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An Investigation of the Effect of Smoking, Alcohol, and Drug Use on Male Infertility

A. Heri Iswanto[1], Yasir Salam Karim[2], Zahidul Islam[3], Ola Kamal A. Alkadir[4], Abduladheem Turki Jalil[5], Ali T. Khlaif[6], Yasser Fakri Mustafa[7], Hamzah H. Kzar[8], Moaed E. Al-Gazally[9], Narmin Beheshtizadeh[10]

[1] Department of Public Health, School of Health Sciences, University of Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia
[2] Al-Manara College for Medical Sciences, Maysan, Iraq
[3] Assistant Professor, Ahmad Ibrahim Kulliyyah of Laws (AIKOL), International Islamic University Malaysia, Selangor, Malaysia
[4] Al-Nisour University College, Baghdad, Iraq
[5] College of Technical Engineering, The Islamic University, Najaf, Iraq
[6] College of Pharmacy, Al-Ayen University, Thi-Qar, Iraq
[7] Department of Pharmaceutical Chemistry, College of Pharmacy, University of Mosul, Mosul, Iraq
[8] Department of Chemistry, College of Veterinary Medicine, Al-Qasim Green University, Al-Qasim, Iraq
[9] College of Medicine, University of Al-Ameed , Karbala, Iraq
[10] Department of Social Sciences, School of Social and Economic Sciences, Al-Zahra University, Tehran, Iran

Corresponding Author: A. Heri Iswanto***; Department of Public Health, School of Health Sciences, University of Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia***
Email: alazzawima123@gmail.com

Emprical Study

Abstract

Background: Infertility in men has increased in recent years. Numerous physical, chemical, biological, and social factors are known to play a role in reducing semen quality, in between, there are high-risk behaviors that affect the quality of semen. In this paper, the effects of three factors: smoking, alcohol consumption, and drugs have been investigated.

Methods: This case-control study was performed from June to September 2021 on 500 people, 250 people with normal semen quality and 250 people with defective semen quality. The data collection tool was a questionnaire made by researchers and semen test results. Finally, the collected data were analyzed by descriptive method with SPSS software. For quantitative variables, mean and standard deviation (SD) were used, while frequency and percentage reports were used for qualitative variables.

Results: Drug use had a significant relationship with the shape and motility of sperm (B = -0.675, P = 0.005). The chance of natural semen decreases by 0.506 times with an increase of one drug use unit; moreover, the older the age of onset of drug use, the more the semen disorders (B = 0.514, P = 0.002)..

Conclusion: Smoking and alcohol consumption were not identified as factors affecting semen quality, but there was a significant relationship between drug use and age of onset and semen disorders.

Keywords: Smoking; Infertility; Alcohol; Drug

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Introduction

One of the problems of countries around the world today is infertility, which has different aspects. The cause of infertility is sometimes related to women (40% to 50%), sometimes related to men (20% to 30%), sometimes related to both (10% to 40%), and in 10% to 20%, is related to unknown factors (Ghasemi, Ghofranipour, Shahbazi, & Aminshokravi, 2020; Prakash, Hatcher, & Shiffman, 2021; Wang et al., 2021). Infertility patterns in developing countries differ from those in developed countries. The incidence of preventable infertility is very high in developing countries. According to World Health Organization (WHO) studies, 42% of women and 29.7% of men suffer from secondary infertility (Rezaei & Vadiati, 2020). Having a history of a past pregnancy, even if it did not lead to a live pregnancy, is called secondary infertility. In most cases, these infertilities are preventable. The ecological causes listed for these infertilities in extensive field studies include environmental toxins such as heavy metals, toxins, pesticides, and mechanical vibrations (Wagner, Stephanson, & Pierson, 2019). Medical causes include chromosomal or hormonal disorders, inflammation of the prostate, inflammation of the testicles, and varicocele (Czyzyk & Krolewski, 1976).

