

Original Article

Asian Pacific Journal of Reproduction

Journal homepage: <https://journals.lww.com/apjr/>

doi: 10.4103/apjr.apjr_87_25

Influence of body mass index on semen quality: Examining sperm DNA fragmentation, protamine deficiency, and hormonal profiles

Mohammed M. Laqqan¹, Maged M. Yassin^{2✉}¹Faculty of Medicine, Islamic University of Gaza, P.O. Box 108, Gaza, Palestine²Department of Human Physiology, Faculty of Medicine, Islamic University of Gaza, P.O. Box 108, Gaza, Palestine

ABSTRACT

Objective: To investigate whether differences exist in DNA fragmentation levels and protamine deficiency in the sperm of obese men compared to those of overweight and proven fertile, normal weight men and evaluate the alterations related to reproductive hormones, semen parameters and their association with body mass index (BMI).

Methods: Participants in this observational study were divided into three groups based on their BMI: proven fertile, normal weight men ($n=200$); overweight men ($n=200$); and obese men ($n=200$). After 3 days of abstinence, seminal fluid was collected from all participants and analyzed. Blood samples were also collected on the same day for hormonal analysis. Sperm DNA fragmentation and protamine deficiency were also assessed.

Results: A total of 600 men with a mean age of (34.3 ± 7.9) years were included in the study. Obese males (BMI 30 kg/m^2 or higher) exhibited significant reductions in semen volume, sperm concentration, total sperm motility percentage, progressive motility, non-progressive motility, and levels of total testosterone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) compared to overweight (BMI 25 to 29.9 kg/m^2) and normal weight males (BMI 18.5 to 24.9 kg/m^2) ($P < 0.001$). Conversely, obese males showed a significant increase in prolactin level, sperm DNA fragmentation, and protamine deficiency compared to overweight and normal weight males ($P < 0.001$). Significant negative correlations were demonstrated between BMI and sperm concentration, motility, total testosterone, FSH and LH ($P < 0.001$), whereas prolactin, sperm DNA fragmentation and protamine deficiency were positively correlated with BMI ($P < 0.001$).

Conclusions: This study provides clear evidence that obesity contributes potentially to male infertility by inducing sperm DNA fragmentation and protamine deficiency, as well as negatively impacting reproductive hormones and semen quality.

KEYWORDS: Body mass index; DNA fragmentation; Protamine deficiency; Reproductive hormonal; Sperm

1. Introduction

People's lifestyles and eating habits have undergone significant change due to the rapid expansion of the economy and improvements in living standards, leading to an increase in the number of overweight and obese individuals. Obesity is not a single disorder but rather encompasses a diverse set of conditions resulting from complex interactions between environmental and genetic factors, ultimately lead to an accumulation of excess body fat, known as the obese phenotype[1]. Globally, the rise in obesity

Key Points

Question: Does obesity affect sperm DNA integrity and reproductive hormone levels in men?

Results: Obese men exhibited significantly higher levels of sperm DNA fragmentation and protamine deficiency, as well as hormonal imbalances, compared to overweight and normal weight men.

Meaning: Obesity may contribute to male infertility by compromising semen quality and altering reproductive hormone levels, highlighting the importance of weight management in fertility care.

✉ To whom correspondence may be addressed. E-mail: myassin@iugaza.edu.ps

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2025 Asian Pacific Journal of Reproduction Produced by Wolters Kluwer- Medknow.

How to cite this article: Laqqan MM, Yassin MM. Influence of body mass index on semen quality: Examining sperm DNA fragmentation, protamine deficiency, and hormonal profiles. *Asian Pac J Reprod* 2025; 14(4): 171-178.

Article history: Received: 10 April 2025; Revision: 19 June 2025; Accepted: 2 July 2025; Available online: 26 August 2025

has raised serious public health concerns[2]. According to the World Health Organization (WHO), the prevalence of obesity has increased nearly five-fold among children and adolescents, and it has almost tripled since 1975[3]. Obesity heightens the risk of developing various diseases, including type 2 diabetes, cardiovascular and respiratory disorders, and cancer[4]. Additionally, research highlights a strong potential association between paternal obesity and infertility. This is particularly concerning given the high prevalence of obesity among young males of reproductive age[5].

