PHARMACIA

Pharmacia 71: 1–14
DOI 10.3897/pharmacia.71.e113854

Review Article

Effect of tobacco smoking and alcohol consumption on semen quality and hormone reproductive levels in infertile males: A systematic review and meta analysis

Ryan Ramon[1], Syah Mirsya Warli[2,3], Nur Rasyid[4], Widi Atmoko[4]

1 *Department of Urology, Faculty of Medicine, Universitas Indonesia – Haji Adam Malik General Hospital, Medan, Indonesia*
2 *Division of Urology, Department of Surgery, Faculty of Medicine, Universitas Sumatera Utara - Haji Adam Malik General Hospital, Medan, Indonesia*
3 *Department of Urology, Universitas Sumatera Utara Hospital – Universitas Sumatera Utara, Medan, Indonesia*
4 *Department of Urology, Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo General Hospital, Jakarta, Indonesia*

Corresponding author: Syah Mirsya Warli (warli@usu.ac.id)

Received 8 October 2023 ♦ **Accepted** 30 November 2023 ♦ **Published** 4 January 2024

Citation: Ramon R, Warli SM, Rasyid N, Atmoko W (2024) Effect of tobacco smoking and alcohol consumption on semen quality and hormone reproductive levels in infertile males: A systematic review and meta analysis. Pharmacia 71: 1–14. https://doi.org/10.3897/pharmacia.71.e113854

Abstract

Aim: This study compared semen quality, FSH, LH, and Testosterone levels in infertile males among smokers and non-smokers and semen quality among alcoholics and non alcoholics.

Methods: A literature search was conducted across five databases in December 2021. The search for this article uses specific keywords tailored to each search database's specifications.

Results: A total of 15 studies with 12,503 infertile male participants included in this study. 8,025 were non-smokers, 4,477 were smokers, 210 were alcoholics and 407 were non alcoholics. The effect of tobacco smoking on sperm were more significant in smokers than in non-smokers. Alcohol consumption affects the quality and quantity of semen. Both tobacco smoking and alcohol consumption combined may amplify their negative effects toward semen parameters.

Conclusion: Smoking and alcohol has a detrimental impact on conventional semen characteristics. Due to the harmful effects of both factors, men seeking reproduction should be advised to avoid these habits.

Keywords

Tobacco smoking, alcohol consumption, semen quality, infertile male, reproductive hormones

Introduction

Infertility refers to the incapacity of a sexually active couple who do not use contraception to naturally conceive a child within a year, where it can be primary, meaning no previous pregnancies; or secondary, meaning previous successful conceptions but subsequent difficulties. (Bundhun et al. 2019). According to the World Health Organization (WHO), Infertility impacts 48 million couples globally, affecting a total of 186 million individuals across

the world. Infertility is a common problem for 8–15% of couples globally and 10–15% of couples in developed countries (Rowe et al. 2000).

In 30–40% of cases, the cause of male infertility remains unknown (idiopathic male infertility), although semen analysis may show abnormalities in the sperm quality (Bundhun et al. 2019). Lifestyle factors that may increase the risk of male infertility include occupational and behavioral factors, including diet, obesity, smoking, alcohol consumption, recreational drug use, and exposure to environmental toxins (Meri et al. 2013). Many studies have proved that cigarette smoking negatively impacts the reproductive systems and fertility of both men and women. The prevalence of smoking is about 37% in men who are in their reproductive age (Tang et al. 2019). These studies indicated that tobacco smoking decreases sperm count, motility, and normal morphology (Rehman et al. 2019 and Mokhtari et al. 2020). However, some studies did not find significant differences in conventional sperm parameters between smokers and non-smokers. Davar et al. 2020 study noted that smokers exhibited reduced semen parameters, including morphology, motility, and concentration. However, these differences among the groups did not reach statistical significance (Davar et al. 2012). Male infertility linked to chronic alcohol use may also result from altered gene expression regulation, affecting the metabolism of proteins crucial for sperm maturation (Finelli et al. 2021). Research by Jensen et al. discovered negative associations between habitual alcohol intake and sperm concentration, total sperm count, and the percentage of sperm with normal morphology (Jensen et al. 2014).