Smoking can lead to infertility in both men and women. If erectile dysfunction in men and increased pregnancy complications also increase with smoking. Chemicals (such as nicotine, cyanide, and carbon monoxide) in cigarette smoke accelerate the destruction of eggs. Unfortunately, once the eggs are destroyed, they cannot be reproduced or replaced (Yi, Ding, Keith, Coffey, & Allison, 2008). This means that menopause occurs 1 to 4 years earlier in women smokers than in non-smokers (Zavidic & Lovrinic, 2018). In men who smoke, smoking is associated with a decrease in sperm count and low sperm motility and an increase in abnormal sperm count, while sperm quality is worse in smokers (Snow, Fonarow, Ladapo, Washington, Hoggatt, & Ziaeian, 2019). The fertility of women smokers is lower than that of non-smokers, so that the infertility rate of women and men smokers is almost twice that of non-smokers. The risk of fertility problems increases with the number of cigarettes smoked daily. Even assisted reproductive therapies such as in vitro fertilization (IVF) may be effective in reducing the effects of smoking on fertility. Women who smoke need more ovarian stimulants during IVF, but they still have fewer eggs during ovulation and are 30% less likely to become pregnant than IVF patients who do not smoke (Abid, Abid, & Abid, 2021). Because smoking damages eggs and sperm, abortions and birth defects are more common in smokers' fetuses. Even smokeless tobacco can increase the rate of miscarriage. The prevalence of chromosomal abnormalities such as Down syndrome is higher in women who smoke than in non-smoking mothers (Gredner, Mons, Niedermaier, Brenner, & Soerjomataram, 2021). In women smokers, the rate of ectopic pregnancy and preterm delivery is also higher. Studies have shown that men whose mothers smoked half a pack (or more) a day had lower sperm counts. In addition, smoking during pregnancy can lead to fetal growth retardation and being underweight before birth. These children are at greater risk for lifelong medical problems (such as diabetes, obesity, and cardiovascular disease). Children whose parents smoke are at higher risk for sudden infant death syndrome and asthma. Some research has shown that non-smokers have twice as much sex as smokers, and smoking affects the shape and motility of semen. Some studies have been inconsistent with these data and have not found a significant relationship between smoking and semen quality (Babakhanzadeh, Nazari, Ghasemifar, & Khodadadian, 2020). Cigarettes are said to contain mutagenic substances that lead to chromosomal

abnormalities in sperm. In addition, by reducing the amount of antioxidants in the blood and semen, it can increase the risk of oxidative damage to sperm deoxyribonucleic acid (DNA) (Fainberg & Kashanian, 2019; Leslie, Siref, & Khan, 2020).

Research has identified alcohol consumption as another socio-ecological factor related to semen quality. According to studies around the world, alcohol can affect any part of the reproductive system in men and cause impotence and infertility. In the testes, alcohol interferes with the secretion of testosterone by affecting the Leydig cells, which are responsible for the production and secretion of testosterone. Chronic alcohol consumption lowers testosterone levels in the blood (Agarwal et al., 2021). Alcohol also disrupts the function of Sertoli cells and impairs the maturation of sperm cells (Choy & Eisenberg, 2018). In the pituitary gland, alcohol consumption also reduces the production, secretion, and function of both luteinizing hormone and follicle-stimulating hormone (Alahmar, 2019). Finally, alcohol can interfere with the production of hypothalamic hormone. Drug use can affect semen parameters and reduce male fertility potential (Alhathal et al., 2020). Drugs act through the morphine receptor in the brain and the limbic system, thalamus, and hypothalamus. Because the testicles function as gonads in men under the control of the endocrine system and the brain-hypothalamus-pituitary axis, hormonal inadequacy is responsible for sperm production disorders. In addition to affecting this axis, narcotics cause defects in spermatozoa. Long-term drug use causes testicular weight loss and impotence. Given that drugs have the ability to affect from the cerebral cortex to the testes themselves, and the spermiogram provides a good view of the various aspects of direct male reproductive function, this paper compared the quality of semen in male consumers without consumption by evaluating the spermiogram. The aim of the present study was to evaluate the effect of smoking, alcohol, and drugs on semen quality to assess male infertility.

