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The impact of obesity on semen parameters and hormone levels in infertile men

Erkan Ozdemir[1], Aytekin Tokmak[2], Ahmet Deniz Tuzluoglu[1], Sezen Bozkurt Koseoglu[3], Mehmet Cinar[2], Ayse Sahin[2], Nafiye Yilmaz[2]

[1]Department of Urology, Dr. Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey
[2]Division of Infertility and Reproductive Endocrinology, Department of Obstetrics and Gynecology, Dr. Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey
[3]Department of Obstetrics and Gynecology, Dr. Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey

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Abstract

Previous studies in overweight men have shown an increased likelihood of abnormal semen parameters. Obesity has been found to be associated with male subfertility. In this study we aimed to investigate the effect of obesity on semen parameters and hormone levels in infertile males. This was a prospective cross-sectional study designed to assess the influence of obesity on semen parameters and hormone levels in infertile men. 88 obese [Body mass index (BMI) ≥30 kg/m2] men and 169 non-obese (BMI<30 kg/m2) men were eligible for the study. All semen samples were obtained by masturbation after 3 days of sexual abstinence. After liquefaction at room temperature, semen volume, sperm concentration, motility, and normal morphology were determined according to World Health Organization (WHO, 2010) guidelines for semen analysis. Serum hormone levels were measured on the same-day with semen analysis. Semen volume was significantly lower in the obese group than in the non-obese group. No significant differences were observed between the groups in term of other semen parameters. Mean serum total testosterone (TT) level and TT/estradiol (E2) ratio were significantly higher in the non-obese group, whereas mean E2 level was significantly higher in the obese group. There was a significant positive correlation between BMI and E2 levels in the obese group. A significant inverse correlation was observed between BMI and TT levels in the non-obese group. Obesity may reduce semen volume in infertile males. This effect may be due to the changes in sex hormone levels. However, it has no impact on more meaningful indicators of male fertility such as sperm concentration, motility, and morphology.

Keywords: Body mass index, male infertility, obesity, sperm parameters, testosteron/estradiol ratio

Introduction

Obesity is now a major public health problem facing the world. The worldwide prevalence of obesity is steadily increasing, and it is estimated that approximately 400 million people were obese in 2005 [1]. Millions of people die each year due to diseases associated with obesity. Nonetheless, obesity has adverse effects on reproductive functions in both women and men. It is clearly known that obesity affects fertility adversely in women of reproductive age by causing insulin resistance, hyperandrogenism and ovulatory dysfunction [2]. Although it impairs the reproductive function in a similar manner in obese men, its effects on sperm parameters are contradictory [3-7].

Obesity reduces serum levels of sex hormone binding globulin (SHBG) and testosterone (T), and increases serum estradiol (E2) levels in men, but the effects of those changes on fertility is not known clearly [8]. In addition, obesity was found to be associated with erectile dysfunction [9].

In this study, we aimed to investigate semen parameters of infertile obese men and also to evaluate the relation between body mass index (BMI) and sex hormone levels.

Materials and Methods

The current study was conducted in the Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara between January 2014 and June 2015. This hospital is a tertiary level referral hospital for infertile couples in the middle of Turkey. The study protocol was performed accordingly to the principles of the Declaration of Helsinki, after receiving approval of the institutional review board. Informed consent was obtained from the each participant.

A total of 257 infertile men aged between 22 and 42 were included in the present study. All participants initially

***Corresponding Author:** Aytekin Tokmak, Division of Infertility and Reproductive Endocrinology, Department of Obstetrics and Gynecology, Dr. Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey. **E-mail:** aytekintokmak@gmail.com

admitted to our infertility outpatient clinics with their wives. The routine infertility workup of all women including baseline hormone levels, antral follicle count and hysterosalpingography were performed and it was noted to be normal for each woman.

Medical and infertility history of each patient were recorded. All patients were examined for genitourinary complaints by two experienced urologist. Exclusion criteria included varicocele more than grade 1, testiculary hypoplasia, and previous history of orchiectomy. Patients were also excluded if any of the following disorders were present: thyroidectomy, epilepsy, asthma, chronic liver and kidney disease, chronic inflammatory bowel disease, steroid and antihyperlipidemic users, history of thromboembolism and cerebrovascular event.

