OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article **Family Medicine**

Impact of Smoking on Reproductive Health: A Systematic Review

Fahad Saad Z Alanazi[1*], Yosef Soltan H Alrawaili[2]

[1]Senior Registrar of Family Medicine, MOH, Arar, Saudi Arabia
[2]Senior Registrar of Family Medicine, MOH, Arar, Saudi Arabia

DOI: 10.36348/sjmps.2023.v09i12.007 | **Received:** 29.10.2023 | **Accepted:** 04.12.2023 | **Published:** 12.12.2023

***Corresponding author:** Fahad Saad Z Alanazi
Senior Registrar of Family Medicine, MOH, Arar, Saudi Arabia

Abstract

Background: Several research endeavours have endeavoured to evaluate the impact of smoking on the physiology of male and female reproduction. Encompassing sperm parameters, male reproductive architecture, and the male hormonal axes. However, the outcomes have been conflicting and ambiguous. ***Objectives:*** To investigate the published literature on the effect of smoking on female and male reproductive health. ***Methods:*** PubMed, SCOPUS, Web of Science, and Science Direct were systematically searched for relevant literature. Rayyan QRCI was employed throughout this comprehensive process. ***Results & interpretation:*** We included thirteen studies with a total of 10092 participants; 4419 (43.8%) were males, and 5673 (56.2%) were females. Smoking is a risk factor in and of itself for male reproductive health. This is more likely to explain smokers' elevated SHBG levels and differential activity of the seminal antioxidant system. These negative effects included abnormal semen motility, volume, count, and morphology. Additionally, smoking had no discernible impact on women's fertility or ovarian reserve, according to this study. More research is needed to determine whether stopping smoking can treat male infertility caused by these substances and to better understand how cigarette smoke affects both female and male fertility.

Keywords: Smoking; Reproductive health; Infertility; Systematic review.

INTRODUCTION

According to the available biological, experimental, and epidemiological data, smoking cigarettes may be responsible for up to 13% of infertility. Smoking may hasten the onset of menopause by one to four years and appears to hasten the loss of reproductive capacity [1].

The cumulative data on cigarette smoking and female fertility have been summarized in a number of thorough assessments, all of which agree that smoking has a negative effect [2-5]. However, there is a lot of room for bias from various sources due to the observational nature of the majority of the current studies and their different demographics [4, 5].

The first extensive population-based study showing that smoking had a deleterious impact on fertility, regardless of other circumstances, was published [6]. To establish the time to conception, the researchers examined data from over 15,000 pregnancies. The potential confounding effects of other variables, such as parental age, ethnicity, education, employment, housing, pre-pregnancy body mass index, and alcohol use, were examined. Active smoking was linked to infertility within the study's 6- and 12-month time frames. Growing daily cigarette smoking rates were connected with growing conception delays. Smokers were 54% more likely than non-smokers to report a pregnancy delay of more than 12 months. The negative effects of passive cigarette smoke exposure alone were only marginally less severe than those of active smoking by either partner [6].

Smoking continues to be a global habit despite the well-known negative effects it has on health in general and the male reproductive system in particular [7]. The World Health Organization (WHO) reports that 30% of all males aged 15 and older smoke [8]. Approximately 46% of men of reproductive age (20–39 years) smoke [9]. The actual number of daily smokers climbed from 721 million in 1980 to 967 million in 2012, despite the fact that the proportion of male smokers, based on nationally representative statistics from 187 countries, declined from 41.2% in 1980 to 31.1% in 2012 [10].

According to the WHO, 8% of couples globally and 10% to 15% of those in industrialized countries struggle with infertility [11], and 30% to 35% of all cases [12] involve male factor infertility. Numerous research has been undertaken to try and find any links between smoking and male infertility, some of which have produced inconsistent results. While much research has identified a link between smoking and male infertility and semen analysis parameters [13-15], other studies have found no such link and, in some cases, have even discovered a positive relationship between smoking and sperm motility [16] and the degree of nuclear DNA damage in sperm [17]. There has been reported inconsistent and conflicting data about the impact of smoking on male infertility [17, 18]. Furthermore, research claiming that smoking has an impact on semen parameters has not conclusively shown that smoking has any impact on male fertility [19, 20].