Traditional semen parameters, the molecular composition of sperm, and the embryo's developmental potential are all considered when evaluating male fertility. Several studies have demonstrated that obesity negatively affects traditional semen parameters, thereby reducing male fertility. Specifically, research has shown that obese and overweight men are more likely to have low sperm counts, poor sperm motility, and a higher percentage of sperm with DNA damage in their ejaculate[6]. Studies have also reported an association between obesity and increased DNA fragmentation, or damage to DNA or chromatin, in human spermatozoa[7]. Moreover, several studies indicate that, in obese men, adipose tissue converts androgens into estrogens, leading to hormonal imbalances and hypogonadism[8]. Additionally, adipose tissue produces pro-inflammatory cytokines and oxidative stress, which can negatively impact testicular function, damage sperm cells, and ultimately decrease male fertility[9]. However, this issue is not so straightforward. Some studies revealed that body mass index (BMI) do not influence sperm semen analysis parameters[10,11]. Furthermore, some authors have found that among couples undergoing *in-vitro* fertilization (IVF), the BMI of the male partner does not affect semen analysis parameters but may influence the number of high-quality embryos obtained during IVF[12], suggesting a potential epigenetic origin and effects in sperm and offspring.

Despite ongoing research, there are still limited studies and conflicting results regarding the impact of obesity on sperm quality, including sperm DNA fragmentation and protamine deficiency. Therefore, this study was conducted to (I) investigate whether differences exist in DNA fragmentation levels and protamine deficiency in the sperm of obese men compared to those of overweight and proven fertile, normal-weight men, (II) evaluate the effect of obesity on sperm parameters and reproductive hormone profiles, and (III) speculate possible associations between BMI and overall sperm quality.

2. Methods

2.1. Study design and study population

This was an observational study conducted between January

2015 and March 2022. Anthropometric measurements included weight in kilograms, height in meters, and BMI, calculated as kg/m^2 . According to the WHO, a BMI of 18.5 to 24.9 kg/m^2 is considered normal weight, 25 to 29.9 kg/m^2 is classified as overweight, and 30 kg/m^2 or higher is considered obese[13]. The male participants were divided into three groups based on their BMI: (group I) normal-weight males who had at least two children ($n=200$), (group II) overweight males ($n=200$), and (group III) obese males ($n=200$). Both the overweight and obese males were considered sub-fertile and had not achieved pregnancy in the past five years. The sample size was determined using the formula for a cross-sectional study with the EPI-INFO statistical package (version 7.2), applying a 99.9% confidence interval (CI), 85% power, and a ratio of 0.4.

The exclusion criteria for all participants were summarized as follows: underweight, diabetes mellitus; smoking; alcohol consumption; anti-sperm antibodies; varicocele; previous reproductive system surgery; known infertility problems; exposure to known reproductive toxins; and the use of medication that may affect semen parameters during the study or within the past 12 months. On the other hand, the inclusion criteria were men aged between 20 and 50 years who shared the same ethnicity and nationality (Arab and Palestinian). According to medical records, all female partners met the following criteria: age between 20 and 39 years, normal BMI, normal hormonal profile, regular menstrual cycles, and no history of endocrine disorders.

2.2. Semen analysis and reproductive hormones evaluation

The semen samples were collected through masturbation after abstaining from sexual intercourse for three days. After a thirty-minute incubation at 37 °C to allow liquefaction, the sperm count was immediately determined using a Makler counting chamber (Sefi-Medica, Haifa, Israel). Sperm morphology was evaluated in this study. Briefly, smears were prepared from each semen sample and allowed to air dry. The smears were then fixed in 95% ethanol for 15 min. After fixation, they were stained with hematoxylin and eosin. To assess the staining results, 100 spermatozoa per smear were examined under brightfield optics at $\times 1\,000$ magnification using oil immersion to determine the percentage of abnormal forms. All semen samples were manually analyzed by a single technologist in accordance with the WHO guidelines[14]. On the day of semen collection, five milliliters of peripheral blood were drawn and centrifuged at $2\,500\times g$ for 20 min to separate the serum. The concentrations of total testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL) were then measured using the Tosoh Instrument (AIA-360, Tokyo, Japan).

2.3. Evaluation of sperm DNA fragmentation

The TUNEL (Terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling) assay was utilized to evaluate sperm DNA fragmentation, which serves as an indicator of sperm apoptosis. An in-situ cell death detection kit (Roche Diagnostics, Germany) was employed following the manufacturer's guidelines. To conduct this assay, ten microliters of a sperm suspension were spread on microscope slides and allowed to air-dry. The smears were then fixed with 4% paraformaldehyde phosphate-buffered saline (PBS) (pH 7.4) for 2 h at room temperature and rinsed with PBS. Permeabilization of the smears was achieved by treating them with 0.1% Triton X-100 for 15 min at room temperature, followed by the addition of fifty microliters of a terminal deoxynucleotidyl transferase (TdT)-labeled nucleotide mixture. The slides were incubated overnight at 37°C in a dark, humidified chamber. Afterward, the slides were rinsed twice with PBS and allowed to air dry. Twenty-five microliters of counterstain were added to the slide, followed by coverslipping. Zeiss Photomicroscope III was used. The slides were investigated to assess DNA fragmentation by distinguishing between TUNEL-positive sperm (bright green stain) and TUNEL-negative sperm (dull green stain)[15].

