Central European Journal of Urology

ORIGINAL PAPER

METABOLIC AND HORMONAL DISORDERS

The impact of body mass index on reproductive hormones, testosterone/estradiol ratio and semen parameters

Unal Oztekin, Mehmet Canikliogluu, Sercan Sari, Abdullah Gurel, Volkan Selmi, Levent Isikay

Bozok Unıversıty Faculty of Medicine, Department of Urology, Yozgat, Turkey

Citation: Oztekin U, Canikliogluu M, Sari S, Gurel A, Selmi V, Isikay L. The impact of body mass index on reproductive hormones, testosterone/estradiol ratio and semen parameters. Cent European J Urol. 2020; 73: 226-230.

Article history
Submitted: March 6, 2020
Accepted: June 1, 2020
Published online: June 12, 2020

Corresponding author
Unal Oztekin
Yozgat Bozok University
Faculty of Medicine
Department of Urology
Ataturk
Road 7th km. 66100 Yozgat, Turkey
phone: 0530 3478 578
dr_unal@hotmail.com

Introduction The aim of this study was to evaluate the relationship between body mass index (BMI) and sperm parameters and reproductive hormone levels in patients with no known risk factors for infertility.
Material and methods Four hundred patients who met the study's inclusion criteria were divided into three groups according to their BMI values as normal weight (BMI: 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI ≥30 kg/m^2). Semen parameters, reproductive hormone levels and testosterone/estradiol ratio were compared retrospectively between the groups.
Results There was no significant difference between the groups in terms of age and infertility period. The mean BMI of all the patients was 26.6 ±4.08, and the BMI in the normal, overweight and obese groups were 22.6 ±1.7, 27.4 ±1.3, and 33.4 ±2.9, respectively (p <0.001). There was no significant difference between the groups in terms of serum follicle stimulating hormone, luteinizing hormone, estradiol, prolactin, semen volume, sperm concentration, total sperm count, and progressive and total motility. Serum testosterone (T) level and testosterone/estradiol (T/E2) ratio were significantly higher in the normal BMI group (p <0.001).
Conclusions Adipose tissue increase was not significantly correlated with change in the semen parameters and it was negatively correlated with T levels and T/E2 ratio.

Key Words: body mass index ‹› reproductive hormones ‹› sperm parameters ‹› testosterone/estradiol ratio ‹› male infertility

INTRODUCTION

Infertility is a serious health problem that occurs in approximately 10% of all families worldwide and may affect couples living in developing countries even more [1]. It can be defined as the failure to conceive despite one year of regular and unprotected intercourse. Endocrine disorders, environmental factors, reactive oxygen radicals, diet, genetic and epigenetic factors have been implicated in the etiology of infertility. Abnormal sperm parameters cause infertility in approximately 50% of couples without children. In 30–40% of couples, the female partner was determined to be fertile, however none of the infertility factors were detected in male partners, and thus these men were diagnosed with idiopathic male infertility. One in six of these pairs present with secondary infertility, whereas primary infertility occurs in one in eight pairs [2].

Obesity is a health-threatening problem with a worldwide prevalence [3]. The relationship between increase in adipose tissue and subfertility has not been clearly demonstrated in the literature yet. However, it has been emphasized that the risk of infertility increases if the male partner is overweight or obese [4]. It has also been reported that increase in adipose tissue negatively affects female fertility [5]. Continuity of spermatogenesis and sperm quality depend on high levels of intratesticular testosterone [6]. Increasing body mass index (BMI) and decreasing testosterone levels may negatively affect spermatogenesis and several factors such as decreased levels

of sex hormone-binding globulin, increased levels of leptin and increased aromatase activity in adipose tissue have been implicated in the etiology [7].
The BMI's effect on semen quality and reproductive hormone levels is not well-known. The aim of this study was to evaluate the relationship between BMI and sperm parameters and reproductive hormone levels in patients with no known risk factors for infertility.