Men whose wives had previously no pregnancy were regarded as primary infertile; if pregnancy occurs at least once it was considered as secondary infertility.

Height and weight of the patients were measured using a professional calibrated device on an empty stomach in the morning. Body mass index (BMI) was calculated as weight divided by height squared. The cohort was mainly divided into the obese and non-obese groups according to their BMI. 88 obese (BMI≥30 kg/m2) men and 169 non-obese (BMI<30 kg/m2) men were eligible for the study.

All of the patients were asked to respect a period of sexual abstinence for 3 days. Semen samples were collected from the patients by masturbation in a private room nearby the laboratory. After liquefaction for half an hour at room temperature, the collected semen specimens (pre-washed) were assessed for conventional semen parameters including sperm concentration and sperm motility by the computer-assisted semen analyzer. The rest of the semen was processed using standard swim up method with a sperm preparation media (Ferticult Flushing medium TM, FertiProNV, Beernem, Belgium). Post wash analysis was again performed by the computer-assisted semen analyzer. Sperm analysis was performed by the same andrology laboratory technician according to a quality control program. Sperm analysis was assessed according to World Health Organization guidelines [10]. Data recorded for each man were semen volume, pH, sperm count, sperm concentration, percentages of motility and normal sperm morphology.

After an overnight fasting, blood samples were taken and evaluated for some hormonal parameters including total testosterone (TT), estradiol (E2) luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL), and thyroid stimulating hormone (TSH).

Statistical analysis

The distributions of all of the continuous variables for normal or non-normal distributions were tested using Kolmogorov-Smirnov test. The variables with normal distributions were compared between groups by the Independent Samples T Test and were expressed as mean + SD. Mann Whitney U Test was applied for non-normal distributed variables and results were expressed as median and inter-quartile range. Categorical variables were analyzed by Pearson's Chi-square Test. Pearson's Correlation analysis was performed to find out a possible association between BMI and sex steroids. Statistical significance was accepted with a probability error of $p < 0.05$. We used the SPSS 17 (Statistical Package for Social Sciences, SPSS Inc) software for statistical analyses.

Results

Two hundred and fifty seven consecutive infertile men were recruited into this prospective cross sectional study during the 1.5-year study period. All female partners of couples were investigated for infertility, and it was shown that they have no known cause of infertility. The male subjects were divided into two groups according to BMI. 88 men with a BMI equal or greater than 30 kg/m2 was defined as obese group, whereas 169 men with a BMI less than 30 were considered for inclusion into the non-obese group.

No significant differences were observed between the two groups in terms of age, marriage duration, infertility type, smoking status, previous infertility treatment, and urological findings. Table 1 depicted demographics and clinical characteristics of the patients. The incidence of diabetes mellitus and hypertension was 3 (3.4%) vs. 1 (0.6%) and 8 (9.1%) vs. 3 (1.8%) in the obese and non obese group, respectively ($p<0.05$).

When the semen parameters were evaluated, semen volume was found to be significantly higher in the obese group than in the non-obese group. Semen volume was found to be significantly higher in the obese group compared to the non–obese group (p: 0.018). There were no statistically significant differences between the two groups according to the other semen parameters ($p<0.05$) (Tablo2).

Serum TT and TT/E2 ratio were statistically significantly lower in the obese group (both $p<0.001$). Conversely, serum E2 levels were significantly higher in this group than in the non–obese group ($p<0.001$) (Tablo3). Mean serum TSH, PRL, and gonadotropin levels were similar between the groups.

Correlation analysis showed that there was a significant positive correlation between BMI and E2 levels in the obese group, whereas there was a significant inverse

correlation between BMI and TT levels in the non-obese group. However, it was noted that there was a significant inverse correlation between BMI and TT/E2 ratio when the entire study population was evaluated conjointly (Table 4).

Table 1. Comparison of demographics and clinical characteristics of the patients.