The heavy metals cadmium and lead are the main active components of smoking that affect semen characteristics. Cadmium has been proven to negatively affect sperm parameters in prior animal investigations [21]. Smokers who smoke more than 20 cigarettes per day have been reported to have elevated seminal cadmium, and blood cadmium levels have been found to have a statistically significant negative link with sperm density and a statistically significant positive correlation with cigarette years [22]. Additionally, it has been demonstrated that infertile smokers have higher amounts of lead in their seminal plasma than infertile smokers who are also fertile men [23]. Negative correlations between sperm concentration, motility, and morphological defects in aberrant spermatozoa and seminal lead and cadmium concentrations have also been noted [24].

Augood *et al.* conducted a systematic review and meta-analysis and found that overall, 1.60 [95% confidence interval (CI) 1.34-1.91] was the odds ratio (OR) for the likelihood of infertility in women smokers compared to non-smokers. Women who smoke have less fecundity, according to studies of in-vitro fertilization (IVF) patients who are sub-fertile. An OR of 0.66 (95% CI 0.49-0.88) for pregnancies per number of IVF-treated cycles in smokers versus non-smokers was discovered by a meta-analysis of nine trials. The consistency of effect across various study designs, sample sizes, and outcome types makes the data given in this review appealing despite the apparent drawbacks of meta-analyses of observational studies. However, ongoing verification is required that confounding factors are not the real cause of the computed total effect [25].

These contradictory and ambiguous outcomes are not shocking. There are three hypotheses that could account for the appearance of inconsistent results. First, a variety of metrics, including semen parameters, spermatozoa function, histologic changes, and others, are utilized to evaluate the impact of smoking on male fertility. The use of various assessments could lead to discrepancies in study conclusions. Second, the processes through which smoking could affect male fertility are not well understood. Thirdly, because it is difficult to account for variables such as exposure to alcohol consumption, medical conditions, pollutants, and socioeconomic level, it is impossible to compare findings between research directly. This systematic review aims to investigate the published literature on the effect of smoking on female and male reproductive health.

METHODOLOGY

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed for this systematic review [26].

Study Design and Duration

This systematic review was conducted in December 2023.

Search Strategy

To retrieve the relevant research, a thorough search was conducted across five major databases, including Google Scholar, PubMed, Web of Science, Science Direct, and EBSCO. We only searched in English and took into account each database's unique criteria. The following keywords were converted into PubMed Mesh terms and used to find studies that were related; "Smoking," "Reproductive health," "Reproduction," "Infertility," "Female," "Women," "Males," and "Men." The Boolean operators "OR" and "AND" will match the required keywords. Among the search results were publications in full English language, freely available articles, and human trials.

Selection Criteria

We considered the following criteria for inclusion in this review:

- Any study designs that investigate the published literature on the effect of smoking on female and male reproductive health.
- Only adult patients (> 18 years).
- Studies conducted between 2019-2023.
- English language.
- Free accessible articles.

Data Extraction

Duplicates in the search strategy output were found using Rayyan (QCRI) [27]. To determine the titles' and abstract relevance, the researchers used a set of inclusion/exclusion criteria to filter the combined search results. The reviewers carefully read each paper that matches the requirements for inclusion. The authors provided other methods of resolving disputes with some thought. The authors extracted data about the study titles, authors, study year, country, participants, gender, risk factors, epidemiological data, and main outcomes.

Strategy for Data Synthesis

Summary tables were created using information from pertinent research to give a qualitative overview of the results and study components given. Following data extraction for the systematic review, the most effective strategy for utilizing data from the included study articles was selected.

Risk of bias assessment

Using the ROBINS-I risk of bias assessment approach for non-randomized trials of therapies, the quality of the included studies was assessed [28]. The seven themes that were assessed were confounding, participant selection for the study, classification of interventions, deviations from intended interventions, missing data, assessment of outcomes, and choosing of the reported result.

RESULTS

Search Results

A total of 390 study articles resulted from the systematic search, and 189 duplicates were deleted. Title and abstract screening were conducted on 201 studies, and 156 were excluded. 45 reports were sought for retrieval, and 2 articles were retrieved. Finally, 43 studies were screened for full-text assessment; 15 were excluded for wrong study outcomes, 14 for the wrong population type, and 1 article was a letter to the editors. Thirteen eligible study articles were included in this systematic review. A summary of the study selection process is presented in Figure 1.