MATERIAL AND METHODS

This retrospective study included patients admitted to our urology clinic due to infertility between January 2018 and June 2019. After approval from the local ethics committee (approval number: 2017-KAEK-189_2019.06.19_08), patients 18 years and older were included in the study. Informed consent was obtained from all patients included in the study. The study was performed in accordance with the declaration of Helsinki. Patients with known risk factors that may affect sperm parameters such as varicocele, history of scrotal surgery (undescended testis, testis tumour, varicocelectomy history in last 6 months), solitary testis, hormonal disorders (diabetes mellitus, hypogonadism, hypo/hyperthyroidism, hyperprolactinemia, etc.), genital tract infection (orchitis, epididymitis, urethritis, etc.), neurologic and psychological disorders and history of medication, chemotherapy and alcohol and tobacco consumption were excluded from the study. Also, patients whose female partners' gynecological examinations revealed abnormalities were excluded from the study. Moreover, patients with azoospermia and cryptozoospermia (≤1 million/ml) were also excluded from the study. Age, BMI, type of infertility, duration of infertility, levels of follicle stimulating hormone (FSH) (0.95–12.5 mIU/ml), luteinizing hormone (LH) (1.5–8.5 mIU/ml), total testosterone (T) (200-950 ng/dl), estradiol (E2) (7.6–42.6 ng/L), and prolactin (PRL) (3.4–19.4 ng/ml), as well as testosterone/estradiol (T/E2) ratios, and semen parameters of 400 patients who met the study's inclusion criteria we recorded. Hormone levels were measured using the ARCHITECT i2000sr immunoassay analyzer (Abbott Laboratories). In the outpatient examination, the height and weight of the patients were measured and recorded. BMI was calculated by the formula of (weight in kg)/(height in m^2). Hormonal analysis was performed on the same day as the sperm specimens were collected from the patients who had at least 72 hours of sexual abstinence. The patients were divided into three groups according to their BMI values as normal weight (BMI: 18.5–24.9 kg/m^2), overweight (BMI: 25–29.9 kg/m^2), and obese (BMI: ≥30 kg/m^2) [8]. Primary infertility was accepted as a failure to achieve pregnancy despite unprotected regular sexual intercourse for at least 12 months. Secondary infertility was defined as the inability to conceive for some time after the birth of one or more biological children. Semen samples were taken after 3–7 days of sexual abstinence and sperm analysis was performed according to the World Health Organization (WHO) 2010 criteria [9]. Sperm analysis results including semen volume, sperm concentration and morphology, total sperm count, progressive and total sperm motility were recorded. The parameters were compared between the three groups divided according to BMI values.

Statistical analyses

All statistical tests were performed using the Statistical Package for Social Sciences version 25 (IBM SPSS®, Chicago, IL). The Kolmogorov-Smirnov test was used to evaluate the data distribution, and a non-parametric test was used for non-normal distributions. Chi-square test was used for categorical data, while Kruskal-Wallis test was used for numerical data. Pairwise multiple comparisons analysis was used to identify the group that provided statistical significance. The relationship between BMI and hormone and semen parameters was determined using Spearman correlation test. A p-value <0.05 was considered statistically significant.

RESULTS

The patients' demographic characteristics and hormonal profiles are summarized in Table 1. A total of 400 patients were included in the study. Of these patients, 274 (68.5%) were primary infertile, while 126 (31.5%) were secondary infertile. There was no significant difference between the groups in terms of type of infertility. Among the patients presenting with primary infertility, 46.7% (128/274) were overweight and 39.0% (107/274) were in the normal weight group. The majority of the patients with secondary infertility (50.7%) were in the overweight group. The mean age was 30.7 ±5.5 years, the mean infertility period was 2.5 ±2.6 years (median 1.5 years, min-max: 1–21 years). There was no significant difference between the groups in terms of age and infertility period. The mean BMI of all the patients was 26.6 ±4.08, and the BMI in the normal, overweight and obese groups were 22.6 ±1.7, 27.4 ±1.3, and 33.4 ±2.9, respectively ($p<0.001$). There was no significant difference between the groups in terms of serum FSH, LH, E2, PRL, semen volume, sperm concentration, total sperm count, and

Table 1. *Demographic and hormonal characteristics of patients according to different BMI groups*

