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The Effect of Smoking on Serum and Seminal Plasma Zinc Levels in Infertile Men: A Comparative Study

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Abstract

Background Male infertility is the inability to conceive due to low sperm count, poor sperm function, or blockages. Smoking has a negative effect on male infertility because it makes breathing and other physiological processes—including respiration—difficult. Chemicals in tobacco smoke, such as oxidants and pro-oxidants, increase oxidative stress in the body, leading to the production of free radicals. Zinc plays a crucial role in combating this oxidative damage, as it is a key component of several antioxidant enzymes like peroxidase, catalase, and superoxide dismutase. Disruptions in zinc metabolism, such as impaired enzyme utilization of zinc, may contribute to oxidative damage caused by smoking. This oxidative stress can negatively impact sperm health and function, highlighting zinc's important role in preserving male fertility.

Objective To assess the effect of smoking on zinc levels in the serum and seminal plasma of infertile males through a comparative analysis between smokers and non-smokers.

Methods A case-control study recruited 60 infertile men, divided into two groups: 30 smokers and 30 non-smokers. Data on their demographics, hematological indices, and key biomarkers were collected, including serum and seminal plasma zinc levels, as well as serum levels of testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH).

Results The zinc levels in both blood and seminal plasma were significantly lower in smokers compared to non-smokers (P <0.05). Specifically, the mean zinc concentration in the serum of smokers was 1.12 µg/dL, compared to 1.24 µg/dL in non-smokers, and in seminal plasma, it was 1.04 µg/mL for smokers versus 1.10 µg/mL for non-smokers.

Conclusion Smoking has negative impact of on zinc levels in the blood and seminal plasma of infertile men. Zinc is essential for reproductive health, playing a crucial role in sperm production and function. This emphasizes the urgent need for smoking cessation programs to protect reproductive health.

Keywords Zinc, cigarette smoking, serum, seminal plasma, male fertility

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List of abbreviations: AMH = Anti-Müllerian hormone, BMI = Body mass index, CEA = Carcinoembryonic antigen, ELISA = Enzyme-linked immunosorbent assay, FSH = Follicle stimulating hormone, LH = Luteinizing hormone, ROS = Reactive oxygen species, SOD = Superoxide dismutase

Introduction

Infertility is defined as the inability to conceive after one year or more of unprotected sexual intercourse [(1)]. It is a significant global health issue affecting both

individuals and society. Men's fertility may decrease as they age, with sperm quality declining after age 35, making aging a common risk factor. Other factors, such as diet, caffeine consumption, weight, exercise, diabetes, exposure to synthetic chemicals, and sleep patterns, can also influence fertility [2]. Approximately 85% of infertility cases have identifiable causes, with the most common being tubal disease, male factor infertility, and ovarian dysfunction. However, 15% of couples experience unexplained infertility, where no clear cause is determined [3]. Lifestyle factors, including smoking and obesity, can further negatively impact fertility [4].

A growing body of evidence links smoking with oxidative stress, which plays a key role in reproductive health. Smokers have higher levels of free radicals and other oxidizing agents than non-smokers, leading to oxidative stress. Tobacco smoke contains oxidants and pro-oxidants that increase this stress and generate free radicals. These can overwhelm the body's antioxidant defense system, damaging proteins, lipids, and DNA [5].

Zinc is a vital component of antioxidant enzymes like superoxide dismutase (SOD), catalase, and peroxidase, which help counter oxidative damage. Smoking can disrupt zinc metabolism, reducing its effectiveness in neutralizing free radicals. Additionally, cadmium from tobacco can displace essential metals like zinc in the body, further contributing to oxidative stress. This is particularly concerning as zinc is essential for reproductive health, particularly in sperm function and testosterone production [6].

Zinc is an essential trace element required for numerous bodily functions, including immunity, learning, and reproduction. It is involved in the activity of over 300 enzymes in the body, highlighting its importance. Low zinc levels may not directly cause infertility, but they can impair reproductive function, particularly in men. Zinc plays a crucial role in male fertility by supporting sperm capacitation, acrosome reactions, and testosterone production, as well as general sexual health and prostate function [7].

Hormonal factors in male fertility

- Testosterone: This primary male hormone regulates sex differentiation, male sexual characteristics, and spermatogenesis [8].
- Luteinizing hormone (LH): In men, LH stimulates the Leydig cells in the testes to produce testosterone, which is essential for sperm production [9].
- Follicle stimulating hormone (FSH): FSH plays a critical role in male reproduction by regulating spermatogenesis. Together with testosterone, FSH ensures the production of adequate sperm quantities and quality [10, 11].

Although the relationship between smoking and zinc depletion is established, the exact mechanisms by which smoking disrupts zinc's role in reproductive health remain incompletely understood. Therefore, the present study aimed to assess the impact of smoking on serum and seminal plasma zinc concentrations among infertile men, and to compare these findings between smokers and non-smokers.

Methods

Study design

The present study was conducted as an observational comparative study involving a total of 60 infertile male subjects, divided into two groups:

1. Smoker group (n = 30): Infertile men who were smokers.
2. Non-smoker group (n = 30): Infertile men who were non-smokers.

The study was carried out at the Department of Chemistry and Biochemistry, College of Medicine, Al-Nahrain University. Samples were collected from patients at the Department of Biochemistry Laboratory in Al-Imamein Al-Kadhimein Medical city, Baghdad, Iraq, between 10/1/2024 and 19/4/2024. All participants had been unable to conceive after

at least one year of unprotected, regular sexual contact. The study protocol was approved by the Institutional Review Board at the College of Medicine, Al-Nahrain University.