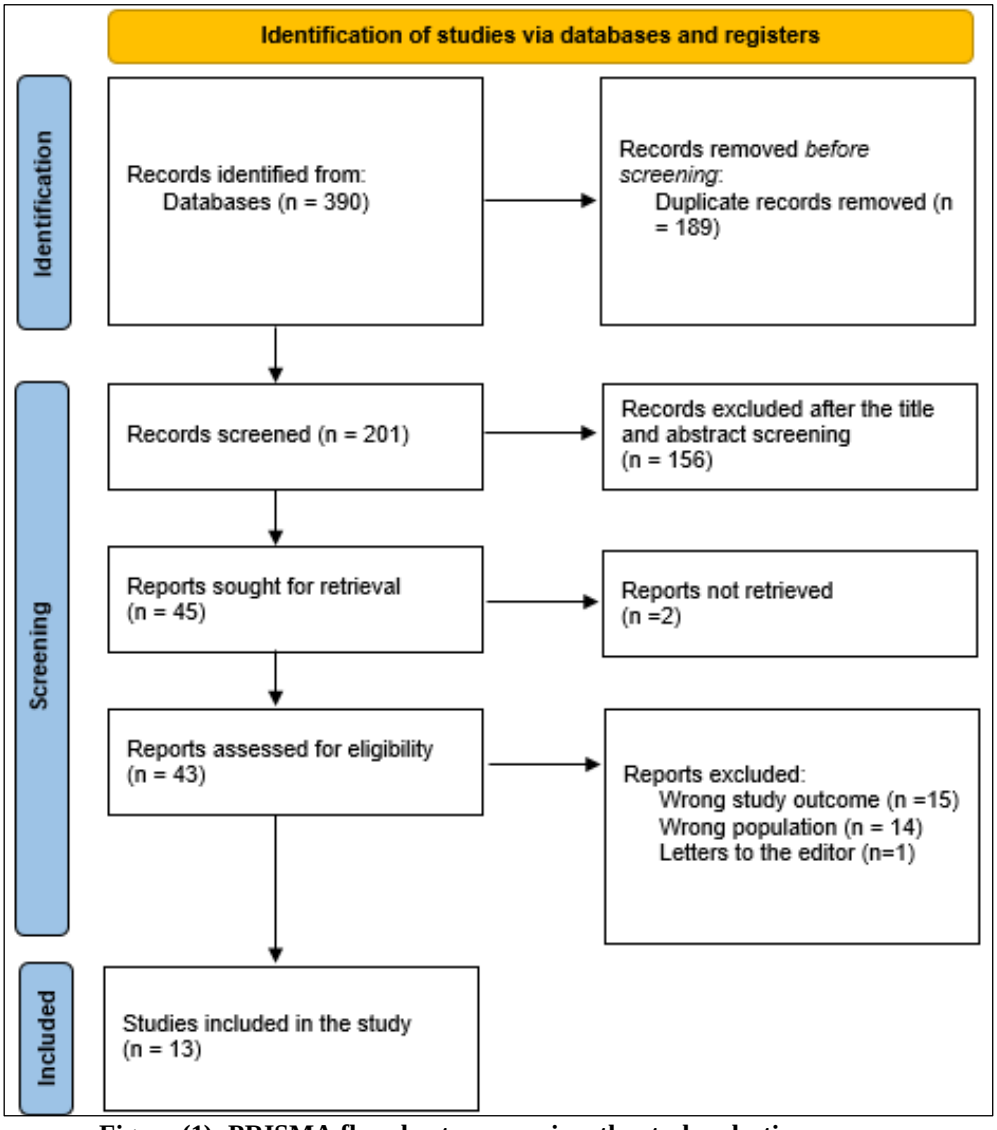

Figure (1): PRISMA flowchart summarizes the study selection process

Characteristics of the included studies

Table (1) presents the sociodemographic characteristics of the included study articles. Our results included thirteen studies with a total of 10092 participants; 4419 (43.8%) were males, and 5673 (56.2%) were females.