2.4. Evaluation of sperm protamine deficiency

Chromomycin A3 (CMA3) staining was used to evaluate the level of protamine deficiency or chromatin decondensation in human spermatozoa. First, smears of semen were generated and treated with methanol-glacial acetic acid in a 3:1 ratio for 15 min at 4°C. The smears were then air-dried at 22°C. Next, fifty microliters of staining solution (Sigma-Aldrich, USA) were added to each smear, which was then incubated in a dark place for 50 min at 22°C. The smears were washed with PBS, and the slides were mounted with 1:1 (v/v) glycerol/PBS and incubated overnight at 4°C. The slides were examined under a fluorescence microscope (Germany's Zeiss Photomicroscope III) to assess the CMA3 staining outcomes. Finally, protamine deficiency was assessed by classifying spermatozoa stained with bright yellow as "bad spermatozoa, positive," and those stained with dull yellow as "good spermatozoa, negative"[15].

2.5. Statistical analysis

All data in this study were analyzed using the IBM SPSS for Windows software package, version 24.0 (SPSS, Inc., Chicago, USA). Based on the results of the skewness test, kurtosis test, and Z-value, the data in this study were found to be non-normally distributed. So, the data were presented as the median and interquartile range (IQR). To compare quantitative variables between study groups, the one-way ANOVA with *post hoc* analysis

was employed. Spearman's rank correlation coefficient was used to assess the relationships between BMI and clinical and biochemical parameters. The multivariate logistic regression analysis was used to determine whether FSH, LH, and PRL are confounding factors. The results of the aforementioned tests were considered statistically significant when the *P*-value was less than 0.05.

2.6. Ethics statement

The Health Research Council in the Palestine provided ethics approval for this study (Reference Number: PHRC/HC/13/14), and all participants gave their informed permission in accordance with the Helsinki Declaration. The samples were analyzed according to the global guidelines and standard procedures.

3. Results

3.1. Semen parameters and reproductive hormones of the study groups

A total of 600 males, with a mean age of (34.3±7.9) years, participated in this observational study. Table 1 outlines the clinical and biochemical characteristics of the study population, including age, semen parameters, sperm DNA fragmentation, protamine deficiency, and hormonal profiles. According to the findings in Table 2, obese males exhibited significant reductions in the following semen characteristics compared to overweight and normal-weight males: semen volume ($P<0.001$), sperm concentration ($P<0.001$), percentage of sperm total motility ($P<0.001$), progressive motility ($P<0.001$), and non-progressive motility ($P<0.001$). On the contrary, obese males exhibited significant increases in the percentage of non-motile spermatozoa ($P<0.001$) and abnormal forms of spermatozoa ($P<0.001$) when compared to overweight and normal weight males, respectively. However, there were no significant differences observed among the study groups in terms of age ($P=0.615$). Additionally, obese males showed significant increases in the following parameters compared to overweight and normal-weight males: the level of sperm DNA fragmentation ($P<0.001$) (Figure 1), and the level of sperm protamine deficiency ($P<0.001$) (Figure 2).

3.2. Level of reproductive hormones among the study groups

As illustrated in Table 2, significant declines are shown in the levels of total testosterone ($P<0.001$), FSH ($P<0.001$), and LH ($P<0.001$) in obese males compared to overweight and normal weight males. In contrast, obese men have a significant elevation in the levels of PRL ($P<0.001$) compared to overweight and normal-weight males.

Table 1. Clinical and biochemical parameters of the study population ($n=600$).

Variables	Median (IQR)
Age, years	32.0 (11.0)
Semen volume, mL	2.5 (2.0)
Sperm concentration, 10^6 per mL	15.4 (26.0)
Percentage of sperm total motility	37.0 (34.2)
Percentage of sperm progressive motility	25.9 (23.9)
Percentage of sperm non-progressive motility	11.1 (10.3)
Percentage of non-motile sperm	63.0 (34.2)
Percentage of sperm abnormal form	72.0 (33.0)
Percentage of sperm DNA fragmentation	14.5 (52.0)
Percentage of sperm protamine deficiency	35.0 (57.0)
Total testosterone level, ng/mL	4.9 (4.4)
FSH level, mIU/mL	4.2 (6.3)
LH level, IU/L	3.8 (5.4)
PRL level, ng/mL	4.6 (9.7)

IQR: interquartile range; FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin.

The results of the logistic regression analysis indicated that the levels of FSH, LH, and PRL hormones were statistically significant, with Exp(B) values less than 10. Therefore, FSH, LH, and PRL are

not considered confounding factors. These findings are presented in Table 3.