The impact factors on semen quality is still a matter of debate. Therefore, our aim was to assess semen parameters in both individuals who smoke and those who do not, and to examine the impact of tobacco smoking on semen quality, as well as the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone in males experiencing infertility.

Methods

The review was done based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. This study aims to analyze the effect of tobacco smoking and alcohol consumption on semen quality in infertile male, so the Patient Interventions Comparisons Outcomes (PICO) used in this systematic review were:

Patients	:	Infertile male
Interventions	:	Tobacco smoking and alcohol consumption
Comparisons	:	-
Outcomes	:	Semen quality, FSH, LH, Testosteron

Eligibility criteria

Inclusion criteria

Inclusion criteria in this systematic review were:

Type of studies

We selected observational studies that measured semen parameters in smokers and non-smokers as well as alcoholics and non alcoholics and reported the following outcomes: semen parameters, sperm morphology, types of structural abnormalities, and hormones related to male reproductive function. The studies had to be fully available (full-text), published within the last decade, and written in English.

Type of participants

The characteristics of participants in the studies included were infertile male participants, who came to the hospital and performed sperm quality checks. Participants were active smokers for at least one year or alcoholics. Age, gender, ethnic, and race were not considered in this study.

Type of outcomes measure

The outcomes of interest in the studies were the total number of cases with oligozoospermia; asthenozoospermia; teratozoospermia; tail, neck, or head defects; sperm morphology defects; testosterone levels; FSH levels; and LH levels.

Exclusion criteria

The following types of studies were excluded from this systematic review:

1. Studies with male participants who were fertile/normal;
2. Did not do comparison to semen parameters between smokers and non-smokers;
3. Did not report any of these outcomes: semen parameters, spermatozoa morphology, structural defect categories, and hormones related to male reproductive function;
4. Studies that were not in English;
5. Studies published more than ten years ago;
6. Studies that were duplicated.

Searching strategy

The search was conducted in December 2021. A literature search in this study used three databases (PubMed/MEDLINE database, Taylor & Francis Online, and ProQuest. The search for this article used specific keywords that were tailored to the specifications of each search database. The keywords used in the investigation were tailored to PICO and used meSH, free text, and title/abstract terminology. Keywords used in literature searching are as follows (Table 1).

Table 1. Literature finding's result.

Database	Keywords	Hit	Selected	Comments
PubMed	((((infertile male* [MeSH Terms]) OR (infertility[MeSH Terms])) OR (male infertility[MeSH Terms])) AND ((((((smoking[MeSH Terms]) OR (cigarette*[MeSH Terms])) OR (cigarette smoking[MeSH Terms])) OR (tobacco[MeSH Terms])) OR (nicotine[MeSH Terms])) OR (tobacco smoking*[MeSH Terms]))) AND ((((((((((((semen quality) OR (semen analysis[MeSH Terms])) OR (sperma[MeSH Terms])) OR (semen[MeSH Terms])) OR (analyses, semen quality[MeSH Terms])) OR (sperm morphology[MeSH Terms])) OR (sperm motility[MeSH Terms])) OR (sperm count[MeSH Terms])) OR (oligozoospermia[MeSH Terms])) OR (asthenozoospermia[MeSH Terms])) OR (teratozoospermia[MeSH Terms])) OR (FSH[MeSH Terms])) OR (LH[MeSH Terms])) OR (testosterone[MeSH Terms]))	269	10	52 not match PICO 1 articles written in Turkey 6 article duplication 12 full text unavailable 180 articles more than 10 years publication 2 article, which participants fertile male 2 article sample is rat 2 article review
ProQuest	ab((infertile male OR infertility OR male infertility)) AND ab((smoking OR cigarette* OR tobacco OR nicotine OR tobacco smoking)) AND ab((semen quality OR semen OR sperm quality OR sperm OR sperm morphology OR sperm count OR sperm motility OR oligozoospermia OR asthenozoospermia OR teratozoospermia OR azoospermia OR testosterone OR FSH OR LH))	74	2	38 not match PICO 1 articles written in French 3 article duplication 15 full text unavailable 13 articles more than ten years publication 2 article sample is rat
Taylor & Francis Online	[Abstract: infertile] AND [[Abstract: male] OR [Abstract: infertility] OR [Abstract: male]] AND [Abstract: infertility] AND [[Abstract: smoking] OR [Abstract: cigarette*] OR [Abstract: tobacco] OR [Abstract: nicotine] OR [Abstract: tobacco]] AND [Abstract: smoking] AND [Abstract: semen] AND [[Abstract: quality] OR [Abstract: semen] OR [Abstract: sperm]] AND [[Abstract: quality] OR [Abstract: sperm] OR [Abstract: sperm]] AND [[Abstract: morphology] OR [Abstract: sperm]] AND [[Abstract: count] OR [Abstract: sperm]] AND [[Abstract: motility] OR [Abstract: oligozoospermia] OR [Abstract: asthenozoospermia] OR [Abstract: teratozoospermia] OR [Abstract: azoospermia] OR [Abstract: testosterone] OR [Abstract: fsh] OR [Abstract: lh]]	11	2	3 not match PICO 1 full text unavailable 5 articles more than ten years publication