Table (2) presents the clinical characteristics. Only one study reported that smoking does not affect

male fertility [29]. On the other hand, eight studies demonstrated that smoking is an independent risk factor for male reproductive health [30-38]. This is more likely caused by the seminal antioxidant system's differing activity [30] and the fact that smokers have higher levels of sex hormone-binding globulin (SHBG) [31]. These negative effects were abnormal semen motility, volume, count, and morphology [33, 35-37].

Three studies found no significant effect of smoking on ovarian reserve and women's fertility [38, 40, 41]. One study reported that there was a higher chance of infertility in women when one was currently smoking [39].

Table (1): Sociodemographic characteristics of the included participants

Study	Study design	Country	Participants	Gender	Age
Iswanto *et al.*, 2022 [29]	Case-control	Indonesia	250	34.7 ± 7.01	Males
Dhair & Abed, 2021 [30]	Case-control	Palastine	320	35.7 ± 10	Males
Osadchuk *et al.*, 2023 [31]	Retrospective cohort	Russia	1222	*25.2 ± 7.1*	Males
Abdulmajeed *et al.*, 2023 [32]	Case-control	Iraq	87	31.2 ± 1.7	Males
Ramgir *et al.*, 2019 [33]	Retrospective observational	India	124	36.7 ± 4	Males
Dupont *et al.*, 2019 [34]	Case-control	France	196	32.2-34.3	Males
Rehman *et al.*, 2019 [35]	cross-sectional	Pakistan	376	35.1 ± 0.4	Males
Mokhtari *et al.*, 2020 [36]	Retrospective	Iran	1744	37.3 ± 7.2	Males
Nagpal *et al.*, 2021 [37]	Case-control	India	100	20-45	Males
Oladipupo et *al.*, 2022 [38]	Cross-sectional	USA	199	21-45	Females
He & Wan, 2023 [39]	Cross-sectional	China	3665	31.4 ± 8.1	Females
Bhide *et al.*, 2022 [40]	Prospective cross-sectional	UK	101	25.5-33.5	Females
Lyngsø *et al.*, 2021 [41]	Cohort	Denmark	1708	31.5 ± 4.3	Females

Table (2): Clinical characteristics and outcomes of the included studies

Study	Diabetes type	Main outcomes	ROBIN-I
Iswanto *et al.*, 2022 [29]	NM	There was a correlation between drug usage and infertility; however, there was no substantial association between smoking and alcohol intake and male infertility.	Moderate
Dhair & Abed, 2021 [30]	59 (18.4) former smokers, 84 (26.3) passive smokers, and 61 (19) current smokers	Men who smoke more than five cigarettes a day have been exposed to secondhand smoke for more than two years or both have a higher risk of infertility.	Moderate
Osadchuk *et al.*, 2023 [31]	NM	Cigarette smoking has an influence on the male reproductive function that is ethnospecific; this effect is likely caused by the seminal antioxidant system's differing activity, which is still unclear.	High
Abdulmajeed *et al.*, 2023 [32]	56 (64.4) smokers and 31 (35.6) nonsmokers	Smokers have higher levels of the hormone SHBG than controls, and they are more likely to acquire diabetes, which is correlated with their larger waist circumferences than males in good health.	Moderate
Ramgir *et al.*, 2019 [33]	29 (23.4) smokers and 95 (85.4) nonsmokers	Men who smoke and drink alcohol have lower-quality sperm, a compromised male endocrine system, and their blood plasma has oxidative damage. These results suggested that alcohol and cigarette smoke are harmful to the male reproductive system.	Moderate
Dupont *et al.*, 2019 [34]	NM	Compared to fertile males, infertile men exhibit worse health and are more likely to smoke. Tobacco use and metabolic syndrome in males seem to be important, separate risk factors for idiopathic infertility.	Moderate
Rehman *et al.*, 2019 [35]	272 (72.3) smokers and 104 (27.7) nonsmokers	Smoking significantly affects sperm count and normal morphology, two factors that are related to fertility. This could be because smoking causes oxidative stress (OS), which drastically affects the characteristics of semen and lowers male fertility.	Moderate
Mokhtari *et al.*, 2020 [36]	379 men were smokers (21.7%), and	It appears that smoking cigarettes negatively affects the standard sperm parameters (semen motility, volume, count, and	High