Methods

This was a case-control study, and in order to find a significant relationship between alcohol, smoking, and drug use and disorders of semen parameters, this paper examined and compared the frequency distribution of these substances in 250 men who had defects in at least one of the semen parameters and 250 people with normal semen. The Jakarta Infertility Clinic, Jakarta, Indonesia, was chosen to select the study population, which included 500 men who were referred to this center in case and control groups based on semen quality. The study lasted from June to September 2021. Sampling was done randomly on different days of the week from men referring to this clinic. Inclusion criteria were 25 to 60 years of age and the duration of marriage being at least 2 years. First, written consent was obtained from the individuals and then an interview was conducted. Persons having a genetic or chromosomal problem, hypogonadism, unilateral testicular hypotrophy, cryptorchidism, and chemotherapy, or taking anticonvulsants, colchicine, sulfasalazine, and retinoic acid over the past year were excluded from the study. The two groups were matched in terms of age, marriage age, and residence in urban or rural areas. To determine the sample size by reviewing similar researches and considering the significance level of 5%, power of 80%, confidence interval (CI) level of 95%, the minimum sample size in each group was calculated as 240, of which 250 people were considered for the study. For ethical reasons, participants in the study were assured that their identities and information would not be disclosed.

Data collection tool was a questionnaire based on the parameters required for the study on epidemiological and observational design by the researcher. First, by

holding a specialized panel with the presence of 5 experts, changes were made in the questionnaire. To evaluate the quantitative face validity, the item effect method was used. The results of the item impact score indicated that all questions with a score greater than 1.5 were included in the questionnaire. To determine the validity of the content, a questionnaire was sent to 10 experts. The answers were calculated according to the content validity ratio (CVR) formula. The results showed that 30 questions were larger than the Lawshe number (0.49). Content validity was also assessed based on the opinion of experts using the content validity index (CVI) formula. The reliability of the questionnaire was assessed through a retest method; 40 patients were asked to answer the questions twice, 15 days apart. The correlation between the questions before and after the test was measured by bivariate correlation test and was reported with a Spearman coefficient above 0.91.

To check sperm parameters, semen analysis was collected according to WHO guidelines performed in the clinic. Spermiogram tests include the following: the volume of semen should be at least 1.5 to 2 cc, the pH of the semen is about 7 to 8, which is in the alkaline range, and the number of sperm is at least 15 million per milliliter or 40 million in total ejaculation; if it is less than this number, it is referred to as oligospermia. Sperm motility should be at least 32% and if it is less than this amount, it is called astenozoospermia. The sample is checked for a maximum of half an hour. After sampling, the sample is placed in an incubator to remove it from the clot. This step is called liquefaction. During this period, the sample is checked and rotated every 10 minutes, if it moves like water in a container, the test can be done. In the next step, the sperm parameters are examined by preparing 3 slides under a microscope.

The content of the questionnaires consisted of four sections. The first part, demographic information, included age, marriage age, number of children, place of birth, and place of residence. The second part included information about the result of semen analysis including sperm count, number of motile sperm, semen volume, sperm shape, semen pH, and finally determining the quality of semen. The third part included risk factors and history of diseases affecting the quality of semen, such as mumps, history of cryptorchidism in childhood, testicular rotation, trauma to the testicles, hernia, varicocele, and urinary and genital infections. Fourth part provided information on personal habits including smoking, alcohol consumption, and drug use. Cigarette smoking was divided into three categories: less than 10, 10 to 20, and more than 20 cigarettes per day. Alcohol consumption was divided into 3 parts: more than one glass per month, more than one glass per week, and more than one glass per day. Drug use was divided into 2 groups: more than 10 times a year and more than once a week and the age of onset of each was determined. Considering the results of the second part and the quality of semen, participants were divided into 2 groups of 250 people with healthy semen as a control group and with defective semen as a case group.

The information was reviewed and controlled after collection. SPSS software (version 22, IBM Corporation, Armonk, NY, USA) was used for data analysis. For final analysis of data, univariate statistical tests, chi-square test (for qualitative variables), and logistic regression with the corresponding odds ratio (OR) and 95% CI level were used. P-values less than 0.05 were considered significant.