Study selection

We used the Mendeley application version 1.19.8 to identify and remove duplicate articles. Two authors independently and in duplication performed the eligibility assessment of all obtained studies. They screened the title and abstract of each remaining study in the initial stages. Then, all authors conducted a full-text evaluation of the remaining articles and categorized them into included, excluded, and ongoing studies or studies awaiting classification. We resolved any discrepancies by discussion. We reported the reasons for excluding some studies after the final assessment. The selection stage of this study followed the PRISMA checklist and flow diagram (Zhang et al. 2016).

Study quality assessment

Two authors conducted assessment of the quality of the studies included then independently assessed the risk of bias for observational studies based on The Joanna Briggs Institute (JBI 2023) Critical Appraisal tools (Page et al. 2021).

Data synthesis and meta-analysis

All data extraction results were analyzed with narrative analysis. A meta-analysis was conducted on relevant studies using the Review Manager v5.4 software. We used the random effects model. The results were visually represented through a forest plot along with a 95% confidence interval (CI). To gauge the level of homogeneity, the I2 statistic was employed, where 30% to 60% indicated moderate heterogeneity, 50% to 90% signified substantial heterogeneity, and 75% to 100% indicated significant heterogeneity. We considered statistical significance to be present when the P-value was less than 0.05.

Results

Literature search outcomes

The literature search identified 357 relevant articles through online databases (269 articles from PubMed database, 74 articles from ProQuest database, and 11 articles from Taylor & Francis Online database; and 3 article found by checking reference lists to identify relevant studies From this set of pieces, 9 articles were excluded because of duplicates. After screening a proper assessment of title and abstract, we excluded 318 articles because 194 articles were published more than ten years ago and two articles were written in languages other than English (French, Turkey); 93 articles were excluded because they did not match with our PICO or the articles did not analyze the endpoints. We also excluded 31 articles because their full-texts were unavailable. Thirty full-text articles were assessed for eligibility, and the articles were excluded based on the inclusion and exclusion criteria. We excluded 15 articles from this analysis for various reasons: 2 had fertile men as participants, 3 used rats as subjects, 2 were review articles, and 8 did not report relevant endpoints for our research question. We included 15 studies that met all our inclusion and exclusion criteria in this narrative analysis. Fig. 1 shows the literature search process.

