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Research Article

Impact of Obesity on Semen Parameters and Sperm DNA Integrity in Infertile Males

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Abstract

Introduction: *The interaction between obesity and fertility has received increased attention owing to the rapid increase in the prevalence of the obesity worldwide. Several studies were done to explain the relationship between obesity and poor semen quality and poor male fertility results has been inconsistent and inconclusive.*

Aim of the Work *is to highlight the effect of obesity on semen parameters and DNA integrity of infertile males. This study was conducted on 88 infertile patients selected from attendants of the Hawa IVF center, Benha, Egypt, in the period from April 2017 to August 2018. divided to 3 groups according to their body mass index (BMI): Group A includes normal weight patients (BMI18-24.9 kg⁄m 2, N 13).Group B includes overweight patients (BMI 25-29.9 kg⁄ m 2, N=31).Group C includes obese patients (BMI ≥30 kg⁄ m 2, N =44).Medical history and general examination were done to exclude patients with male factors known to affect fertility. BMI was calculated and semen analysis and sperm DNA fragmentation index (DFI) were estimated for all patients.*

Results: *According to BMI there was significant decrease between groups (B and C) regarding the percent of sperms progressive motility (P-value=0.045) which was negatively correlated with BMI (r=-0.216, p-value=0.043). Significant increase DFI was found in group B (overweight) and group C (obese) compared to group A (normal) and a positively correlated with BMI (r=0.225, p=0.035).*

Conclusion: *Obesity is associated with low progressively motile sperms and increased percentage of sperm DNA fragmentation index (DFI).*

Keywords: obesity, semen parameters, sperm DNA integrity, infertile males

Introduction

Obesity, defined by the World Health Organization (WHO) as a body mass index (BMI) 30 ≥kg/ m^2, is a medical condition of excess body fat that negatively influencing morbidity and mortality via non-communicable disease risks [1,2].

Infertility is defined by the World Health Organization (2010) as 'the inability of a couple to achieve conception or bring a pregnancy to term after 12 months or more of regular unprotected sexual intercourse [3].

Alongside an increased incidence of obesity, infertility is a growing concern affecting up to 15%of couples trying to conceive globally, with approximately 25 % of cases attributed to the male partner [4].

In males, the effect of obesity on the hormone regulation of spermatogenesis is underpinned by the hypothesis that the hypothalamic pituitary gonadal (HPG) axis is deregulated by obesity. Several studies documents that increased male body mass index (BMI) is associated with decreased plasma concentrations of sex hormone binding globulin (SHBG) testosterone, and a concomitant increased plasma concentration of estrogen [5,6,7,8].

There is a clear consensus in literature that male obesity is associated with higher levels of sperm DNA damage, despite the use of various methodologies to measure sperm DNA integrity (i.e., TUNEL, COMET and SCSA) [9-15].

The effect of BMI on sperm characteristics remains controversial; various studies have shown obesity to be associated with a reduction in sperm count, concentration, motility, vitality, morphology, and /or DNA integrity [16,17]. In contrast, other researchers have not found similar relationships [5,18]. This is highlighted by two meta -analytical reviews that had numerous opposing conclusions [19,20].

Aim of Work

The aim of this work is to highlight the effect of obesity on semen parameters and DNA integrity of infertile males.

Patients and Methods

The study was conducted at the Andrology outpatients' clinic, Hawa IVF center, Benha, Egypt, in the period from April 2017 to August 2018, included 88 male patients complaining of infertility, divided to 3 groups according to their BMI:

- **Group A** includes normal patients (BMI18-24.9 kg/m ^{2}, N =13).
- **Group B** includes overweight patients (BMI 25-29.9 kg/ m ^{2}, N=31).
- **Group C** includes obese patients (BMI ≥30 kg/ m ^{2}, N =44).