3.3. Association between BMI and investigated clinical and biochemical parameters

Table 4 has demonstrated significant negative correlations between BMI and semen volume ($r=-0.781$, $P<0.001$), sperm concentration ($r=-0.823$, $P<0.001$), percentage of sperm total motility ($r=-0.800$, $P<0.001$), progressive motility ($r=-0.800$, $P<0.001$), sperm non-progressive motility ($r=-0.801$, $P<0.001$). Also, significant negative correlations between BMI and the levels of total testosterone ($r=-0.813$, $P<0.001$), FSH ($r=-0.822$, $P<0.001$), LH ($r=-0.863$, $P<0.001$) have been demonstrated. Conversely, significant positive associations have been observed between BMI and percentage of non-motile sperm ($r=0.800$, $P<0.001$), sperm abnormal form ($r=0.309$, $P<0.001$), PRL ($r=0.854$, $P<0.001$), levels of DNA fragmentation ($r=0.439$, $P<0.001$) and sperm protamine deficiency ($r=0.604$, $P<0.001$).

Table 2. Semen parameters and reproductive hormones of the studied groups ($n=600$).

Variables	Normal weight ($n=200$)	Overweight ($n=200$)	Obesity ($n=200$)	P-value
Age, years	32.0(13.0)	32.0(10.0)	32.0(10.0)	0.615
Semen volume, mL	3.8(1.0)	2.5(1.5) ^a	1.2(0.6) ^{ab}	< 0.001
Sperm concentration, 10^6 per mL	49.7(52.2)	14.3(4.1) ^a	8.0(8.0) ^a	< 0.001
Percentage of sperm total motility	62.2(17.0)	37.0(18.3) ^a	18.0(14.1) ^{ab}	< 0.001
Percentage of sperms progressive motility	43.5(11.9)	25.9(12.8) ^a	12.6(9.9) ^{ab}	< 0.001
Percentage of sperm non-progressive motility	18.7(5.1)	11.1(5.5) ^a	5.4(4.2) ^{ab}	< 0.001
Percentage of non-motile sperm	37.9(17.0)	63.0(18.3) ^a	82.0(14.1) ^{ab}	< 0.001
Percentage of sperm abnormal form	50.0(48.0)	71.6(20.0) ^a	81.0(27.0) ^{ab}	< 0.001
Total testosterone level, ng/mL	7.3(2.7)	4.9(1.6) ^a	2.0(1.0) ^{ab}	< 0.001
FSH level, mIU/mL	8.7(1.9)	4.3(2.7) ^a	1.5(0.9) ^{ab}	< 0.001
LH level, IU/L	7.5(4.5)	3.9(2.0) ^a	0.9(0.4) ^{ab}	< 0.001
PRL level, ng/mL	1.5(1.8)	4.3(2.0) ^a	14.2(4.0) ^{ab}	< 0.001

Data are expressed as median (IQR). FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin. ^a $P<0.05$: compared to the normal weight; ^b $P<0.05$: compared to the overweight.

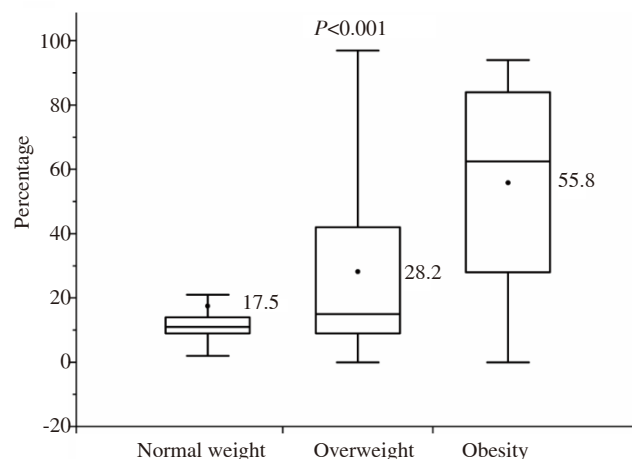
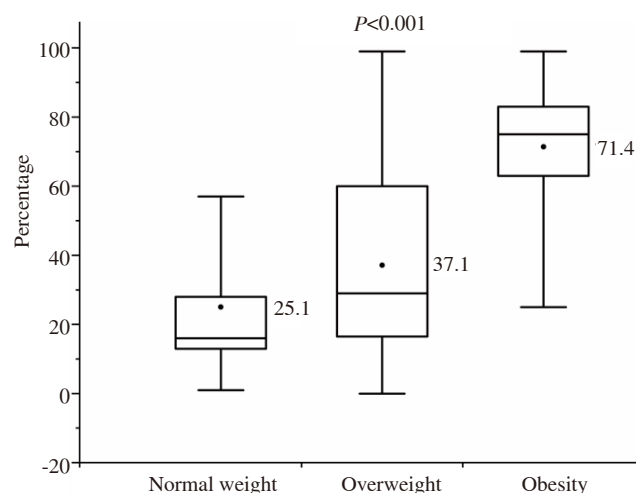
**Figure 1.** Levels of DNA fragmentation in human spermatozoa among the study groups. The dots represent the average value for each group.**Figure 2.** Levels of protamine deficiency in human spermatozoa among the study groups. The dots represent the average value for each group.

