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Effects of Obesity in Male Fertility in Khartoum State

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ABSTRACT

Obesity is a severe medical condition causing health issues and reducing life expectancy, affecting 400 million adults and 1.6 million overweight individuals, is a severe medical condition affecting fertility, with extreme obesity causing fertility issues. This study aimed to investigate the effect of obesity on male fertility in Khartoum state; it is a cross-sectional facility-based study studying All males of Infertile couples who come to the infertility clinic. The study discussed patient demographics, past medical and surgical history, and self-reported male sexual dysfunction in addition to the factors that affect male infertility, Body Mass Index (BMI), and spermatic parameters (motility, morphology, concentration) by seminal analysis. The statistical package SPSS 23.0 was used for analysis. The study revealed that 40 men (20.5) were of age <30 years old, 57 men (29.9%) of age 30 – 40 years old, and 98 men (50.3%) were of age >40 years old. "One hundred five men (53.8%) were from North Sudan", "58 men (29.7%) were from Eastern Sudan,30 men (15.35%) were from Western Sudan overweight, and 2 men (1.15%) were from Southern Sedan, 56 men (28.7%) have BMI <25,81(41.5%) had BMI 25 -30 and 58(29.8%) have BMI of >30, 110 men (56.4%) have normal sperm counts and 85 (43.6) have abnormal sperm counts, 105 men (53.8%) have normal sperm morphology". In contrast, 90 (46.2) have abnormal morphology. Eighty-eight men (45.1%) have progressive motility, while 107 men (54.9%) have impaired motility. Fifty-six men (28.8%) of participants have erectile dysfunction, while 139 (71.2%) have not. It concluded that increasing the age of the male partner increases the risk of infertility, and ethnicity has an unclear effect on infertility and still needs further studies to prove it. Obesity rates are increasing among men in Khartoum, impacting seminal parameters like motility and erectile dysfunction, as highlighted in a study.

INTRODUCTION

Obesity is a severe medical condition characterized by the deposition of excess body fat, which might adversely affect health and reduce life expectancy. A person could be classified as overweight if his/her BMI is 25–30 kg/m2, and obese if BMI exceeds 30 kg/m2 (Bullen *et al.*, 2015).

Obesity is a global health issue with an epidemic proportion, with 400 million adults obese and 1.6 million overweight, accounting for 7.5% of the disease burden (Palmer *et al.*, 2012). It is associated with hormonal disturbance which negatively impact fertility, with women experiencing fertility in extreme obesity and weight loss, but this association is poorly characterized in males (Hammoud *et al.*, 2008; Rufus *et al.*, 2018).

Obesity in women leads to unproductive ovulation, decreased conception rates, and increased risk of miscarriage, while weight loss in ovulatory women improves fertility and conception rates. Obesity in male patients is linked to increased infertility, highlighting the need for increased clinician awareness and the increasing use of Artificial Reproductive Technologies, particularly Intra-Cytoplasmic Sperm Injection (ICSI) (Barbagallo *et al.*, 2021; Bullen *et al.*, 2015).

Total body fat, intra-abdominal fat, and subcutaneous fat are all associated with low levels of free and total testosterone in men, and most obese men looking for infertility treatment present with a decreased testosterone / estrogen ratio (Carrageta *et al.*, 2019). This is due to over activity of the aromatase cytochrome P450 enzyme, which is expressed at high levels in white adipose tissue and is responsible for a key step in the biosynthesis of estrogens (Li *et al.*, 2015; Steiner & Berry, 2022).

High levels of estrogens in obese males result from the increased conversion of androgens into estrogens owing to the high bioavailability of these aromatase enzymes. Dysregulated levels of sex hormones can cause great changes in both spermatogenesis and other aspects of male reproduction. This observation indicates that estrogens might have a part in regulating the Hypothalamic Pituitary Gonadal (HPG) axis, suggesting that any amount of excess estrogen could be detrimental (Chimento *et al.*, 2014).