Study	Diabetes type	Main outcomes	ROBIN-I
	1365 men were non-smokers (78.3%)	morphology). Men who smoke and are infertile should be advised to give up by their doctors.	
Nagpal *et al.*, 2021 [37]	50 Nonsmokers and 50 Smokers	Smoking has a negative impact on sperm count, and the quantity of cigarettes smoked directly correlates with the decline in semen quality.	High
Oladipupo *et al.*, 2022 [38]	71 nonsmokers, 70 passive smokers, and 58 active smokers	There was no correlation between decreased ovarian reserve and current smoking. On the other hand, the concept that prolonged or heavy smoking can lower ovarian reserve was supported by other study findings and trends.	Moderate
He & Wan, 2023 [39]	2544 (69.2) nonsmokers, 431 (11.7) passive smokers, and 689 (18.8) current smokers	There was a higher chance of infertility when one was currently smoking. Subgroup analysis revealed that the relationships between smoking status and infertility were limited to Mexican American women and those between the ages of 25 and 38.	Moderate
Bhide *et al.*, 2022 [40]	64 (63.3) nonsmokers, 25 (24.8) former smokers, and 12 (11.8) current smokers	They were unable to discover a statistically significant difference in quantitative ovarian reserve indicators between current smokers, ex-smokers, and never smokers. They verified that there is a strong correlation between self-reported smoking and quantitatively assessed smoking biomarkers. Biomarkers of smoking and biomarkers of ovarian reserve did not significantly correlate.	Moderate
Lyngsø *et al.*, 2021 [41]	1623 (90.5) ex-smokers and never smoked and 85 (9.5) smokers	When undergoing medically assisted reproduction therapies, there was no correlation found between the likelihood of a clinical pregnancy or a live birth and the occasional or daily smoking of cigarettes by females. Tobacco use, however, should be aggressively discouraged as it remains a major cause of decreased fertility as well as morbidity and mortality in mothers, foetuses, and infants.	Moderate

DISCUSSION

There is still some evidence to support the hypothesis that smoking affects male fertility. It is challenging to draw conclusions about the precise impact of smoking and nicotine on male reproductive physiology due to conflicting research. This comprehensive review reported that smoking is an independent risk factor for male reproductive health [30-38]. This is more likely caused by the seminal antioxidant system's differing activity [30] and the fact that smokers have higher levels of SHBG [31]. These negative effects were abnormal semen motility, volume, count, and morphology [33, 35-37]. Smoking has been found to have an adverse effect on semen parameters by two meta-analyses that assessed semen parameters. According to Sharma *et al.*, [42], smoking cigarettes was associated with aberrant morphology and reduced sperm motility. The other meta-analysis, which comprised 16 trials, supported the previous studies showing that smoking decreased sperm counts and increased spermatozoa morphological defects [43]. In terms of sperm motility, sperm count, and sperm morphology, the results of these two meta-analyses and systematic reviews were fairly similar.

The 2014 Surgeon General's report on tobacco use changed the way that people thought about smoking and anti-smoking policies. It came to the conclusion that 5.6 million young persons under the age of 18 would pass away prematurely from cigarette effects if smoking rates kept rising as predicted [44]. Hazardous free radicals are introduced into a homeostatic system by cigarette smoking [45]. This delicate balance is constantly assaulted by cigarette use, leading to a series of stresses that have a significant impact on normal reproductive physiology both macroscopically and molecularly [46]. The increased oxidative stress brought on by cigarette smoking leads to reduced semen quality, decreased auxiliary gland functions, tube blockage, and defective spermatogenesis [47]. Sperm is the primary product of all these male reproductive activities, and it can be fatally destroyed by these strong oxidative stresses.

In the male genitourinary tract, this type of oxidative stress also causes an increase in inflammatory responses. This causes harm to the nearby tissues, which intensifies the inflammatory reaction [47]. The release of reactive oxygen species boosts the immune system's defences. Proinflammatory cytokines and other provocative inflammatory mediators are released locally, which further exacerbates the local immune responses [46].

