

## Effect of Anabolic-Androgenic Steroids on Men's Semen among Gym-Goers: A Cohort Study

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### ABSTRACT

Anabolic-Androgenic steroids (AAS) misuse are growing worldwide and used especially among male bodybuilders and gym-goers for building muscle to improve their physical appearance. AAS misuse is considered a preventable factor of male fertility because it affects the hypothalamic-pituitary-gonadal axis resulting in transient or persistent suppression of spermatogenesis. The study Objective is to investigate the effect of anabolic steroids misuse on the semen parameters, suggestive of decreased male bodybuilders fertility whose anabolic steroids abuse. A prospective cohort study was conducted on 80 healthy male gym-goers divided into the case and control group who attending gyms in Mosul city. A structured interviewing questionnaire was used to collect information related to AAS misuse, semen specimen for evaluation of sperm parameters in a private analytics Lab, for a period 1st November 2020 until 15th March 2021. Semen analysis of AAS group exhibited highly significant ( $P=0.000$ ) in the overall mean of total sperm count/ ejaculate was ( $18.83 \pm 24.02$  vs.  $139.5 \pm 24.80$ ) and the percentage of sperm motility was significantly lower than the control group. AAS group have five times more likely to develop oligospermia than the control group (RR: 5; 95% CI: 2.690-9.293;  $P=0.000$ ). The use of AAS has a severe effect on male fertility, AAS users exhibited a severe decrease in sperm counts indicative of impaired spermatogenesis.

**Keywords:** Anabolic-Androgenic steroids, Semen, Gym-Goers, male fertility

### Introduction

Anabolic steroids, or also known as androgenic steroids are manmade derivatives of testosterone and abbreviated as (AAS). Legal, as well as the illegal use of anabolic steroids, is gaining popularity (Odoardi et al., 2021). AAS considered the most used agents worldwide to enhance performance, muscle growth, and body fat loss, as well as physical attractiveness. Anabolic-androgenic steroids are a synthetic steroid hormone that has anabolic and androgenic properties, and they are classified as steroids due to the inclusion of a steroid ring in their structure (Althobiti et al., 2018; Harvey et al., 2019). Anabolic term indicates to hypertrophy of the body, while androgenic term indicates to enhance characteristics of the male sex that include muscle mass, deep voice, and facial hair. It has historically been used clinically to treat several medical cases, including delayed puberty, loss of muscle mass, AIDS, and cancer, but more recently, it has been used to encourage fat reduction and muscle building in a recreational sporting sense. Several studies have shown that these treatments have a wide range of side effects, including fertility and physiological complications, psychological problems, cardiovascular disease, and renal and hepatic disorders (Perry et al., 2020). Testosterone is the most active endogenous androgen and is a 19-carbon steroid. Some athletes or gym-goers use AAS on a regular basis, while others want to minimize their possible side effects by using them in other ways, as Cycling (for periods of six to twelve weeks, users take AAS, followed by several weeks or even months off), Stacking (to increase the potency of the steroids, users mix many different steroid forms or add other supplements), Pyramiding (users steadily increase the dose until it reaches a peak, after which they reduce it), Plateauing (alternating, overlapping, or substituting with another steroid, where they alternate between periods with low and high doses to avoid developing a tolerance, also