Resistin is another adipose tissue specific factor, which is reported to induce insulin resistance (Steppan & Lazar, 2002). Hyperinsulinemia, which often occurs in obese men, has an inhibitory effect on normal spermatogenesis and can be linked to decreased male fertility in a group of diabetic men, semen parameters (concentration, motility and morphology) did not differ from the control group, but the amount of nuclear and mitochondrial DNA damage in the sperm was significantly higher (Maresch *et al.*, 2018; Oghbaei *et al.*, 2021).

The sperm DNA damage can impair male fertility

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and reproductive health (Panner Selvam *et al.*, 2021), in addition to inducing sperm DNA damage, insulin levels also have been shown to influence the levels of sex hormone binding globulin (sHBG), a glycoprotein that binds to sex hormones, specifically testosterone and estradiol, thereby inhibiting their biologic activity as carrier (Qu & Donnelly, 2020; Winters *et al.*, 2014).

Obesity can lead to altered sperm production and parameters due to increased gonadal heat, which is a side effect of increased scrotal adiposity (Chaudhuri *et al.*, 2022; Liu & Ding, 2017). The process of spermatogenesis is highly sensitive to heat, with optimal temperature ranging between 34–35°C in humans. Increased testicular heat is associated with reduced sperm motility, increased sperm DNA damage and increased sperm oxidative stress (Hoang-Thi *et al.*, 2022).

Obesity and its causative agents, such as insulin resistance and dyslipidemia, are linked to increased oxidative stress, resulting in impaired sperm DNA damage and oxidative stress in obese patients (Leisegang, 2022; Manna & Jain, 2015). This association is most likely the result of the higher than usual metabolic rates required to maintain normal biological processes and an increased level of stress in the local testicular environment, both of which naturally produce Reactive Oxygen Species (ROS). ROS is an independent marker of male factor infertility and can lead to DNA damage, deformity and damaged plasma membrane integrity in sperm (Alahmar, 2019; Hosen *et al.*, 2015).

Excess body weight can impair the feedback regulation of the HPG axis, and all of the factors above might contribute to, or be a result of, this dysregulation, which can contribute to apparent semen quality abnormalities. Obese, infertile men exhibit endocrine changes that are not observed in men with either obesity or infertility alone (Craig *et al.*, 2017; Katib, 2015). This defective response to hormonal changes might be explained by partial or complete dysregulation of the HPG axis (Dutta *et al.*, 2019; Mintziori *et al.*, 2020).

Because obesity can result from an unfavorable genotype and because obesity can cause infertility, a genetic link between these two factors might explain this discrepancy. Patients with Klinefelter, Prader–Willi or Laurence–moon–Bardet–Biedel syndromes all display, to varying degrees, both obesity and infertility (Chaudhuri *et al.*, 2022; Krausz *et al.*, 2022; Tornese *et al.*, 2020). In addition, men who are both infertile and obese show significantly lower testosterone levels than obese fertile men (Stokes *et al.*, 2015).

Due to difficulties in interpreting data from human studies, rodent models of male obesity have now been established to assess the impact of male obesity on sperm function, however it is necessary to be aware of the differences between species. These studies have demonstrated that males fed a high fat diet to induce obesity had reduced sperm motility and a decrease in percentage of sperm with normal morphology (Mu *et al.*, 2017).

Numerous human studies as well as animal study have determined that a relationship between obesity and reduced sperm DNA integrity exists, despite the use of a variety of different methodologies to measure sperm DNA integrity (TUNEL, COMET, SCSA, etc.) (Evenson, 2017; Javed *et al.*, 2019; Román Montañana, 2020). Only two studies, one human and one rodent have directly linked levels of sperm oxidative stress with male BMI. Both studies concluded that a positive association between increasing BMI and increased sperm oxidative stress exists (Jing *et al.*, 2023).