Parameters	All patients	Distribution of groups according to BMI (kg/m²)			
		Normal (18–24.9)	Overweight (25–29.9)	Obese (>30)	P value
Number (n) (%)	400 (100)	146 (36.5)	192 (48)	62 (15.5)	
BMI (mean ±SD) (18.6–41.5)	26.6 ±4.0	22.6 ±1.7 (18.6–24.9)	27.4 ±1.3 (25.0–29.8)	33.4 ±2.9 (30.0–41.52)	<0.001
Age (mean ±SD)	30.7 ±5.5 (18–54)	30.2 ±5.2 (21–54)	31.0 ±5.7 (18–54)	31.2 ±5.5 (21–50)	0.229
Type of infertility (n) (%)					
Primary	274 (68.5)	107 (73.3)	128 (66.7)	39 (62.9)	0.253
Secondary	126 (31.5)	39 (26.7)	64 (33.3)	23 (37.1)	
Duration of infertility, year (mean ±SD)	2.5 ±2.6	2.3 ±2.3	2.5 ±2.9	2.6 ±2.4	0.366
Serum FSH, mIU/ml (mean ±SD)	3.8 ±2.3 (1.0–12.4)	3.8 ±2.2 (1.2–12.4)	3.8 ±2.4 (1.0–12.0)	3.7 ±1.9 (1.1–10.9)	0.919
Serum LH, mIU/ml (mean ±SD)	3.5 ±1.5 (1.5–8.4)	3.5 ±1.4 (1.5–8.4)	3.5 ±1.6 (1.5–8.1)	3.3 ±1.4 (1.5–7.3)	0.472
Serum T, ng/dl (mean ±SD)	478.6 ±198.4 (220.4–923.14)	558.7 ±184.7 (221.8–923.1)	444.5 ±202.3 (225.4–921.4)	395.7 ±149.4 (220.4–832.1)	<0.001[a]
Serum E2, ng/L (mean ±SD)	24.4 ±9.9 (10.0–88.0)	23.7 ±9.3 (10.0–63.0)	24.5 ±10.7 (10.2–88.0)	25.5 ±9.0 (10.6–50.0)	0.315
Serum PRL, ng/ml (mean ±SD)	9.7 ±4.8 (3.1–16.8)	10.0 ±5.2 (4.5–16.8)	9.5 ±4.7 (3.2-15.7)	9.9 ±4.0 (3.1–15.4)	0.439
Semen volume, ml (mean ±SD)	3.2 ±1.4 (1.5–8.5)	3.2 ±1.3 (1.5–7.5)	3.3 ±1.5 (1.5–8.5)	3.0 ±1.3 (1.5–6.5)	0.653
Sperm conc. mil/ml (mean ±SD)	46.6 ±32.3 (1.5–140.5)	44.5 ±32.1 (1.5–120)	49.0 ±31.4 (2.2–140.5)	44.1 ±35.3 (1.5–120.4)	0.259
Total sperm, mil (mean ±SD)	152.4 ±128.2 (2.3–812.07)	143.3 ±119.7 (2.3–552.8)	163.2 ±131.2 (2.5–812.7)	140.0 ±137.7 (2.8–611.4)	0.110
Progressive motility (type A) (%)	27.5 ±12.8 (0–70)	27.0 ±11.8 (0–50)	28.2 ±12.2 (5–60)	26.6 ±16.4 (0–70)	0.618
Total motility (type A+B) (%)	45.5 ±16.0 (0–80)	44.9 ±15.4 (0–75)	46.7 ±14.8 (11–80)	43.2 ±20.1 (578)	0.543
T/E2 (mean ±SD)	22.7 ±14.2 (3.1–83.8)	26.6 ±12.7 (7.0–77.6)	21.3 ±15.7 (4.1–83.8)	17.8 ±9.9 (3.1–56.6)	<0.001[b]

[a]Pairwise multiple comparisons: normal – overweight (P ≤0.001); normal – obese (P ≤0.001); overweight – obese (P = 0.150)
[b]Pairwise multiple comparisons: normal – overweight (P ≤0.001); normal – obese (P ≤0.001); overweight – obese (P = 0.087)
BMI – body mass index; SD – standard deviation; FSH – follicle stimulating hormone; LH – luteinizing hormone; T – testosterone; E2 – estradiol; PRL – prolactin; T/E2 – testosterone/estradiol

progressive and total motility. Serum T level and T/E2 ratio were significantly higher in the normal BMI group (p <0.001).

The BMI was negatively correlated with semen volume, normal sperm morphology, total sperm count, and T and T/E2 ratio. However, this correlation was significant only with serum T levels and T/E2 ratio (p <0.001) (Table 2).