Study quality

In this study, two authors independently assessed the quality of the studies using the assessment risk of bias in observational articles based on The Joanna Briggs Institute (JBI 2023) Critical Appraisal tools for use in JBI systematic reviews, Checklist for Cross-sectional and Cohort Studies. We found that almost all studies showed good quality, only one study exhibited moderate quality, which was the study conducted by Zhang et al. 2016. The retrospective study

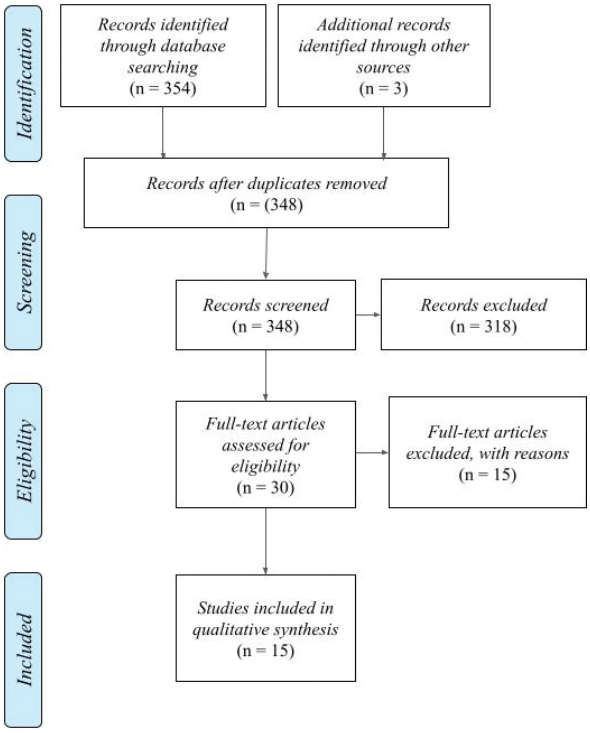

Figure 1. Literature search flow diagram.

doesn't report confounding factors and strategies to deal with the confounding factors stated; it can present a risk of bias in the study because any factors may impact infertile males. This study included observational studies such as cross-sectional, cohort retrospective, and prospective. The cross-sectional studies (Caserta et al. (2013), Asare-Anane et al. (2016), Chitta et al. (2016), and Mitra et al. (2012), were not followed up because they carried out the exposure assessment at one time. The strategy of follow-up participant exposure in the study prospective (Cui et al. (2016), Mostafa et al. (2018), was carried out for each control patient during treatment at the infertility clinic and presented a detailed assessment of the risk of bias in Table 2.

Characteristics of included studies

A total of 15 studies (Table 3), with 12,503 infertile male participants included in this study. Of these infertile male participants, 8,025 were non-smokers with a mean age of 29.7–38.5, while 4,477 were smokers with a mean age of 29.6–40, 210 were identified as alcoholics and 407 were non alcoholics. However, not all articles in this study explained the participants' ages. Participants in this study were infertile males seeking infertility treatment at the infertility clinic, IVF unit,

Table 2. Assessment of the risk of bias for each study observational.

Question	Al-Turki et al. 2014	Anane et al. 2016	Brucker et al. 2020	Caserta et al. 2012	Cui et al. 2016	Chitta et al. 2016	Jain et al. 2015	Meri et al. 2013	Mitra at al. 2013	Mostafa et al. 2017	Zhang et al. 2013	Zhang et al. 2015	Anifandis et al. 2014	Komiya et al. 2014	Keskin et al. 2015
Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
Were the two groups similar and recruited from the same population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were objective, standard criteria used for measurement of the condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were confounding factors identified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Were strategies to deal with confounding factors stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Unclear	No	Unclear	No	Yes	No	Unclear	Unclear	No	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Were strategies to address incomplete follow up utilized?	Unclear	No	Unclear	No	Yes	No	Unclear	Unclear	No	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	YA	Ya	Yes	Yes	Yes	Yes	Yes	Yes
Quality Study	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Good Quality	Moderate Quality	Good Quality	Good Quality	Good quality

Table 3. Characteristics of studies included in this review.