Table 3. Multiple logistic regression analysis to identify confounding factors.

Factors	B	S.E.	Wald	df	P-value	OR	95% CI for OR	
							Lower	Upper
FSH level, mIU/mL	-0.816	0.118	47.880	1.00	< 0.001	0.442	0.351	0.557
LH level, IU/L	-0.491	0.103	22.955	1.00	< 0.001	0.612	0.500	0.748
PRL level, ng/mL	1.441	0.216	44.430	1.00	< 0.001	4.226	2.766	6.455

FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin; B: intercept, SE: standard error of the intercept, OR: odds ratio, CI: confidence interval. A variable is considered a confounder if the OR changes by $\geq 10\%$.

Table 4. Correlation between the body mass index (BMI) and investigated clinical and biochemical parameters ($n=600$).

Parameters	BMI (kg/m ²)		Parameters	BMI (kg/m ²)	
Age, years	<i>r</i>	-0.060	Percentage of sperm abnormal form	<i>r</i>	0.309
	<i>P</i> -value	0.110		<i>P</i> -value	< 0.001
Semen volume, mL	<i>r</i>	-0.781	Percentage of sperm DNA fragmentation	<i>r</i>	0.439
	<i>P</i> -value	< 0.001		<i>P</i> -value	< 0.001
Sperm concentration, 10 ⁶ per mL	<i>r</i>	-0.823	Percentage of sperm protamine deficiency	<i>r</i>	0.604
	<i>P</i> -value	< 0.001		<i>P</i> -value	< 0.001
Percentage of sperm total motility	<i>r</i>	-0.800	Total testosterone level, ng/mL	<i>r</i>	-0.813
	<i>P</i> -value	< 0.001		<i>P</i> -value	< 0.001
Percentage of sperm progressive motility	<i>r</i>	-0.800	FSH level, mIU/mL	<i>r</i>	-0.822
	<i>P</i> -value	< 0.001		<i>P</i> -value	< 0.001
Percentage of sperm non-progressive motility	<i>r</i>	-0.801	LH level, IU/L	<i>r</i>	-0.863
	<i>P</i> -value	< 0.001		<i>P</i> -value	< 0.001
Percentage of non-motile sperm	<i>r</i>	0.800	PRL level, ng/mL	<i>r</i>	0.854
	<i>P</i> -value	< 0.001		<i>P</i> -value	< 0.001

Spearman's test is used. *r*: correlation coefficient; FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin.

4. Discussion

The global increase in obesity rates has coincided with reports of rising rates of male infertility, low sperm quality, and other health issues[16]. Male-related infertility accounts for 45%–50% of infertile couples[17]. In recent years, significant efforts have been made to investigate the influence of BMI on human spermatozoa, specifically DNA fragmentation and protamine deficiency, as well as its relationship with infertility. Fat may impose negative impact on spermatogenesis through various mechanisms such as thermal effects, hyperestrogenism, hyperglycemia, sexual dysfunction, and sperm genetic disturbances. Furthermore, study indicated that paternal obesity has detrimental effects that can be transmitted to offspring through genetic alterations in germ cell DNA[18]. Despite these efforts, there is still conflicting evidence and limited research on the association of obesity with the decline in male fertility, as well as the decline in sperm quality. Therefore, this study was conducted to clarify the impact of obesity on semen parameters, sperm DNA fragmentation and protamine deficiency.

This study found that obese males had significant declines in the volume of seminal fluid, sperm concentration, percentage of sperm total motility, progressive motility, and non-progressive motility compared to overweight and normal-weight males. Conversely, significant elevations have been shown in the percentage of non-motile spermatozoa and abnormal sperm forms in obese males compared to other groups. These findings are in agreement with

previous studies that have revealed significant declines in semen parameters such as semen volume, sperm count, total sperm motility, and sperm progressive motility in obese and overweight males in comparison to normal-weight males[19]. The percentage of sperm with abnormal morphology and non-motile sperm was significantly higher in obese males than in normal-weight males[20]. A previous study has revealed that obesity negatively affects spermatogenesis by impairing the blood-testis barrier and Leydig cell function[21]. In this context, oxidative stress and inflammatory responses in the semen of obese males are increased, sperm motility is reduced, morphological defects are increased, and DNA damage and apoptotic rate of germ cells are increased, each of which leads to decreased spermatogenesis[22]. In contrary, a study showed that obesity had no effect on sperm concentration and percentage of normal sperm morphology[23].