DISCUSSION

In this study, we excluded patients with known risk factors and aimed to evaluate the relationship between BMI and reproductive hormones and semen parameters. Changes in hormonal and semen param-

Table 2. *Correlation between BMI and sperm and hormonal parameters*

Parameters	BMI (kg/m²)	
	r	p[a] value
Semen volume (ml)[a]	-0.027	0.596
Sperm concentration (mil/ml)[a]	0.009	0.853
Normal morphology (%)[a]	-0.010	0.148
Total sperm count (mil)[a]	-0.003	0.957
Serum E2 (ng/L)[a]	0.088	0.079
Serum T (ng/dl)[a]	-0.402	<0.001
T/E2 ratio	-0.367	<0.001

[a]Spearman correlation test; BMI – body mass index, E2 – estradiol, T – testosterone, T/E2- testosterone/estradiol

eters are expected in response to increasing adipose tissue that comes with increased BMI [10]. According to our results, there was no significant relationship between BMI and semen parameters, however serum T levels and T/E2 ratios differed between the groups and were negatively correlated with increasing BMI.

The relationship between obesity, male subfertility and sperm parameters can be multifactorial and different pathophysiological hypotheses have been proposed. Firstly, a decrease in sex hormone binding globulin (SHBG) levels has been shown to be facilitated by hyperinsulinemia caused by insulin resistance due to obesity and by the negative feed-back effect of elevated total E2 levels [4, 11]. Secondly, the increase in leptin levels lead to suppression of the effect of LH on testicular Leydig cells [7]. Finally, the reduction of T/E2 ratio due to steroid aromatization in the adipose tissue causes an increase in estrogen levels and leads to hypogonadotropic hyperestrogenic hypogonadism [7].

There are conflicting opinions in the literature regarding the correlation between BMI and semen parameters because there is lack of studies evaluating male infertility in obese patients and obesity may be accompanied by comorbid diseases that may affect fertility. Sermondade et al. [4] conducted a meta-analysis with 1307 patients and concluded that the increase in BMI negatively affected some semen parameters. Some other studies have also reported that obese males had decreased semen volume, sperm concentration and total sperm count, and had sperm quality disorders 3 times more frequently than the normal group [12, 13]. However, a meta-analysis that included 31 studies reported that increased BMI had no effect on sperm parameters [14]. In addition, it was emphasized that fertilization rates were higher in obese men as a result of the in vitro fertilization cycle compared to normal weight men. However, the live birth rate was reported to be lower for the obese patients group [15]. When the literature data was analysed, the interaction between the increase of the adipose tissue and the reproductive system was not clearly explained. In our study, we did not find a significant correlation between BMI increase and parameters such as semen volume, sperm morphology, and total sperm count. In addition, we did not see any significant correlation between BMI and sperm motility and ejaculate volume.

There are also studies reporting the negative effect of obesity on motility and ejaculate volume [16, 17]. In a study similar to ours, where the infertility-associated risk factors were excluded, the sperm concentration was found to be negatively correlated with increased BMI [10, 18] but we did not detect any such correlation in our study. It has been reported that differences in standardization used during the sperm's morphological evaluation may cause variability in results [19]. While some studies have shown that the increase in adipose tissue is positively correlated with the increase in the rate of morphologically abnormal sperm [20] other studies claimed that adiposity had no effect on morphology [10, 14, 21]. In our study, we did not find any significant correlation between increased adipose tissue and abnormal sperm morphology.

Local hormonal balance of testicular testosterone and estradiol ratio has an impact on spermatogenesis. The deterioration of this balance may lead to infertility by affecting normal spermatogenesis negatively. Thus, evaluating the alteration of T/E2 ratio may give beneficial information [22]. A study by Keskin et al. [23] conducted with 454 patients reported no significant correlation between BMI increase and semen parameters as well as T/E2 ratio, however a negative correlation between BMI and total testosterone and PRL was observed. In our study, increased BMI was negatively correlated with total testosterone levels and T/E2 ratio, but was not significantly correlated with PRL and gonadotropin levels. Our results are in line with another study that has reported that adiposity significantly reduces T levels, but has no effect on gonadotropin levels [24]. The results of our study as well as other studies suggest that obesity negatively affects male reproductive potential by decreasing T levels and T/E2 ratio [11].

This study has some limitations due to its retrospective design. Due to the insufficient number of patients, a low-weight group with a BMI of less than 18 could not be established. Furthermore, since the patients included in the study were men presenting with infertility, they may have higher abnormal semen parameters than the general population. The absence of free testosterone measurement and the patients who have sperm count under 5 million without genetic analysis may also be considered a limitation.

CONCLUSIONS

In our study, while adipose tissue increase was not significantly correlated with change in the semen parameters, it was negatively correlated with T levels and T/E2 ratio. Although increased BMI has been shown to adversely affect fertility potential by various mechanisms of action, larger randomized and prospective studies are needed to determine the effects of adiposity on sperm quality, hormonal axis and male infertility.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007; 22: 1506-1512.