Studies	Study Design	Years of patient's enrollment	No. of infertile		No. of infertile		Age (years) S/NS	Endpoint	Outcome	Study Quality
			Smokers	Non Smokers	Alcoholics	Non Alcoholics				
Al-Turki et al. (2014)[17]	Retrospective	2010–2012	90	168	–	–	34.2/34.1	Testosterone level, FSH level, LH level	Reduced hormonal levels and semen parameters in smokers than non smokers	Good Quality
Anane et al. (2016)[15]	Cross Sectional	2010–2011	95	45	–	–	35,0/37,3	Oligozoospermia, Asthenozoospermia, Teratozoospermia	Reduced semen volume, sperm viability, sperm motility, sperm morphology and concentration in smokers than non nonsmokers	Good Quality
Brucker et al (2020)[18]	Retrospective	2010–2017	586	4.560	–	–	35,99/36,45	Testosterone level, FSH level, LH level	Reduced sperm concentration in smokers than non smokers. Semen volume, sperm motility, sperm vitality and sperm morphology not influenced in smoking	Good Quality
Caserta et al. (2012)[16]	Cross Sectional	2006–2011	200	448	–	–	38,3/38,5	Oligozoospermia, asthenozoospermia, teratozoospermia, FSH level, LH level	Lower count and motility in smokers than nonsmokers. No correlation between sperm parameters and smoking intensity	Good Quality
Cui et a.l (2016)[7]	Prospective	2013–2015	920	298	–	–	–	Abnormal sperm head, abnormal sperm body, abnormal sperm tail	Abnormal head rete in the heavy smoking group and long-term smoking group were significantly	Good Quality
Chitta et al. (2016)[19]	Cross Sectional	2011–2012	100	100	–	–	–	Semen parameter: sperm concentration, motility, semen volume, normal morphology	Reduced sperm count, motility and morphology in smokers than non smokers	Good Quality
Jain et al. (2015)[20]	Retrospective	Jan–May 2015	118	211	–	–	35,51/34,89	Abnormal morphology	Reduced progressive motility and concentration sperm in smokers than non smokers. Abnormal morphology in smokers more than non smokers	Good Quality
Meri et al. (2013)[4]	Retrospective	2010–2011	396	564	–	–	34,35/36,45	Abnormal morphology	Reduced motility and morphology in smokers compared with nonsmokers. Lower count, motility, and morphology in heavy smokers compared with non– heavy smokers	Good Quality
Mitra et al. (2012)[8]	Cross Sectional	–	178	126	–	–	40/35	Asthenozoospermia (reduced motility), oligozoospermia (low sperm count), teratozoospermia (sperm with abnormal morphology), azoospermia (no sperm count), immotility, sperm head defect, sperm tail defect	Lower sperm motility, reduced morphology, lower DNA integrity, higher FSH and LH levels, and decreased testosterone levels in smokers compared with nonsmokers	Good Quality
Mostafa et al (2018)[21]	Prospective	Apr–Des 2014	50	45	–	–	30,8/29,7	Semen parameter: sperm concentration, motility, semen volume, abnormal morphology	Reduced total motility, viability and count of sperm in smokers than non smokers	Good Quality
Zhang et al. (2013)[23]	Retrospective	2007–2010	737	775	–	–	29.6/29.9	Semen pH, sperm head defects, sperm neck defect, sperm tail defect	Lower volume, progressive motility, viability, and morphology, and higher number of leukocytes in smokers than nonsmokers. Dose-response correlation between morphology and amount of smoking	Good Quality
Zhang et al. (2015)[11]	Retrospective	2013–2014	704	372	–	–	29.9/30.4	FSH level, LH level, testosterone level	Lower sperm viability and motility in smokers than nonsmokers.	Moderate Quality
Anifandis et al. (2014)	Cross sectional		109	98	83	124	37.43 + 0.3	Semen parameter: sperm concentration, volume, progressive motility, non progressive motility, immotility, small halos, no halos, degenerative spermatozoa, sperm DNA fragmentation	Semen volume, the proportion of degenerated spermatozoa, and sperm DNA fragmentation (SDF) exhibited notable correlations with different smoking statuses. Conversely, the percentage of spermatozoa with small halos showed a significant correlation with alcohol consumption. Additionally, the smoking habits of the individuals were linked to their alcohol consumption patterns.	Good Quality
Komiya et al. (2014)	Cross sectional	Oct 2012–Feb 2014	10	43	27	27	34.9/35	LH level, FSH level, serum total testosterone, serum free testosterone, semen volume, normal sperm morphology, sperm count, progressive sperm motility, motile sperm count, computer-assisted semen analysis (linear velocity, curvilinear velocity, linearity, ALH, beat/cross frequency), high-magnification microscopy (proportion of vacuolated sperm), sperm DNA fragmentation index	The Sperm DNA Fragmentation Index (SDFI) measured at 41.3% ± 22.2% (mean ± standard deviation) was consistent across various infertility causes. However, chronic alcohol consumption elevated the SDFI to 49.6% ± 23.3%, whereas it remained at 33.9% ± 18.0% among nondrinkers. The SDFI was linked to unfavorable traditional semen parameters and sperm motility traits, and it also showed a correlation with serum FSH levels. Moreover, there was an inclination for the Sperm Nuclear Vacuolation (SNV) to increase in tandem with the SDFI. In a multivariate analysis, it was evident that sperm progressive motility and chronic alcohol use emerged as significant predictors of SDFI.	Good Quality
Keskin et al. (2016)	Prospective	January–March 2015	184	172	100	256	33.04 + 5.43	Semen parameter: volume, concentration, total motility, progressive motility, normal morphology, head anomaly, neck anomaly, tail anomaly	In relation to cigarette usage, it was observed that only in group 4 (comprising individuals with over 20 pack-years of cigarette use) did semen volume exhibit a significant decrease compared to the control group (determined by Mann-Whitney U test, $p = 0.009$). No noteworthy differences were found in any other parameters or groups when compared to the control group (Mann-Whitney U test, $p > 0.05$).	Good Quality