Results

In order to separate the case and control groups, first the results of spermiogram test were examined. In this experiment, the number of sperms, semen volume, number of motile sperms, sperm shape, semen pH, etc. were tested. The test results are shown in figure 1.

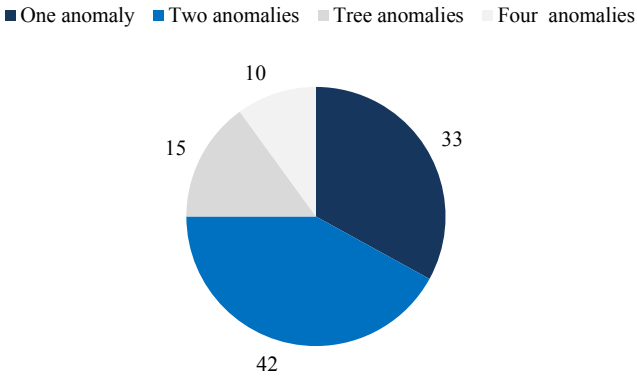

Figure 1. Percentage of sperm anomalies in the case group

As shown in figure 1, 33% had one anomaly, 42% had 2 anomalies, 15% had 3 anomalies, and 10% had 4 or more anomalies.

The results showed that the mean age (P = 0.082) and age of marriage (P = 0.486) were not significantly different between the two groups, but the mean duration of infertility (P = 0.001) was significantly different between the two groups. The results for this section are presented in table 1.

The living conditions in the case and control groups were as follows: 31.2% of the men in the case group and 29.1% of the men in the control group lived in rural areas and the rest lived in cities. As can be seen in table 2, the frequency of smoking in the case group was 34% and in the control group was 25.7%. Table 3 also shows the consumption of alcohol and drugs in the two groups.

According to these findings, the frequency of smoking in the two groups was significantly different (P = 0.031). The highest frequency of smoking in both groups was 10 to 20 cigarettes per day, which was 22% in the case group and 15.5% in the control group. The highest frequency of age of onset of smoking was 21 to 29 years; the frequency of this group was 17% in the case group and 11.2% in the control group. There was a significant difference between the two groups according to the P-value (P = 0.001).

Frequency of drug users in the case group was 33 people, which was equal to 13.3% of the people in the case group, and among the control group was 15 people, which was equal to 6.1% of the control group. The P-value (P = 0.004) indicates a significant difference in drug use between the two groups.

According to the results of a total of 500 people in the study, 9.6% were drug users who had 6.6% defective semen. 29.8% of the total study sample were smokers, of which 17% had defective semen. Data were entered into logistic regression to find the relationship between smoking, alcohol and drug use with defects in semen parameters.

Table 1. Comparison of mean age, age of marriage, and duration of infertility in case and control groups

Variables	Case group (mean ± SD)	Control group (mean ± SD)	P-value
Age (year)	34.65 ± 7.01	33.85 ± 6.36	0.082
Marriage age (year)	27.21 ± 5.01	27.18 ± 5.01	0.048
Duration of infertility (year)	6.40 ± 4.60	5.12 ± 3.85	0.001

SD: Standard deviation

Table 2. Comparison of smokers' frequency, smoking rate, and age of onset of smoking in the two groups

Factor	Group	Case [n (%)]	Control [n (%)]	P-value
Smoking	Yes	85 (34.0)	64 (25.5)	0.031
	No	165 (66.0)	186 (74.5)	
	Total	250 (100)	250 (100)	
Daily smoking rate	≤ 10	14 (5.8)	21 (8.5)	0.017
	10 to 20	55 (22.0)	39 (15.5)	
	> 20	16 (6.2)	4 (1.5)	
Age of onset of smoking (year)	≤ 20	18 (7.2)	22 (8.8)	0.001
	21-29	42 (17.0)	28 (11.2)	
	≥ 30	25 (9.8)	14 (5.5)	

At 95% CI, smoking and alcohol consumption did not have a significant weight in relation to semen disorders, but drug use had a significant relationship with defects in sperm shape and motility (OR = 0.506, CI = 0.485-0.515, B = -0.675, P = 0.005). In other words, by increasing one unit of drug consumption, the chance of normal semen decreases by 0.506. There was also a relationship between the age of onset of drug use and abnormalities in semen parameters (OR = 1.00, CI = 1.000-1.001, B = 0.514, P = 0.002), that is, the older the age of onset, the more the abnormalities observed in semen parameters.