2. Jungwirth A, Diemer T, Kopa Z, Krausz C, Minhas S, Tournaye H. EAU Guidelines on Male Infertility. In: Jungwirth A, ed. EAU Guidelines 2018. Arnhem: EAU Guidelines Office; 2018. pp. 722-723.

3. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014; 384: 766-781.

4. Sermondade N, Faure C, Fezeu L, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013; 19: 221-231.

5. Fedorcsak P, Dale PO, Storeng R, et al. Impact of overweight and underweight on assisted reproduction treatment. Hum Reprod. 2004; 19: 2523-2528.

6. Helo S, Ellen J, Mechlin C, et al. A Randomized Prospective Double-Blind Comparison Trial of Clomiphene Citrate and Anastrozole in Raising Testosterone in Hypogonadal Infertile Men. J Sex Med. 2015; 12: 1761-1769.

7. Xu X, Sun M, Ye J, et al. The Effect of Aromatase on the Reproductive Function of Obese Males. Horm Metab Res. 2017; 49: 572-579.

8. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000; 894: 1-253.

9. World Healt Organization: Laboratory manual for the examination and processing of human semen, 5th ed. Geneva: WHO press; 2010.

10. Alshahrani S, Ahmed AF, Gabr AH, Abalhassan M, Ahmad G. The impact of body mass index on semen parameters in infertile men. Andrologia. 2016; 48: 1125-1129.

11. Davidson LM, Millar K, Jones C, Fatum M, Coward K. Deleterious effects of obesity upon the hormonal and molecular mechanisms controlling spermatogenesis and male fertility. Hum Fertil (Camb). 2015; 18: 184-193.

12. Sharma R, Biedenharn KR, Fedor JM, Agarwal A. Lifestyle factors and reproductive health: taking control of your fertility. Reprod Biol Endocrinol. 2013; 11: 66.

13. Shukla KK, Chambial S, Dwivedi S, Misra S, Sharma P. Recent scenario of obesity and male fertility. Andrology. 2014; 2: 809-818.

14. MacDonald AA, Herbison GP, Showell M, Farquhar CM. The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis. Hum Reprod Update. 2010; 16: 293-311.

15. Colaci DS, Afeiche M, Gaskins AJ, et al. Men's body mass index in relation to embryo quality and clinical 491 outcomes in couples undergoing in vitro fertilization. Fertil Steril. 2012; 98: 1193-1199.e1

16. Hadjkacem Loukil L, Hadjkacem H, Bahloul A, Ayadi H. Relation between male obesity and male infertility in a Tunisian population. Andrologia. 2015; 47: 282-285.

17. Eisenberg ML, Kim S, Chen Z, Sundaram R, Schisterman EF, Buck Louis GM. The relationship between male BMI and waist circumference on semen quality: data from the LIFE study. Hum Reprod. 2014; 29: 193-200.

18. Hammoud AO, Wilde N, Gibson M, Parks A, Carrell DT, Meikle AW. Male obesity and alteration in sperm parameters. Fertil Steril. 2008; 90: 2222-2225.

19. Hammoud AO, Gibson M, Peterson CM, Meikle AW, Carrell DT. Impact of male obesity on infertility: a critical review of the current literature. Fertil Steril. 2008; 90: 897-904.

20. Hofny ER, Ali ME, Abdel-Hafez HZ, et al. Semen parameters and hormonal profile in obese fertile and infertile males. Fertil Steril. 2010; 94: 581-584.

21. Chavarro JE, Toth TL, Wright DL, Meeker JD, Hauser R. Body mass index in relation to semen quality, sperm DNA integrity, and serum reproductive hormone levels among men attending an infertility clinic. Fertil Steril. 2010; 93: 2222-2231.

22. Parekattil SJ, Agarwal A. Male Infertility: Contemporary Clinical Approaches, Andrology, ART & Antioxidants. Male Infertility: Springer Science & Business Media; 2012; pp. 247-259.

23. Keskin MZ, Budak S, Aksoy EE, et al. Investigation of the effect of body mass index (BMI) on semen parameters and male reproductive system hormones. Arch Ital Urol Androl. 2017; 89: 219-221.

24. Ehala-Aleksejev K, Punab M. Relationships between total testicular volume, reproductive parameters and surrogate measures of adiposity in men presenting for couple's infertility. Andrologia. 2017, Dec 28 [Epub ahead of print]. ■