or urology polyclinic. Overall, participants were primary infertile couples. Routine semen analysis was carried out under light microscopy according to WHO guidelines.

We included cross-sectional, retrospective, and prospective studies that enrolled participants from 2007 to 2017. We also excluded participants who had confounding factors that could affect male infertility, such as systemic diseases (e.g., diabetes, hypertension, thyroid disorders, cancer, or tuberculosis); current or recent smoking (less than six months); occupational exposure to chemicals; history of orchitis, prostatitis, or external genital abnormalities; varicocele grade 2–3; cryptorchidism or its surgery; previous surgery for inguinal hernia, orchidopexy, or any scrotal procedure; abnormal karyotype or Y chromosome microdeletions (Table 4). In our opinion the characteristics of included studies is sufficient to be used in our meta analysis and representing our paper to achieve analytical conclusion.

Table 4. Other characteristics and criteria exclusion of participants each study.

Studies	Type of Infertility	Exclusion of Participants	Alcohol Consumption	Patients Identification	Assessment of infertile
Al-Turki et al. (2014)[17]	Primary and secondary infertility	Patients with azoospermia	Alcohol consumption was controlled	Infertility clinic	History, physical examination, USG, and semen analysis
Anane et al. (2016)[15]	Primary infertility	Patients with varicocele, history of testes injury, occupational exposure and use of pesticides, subjects with a history of chronic urinary tract infection, subjects with disorders such as diabetes mellitus, hypertension and coronary heart diseases.	Not specified	Infertility clinic	History, physical examination, USG, and semen analysis
Brucker et al (2020)[18]	Primary infertility	patients with azoospermia, ex-smokers, history of secondary infertility, alcohol abuse, varicocele/ hydrocele, postvasectomy reconstructive surgery, injury to the testes or chronic diseases (such as diabetes, tuberculosis, hypertension, thyroid disease,chronic urinary tract infection).	Not specified	Infertility clinic	History, physical examination, USG, and semen analysis
Caserta et al.[16] (2012)	Primary infertility	Patients with azoospermia, orchitis or prostatitis, grade 2 or 3 varicocele, undescended testes or its surgery, altered karyotype	Not specified	Infertility clinic	History, physical examination, USG, and assessment of hormonal and semen parameters
Cui et al (2016)[7]	Primary infertility	Cryptorchidism, varicocele, infections, anti-sperm antibodies, chromosomal abnormalities	Not specified	Infertility clinic	history was obtained from each subject to exclude systemic diseases and assess alcohol assumption; careful physical examination was performed, with measurement of testicular size to exclude abnormalities of the external genitalia and cryptorchidism; ultrasonographic examination was performed to exclude varicoceles; microbiological examination and spermioculture were performed to exclude infections; an immunobead binding test was performed to exclude the presence of anti-sperm antibodies; karyotyping was used to exclude any chromosomal abnormality; and genetic examination was performed to exclude Y chromosome microdeletions and cystic fibrosis gene mutations.
Chitta et al. (2016)[19]	Primary infertility	Patients suffering from secondary infertility, Persons with occupation near hot furnace and workers of chemical industries, Persons with history of infections, drug addiction and previous history of operation on genitourinary track	Not specified	Infertility clinic	History, physical examination, USG, and semen analysis
Jain et al. (2015)[20]	Primary infertility	patients with a history of sexual transmitted diseases, surgery for an inguinal hernia, orchidopexy or any scrotal surgery. Male patients with chronic medical illness (renal, liver, hypertension, diabetes mellitus, etc.) and with abnormal genital examination (hydrocele, varicocele, and ectopic testes)	Not specified	Infertility clinic	History, physical examination, USG, and semen analysis
