genesis, which may be relevant to explain the link between decreased testosterone secretion and hyperleptinemia in obese men [20]. Yu et al., in 2007. [21]. Correlated serum leptin and pituitary hormones as having a potent stimulating effect of Prolactin (PRL) release at high leptin concentration and they showed that the increase of serum leptin decreases testosterone synthesis in Leydig cells, thereby inhibiting sperm maturation. Suppression of Sertoli cell function may also occur, as decreased inhibin B had been observed in obese people (Margetic et al., 2004 [22]. In our study it was found that serum Testosterone level negatively correlated with serum leptin, Further research focusing on the obesity impact on male infertility has been attributed to higher testosterone level, given the fact that testosterone administration to hypogonadal men caused reduction of serum leptin (Bardin (1996): [23]. Testosterone supplementation has been reported to normalize elevated plasma leptin levels in both young and old hypogonadal men without concomitant changes in body habits, body fat content, or BMI, confirming a strong correlation between leptin and BMI, a gender difference in the levels of leptin. A population-based study reported an inverse relation between leptin and testosterone that was independent of BMI (Luukkaa et al., 1998). [24]. this study also showed that leptin in obese infertile male was elevated significantly compared to other groups. These results were consistent with many other studies, which explained that serum leptin in obese infertile patients was significantly higher than in obese fertile subjects. Several reports showed that the

accumulation of fatty tissue in men was associated with decreased total testosterone and increased estrogen levels (Zohdy et al., 2007). [17].

6. Conclusion

This study show that the mean BMI, as well as serum leptin levels in obese infertile were significantly higher than obese fertile men. Serum leptin had significant negative relation with sperm concentration, sperm motility and testosterone level. Also leptin had significant correlation with the abnormal sperm morphology, sperm concentration, sperm motility and serum testosterone. But had non-significant relation with infertility duration. Men with high BMIs were found to have an abnormal semen analysis in the form of decrease in sperm count, decrease in sperm motility as well as increase in the abnormal forms of spermatozoa.

7. Recommendations

We recommend that more studies are needed to detect link between leptin and reproduction in male. Also recommend studying the effect of weight reduction on improvement of semen quality and serum testosterone level.

8. Conflict of interest

Dr. Mohamed Mashahit has nothing to disclose.

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