Variables	Obese group; BMI≥ 30 kg/m2 (n:88)	Non-obese group; BMI<30 kg/m2 (n:169)	P value
Age(years)	31.1±4.0	30.1±4.5	0.070
BMI(kg/m2)	34.5±4.4	24.5±2.8	**<0.001**
Spouse age(years)	28.4±4.5	26.3±5.1	**0.001**
Marriage duration(years)	4.1±3.0	3.9±3.2	0.430
Smoker ***n(%)***	43(48.9)	85(50.3)	0.828
Infertility type ***n(%)***			0.114
Primary	76(86.4)	156(92.3)	
Secondary	12(13.6)	13(7.7)	
Live children	0(0–1)	0(0–3)	0.139
IUI cycles ***n(%)***			0.320
1	7(8)	17(10.1)	
2	4(4.5)	12(7.1)	
3	3(3.4)	4(3.4)	
IVF ***n(%)***			0.579
1	7(8)	18(7)	
≥2	2(2.2)	2(1.2)	
Grade 1 varicocele n(%)	8(9.1)	29(17.2)	0.080
Previous Urologic Surgery n(%)			0.268
Orchiopexy	4(4.5)	2(1.2)	
Spermatic vein ligation Inguinal	10(11.4)	27(16)	
hernia	3(3.4)	8(4.7)	

BMI: body mass index, IUI: intrauterine insemination, IVF: invitro fertilization.
Data are presented as mean±standar deviation, median(minimum–maximum) I, and median±interquartile range. P<0.05 is considered statistically significant

Table 2. Comparison between semen parameters in the two groups.

Variables	Obese group (n:88)	Non-obese group (n:169)	P value
Sperm volume(cc)	2.1±1.4	2.5±1.4	0.018
pH	8.0(7.0–8.0)	8.0(7.0–8.5)	0.677
Liquefactions n(%)	8(9.1)	17(10.1)	0.804
Leukocyte n(%)	6(6.8)	24(14.2)	0.080
Sperm count (mil)	36.9±40.5	35.6±38.8	0.916
Concentration(mil/mL)	19.7±25.0	16.1±24.5	0.417
Progressively motility (%)	28.6±20.3	23.9±18.6	0.060
Postwash sperm count(mil/mL)	17.2±18.0	19.1±19.5	0.504
Postwash progressively motility(%)	64.4±40.2	68.3±39.5	0.238
Kruger (%)	4.4±3.5	4.0±3.2	0.547
TPMSC(mil)	15.3±17.3	18.2±19.8	0.405
Sperm count <39 mil n(%)	54(61.4)	112(66.3)	0.436
Sperm volume<1.5 cc n(%)	27(30.7)	30(17.8)	0.018
Concentration <15 mil/cc n(%)	56(63.6)	119(70.4)	0.269
Motility<32% n(%)	42(47.7)	97(57.4)	0.140
Kruger<4% n(%)	46(52.3)	81(47.9)	0.509
Azoospermia n(%)	20(22.7)	32(18.9)	0.473

TPMSC: total progressively motile sperm count.

Table 3. Serum hormone levels according to the presence of obesity

Variables	Obese group (n:88)	Non-obese group (n:169)	P value
FSH (U/L)	5.6±4.5	7.2±9.2	0.760
LH(U/L)	4.7±3.1	5.7±5.6	0.373
TT (ng/dL)	321.3±130.8	455.0±174.7	**<0.001**
E2 (pg/mL)	27.8±12.8	22.2±7.3	**<0.001**
TT/E2	13.1±6.0	23.1±13.7	**<0.001**
PRL (mU/L)	8.6±3.3	8.8±3.7	0.999
TSH(mU/L)	2.0±2.2	1.9±1.7	0.523
free T3 (pmol/L)	3.6±0.4	3.5±0.4	0.499
free T4(pmol/L)	1.1±0.3	1.1±0.2	0.311

FSH: follicle stimulating hormone, LH: luteinizing hormone, TT: Total testosterone, E2: Estradiol, PRL: prolactin, TSH: thyroid stimulating hormone.

Table 4. Correlation analysis between BMI and sex hormones

		Obese group (n:88)	Non-obese group (n:169)
TT	r	–0.084	–0.281
	p	0.434	**<0.001**
E_2	r	0.317	–0.004
	p	**0.003**	0.961
TT/E_2	r	–0.349	–0.216
	p	**0.001**	**0.005**

Discussion

The main finding of the present study is that there were no meaningful differences between obese and non-obese infertile patients in terms of semen parameters with the exception of semen volume. It was also found that TT levels were lower and E2 levels were higher in obese infertile men when compared to non-obese ones, and obesity reduces TT/E2 ratio.