Inclusion criteria

Infertile men aged 20-50 years. They underwent a physical examination and semen analysis. Smoking intensity and duration were also recorded for the smoker group.

Exclusion criteria

Participants with chronic illnesses, a history of hormone therapy, testicular cancer, or other conditions known to affect reproductive health were excluded to minimize confounding factors influencing zinc levels. Additional exclusions included occupational exposure to zinc or other relevant chemicals, use of zinc supplements, alcohol consumption, or medications that may impact zinc metabolism.

Outcome measurements

- Serum and seminal plasma zinc levels were measured using Enzyme-linked immunosorbent assay (ELISA) [12].
- Hormonal parameters: FSH, LH, and testosterone were assessed from venous blood samples using the TOSOH ALA 360 analyzer system.

Statistical analysis

Data were presented as means and standard deviations (SD). The statistical analysis was performed using statistical package for the social sciences (SPSS) analysis version 25. The Shapiro-Wilk test was used to assess the normality of the data distribution. For parametric data, an unpaired t-test was used to compare the groups, while non-parametric data were analyzed using the Mann-Whitney U test [13].

Results

The results showed no significant differences between smokers and non-smokers in terms of age, and BMI (Table 1).

Table 1. Comparison of age, body mass index serum between infertile smokers and non-smokers

Parameter	Groups	Median (IQR)	Mean±SD	P value
Age (yr)	Smoker	34.50 (28.25-40.75)	34.63±8.62	1.000
	non-Smoker	36.50 (28.25- 40.75)	34.63±8.24	
BMI (kg/m^2)	Smoker	26.15 (25.20- 27.53)	26.37±2.49	0.437
	non-Smoker	26.60 (25.63- 28.58)	26.88±2.54	

P value by unpaired ttest

Current study revealed that smokers exhibited significantly lower serum zinc (1.12±0.09 µg/dL vs. 1.24±0.12 µg/dL, P <0.001), seminal zinc (1.04±0.07 µg/dL vs. 1.10±0.09 µg/dL, P = 0.004), compared with non-smokers, as shown in table (2).

Table 2. Comparison of serum and seminal zinc between infertile smokers and non-smokers

Parameter	Groups	Median (IQR)	Mean±SD	P value
Serum Zinc (µg/dL)	Smoker	1.15 (1.02- 1.19)	1.12±0.09	<0.001
	non-Smoker	1.29 (1.25- 1.32)	1.24±0.12	
Seminal plasma Zinc (µg/dL)	Smoker	1.00 (0.99- 1.08)	1.04±0.07	0.004
	non-Smoker	1.15 (0.99- 1.19)	1.10±0.09	

P value by Mann–Whitney U test

Discussion

In this study, the results showed that cigarette smoking had a significant negative effect on zinc concentrations in both serum and seminal plasma among infertile men. These findings agree with several studies that reported the adverse influence of smoking on micronutrient status and male reproductive function. Tobacco smoke contains numerous oxidants and pro-oxidants that increase reactive oxygen species (ROS), causing oxidative stress and damage to lipids, proteins, and DNA [10,11]. The depletion of zinc observed in smokers can therefore be attributed to the increased oxidative burden and the disruption of zinc-dependent antioxidant enzymes such as superoxide dismutase, catalase, and peroxidase [12,13].

Zinc plays a vital role in maintaining sperm integrity and function. It stabilizes cell membranes, protects DNA from oxidative injury, and supports the activity of key antioxidant systems. The reduction of zinc in both serum and seminal plasma among smokers in this study is consistent with previous work by Colagar et al. [15] and Zečević et al. [16], who reported that seminal zinc levels are directly associated with sperm count, motility, and morphology. Similarly, Osadchuk et al. [6] found that smoking decreases seminal zinc and increases sperm DNA fragmentation, confirming the oxidative impact of tobacco exposure. Cadmium, a toxic metal present in cigarette smoke, may also replace zinc in metalloproteins and enzymes, further aggravating zinc deficiency and oxidative stress [14].

Some research has shown contrasting results; for example, Eggert-Kruse et al. [17] did not find a significant association between serum or seminal zinc levels and semen quality parameters. Likewise, certain studies observed minimal differences in serum zinc despite clear declines in seminal zinc among smokers [14]. These inconsistencies may arise from methodological differences, variations in dietary zinc intake, lifestyle factors, or genetic differences in antioxidant capacity. However, the consistent pattern of lower seminal zinc in smokers across multiple studies including ours strongly supports the role of smoking in inducing oxidative imbalance and reproductive dysfunction.

In conclusion, the findings of this study emphasize the importance of zinc as a protective factor against smoking-induced oxidative stress and male infertility. Smoking cessation should be considered a key recommendation for infertile men, as it can restore antioxidant balance and improve sperm health. Moreover, evaluating zinc levels particularly in seminal plasma can serve as an additional diagnostic tool in infertile smokers and may guide targeted nutritional or supplemental interventions.

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Author contribution

Hadi: designed outlines and drafted the manuscript. Hadi and Dr. Abd Ali: performed the experiments and analyzed the data. Dr. Abd Ali and Dr. Hamed reviewed the scientific information evident in the manuscript. reviewed the scientific contents described in

the manuscript. Ali assisted in collection the samples. All authors read and approved the final submitted version of the manuscript.

Conflict of interest

The authors have no conflicts of interest to disclose.

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