Another Retrospective study done in a Referral fertility center in UK 2008 revealed that "the incidence of oligozoospermia increased with increasing BMI: normal weight ¼ 5.32%, overweight ¼ 9.52%, and obese ¼ 15.62%. The prevalence of a low progressively motile sperm count was also greater with increasing BMI: normal weight ¼ 4.52%, overweight ¼ 8.93%, and obese ¼ 13.28%. The incidence of erectile dysfunction did not vary across BMI categories when corrected for potential contributing factors (9).

The study aimed to investigate the impact of male obesity on spermatic parameters (morphology, motility and concentration), erectile dysfunction rates, and the relationship between personal characteristics and infertility.

MATERIALS AND METHODS

Study Design & Area

The present research study is a Cross-sectional facility-based study, conducted at Bnoon Infertility Center and Saad Abu Alaa Infertility Center in Khartoum state.

Saad Abu Ellaa Infertility Center, the first governmental specialized center in Sudan, is managed by Khartoum University and has highly qualified staff. It offers IVF at the lowest possible cost, with an average of 1000-1200 patients per year. Bnoon Infertility Center, a private specialized center in Khartoum, Sudan, is well-known with an average of 1500-2000 patients seen annually, representing the private sector.

Study Duration

The study was conducted for approximately six months spanning from January 2018 to June 2018.

Study Population

All male individuals from infertile couples seeking treatment at the infertility center.

Inclusion Criteria

Males from couples who have been married for at least one year and do not have any siblings.

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Exclusion Criteria

- Males from couples who have been married for less than one year.
- Males who do not engage in regular intercourse due to the reasons such as husbands travelling abroad.

• Males who decline to sign the consent form.
• Males with co-existing conditions such as diabetes mellitus, hypertension, or a history of undescended testis.

Sample Size

The sample size will be calculated by using the given formula:

N=Z2 PQ/D2

Where,

N= Sample Size

Z= Standard Deviation taken as 1.96 at a 95% confidence interval

P= Estimated Prevalence, assumed as 0.5 or 50%

Q= 1-P, also 0.5 in this case

D= Total Coverage initially set at a 385 patients.

Independent Variables

Age of individuals measured in years

Ethnicity: The cultural or ancestral background of individuals, categorized in specific ethnic groups.

Body Mass Index (BMI): A measurement of body fats based on height and weight used to access health status related to weight.

Dependent Variables

The dependent variables include oligospermia, azoospermia, abnormal sperm morphology, abnormal sperm motility, and erectile dysfunction.

Data Collection

Confidential questionnaires were used to gather data on patient demographics, medical history, male sexual dysfunction, factors influencing infertility, BMI, and seminal analysis parameters such as motility, morphology, and concentration. The participants filled out the questionnaire in a highly confidential manner.

Data Analysis

The means were reported as Mean ± Standard error. The Chi-Square test for trend was utilized to compare frequencies and logistic regression analysis was applied and deemed suitable. Statistical analysis was conducted by using the SPSS 23.0 software package (SPSS, Chicago, IL).

Ethical Considerations

Ethical approval was obtained from the infertility centers before the intervention, including approval from the ethical committee. All men included in the study received written consent, with the study purpose explained to them. The questionnaire was filled out confidentially and voluntarily by the nominated participants. Patients had the right to decide whether to participate in the study or not.

RESULTS AND DISCUSSION

Results

Selected Participants

In the present study, 40 men (20.5%) were under the age of 30, and 57mean (29.9%) were between the ages of 30 and 40, while 98 men (50.3%) were over the age of 40.

Table 1: Frequency of Age Groups Among Participants

Age group	No. of participant	Percentage of participants
<30 years old	40	20.5%
30 – 40 years old	57	29.2%
>40 years old	98	50.3%