Exclusion criteria

Patients with known reproductive tract pathology (e.g. genital tract infections, prostatitis, varicocele, etc), Patients with azoospermia, Patient on hormonal therapy (e.g. testosterone, insulin, thyroid replacement) or If they were hospitalized or had any surgery in the last six months, Patients with any chronic disease (specifically obesity related pathology such as Cushing's syndrome, hypothyroidism and type two diabetes mellitus (T2DM|)), Those on medications associated with increased obesity risk (e.g. antidepressant medications, cortisone, metformin, etc.) or with history of smoking or recreational drug use in the last six months and patients with diagnosed female factor infertility.

Ethical consideration

- The steps and the aim of the research were explained to participants before they were involved.
- The participants were not exposed to any hazardous interventions in the research.
- The participants were included on their full well.
- A written consent was taken from all participants before they were involved.

Methods

Detailed medical history and examination were done to all patients to exclude those with any excluded criteria.

Calculation of BMI

Men height (cm) and weight (kg) were reported. Then BMI was calculated as weight (kg) divided by height (m) squared (BMI = weight/ height ^{2}) [21].

Participants included in data analysis were divided into three groups based on the WHO definitions of obesity [1,2].

Investigations

Semen analysis

Semen analysis was done after a sexual abstinence for at least 3 days. Semen was obtained by masturbation into a sterile plastic container. Participants were instructed to collect all semen and report any semen loss. Semen analysis was carried out according to the criteria mentioned in the World Health Organization laboratory manual [22].

Assessment of DNA integrity

By Acridine Orange (AO) Assay

The AO assay measures the ability of sperm nuclear DNA to denature by acid which forms metachromatic shift of AO fluorescence from green (native DNA) to red (denatured DNA). The fluorochrome AO intercalates in double-stranded DNA as a monomer which binds to single-stranded DNA. The monomeric AO bound to native DNA fluoresce green, whereas the aggregated AO on denatured DNA fluoresces red [23].

Statistical analysis

Date entry and data analysis were done using SPSS version 19 (Statistical Package for Social Science). Data were presented as number, percentage, mean, median and standard deviation. Mann-Whitney test was used to compare quantitative variables between groups in case of non-parametric data. Spearman correlation was done to measure correlation between quantitative variables. P-value considered statistically significant when $P < 0.05$.

Results

BMI of included patients

The mean body mass index (BMI) of the cohort was 28.93 ± 4.23 (Range=19.96 – 42.52), 14.8% of patients were normal weight (BMI 18–24.9), 35.2% were overweight (BMI 25 – 29.9) with a mean 28.93 ± 4.23 (Range=19.96 – 42.52), 50% of participants were obese (BMI ≥30 kg/ m 2), (table1).

	No. (n= 88)	%
Body mass index (BMI):		
Normal weight (18–24.9).	13	14.8
Overweight (BMI 25 – 29.9).	31	35.2
Obese BMI ≥30 kg/ m ^{2}	44	50
Mean ± SD (Range)	28.93 ± 4.23 (19.96 – 42.52)	

Table 1: BMI of included patients.

Relation between obesity and semen parameters according to body mass index (BMI)

According to BMI, patients were divided to three groups, 13 patients were normal weight (BMI 18–24.9), 31 patients were Overweight (BMI 25 – 29.9) and 44 patients were obese (BMI ≥30). The three groups were compared to each other as regard semen parameters and DNA integrity.

There was only significant decrease of sperm motility grade A (Rapid progressive motility) and the total progressive motility (grade A+B) in obese group than overweight group.

There were no significant differences (P value >0.05) neither between normal and neither overweight groups nor does normal and obese group (table 2).

As regard sperm DNA fragmentation index (DFI), there were significant increase of sperm DFI in overweight and obese groups (p-value= 0.040 and 0.010 respectively) than normal weight group, (table 2).