In the present study, obese men exhibited significantly elevated levels of DNA fragmentation and protamine deficiency in their spermatozoa when compared to overweight and normal-weight males. These findings are consistent with a previous study[24]. It is acceptable that elevated reactive oxygen species (ROS) in seminal fluid of obese men can detrimentally affect germ cells by altering cell membranes, leading to irreversible cellular abnormalities. In this regard, high levels of ROS induce DNA damage in fully developed sperm and spermatids[25].

Regarding the reproductive hormonal profile, significant reductions have been shown in levels of testosterone, FSH, and LH in obese

males compared to overweight and normal-weight males. These findings are in agreement with a study indicating that obesity could negatively impact sperm quality through reduction of reproductive hormones levels[20]. One hypothesis to explain this decline suggests that obese males may encounter challenges in producing sex hormone-binding globulin[26]. Furthermore, obese men exhibit heightened activity of the aromatase enzyme, resulting in an increased conversion of androgens to estrogen[27]. The resulting hyperestrogenemia establishes a negative feedback loop on the hypothalamic-pituitary-gonadal axis, leading to the suppression of LH and FSH production. Consequently, testosterone output from the testes is diminished, resulting in a condition known as hypogonadotropic hypogonadism[28]. An alternative hypothesis suggests that the increase in the level of leptin hormone produced by adipose tissue[29] may contribute to the suppression of steroid synthesis in the testicles, thus elucidating the connection between hyperleptinemia, decreased gonadotropin levels, and testosterone production in obese men[30].

In this study, significant negative correlations were found between BMI and various semen parameters including semen volume, sperm concentration, and sperm motility. Similar findings were previously reported[30,31]. These correlations may be caused by a number of reasons accompanied by obesity, including hormone imbalance, oxidative stress, and inflammation, as these conditions can inhibit spermatogenesis and sperm maturation, potentially leading to infertility[32]. However, few authors failed to find an association between increases in BMI and changes in semen characteristics[33]. On the other hand, this study revealed positive correlations between BMI and sperm DNA fragmentation and protamine deficiency. Such results are supported by the findings that higher levels of sperm DNA damage and increased BMI are interconnected[34]. One possible explanation for these findings is the oxidative stress caused by an excess of ROS, which damages the DNA and compromises the integrity of the plasma membrane in sperm[29,35]. This explanation is strengthened by positive associations of oxidative stress in semen and testes with an increase in BMI and sperm DNA damage, and a negative correlation with sperm motility[36].

Regarding the association between BMI and reproductive hormones, significant negative associations were found between the levels of total testosterone, FSH, and LH hormones and BMI. These findings were accepted that men obesity has been associated with hypogonadism[37]. Indeed, reproductive hormone irregularities may be one of the most significant causes of male infertility or subfertility caused by obesity. It is well understood that an elevated level of testosterone is required for both testicular development and spermatogenesis maintenance. Furthermore, a high quantity of testosterone is related to Sertoli cells, which build a niche suitable for growing germ cells during the various phases

of spermatogenesis[38]. FSH is also an essential regulator of Sertoli cells, boosting nearly all spermatogenesis-related processes[39]. As a result, decreased testosterone and FSH levels in obese men might impair spermatogenesis, resulting in lower sperm counts and male infertility[29]. Additionally, a study exhibited negative correlations between the levels of LH, FSH, and BMI; this association may be related to the conversion of androgens to estradiol, resulting in increased serum estrogen levels[40]. The higher levels of estradiol in obese individuals decrease the production and secretion of LH and FSH, leading to reduced testicular function and testosterone production, which has a direct harmful effect on spermatogenesis[41]. On the other hand, this study demonstrated a positive association between BMI and PRL levels, which aligns with a previous study[42].

This study had a few limitations, including not assessing obesity through waist circumference, hip circumference, or the waist-to-hip ratio. Furthermore, additional genetic research is required to better understand how obesity affects sperm DNA methylation and the genes involved in sperm development and maturation, which would clarify the relationship between obesity and male fertility.

In conclusion, obese males exhibited lower semen volume, sperm concentration, motility, and levels of total testosterone, FSH, and LH. In contrast, they showed higher levels of non-motile and abnormally shaped sperm, PRL, sperm DNA fragmentation, and protamine deficiency compared to overweight and normal-weight males. BMI demonstrates significant negative associations with semen volume, sperm concentration, sperm motility, total testosterone, FSH, and LH, while it is positively associated with PRL, sperm DNA fragmentation, and protamine deficiency.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Funding

The study received no extramural funding

Authors' contributions

Mohammed M. Laqqan and Maged M. Yassin contributed equally to the conceptualization, formal analysis, and visualization. Maged M. Yassin led the data curation, investigation, methodology, and writing of the original draft, while Mohammed M. Laqqan provided support in data curation and contributed to the review and editing of the manuscript.