Meri et al. (2013)[4]	Primary infertility	males with abnormal genital examination (varicocele, undefended testicles, hydrocele, small sized testes);males with azospermia; males with history of mumps; d) males with history of surgery for inguinal hernia, orchidopexy, or any scrotal surgery; e) males with chronic medical illness (diabetes mellitus, hypertension, thyroid disease, cancer patients, and tuberculosis; and males who quit smoking for a period of less than 6 months.	No	Infertility clinic	History, physical examination, USG, and semen analysis
Mitra et al. (2012)[8]	Not specified	Pathology of chronic diseases	Not specified	Infertility clinic	History, physical examination, USG, and semen analysis

Studies	Type of Infertility	Exclusion of Participants	Alcohol Consumption	Patients Identification	Assessment of infertile
Mostafa et al[21] (2018)	Primary infertility	patients with a history of recreational drug use (i.e., marijuana use and/or narcotic agents), shisha smoking, chronic alcohol consumption (including social drinking), medication use (affecting male fertility), chronic illnesses or genitourethral surgery, azoospermia, severe oligozoospermia (sperm count less than 5 millions), leukocytospermia, hemospermia, chronic urinary tract infection, older than 45 years of age, obese (BMI ≥30) or who had occupational exposure to chemicals, insecticides or excessive hea	No	Infertility clinic	History, physical examination, USG, and semen analysis
Zhang et al. (2013)[23]	Primary infertility	Azoospermia, excessive alcohol intake, hallucinatory drugs, serious systemic disease, abnormality of the external genitalia, known family genital disorders, infection or trauma to genitals	No	Infertility clinic	History, physical examination, USG, and semen analysis
Zhang et al. (2015)[11]	Not specified	Not specified	Not specified	Infertility clinic	History, physical examination, USG, and semen analysis
Anifandis et al. (2014)	Not specified	Not specified	Subjects were classified into 3 groups based on their alcohol intake: no alcohol users, moderate alcohol users (>0 to <7 units/ week), heavy alcohol users (>7 units/week)	IVF unit	History, physical examination, semen analysis, sperm chromatin dispersion assay
Komiya et al. (2014)	Not specified	Patients who showed a sperm count less than 5 million/mL were excluded.	Subjects were classified into 2 groups: patients with and without chronic alcohol use (the consumption of ≥350 mL of beer per week or a corresponding amount of other alcoholic-containing drinks)	Infertility unit	History taking, physical examinations, conventional semen analysis, computer-assisted semen analysis by the SMAS, high-magnification observation of the sperm heads, and sperm DNA integrity testing during the evaluation for male infertility
Keskin et al. (2016)	Not specified	Patients factors potentially impacting semen parameters, such as systemic illnesses, medication use, a history of inguinal or testicular surgery, varicocele, undescended testicles, small testicle size upon physical examination, abnormalities in serum gonadotropin, androgen, and prolactin levels, as well as genetic analysis-related issues; patients with a cigarette use history of 1 package-year or more and those who had never smoked; patients with alcohol consumption rates exceeding 1 unit every 3 months and those who abstained from alcohol. Excluded were patients with alcohol use rates less than 1 unit every 3 months.	Patients were divided into 5 groups according to alcohol use: patients who do not use alcohol were determined as group 0 (control), patients who use alcohol 1 unit/3 months were determined as group 1; patients who use alcohol 1 unit/ month were determined as group 2; patients who use alcohol 1 unit/ week were determined as group 3 (n = 3); patients who use alcohol 1 unit/day were determined as group 4 (n = 19)	Hospital urology polyclinic	History taking, physical examinations, semen analysis