called “cruise and blast”) (Conchin et al., 2020; Hauger et al., 2020). In the Middle East, a high prevalence of AAS abuse. In Lebanon was 10.7% (Mufarrij, 2020). In Saudi Arabia reports that using AAS 29.3% and the use of AAS was more prevalent among gym members who practiced weightlifting (45.5%) (Al-Harbi et al., 2020). Furthermore, a survey of 200 gym users in Kuwait revealed a lifetime prevalence of (34%) (Khullar et al., 2016). In Iraq, a nationally representative poll of 3200 people revealed that (1.4%) of people had used AAS at some point in their lives (Al-Hemiery et al., 2017). “Taking testosterone is almost male contraception,” says Dr. Brian Levine, managing partner and practice director of CCRM (The Colorado Center for Reproductive Medicine) New York. The Mossman-Pacey paradox, named after the two researchers who first identified it, refers to the use of testosterone or anabolic steroids to obtain muscle mass and thus look more pregnant while potentially raising one's chances of infertility (Mossman & Pacey, 2019). Anabolic steroids promote muscle development quickly, but they can increase the risk of infertility and erectile dysfunction (Horwitz, Andersen, et al., 2019). Mossman and Pacey point out in a recent issue of the Journal of Internal Medicine, while anabolic steroid abusers may appear superior at first glance, they are extremely likely to be unfit for reproductive purposes. This appears to be an evolutionary anomaly because we think reproduction is the underlying explanation for bodybuilding and gym-goers are aware of the side effects of anabolic steroids (Horwitz, Dalhoff, et al., 2019). The normal spermatogenesis mechanism necessitates a combination of follicle-stimulating hormone and luteinizing hormone, which is compromised by AAS misuse, leading to infertility. Fortunately, research indicates that AAS-related infertility can be reversed, while sperm production can take up to a year to return to normal (de Ronde, 2019; Esparza et al., 2020). Infertility is a medical and societal concern that affects many people. Changes in sperm concentration, motility, and/or morphology are responsible for about half of all cases of infertility in men. Recent advancements around infertility have had a significant impact on our perception of the various causes of male factor infertility. Though environmental, physiological, and genetic factors have been identified, misuse of anabolic-androgenic steroids (AASs) tends to affect sperm function and cause pregnancy delays (Dcunha et al., 2020). There are some significant physiological effects of AAS on genital function, including development and growth of the penis, glands as seminal vesicles, and prostate, as well as effects on libido, orgasm, and arousal that regulated by the CNS, researches show the prolonged use for AAS supplementation with high-dosage, influence sexual function and it associated with higher rates of erectile dysfunction and decreased libido after cessation to use (Armstrong et al., 2018). Exogenous testosterone and AAS inhibit the hypothalamic-pituitary system, which is not unexpected given that endogenous testosterone is the main regulator of the hypothalamic-pituitary-testicular axis. The resulting reduction in testosterone secreted and intratesticular testosterone, as well as spermatogenesis and sperm production, is caused by the deficiency of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Several experiments have shown that bodybuilders who use AAS have lower sperm concentrations and a greater incidence of azoospermia than controls. Clinical studies in male hormonal contraceptives are based on this impact (McBride & Coward, 2016).

### **Specific Objectives of the Study**

To evaluate the semen parameters for AAS abuser, And to explore the influence duration of using anabolic steroids and period of cessation on the sperm analysis.

## **Method and Material**

Ethical approval was obtained to conduct the study from the University of Mosul/collegiate committee for medical research ethics (No.29, in 18/10/2020). The study's purpose and procedures were explained and emphasize the study participant's right to self-determination, confidentiality, and anonymity.

### **Study Design:**

This study is a non-experimental, prospective cohort study with a nested case-control study to accomplish the objectives of the study for the period extended from 1<sup>st</sup> November 2020 until 15<sup>th</sup> March 2021.

### **Study Setting:**

This study was conducted in Mosul city, capital of Nineveh Governorate, in northern Iraq, at 30 gymnasiums, 20 of it distributed on the left side of the city and 10 distributed on the right side of the city.

### **Data Collection Period:**

The study has been conducted in a period extending from 15<sup>th</sup> of November 2020 to 15<sup>th</sup> of February 2021 at thirty gyms in Mosul city.

### **Sample of the Study:**

A non-probability sample was purposively selected according to the inclusion and exclusion criteria of gym-goers, invited from 30 gymnasiums, for the purpose of voluntarily participating in the study, a total number of 90 gym-goers were interviewed during the study period, and 10 of them were excluded due to did not match the study criteria.

### **Data Collection Method:**

The interview was conducted to fill out the questionnaire with the gym-goers in the laboratory, as well as performing the hormonal assay in addition to analyzing the semen of them, and each participant needed approximately (15-20) minutes to complete the data collection and perform tests.

### **Semen Analysis:**

All participants provided a sample of semen after (2 - 7) days of sexual activity abstinence by Masturbation in a private space inside the laboratory. After liquefaction at 37C, the semen sample was examined for volume, sperm concentration per milters, total sperm count per ejaculate, percentage of spermatozoa motility, and morphologically, according to the standards guidelines of World Health Organization at the present time.

### **Statistical Analysis:**

Statistical analysis of data was done by (SPSS) version 26, MedCalc Statistical Software for ROC curve analysis, as well as Microsoft Excel 365 for graphing. A descriptive approach was applied. Mean  $\pm$  SD, median (range), or frequency (percentage) were computed. The parameters of gym-goers who use anabolic steroids and those who do not were compared using a Chi-square test. Mann-Whitney U test for continuous variables that following non-normal distribution, the relative risk was calculated to determine the size of an effect.