Infertility is defined as inability to conceive after one year of sexual intercourse without the use of any contraceptive methods. This condition affects about 15% of couples with an estimated 48.5 million couples worldwide. Approximately 30% of infertility cases are purely male originated [11]. Male infertility may be due to many reasons. Sperm production disorders, blockage in the sperm ducts, the presence of antibodies against sperm, testicular trauma, hormonal disorders, anatomical problems, varicocele, past illnesses, infections and certain medications can cause infertility in males.

Obesity defined as global epidemic of our age is one of the most important health problems. This is a major cause of morbidity and mortality worldwide. It is well known that obesity adversely affects cardiovascular system as well as reproductive system in both men and women. A recent study demonstrated that increased paternal BMI was associated with decreased blastocyst development, clinical pregnancy rates and live birth outcomes as well as increased risk of miscarriage following assisted reproductive technology (ART) [12]. And the authors suggested that further studies are needed to elucidate the mechanisms involved in this relation.

There is an accumulating data that male obesity is associated with impaired endocrine dysfunction. It leads to sexual dysfunction such as erectile dysfunction. Epidemiologic studies showed that this decrease is not solely mediated by sexual dysfunction in obese men [4], deteriorated molecular mechanism of sperm may be responsible for this situation. However the effect of obesity on sperm parameters is conflicting.

Despite the use of semen parameters set by the World Health Organization, different results from various studies regarding the impact of obesity on sperm parameters were obtained. A study conducted with a large group of patients in 2008 showed that overweight men (BMI: 25.1-30.0 kg/m2) had a slightly lower adjusted sperm concentration and total sperm count than did men with a normal BMI (20.0-25.0 kg/m2) [6]. However, no significant differences were found between overweight and obese men with regard to sperm parameters in that study. In contrast to this study, a study conducted with young (mean age: 19) healthy volunteers demonstrated that sperm concentration and total sperm count were significantly lower in the overweigh men compared to men with normal BMI [13]. In our study, we found similar sperm concentration and total sperm count in both obese and non-obese men. Unlike these studies, mean semen volume was significantly lower in obese infertile men than in those with a BMI less than 30.

Besides sperm concentration and count, the relationship between sperm morphology, progressive motility and obesity has been shown in previous studies [14,15]. A study with small sample size depicted that weight loss led to improvement in semen quality including sperm count and normal sperm morphology [15]. Accordingly, the importance of controlled weight loss and lifestyle changes was highlighted in that paper. We found no significant differences between the groups in terms of semen parameters in term of normal sperm morphology, progressive motility, and total sperm count. In a review of 23 studies investigating paternal obesity and their effect on basic sperm parameters; sperm concentration was found to be decreased in 15 studies, motility decreased in 7, and 7 studies showed that sperm morphology was impaired by obesity [16].

Spermatogenesis is a highly complex and a selective process which is regulated by the hypothalamus, hypophysis and Sertoli-Leydig cells located in the testes, respectively. This cycle starts at puberty in men and continues until death. It has been hypothesized that obesity disturbs spermatogenesis through the hypothalamic-pituitary axis [16]. Obesity alters sex hormone levels as in women, and consequently hormonal changes affect male fertility [13,17].

Testosterone and SHBG levels decrease while E2 and TT/E2 increase in obese men [8, 17]. Decreased TT and increased E2 in men have been associated with reduction in sperm count and subfertility [18]. Adhesions between Sertoli cells and spermatids are T dependent since androgen action is required for the release of mature sperm [19]. A significant reduction of the total sperm count in obese men has been reported due to the reduction in T levels [20]. Consistent with the literature, we found that TT levels were lower and E2 levels were higher in obese

infertile men when compared to non-obese group, and that there was a significant inverse correlation between BMI and TT/E2 ratio. Although we have designed a prospective study, the lack of validation cohort is our main limitation.

In conclusion, semen volume was lower in obese infertile men when compared to non-obese infertile men. This effect may be due to the changes in sex hormone levels. In contrast to other studies, our results indicate that there were no significant differences among infertile men in terms of total sperm count, sperm motility, and normal sperm morphology when this cohort evaluated according to their body mass index. There is a growing body of contradictory literature on the relationship between obesity and semen parameters. These finding should be supported by large prospective randomized clinical studies with the inclusion of the men without infertility problems.

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