Semen parameters	Normal weight (n= 13)	Overweight (n= 31)	Obese (n= 44)	P-value[1]	P-value[2]	P-value[3]
Liquefaction Time: (min)				0.707	0.646	0.951
Mean ± SD	30.39 ± 6.60	32.42 ± 8.15	33.52 ± 11.74			
Median (Range)	30 (20-40)	30 (20-50)	30 (20.0-60.0)			
Volume: (ml)				0.319	0.184	0.931
Mean ± SD	2.55 ± 1.16	3.04 ± 1.46	3.07 ± 1.40			
Median (Range)	2.5 (1.2-5.2)	2.5 (1-6.5)	2.5 (1.2-7.0)			
Sperm Rapid progressive motility (grade A)				0.863	0.213	0.016*
Mean ± SD	10.39 ± 9.89	9.84 ± 7.47	6.36 ± 8.72			
Median (Range)	10 (0-25)	10 (0-25)	5 (0.0-40.0)			
Sperm motility B: (slow progressive motility)				0.865	0.684	0.764
Mean ± SD	31.92 ± 10.52	32.90 ± 10.86	32.05 ± 9.04			
Median (Range)	35 (10-40)	30 (10-55)	32 (5.0-50.0)			
Sperm progressive motility (A+B):				0.637	0.151	0.045*
Mean ± SD	42.31 ± 17.03	42.74 ± 11.61	38.41 ± 12.70			
Median (Range)	50 (10-65)	45 (10-60)	37.5 (5.0-70.0)			
Sperm motility C: (non-progressive motility)				0.723	0.309	0.256
Mean ± SD	15.00 ± 6.12	14.84 ± 3.98	16.84 ± 6.82			
Median (Range)	15 (10-30)	15 (10-20)	15 (10.0 - 45.0)			
Sperm motility D (non-motile sperm)				0.658	0.352	0.268
Mean ± SD	42.69 ± 17.98	42.42 ± 12.24	44.77 ± 15.21			
Median (Range)	40 (20-75)	40 (25-80)	45 (10.0 - 85.0)			
Sperm concentration (million/ml):				0.348	0.536	0.352
Mean ± SD	43.78 ± 33.68	33.68 ± 32.88	37.58 ± 30.83			
Median (Range)	38 (1.1-98)	21 (3-120)	28 (1.4 - 128.0)			
Total sperm count:				0.487	0.932	0.294
Mean ± SD	117.28 ± 115.13	95.57 ± 103.54	111.85 ± 97.21			
Median (Range)	100 (1.3-426)	69 (11-472)	80.2 (2.8-400.0)			
Abnormal forms:				0.060	0.051	0.892
Mean ± SD	52.31 ± 12.52	60.65 ± 14.30	60.14 ± 12.38			
Median (Range)	50 (30-80)	60 (30-90)	60 (35.0-90.0)			
DFI				0.040*	0.010*	0.684
Mean ± SD	45.00 ± 9.35	52.45 ± 12.50	53.18 ± 10.57			
Median (Range)	45 (35-70)	50 (30-76)	50 (35.0 -75.0)			

P-value1: Comparison between Normal and Overweight.
P-value2: Comparison between Normal and Obese.
P-value3: Comparison between Overweight and Obese.
* P-value < 0.005.

Table 2: Comparison of patients' semen analysis according to categories of BMI in patients.

Correlations between BMI and semen parameters

Significant negative correlation was found between body mass index and sperm progressive motility (grad A+B) with p-value=0.043. Also, Significant positive correlations were found between body mass index and **s**perm DNA fragmentation index (DFI) with p-value=0.035, (table 3).

Semen parameters, insulin and glucose in serum and semen	BMI	
	r-value	P-value
Liqufaction Time (min)	0.000	0.999
Volume (ml)	0.032	0.769
Sperm motility A+B	-0.216	0.043*
Sperm concentration (million/ml)	-0.033	0.761
Sperm count	-0.002	0.982
Abnormal forms	0.164	0.128
DFI	0.225	0.035*

Table 3: Correlations between BMI and semen parameters

Discussion

Obesity and male factor infertility have coincidently been increasing globally. Obesity is associated with various metabolic changes, chronic inflammation and males, hypogonadism [26,25].

Results of the present study found significant decrease of sperm progressive motility in obese patients compared to overweight (p-value=0.045), and negative significant correlation between sperm progressive motility and body mass index (BMI).