This study also found no significant effect of smoking on ovarian reserve and women's fertility [38, 40, 41]. One study reported that there was a higher

chance of infertility in women when one was currently smoking [39]. Tobacco smoke contains substances such as carbon monoxide, nicotine, cadmium, and polycyclic aromatic hydrocarbons (PAHs), like benzo[a]pyrene (B[a]P), which are known to have harmful effects on reproductive health [48]. Tobacco smoke is thought to affect ovarian reserve through a number of biological mechanisms, including cytotoxicity, impaired steroidogenesis, increased chromosomal errors, atresia of oocytes in primordial and small primary follicles, early luteinization of the preovulatory follicle, and inhibition of follicular development [49].

CONCLUSION

For male reproductive health, smoking is an independent risk factor. Smokers' higher levels of SHBG and the seminal antioxidant system's differential activity are more likely to be a consequence of this. Abnormal semen motility, volume, count, and morphology were these detrimental outcomes. This study also found no significant effect of smoking on ovarian reserve and women's fertility. To better understand how cigarette smoke affects male and female fertility and whether quitting smoking can treat male infertility caused by these chemicals, more research is required.

REFERENCES

1. Practice Committee of the American Society for Reproductive Medicine. (2008). Smoking and infertility. *Fertility and Sterility*, *90*(5), S254-S259.
2. Stillman, R. J. (1989). Seminar in reproductive endocrinology: smoking and repr
3. Fredricsson, B., & Gilwam, H. (1992). Smoking and reproduction: Short and long term effects and benefits of smoking cessation. *Acta obstetricia et gynecologica Scandinavica*, *71*(8), 580-592.
4. Wallach, E. E., Hughes, E. G., & Brennan, B. G. (1996). Does cigarette smoking impair natural or assisted fecundity?. *Fertility and sterility*, *66*(5), 679-689.
5. Augood, C., Duckitt, K., & Templeton, A. A. (1998). Smoking and female infertility: a systematic review and meta-analysis. *Human Reproduction (Oxford, England)*, *13*(6), 1532-1539.
6. Hull, M. G., North, K., Taylor, H., Farrow, A., & Ford, W. C. L. (2000). Delayed conception and active and passive smoking. *Fertility and sterility*, *74*(4), 725-733.
7. Zhang, Z. H., Zhu, H. B., Li, L. L., Yu, Y., Zhang, H. G., & Liu, R. Z. (2013). Decline of semen quality and increase of leukocytes with cigarette smoking in infertile men. *Iranian journal of reproductive medicine*, *11*(7), 589.
8. Saleh, R. A., Agarwal, A., Sharma, R. K., Nelson, D. R., & Thomas Jr, A. J. (2002). Effect of cigarette smoking on levels of seminal oxidative stress in infertile men: a prospective study. *Fertility and sterility*, *78*(3), 491-499.
9. Ng, M., Freeman, M. K., Fleming, T. D., Robinson, M., Dwyer-Lindgren, L., Thomson, B., ... & Gakidou, E. (2014). Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. *Jama*, *311*(2), 183-192.