Discussion

The current study examines the effects of three factors on semen quality parameters in men: smoking, alcohol, and drugs. There was no significant relationship between the frequency of history of semen-related disease and spermiogram abnormalities in the two groups. In both groups, no history of infectious diseases related to the quality of semen parameters was reported. Although in the past, varicocele was known as the most important cause of male infertility, based on recent studies, it is not possible to speak with certainty about the relationship between varicocele and infertility (Lotti & Maggi, 2018). Rather, we can talk about the relationship between this disease and infertility in men; this relationship may be multifactorial. Smoking in some studies has shown a significant relationship with semen quality; in some studies, contradictory results have been obtained and similar to this study, no significant relationship has been observed between smoking and semen quality (Durairajanayagam, 2018). A significant issue in relation to the study of the frequency of this type of behavioral habits is the cultural, social, and belief differences affecting different societies, which overshadow the results of studies (Houston et al., 2022). Based on the evidence, the pattern of infertility sauce varies according to different ecological, health, and cultural conditions in different parts of the world. Regarding drug use and semen quality, the results showed that there was a significant relationship between semen quality with drug use and age of onset (Turner et al., 2020).

Cigarette smoke contains harmful substances that disrupt the hypothalamic cycle of sex hormone production and prevent adequate sperm production.

Table 3. Comparison of alcohol and drug use in 2 groups

Factor	Group	Case [n (%)]	Control [n (%)]	P-value
Drug	Yes	33 (13.3)	15 (6.1)	0.004
	No	217 (86.7)	235 (93.9)	
Alcohol	Yes	5 (1.8)	3 (1.0)	0.725
	No	245 (98.2)	297 (99.0)	

The cultural, social, and belief differences affecting different societies that overshadow the results of studies are a significant issue in the study of the frequency of this type of behavioral habit. Because according to the evidence, the etiology of infertility varies according to ecological, health, and cultural conditions worldwide (Takeshima et al., 2021).

Alcohol consumption is linked to people's cultural status and religious beliefs; thus, naturally, the frequency of consumption varies greatly across regions. The difference in results appears to be due to differences in behavioral habits between regions (Gunes & Esteves, 2021). In terms of opium use and sperm quality, the findings show a significant link between opium use and sperm disorders, as well as the age of onset of use. More detailed studies are needed to identify the intervening and controlling socio-ecological factors in different regions to achieve more definite results in this field (Henkel, Sandhu, & Agarwal, 2019). Smoking, drinking, and using drugs are high-risk reproductive health behaviors. It appears that paying attention to ecological differences in different regions can justify differences in consumption frequency in different regions. Increasing awareness and changing people's behaviors, particularly in couples, can be effective in preventing infertility and maintaining reproductive potential, as well as providing more effective infertility treatment (Colaco & Modi, 2018).

Among the limitations of this study are the absence of educational intervention and the failure to compare results to international benchmarks. In order to achieve more conclusive results in this field, it is suggested that future research be conducted to determine the intervening and controlling social and ecological factors in various regions. Moreover, raising awareness and modifying the behavior of individuals, particularly child-seeking couples, can effectively prevent infertility, particularly secondary infertility; therefore, it is recommended to implement educational interventions in this area.

Conclusion

Infertility occurs in men for a variety of reasons. Semen quality is the most important indicator of the cause of infertility in men. By examining the factors affecting the quality of semen, in this paper, we tried to investigate the effect of three factors: smoking, alcohol consumption, and drug use on semen quality. There was no significant relationship between male infertility and smoking and alcohol consumption, but there was a relationship between drug use and infertility. By increasing one unit of drug use, the chance of natural semen decreases by 0.506. There was also a relationship between the time of drug use and the quality of semen, so that the older the age of onset, the more the abnormalities in semen.

Conflict of Interests

Authors have no conflict of interests.

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