Publisher's Note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

- [1] Qasim A, Turcotte M, de Souza RJ, Samaan MC, Champredon D, Dushoff J, et al. On the origin of obesity: Identifying the biological, environmental and cultural drivers of genetic risk among human populations. *Obes Rev* 2018; **19**(2): 121-149.
- [2] Munir M, Zakaria ZA, Baig AA, Mohamad MB, Arshed N, Alhajj R. Global impact on human obesity—A robust non-linear panel data analysis. *Nutr Health* 2024; **30**(3): 531-548.
- [3] Park H, Choi JE, Jun S, Lee H, Kim HS, Lee HA, et al. Metabolic complications of obesity in children and adolescents. *Clin Exp Pediatr* 2024; **67**(7): 347-355.
- [4] Costanian C, Bennett K, Hwalla N, Assaad S, Sibai AM. Prevalence, correlates and management of type 2 diabetes mellitus in Lebanon: Findings from a national population-based study. *Diabetes Res Clin Pract* 2014; **105**(3): 408-415.
- [5] Raad G, Azouri J, Rizk K, Zeidan NS, Azouri J, Grandjean V, et al. Adverse effects of paternal obesity on the motile spermatozoa quality. *PLoS One* 2019; **14**(2): e0211837.
- [6] Vozdova M, Kubickova S, Kopecka V, Sipek J, Rubes J. Effect of body mass index on semen quality, sperm chromatin integrity and sperm DNA methylation. *Obes Res Clin Pract* 2024; **18**(5): 380-387.
- [7] Fariello RM, Pariz JR, Spaine DM, Cedenho AP, Bertolla RP, Fraietta R. Association between obesity and alteration of sperm DNA integrity and mitochondrial activity. *BJU Int* 2012; **110**(6): 863-867.
- [8] Genchi VA, Rossi E, Lauriola C, D'Oria R, Palma G, Borrelli A, et al. Adipose tissue dysfunction and obesity-related male hypogonadism. *Int J Mol Sci* 2022; **23**(15): 8194.
- [9] Kahn BE, Brannigan RE. Obesity and male infertility. *Curr Opin Urol* 2017; **27**(5): 441-445.
- [10] MacDonald A, 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**(3): 293-311.
- [11] Anifandis G, Dafopoulos K, Messini CI, Polyzos N, Messinis IE. The BMI of men and not sperm parameters impact on embryo quality and the IVF outcome. *Andrology* 2013; **1**(1): 85-89.
- [12] Nikolic AZ, Dragojevic-Dikic S, Kocic J, Babic U, Joksimovic A, Radakovic-Cosic J, et al. Influence of male body mass index on semen analysis parameters and *in vitro* fertilization outcomes. *Medicine* 2024; **103**(31): e38949.
- [13] Alam K, Kumar T, Jha K, Zabihullah M, Alam Sr MK. Impact of body mass index and anthropometric measures on cardiorespiratory fitness in non-obese adult males: A cross-sectional observational study. *Cureus* 2024; **16**(12): e75329. doi: 10.7759/cureus.75329.
- [14] Chung E, Arafa M, Boitrelle F, Kandil H, Henkel R, Saleh R, et al. The new 6th edition of the WHO Laboratory Manual for the Examination and Processing of Human Semen: Is it a step toward better standard operating procedure? *Asian J Androl* 2022; **24**(2): 123-124.
- [15] Laqqan MM, Yassin MM. Potential effect of tobacco cigarettes smoking on global DNA methylation status and protamines transcripts in human spermatozoa. *Middle East Fertil Soc J* 2021; **26**(1): 21.
- [16] Martins AD, Majzoub A, Agawal A. Metabolic syndrome and male fertility. *World J Mens Health* 2019; **37**(2): 113-127.
- [17] Agarwal A, Baskaran S, Parekh N, Cho CL, Henkel R, Vij S, et al. Male infertility. *Lancet* 2021; **397**(10271): 319-333.
- [18] Potabattula R, Ditttrich M, Schorsch M, Hahn T, Haaf T, El Hajj N. Male obesity effects on sperm and next-generation cord blood DNA methylation. *PLoS One* 2019; **14**(6): e0218615.
- [19] Li Y, Lin Y, Ou C, Xu R, Liu T, Zhong Z, et al. Association between body mass index and semen quality: A systematic review and meta-analysis. *Int J Obes (Lond)* 2024; **48**(10): 1383-1401.
- [20] Maghsoumi-Norouzabad L, Zare Javid A, Aiiashi S, Hosseini SA, Dadfar M, Bazyar H, et al. The impact of obesity on various semen parameters and sex hormones in Iranian men with infertility: A cross-sectional study. *Res Rep Urol* 2020; **12**: 357-365.
- [21] Chojnacka K, Bilinska B, Mruk DD. Interleukin 1alpha-induced disruption of the Sertoli cell cytoskeleton affects gap junctional communication. *Cell Signal* 2016; **28**(5): 469-480.
- [22] Tunc O, Bakos HW, Tremellen K. Impact of body mass index on seminal oxidative stress. *Andrologia* 2011; **43**(2): 121-128.
- [23] Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality? A meta-analysis and systematic review from the general population rather than the infertile population. *Andrologia* 2021; **53**(7): e14099.
- [24] Peel A, Saini A, Deluao JC, McPherson NO. Sperm DNA damage: The possible link between obesity and male infertility, an update of the current literature. *Andrology* 2023; **11**(8): 1635-1652.
- [25] Nowicka-Bauer K, Nixon B. Molecular changes induced by oxidative stress that impair human sperm motility. *Antioxidants*. 2020; **9**(2): 134.
- [26] Cooper LA, Page ST, Amory JK, Anawalt BD, Matsumoto AM. The association of obesity with sex hormone-binding globulin is stronger than the association with ageing—implications for the interpretation of total testosterone measurements. *Clin Endocrinol* 2015; **83**(6): 828-833.
- [27] Colleluori G, Chen R, Turin CG, Vigeveno F, Qualls C, Johnson B, et al. Aromatase inhibitors plus weight loss improves the hormonal profile of obese hypogonadal men without causing major side effects. *Front Endocrinol* 2020; **11**: 277.
- [28] Xu X, Sun M, Ye J, Luo D, Su X, Zheng D, et al. The effect of aromatase on the reproductive function of obese males. *Horm Metab Res* 2017; **49**(8): 572-579.
- [29] Leisegang K, Sengupta P, Agarwal A, Henkel R. Obesity and male