10. World Health Organization. (1987). Infections, pregnancies, and infertility: perspectives on prevention. *Fertility and Sterility*, *47*(6), 964-968.
11. Odisho, A. Y., Nangia, A. K., Katz, P. P., & Smith, J. F. (2014). Temporal and geospatial trends in male factor infertility with assisted reproductive technology in the United States from 1999–2010. *Fertility and Sterility*, *102*(2), 469-475.
12. Zinaman, M. J., Brown, C. C., SELEVAN, S. G., & CLEGG, E. D. (2000). Semen quality and human fertility: a prospective study with healthy couples. *Journal of andrology*, *21*(1), 145-153.
13. Chia, S. E., Lim, S. T. A., Tay, S. K., & Lim, S. T. (2000). Factors associated with male infertility: a case-control study of 218 infertile and 240 fertile men. *BJOG: An International Journal of Obstetrics & Gynaecology*, *107*(1), 55-61.
14. Künzle, R., Mueller, M. D., Hänggi, W., Birkhäuser, M. H., Drescher, H., & Bersinger, N. A. (2003). Semen quality of male smokers and nonsmokers in infertile couples. *Fertility and sterility*, *79*(2), 287-291.
15. Adelusi, B., Al-Twaijiri, M. H., Al-Meshari, A., Kangave, D., Al-Nuaim, L. A., & Younnus, B. (1998). Correlation of smoking and coffee drinking with sperm progressive motility in infertile males. *African journal of medicine and medical sciences*, *27*(1-2), 47-50.
16. Sergerie, M., Ouhilal, S., Bissonnette, F., Brodeur, J., & Bleau, G. (2000). Lack of association between smoking and DNA fragmentation in the spermatozoa of normal men. *Human Reproduction*, *15*(6), 1314-1321.
17. Vogt, H. J., Heller, W. D., & Borelli, S. (1986). Sperm quality of healthy smokers, ex-smokers, and never-smokers. *Fertility and sterility*, *45*(1), 106-110.
18. Brugo-Olmedo, S., Chillik, C., & Kopelman, S. (2001). Definition and causes of infertility. *Reproductive biomedicine online*, *2*(1), 173-185.
19. Practice Committee of the American Society for Reproductive Medicine. (2008). Smoking and infertility. *Fertility and Sterility*, *90*(5), S254-S259.
20. Oliveira, H., Spanò, M., Santos, C., & de Lourdes Pereira, M. (2009). Adverse effects of cadmium exposure on mouse sperm. *Reproductive Toxicology*, *28*(4), 550-555.
21. Oldereid, N. B., Thomassen, Y., & Purvis, K. (1994). Seminal plasma lead, cadmium and zinc in relation to tobacco consumption. *International journal of andrology*, *17*(1), 24-28.
22. Chia, S. E., Xu, B., Ong, C. N., Tsakok, F. M., & Lee, S. T. (1994). Effect of cadmium and cigarette smoking on human semen quality. *International journal of fertility and menopausal studies*, *39*(5), 292-298.
23. Pant, N., Kumar, G., Upadhyay, A. D., Gupta, Y. K., & Chaturvedi, P. K. (2015). Correlation between lead and cadmium concentration and semen quality. *Andrologia*, *47*(8), 887-891.
24. Augood, C., Duckitt, K., & Templeton, A. A. (1998). Smoking and female infertility: a systematic