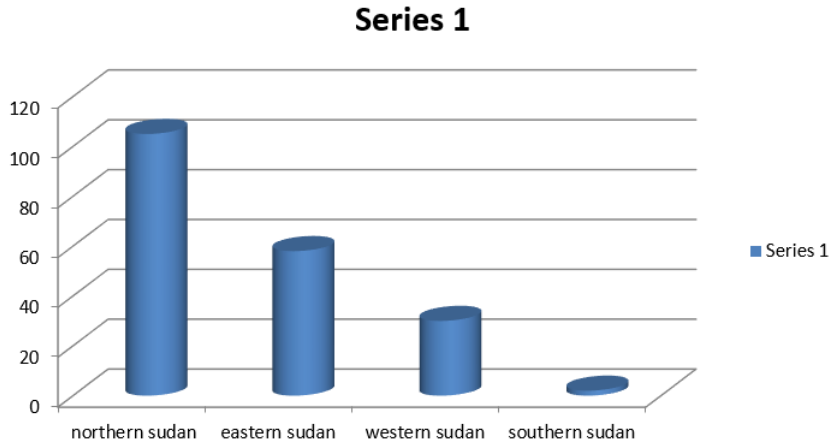

Figure 1: Frequency of Ethnic Groups Among Participants

Of this study 105 men (53.8%) were from North Sudan, 58 men (29.7%) were from Eastern Sudan, 30 men (15.35%) are from Western Sudan overweight and 2 men (1.15%) were from Southern Sudan. of the study, 110 men (56.4%) have normal sperm counts and 85 (43.6) have abnormal sperm counts, 105 men (53.8%) have normal sperm morphology while 90 (46.2) have abnormal morphology. 88 men (45.1%) have progressive motility while 107 men (54.9%) have impaired motility.

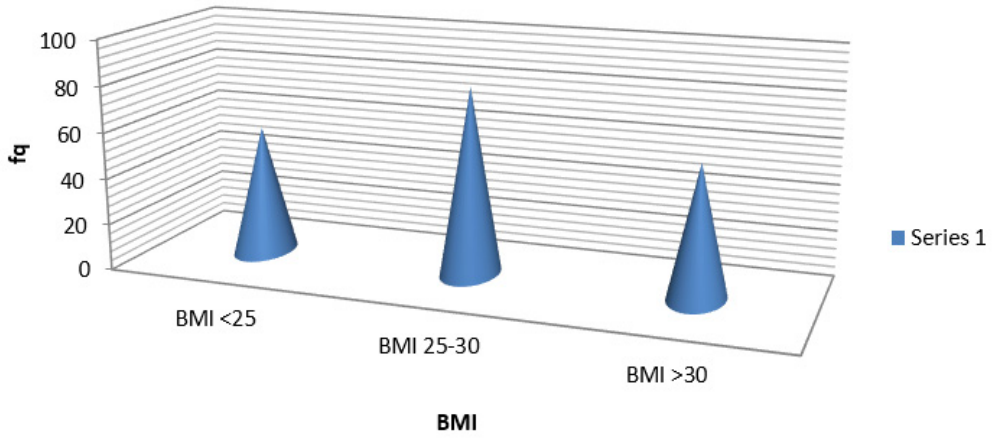

Figure 2: Frequency of Body Mass Index Among Participants

Table 2: Frequencies of Seminal Parameters Among Participants

Seminal analysis	**No. of participant**	
	Normal	**Abnormal**
Sperms count	110	85
Sperms morphology	105	90
Sperms progressive motility	88	107