In agree with these results, Hofny et al., (2010) found a significant negative correlation between sperm motility and BMI (7). Hammoud et al., (2008) also observed a significant increase in the prevalence of low progressively motile spermatozoa with increased BMI [26]. Other studies also reported a negative relationship between obesity and sperm motility [8,12, 13].

In contrast with the results in the present study Jensen et al., (2004), reported a higher prevalence of oligozoo-spermia in overweight and obese men compared with normal-weight men. However, they did not find any relationship between increasing male BMI and percentage of motile sperm. The study was carried out on 1558 young males' military recruits from Denmark [16]. These differences might be due to that the populations included in their study which were general young age even not complaining from infertility, while the populations of this study were all complaining from male factor infertility, most of them have bad semen analysis and their age were between 20 to 48 years.

Results of the present study found no significant difference of sperm count and concentration with increasing BMI. Similar results in accordance with our result were reported [5,10,25,27,28,29]. Chavarro et al. (2010) did not observe statistically significant differences in sperm morphology, sperm motility or sperm concentration in relation with levels of BMI [10]. Also, Duits et al. (2010), found no association between BMI and sperm motility & sperm count [18].

In contrast other studies found a decrease of sperm count and concentration with increasing BMI [11,16,30]. Tunc et al., (2011) found that, increased BMI was significantly linked with a fall in sperm concentration [11]. Sermondade et al. (2013), on meta-analysis study showed that overweight and obese men had a significantly elevated risk of abnormal sperm count compared with normal weight men [20].

Hofny et al., (2010), also reported a significant positive correlation between BMI and abnormal sperm morphology as well as significant negative correlation with sperm concentration, sperm motility [7]. This in agreement with our results as regard negative correlation between BMI and sperm motility but disagree with us as regard sperm concentration and morphology. These differences might be due to that the population included in their study which were only obese fertile and infertile while all our population were infertile with different BMI.

The present study found significant increase of sperm DNA fragmentation index (DFI) in obese and overweight (p-value= 0.040 and0.010 respectively) compared to normal patients, also significant positive correlation between body mass index and DFI.

Several studies have examined associations between body weight and Sperm DNA integrity**.** Most of these studies indicate a negative impact of sperm DNA integrity with increasing weight [8,9,10,12,27]. Kort et al. (2006), suggests that both overweight and obesity are associated with a higher DFI [9].

In contrast Eisenberg et al. (2014) published a report on 501 couples attempting to conceive and did not indicate any significant relationship between BMI and DFI [15]. In agreement with this, Hakonsen et al. (2012) did not find any significant improvement in DFI upon weight loss in a cohort of 43 obese men [31]. The results are contradictory, perhaps due to differences in populations this were complaining of couple infertility not male factor only infertility and in the methods of assessing DFI.

Reactive oxygen species (ROS) are one of the main contributors for impairing sperm DNA structure which is commonly elevated in subfertile men [32]. Obesity may be associated with significant perturbations to oxidative state and DNA integrity of sperm, and have repercussions not only on sperm function, but on the resultant embryo [33].

The current study found no significant difference of sperm abnormal forms with increasing BMI. Most of the studies agree with this result and have shown no correlation between obesity and abnormal sperm morphology [12,14,27,29], while some studies found that obesity is associated with increased sperm abnormal forms [7,9,16, 17,13].

The discrepancies observed in the literature likely result from several limitations that are inherent in human studies. First, these studies can be confounded by lifestyle factors such as smoking, alcohol consumption and recreational drug use as well as co-factors such as metabolic syndrome, all which can impair sperm function. Second, as most studies originate from fertility clinics where patient cohorts are frequently biased toward subfertile men, this may also confound findings. Thirdly, some studies rely on self-reporting of parameters, such as lifestyle factors and BMI, which can lead to inaccurate reporting.

Conclusion

- The results of this study found that male obesity may negatively impact reproductive function and fertility:
- Obesity is associated with low progressively motile sperms.
- Obesity is associated with increased percentage of sperm DNA fragmentation index (DFI).

Recommendations

- Further studies should be performed to define the extent of the relationship between obesity and altered sperm parameters and mechanisms responsible for alteration of sperm parameters.

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