review and meta-analysis. *Human Reproduction (Oxford, England)*, *13*(6), 1532-1539.
25. Tugwell, P., & Tovey, D. (2021). PRISMA 2020. *Journal of Clinical Epidemiology*, *134*, A5-A6.
26. Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—a web and mobile app for systematic reviews. *Systematic reviews*, *5*, 1-10.
27. Jüni, P., Loke, Y., Pigott, T., Ramsay, C., Regidor, D., Rothstein, H., ... & Shea, B. (2016). Risk of bias in non-randomized studies of interventions (ROBINS-I): detailed guidance. *Br Med J*, *355*, i4919.
28. Iswanto, A., Karim, Y. S., Islam, Z., Jalil, A. T., Khlaif, A. T., Mustafa, Y. F., ... & Beheshtizadeh, N. (2022). An Investigation of the Effect of Smoking, Alcohol, and Drug Use on Male Infertility. *International Journal of Body, Mind & Culture (2345-5802)*, *9*(3).
29. Dhair, A., & Abed, Y. (2021). Dose-dependent effect of smoking on fertility status among men in Gaza strip, Palestine. *Dubai Medical Journal*, *4*(3), 190-197.
30. Osadchuk, L., Kleshchev, M., & Osadchuk, A. (2023). Effects of cigarette smoking on semen quality, reproductive hormone levels, metabolic profile, zinc and sperm DNA fragmentation in men: results from a population-based study. *Frontiers in Endocrinology*, *14*.
31. Abdulmajeed, A. I., Al _ Zuhairi, W. S., Hassan, E. A., & Imran, N. A. (2023). Study the effect of smoking on reproductive hormones in (Iraqi Adults Men). *Egyptian Journal of Chemistry*, *66*(6), 69-74.
32. Ramgir, S. S., & Abilash, V. G. (2019). Impact of Smoking and Alcohol Consumption on Oxidative Status in Male Infertility and Sperm Quality. *Indian Journal of Pharmaceutical Sciences*, *81*(5).
33. Dupont, C., Faure, C., Daoud, F., Gautier, B., Czernichow, S., Lévy, R., & ALIFERT collaborative group Isabelle Aknin Isabelle Cedrin-Durnerin Steven Cens Pascale Chavatte-Palmer Serge Hercberg Khaled Pocate Nathalie Sermondade Claude Uthurriague Jean-Philippe Wolf. (2019). Metabolic syndrome and smoking are independent risk factors of male idiopathic infertility. *Basic and clinical andrology*, *29*, 1-7.
34. Rehman, R., Zahid, N., Amjad, S., Baig, M., & Gazzaz, Z. J. (2019). Relationship between smoking habit and sperm parameters among patients attending an infertility clinic. *Frontiers in Physiology*, *10*, 1356.
35. Mokhtari, G. R., Esmaeili, S., Mahsa Zeinali Moghaddam, M., & Ghanbari, A. (2020). Effect of Cigarette Smoking on Sperm Parameters in Men with Idiopathic Infertility. *Journal of Guilan University of Medical Sciences*, *29*(3), 14-21.
36. Nagpal, A., Girotra, P., Nagpal, D., Nagpal, L., & Nagpal, S. K. (2021). Study of the effect of smoking on sperm count in male infertility. *Int J Gynaecol Obstet*, *5*(5), 67-69.
37. Oladipupo, I., Ali, T. S., Hein, D. W., Pagidas, K., Bohler, H., Doll, M. A., ... & Taylor, K. C. (2022). Association between cigarette smoking and ovarian reserve among women seeking fertility care. *Plos one*, *17*(12), e0278998.
38. He, S., & Wan, L. (2023). Associations between smoking status and infertility: a cross-sectional analysis among USA women aged 18-45 years. *Frontiers in Endocrinology*, *14*, 1140739.
39. Bhide, P., Timlick, E., Kulkarni, A., Gudi, A., Shah, A., Homburg, R., & Acharya, G. (2022). Effect of cigarette smoking on serum anti-Mullerian hormone and antral follicle count in women seeking fertility treatment: a prospective cross-sectional study. *BMJ open*, *12*(3), e049646.
40. Lyngsø, J., Kesmodel, U. S., Bay, B., Ingerslev, H. J., Pisinger, C. H., & Ramlau-Hansen, C. H. (2021). Female cigarette smoking and successful fertility treatment: A Danish cohort study. *Acta obstetricia et gynecologica Scandinavica*, *100*(1), 58-66.
41. Sharma, R., Harlev, A., Agarwal, A., & Esteves, S. C. (2016). Cigarette smoking and semen quality: a new meta-analysis examining the effect of the 2010 World Health Organization laboratory methods for the examination of human semen. *European urology*, *70*(4), 635-645.
42. Bundhun, P. K., Janoo, G., Bhurtu, A., Teeluck, A. R., Soogund, M. Z. S., Pursun, M., & Huang, F. (2019). Tobacco smoking and semen quality in infertile males: a systematic review and meta-analysis. *BMC public health*, *19*(1), 1-11.
43. United States. Public Health Service. Office of the Surgeon General, & United States. Office on Smoking. (2004). *The health consequences of smoking: a report of the Surgeon General*. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health.
44. Kumar, S., Murarka, S., Mishra, V. V., & Gautam, A. K. (2014). Environmental & lifestyle factors in deterioration of male reproductive health. *The Indian journal of medical research*, *140*(Suppl 1), S29.
45. Thompson, J., & Bannigan, J. (2008). Cadmium: toxic effects on the reproductive system and the embryo. *Reproductive toxicology*, *25*(3), 304-315.
46. Fraczek, M., & Kurpisz, M. (2007). Inflammatory mediators exert toxic effects of oxidative stress on human spermatozoa. *Journal of andrology*, *28*(2), 325-333.
47. Dechanet, C., Anahory, T., Mathieu Daude, J. C., Quantin, X., Reyftmann, L., Hamamah, S., ... & Déchaud, H. (2011). Effects of cigarette smoking on reproduction. *Human reproduction update*, *17*(1), 76-95.
48. Sadeu, J. C., & Foster, W. G. (2013). The cigarette smoke constituent benzo [a] pyrene disrupts metabolic enzyme, and apoptosis pathway member gene expression in ovarian follicles. *Reproductive toxicology*, *40*, 52-59.