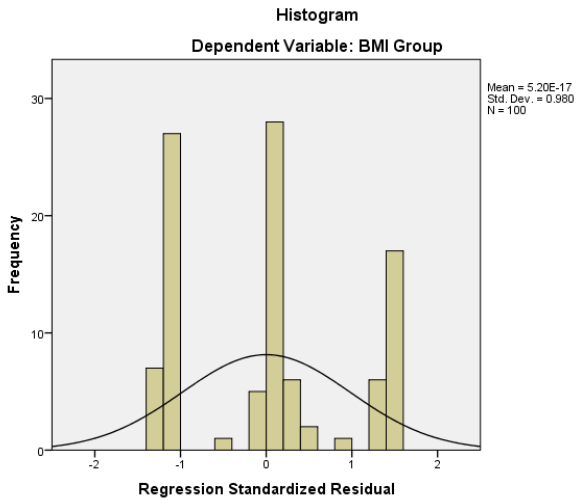

Figure 3: Multiple Liner Regression for BMI & Seminal Parameters

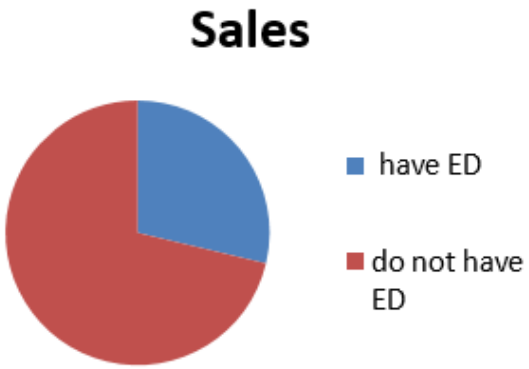

Figure 4: Frequency of Participants With Erectile Dysfunction

Discussion

In the present research study, it was observed that the majority of participants, out of a total of 195 men, were aged over 40 years, accounting for 50.3% of all participants. This was followed by individuals aged between 30 and 40 years, representing 29.95%, while those below 30 years old constituted the smallest proportion at 20.5% of all participants (Harris *et al.*, 2011).

This finding is corroborated by a French study that investigated 901 cycles of intrauterine artificial insemination. The study identified the age of the male partner as the most influential factor affecting the likelihood of pregnancy. After six cycles, men aged 35 years or older exhibited a fertility rate of 25%, contrasting with a fertility rate of 52% among men under 35 years old, reflecting 52%reduction in fertility rate.

The majority of participants, compromising 53.8%, hailed from North Sudan with Eastern Sudan contributing 29.7% of the participants. Western Sudan accounted for 15.35% of the sample, while Southern Sudanese participants constituted the smallest group at 1.15%. Despite the evident disparity in participant distribution across ethnic groups, statistical analysis revealed no significant association between BMI, infertility and ethnic groups, with respective p-values of 0.4 and 0.7.

Among the participants, 81% had a BMI ranging from 25 to 30, with 58% having a BMI exceeding 30 kg/m2, and only 28.7% having a BMI below 25 kg/m2. Figure 2 provided a visual depiction of these distributions. These results are consisted with prior research indicating a troubling rise in male obesity among men of reproductive age, nearly tripling over the past three decades, coinciding with a global increase in male fertility rates. Emerging evidence suggests that male obesity adversely effects

reproductive potential, impacting not only sperm quality but also inducing structural and molecular changes in germs cells within the testes and ultimately in mature sperm. Direct associations have been found between male BMI and DNA fragmentation in sperm, with higher BMI levels correlating with increased sperm fragmentation (Harris *et al.*, 2011).

In April 2016, a study conducted in the UK found a significant decrease in sperm quality among men with a BMI over 25, with even more severe effects observed in those with a BMI over 30. This decline in sperm quality, particularly characterized by fragmented sperm DNA, is associated with an increased risk of early miscarriage. The silent challenge of infertility among obese men underscores the importance of addressing this health issue, as highlighted in the present research. These findings emphasize the need for attention from policymakers and the media to raise awareness and promote inventions in this area (G Alves *et al.*, 2016; Hammoud *et al.*, 2008).

Although it was found that 56.4% of participants had normal sperm counts, and 53% exhibited normal sperm morphology. However, only 45.1% showed normal progressive motility, as presented in Table 3. A study conducted in the USA in 2008 at a referral clinic revealed that the incidence of oligozoospermia increased with higher BMI categories: 5.32% among normal weight individuals, 9.52% among overweight individuals, and 15.62% among obese individuals. Similarly, the prevalence of a low progressively motile sperm counts also increased with increasing BMI: 4.52% among normal weight individuals, 8.93% among overweight individuals, and 13.28% among obese individuals (Hammoud *et al.*, 2008). Recent population based studied conducted over the past 5-10 years have revealed a higher prevalence of abnormal semen parameters among overweight and obese men, suggesting a potential association with subfertility in couples where the male partner is obese (Du Plessis *et al.*, 2010).