## **Results**

Table 1 shows there were statistically significant differences between groups of the study at ( $P < 0.01$ ) in the semen volume (ml), sperm concentration, total sperm count, sperm motility, and Sperm Morphology. Table 2 shows that gym-goers who take anabolic steroids have five times more likely to develop low sperm count than those who do not use these steroids. The ROC (Receiver Operating Characteristic) analysis of total sperm count shows (Area Under the Curve= 0.983) with significant differences ( $P < 0.001$ ).

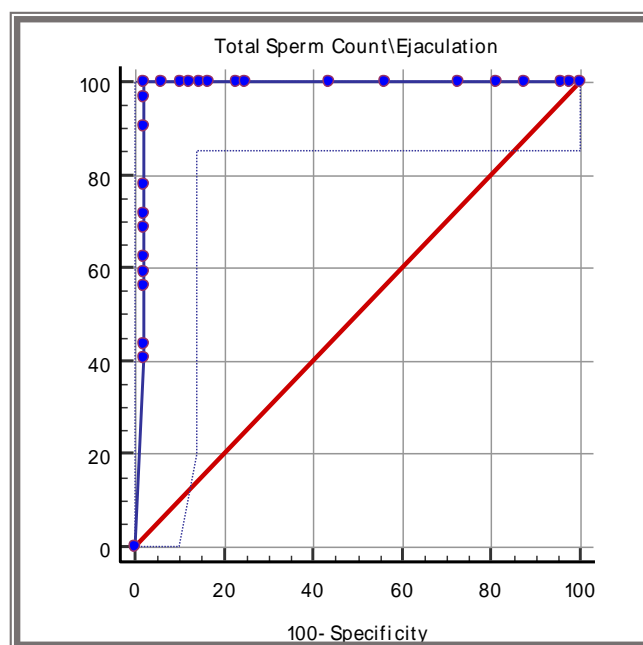
**Table (1):** Descriptive statistics and Z-Score of Mann–Whitney U test for the mean of semen parameters for both AAS group and control groups.

Semen Parameters	$\bar{x}$	SD	$\bar{x}$	SD	Z-Score	P-value
Abstains Periods (days)	3.45	1.50	3.78	1.56	-1.01	0.310
Semen Volume (ml)	3.00	0.75	3.52	0.71	-3.02	0.003
Semen PH	7.71	0.29	7.74	0.27	-0.40	0.682
Liquification (min.)	29.88	4.86	29.25	4.87	-0.62	0.531
Sperm Concentration*10 <sup>6</sup> /ml	6.50	9.41	41.25	11.05	-7.31	0.000
Total Sperm Count*10 <sup>6</sup> /ejaculate	18.19	24.39	139.9	24.66	-7.70	0.000
Active Sperm Motility (%)	23.63	18.60	63.88	8.04	-7.49	0.000
Sluggish Sperm Motility (%)	22.25	18.46	21.38	6.30	-0.70	0.479
Immotile Sperm (%)	41.63	30.85	14.25	5.37	-4.53	0.000
Normal Sperm Morphology (%)	53.38	22.54	75.63	22.54	-6.42	0.000
Abnormal Sperm Morphology	34.13	16.16	24.38	4.55	-4.46	0.000

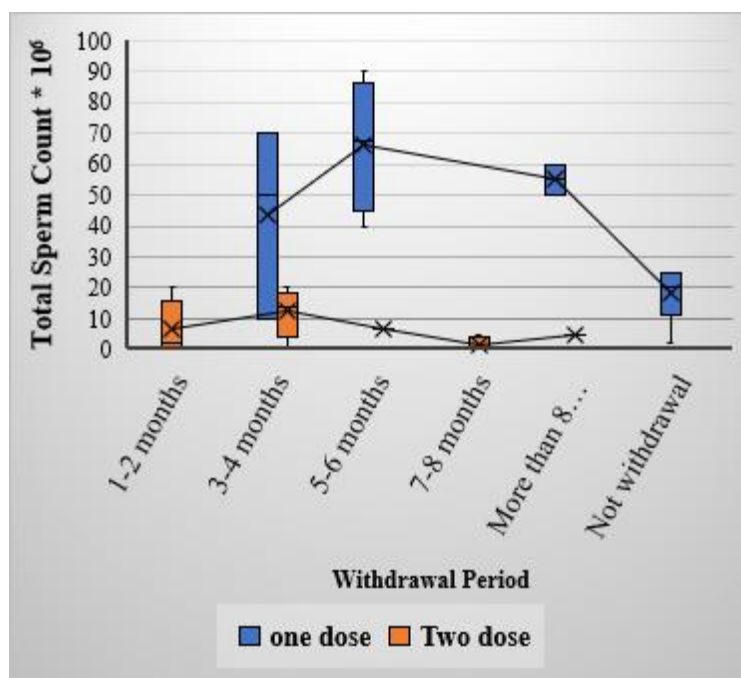
**Table (2):** Relative Risk and Confidence Interval for Significance Risk Factor

Variable	RR	95% CI		P. value
		Lower	Upper	
Oligospermia	5.00	2.690	9.293	0.000

**\*\*Note:** RR: Relative Risk, CI: Confidence Interval.



**Figure 1.** ROC Analysis for Total Sperm Count per Ejaculate.



**Figure 2.** The effect of withdrawal periods of AAS used and the doses/week of AAS used on the total sperm count per ejaculate.