- infertility: Mechanisms and management. *Andrologia* 2021; **53**(1): e13617.
- [30]Di Nisio A, Sabovic I, De Toni L, Rocca MS, Dall'Acqua S, Azzena B, et al. Testosterone is sequestered in dysfunctional adipose tissue, modifying androgen-responsive genes. *Int J Obes* 2020; **44**(7): 1617-1625.
- [31]Bansal S, Mundkur A, Adiga P, Kumar P, Kumar S, Poojary V, et al. The effect of body mass index on semen quality. *Int J Infertil Fetal Med* 2022; **13**(3): 121-124.
- [32]Bieniek JM, Kashanian JA, Deibert CM, Grober ED, Lo KC, Brannigan RE, et al. Influence of increasing body mass index on semen and reproductive hormonal parameters in a multi-institutional cohort of subfertile men. *Fertil Steril* 2016; **106**(5): 1070-1075.
- [33]Baydilli N, Selvi İ, Akınsal EC, Zararsız GE, Ekmekçioğlu O. How does body mass index affect semen parameters and reproductive hormones in infertile males? *Turk J Urol* 2020; **46**(2): 101-107.
- [34]Zhu G, Zhang Y, Dong J, Liu Y, Zhao F, Li T, et al. Association between body mass index and male sperm apoptosis and apoptosis-related factors. *Diabetes Metab Syndr Obes* 2021; **14**: 1043-1051.
- [35]Rato L, Alves MG, Cavaco JE, Oliveira PF. High-energy diets: A threat for male fertility? *Obes Rev* 2014; **15**(12): 996-1007.
- [36]Kurkowska W, Bogacz A, Janiszewska M, Gabry E, Tiszler M, Bellanti F, et al. Oxidative stress is associated with reduced sperm motility in normal semen. *Am J Mens Health* 2020; **14**(5): 1557988320939731. doi: 10.1177/1557988320939731.
- [37]Dutta S, Sengupta P, Biswas A. Adiponectin in male reproduction and infertility. *Asian Pac J Reprod* 2019; **8**(5): 244-250.
- [38]Chen YA, Chang HC, Liao CH. The impact of obesity on serum testosterone levels and semen quality in a population of infertile men. *Urol Sci* 2019; **30**(3): 118-123.
- [39]Oduwole OO, Peltoketo H, Huhtaniemi IT. Role of follicle-stimulating hormone in spermatogenesis. *Front Endocrinol* 2018; **9**: 763.
- [40]Palmer NO, Bakos HW, Fullston T, Lane M. Impact of obesity on male fertility, sperm function and molecular composition. *Spermatogenesis* 2012; **2**(4): 253-263.
- [41]Pavlovich CP, King P, Goldstein M, Schlegel PN. Evidence of a treatable endocrinopathy in infertile men. *J Urol* 2001; **165**(3): 837-841.
- [42]Al Sabie F, Tariq Z, Erickson D, Donegan D. Association between prolactinoma and body mass index. *Endocr Pract* 2021; **27**(4): 312-317.

Edited by Lin LY, Lei Y