Additionally, it was found that obesity impacts genetic and epigenetic mechanisms, inhibiting chromatin condensation, increasing DNA fragmentation, causing apoptosis and alteration in spermatozoa, disrupting sperm morphology and functions, and potentially causing inherited epigenetic alterations in offspring (Dutta *et al.*, 2019; Leisegang *et al.*, 2021).

Leptin, a hormone produced by adipose tissue, increases with body fat, affecting reproductive function. Obese men may not be sensitive to increased leptin production, leading to functional leptin resistance. While Kisspeptin neurons mediate leptin's effects on the reproductive system, potentially causing increased infertility (Ghaderpour *et al.*, 2022).

Furthermore, through, endocrinopathy obesity effects male fertility, aromatization, erectile dysfunction, psychological effects, sleep apnea, leptin, oxygen free radicals, and epididymitis. Treatment includes weight reduction, aromatase inhibitors, gonadotropins, phosphodiesterase inhibitors, and insulin-sensitizing agents (El Salam, 2018).

The present study assessed the impact of obesity on epididymal and germinal epithelia revealed significant finding. Circulating leptin and estradiol levels exhibited a notable increase, while testosterone levels declined. Additionally, there was an observed increase in lipid peroxidation in the epididymis and a reduction in spermatobioscopic parameters. Morphological differences were noted in the heads of the epididymis in obese rats, although no significant variance was observed in the testes between the two groups (Vigueras-Villaseñor *et al.*, 2011). These results provide clear evidence of an adverse effect on sperm in obese rats, particularly evident in the epididymis.

However, all studies consistently demonstrated a clear association between obesity and male fertility, this particular study was found no significant association in terms of reduced progressive sperm motility. The linear regression analysis yielded a non-significant p-value of 0.3, as illustrated in Figure 3 of the histogram. This lack of significance can be attributed mainly to the suboptimal sample size used in the study.

Only 25.2% of the participants experienced erectile dysfunction. An Italian study published in The Journal of Sexual Medicine, examined 2,435 Italian male patients who sought outpatient treatment for sexual dysfunction from 2001 to 2007. The participants were categorized as follows: 41.5% were normal weight, 42.4% were overweight, 12.1% were obese and 4% were severely obese. The average age of the participants was 52 years old. Patients underwent laboratory blood tests and a penile Doppler ultrasound to assess penile blood flow. Additionally, they were interviewed regarding their erectile dysfunction and completed a mental health assessment (Esposito *et al.*, 2008).

LIMITATIONS

- The study's small sample size hindered the detection of significant differences, particularly regarding the impact of obesity on infertility.
- The study's generalizability was limited, because it purely focused on men in Khartoum, requiring a more diverse sample to better understand ethnicity's impact on infertility.
- The use of self-reported data, particularly in erectile dysfunction and lifestyle factors like obesity, can introduce potential bias and inaccuracies.

CONCLUSION

The study concluded various factors related to male fertility, including age, ethnicity and obesity. It found that advancing age of the male partner increases the risk of infertility, while the impact of ethnicity on infertility remains uncertain and requires further research. Additionally, the study noted a rising trends of obesity among men in Khartoum and highlighted its detrimental effects on seminal parameters, particularly sperm motility. Moreover, obesity was linked to an increased risk of

erectile dysfunction. However, the study failed to identify a statistically difference in infertility related to obesity, possibly due to the small sample size.

RECOMMENDATIONS

• Large-scale studies with a diverse participant pool can improve the statistical power and generalizability of findings on obesity's impact on infertility.

• Longitudinal research designs can help track changes over time and establish causal relationships between advancing age, obesity, and infertility outcomes.

• Biomarkers, including objective measures like obesity, reproductive hormones, and semen quality, can offer more reliable data and reduce reliance on self-reported information.

• Collaborating with multiple research centers across different regions can expand the study's scope and better understand infertility risk factors among diverse populations.

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