## Discussions

Table 1 shows the overall mean and standard deviation of semen parameters for the AAS group and the control group; those semen parameters have a highly significant decrease at ( $P < 0.01$ ) in the AAS group for sperm concentration ( $6.5 \pm 9.41$ )  $10^6/\text{ml}$ , total sperm count ( $18.19 \pm 24.39$ )  $10^6/\text{ejaculate}$ , active sperm motile ( $23.63 \pm 18.6$ )%, non-motile sperm ( $41.63 \pm 30.85$ )%, normal sperm morphology ( $53.38 \pm 22.54$ )%, abnormal sperm morphology ( $34.13 \pm 16.16$ )%, compared to control group was within the normal ranges. The sperm count of the AAS users group shows a significant difference by using the Mann-Whitney U test, and the steroid user group shows a highly significant reduction in sperm count compared to the control group ( $P\text{-value} = 0.00$ ); similar data were obtained from another study conducted by (Anwar & Abboud, 2016) agree with finding related to sperm counts, and disagree with finding related to sperm motility and morphology. But another study conducted by (Sharef et al., 2017) on just Nandrolone effects on semen quality agrees with all our results regarding sperm count, motility, and morphology. The AAS use by bodybuilding players have a direct effect on the sperm count; the reduction of sperm count can be explained by the hormone imbalance that occurred due to the AAS abuse, which indicates the impact of AAS users on their testes by downregulation of sperm production by these testes, while the sperm counts of the control group are not affected, which suggests that weightlifter exercise without taking AAS has no significant effect on spermatogenesis, even if taking protein supplements as the study conducted by (Tøttenborg et al., 2020). Table 2 shows that gym-goers who take anabolic steroids have five times more likely to develop low sperm

count (severe, moderate, or mild oligospermia) than those who do not use these steroids (RR: 5; 95% CI: 2.690-9.293; P.=0.000), and a new study conducted by (Windfeld-Mathiasen et al., 2021), agreed with our finding, which reported " The group of androgen users had a 26% lower fertility rate than the controls over the 10-year period before testing positive (P = 0.0028; rate ratio [RR] 0.74; 95% CI, 0.60-0.90)", suggesting that if the capability to spermatogenic was permanently damaged due to abuse of AAS with long-period, this would result in sperm count excessively reduction and low fertility rates. Figure 1 illustrates the Reserve Operating Characteristic (ROC) test for total sperm count\ejaculate, with an excellent rate for accuracy of the test (AUC= 0.983) with (P. = < 0.001), and it has a significant diagnostic ability to determine the impact of AAS use on male gym-goers' fertility, agreed with our finding the results of the study conducted by (Anwar & Abbood, 2016). Figure 2 illustrates that cessation of AAS use of participants in the AAS group with two doses/week has a severe effect more than one dose/week on returning sperm count to the range of normality, in which the participants who took two doses/week have oligospermia even with more than 18 months of cessation AAS use, however, most users on a dose of no more than 400 mg \ week gradually returned to baseline values of gonadotropins, free testosterone. Sperm count within 5-6 months agrees with the finding of a study conducted by (Christou et al., 2017), indicating that the degree of AAS misuse can have a major impact on spermatogenesis recovery and may raise the risk of permanent fertility disability.

### Conclusions

the study concluded that more than two-thirds of the AAS consumer gym-goers have oligospermia; on the other hand, the control group was normal sperm densities. A highly significant decrease in the AAS group sperm motility compared to the control group was within the normal ranges, and there is no effect on sperm morphology. The bodybuilders whom AAS abuse have five times more likely to decrease fertility rate than those who do not use these steroids.

### Recommendations

the study recommended that community health education through health promotion programs for gyms-goers about the long-term adverse effects that consequence using AAS, and especially on fertility. More research studies are needed for a larger sample, including both genders, and the effects of the AAS on other body systems to assess the problem of AAS abuse more accurately in Iraq.

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