Oligozoospermia in smokers

Table 5 shows that the above three studies' results of oligozoospermia are significantly higher in smokers than non-smokers, with a p-value <0,05. The meta-analysis using the random effects model demonstrated a notably elevated risk of oligozoospermia among smokers compared to non-smokers, with an odds ratio (OR) of 1.86 [1.27, 2.71], as depicted in Fig. 2. Notably, the overall dataset exhibited homogeneity.

Teratozoospermia in smokers

As shown in Table 5, teratozoospermia is significantly higher in smokers than non-smoker in a study by Anane et al. (2016) and Mitra et al. (2012). In the study Caserta et al. (2013) there were no significant differences among the smokers and non-smokers (Caserta et al. 2013; Asare et al. 2016; Mitra et al. 2012) The analysis using the random effects model unveiled a notably increased risk of teratozoospermia among smokers compared to non-smokers, with an odds ratio (OR) of 1.95 [1.29, 2.95], as illustrated in Fig. 3. Nonetheless, the I2 value of 74% suggested substantial heterogeneity across the studies.

Table 5. Percentage of Oligozoospermia, Teratozoospermia, Asthenozoospermia in patient smoker and non-smokers.

Oligozoospermia			
Study	**Smokers (%)**	**Non- smokers (%)**	**p-value**
Anane et al. (2016)	27.8	11.1	0.00047
Caserta et al. (2012)	34 (17%)	45 (10.3%)	0.02
Mitra et al. (2013)	22 (12.36%)	11 (8.73%)	0.000
Teratozoospermia			
Study	**Smokers (%)**	**Non- smokers (%)**	**p-value**
Anane et al. (2016)	76.0	39.8	0.0003
Caserta et al. (2012)	7 (3.5%)	9 (2%)	0.26
Mitra et al. (2013)	40 (22.47%)	24 (19.05%)	0.000
Asthenozoospermia			
Study	**Smokers (%)**	**Non- smokers (%)**	**p value**
Anane et al. (2016)	57.4	24.4	0.0010
Caserta et al. (2012)	99 (49.5%)	194 (43.3%)	0.14
Mitra et al. (2013)	15 (8.4%)	5 (3.96%)	0.000

Asthenozoospermia in smokers

Results of the three studies show that asthenozoospermia in smokers is higher than in non-smokers, but the p-value in a

study by Caserta et al. (2013) showed no statistically significant difference (p>0,050) (Caserta et al. 2015). The analysis using the random effects model uncovered a significantly elevated risk of asthenozoospermia among smokers compared to non-smokers, with an odds ratio (OR) of 1.58 [1.18, 2.13], as depicted in Fig. 4. Nevertheless, the I2 value of 75% signified substantial heterogeneity among the studies.

Morphology defect of spermatozoa in smokers

Table 6 showed that the morphology defect of spermatozoa was increased in patients who were smokers. Our analysis using the random effects model revealed that smokers demonstrated slightly higher mean differences in head defects, with a mean difference of 2.66 [0.57, 4.74], neck defects with a mean difference of 1.95 [0.46, 3.45], and tail defects with a mean difference of 1.30 [0.28, 2.32], as shown in Figs 5–7. Nonetheless, the I^2 values indicated significant heterogeneity among the studies.

Male reproductive hormones in smokers

The above studies in Table 7, showed the relationship of smoking with male hormone levels. Our meta-analysis revealed that there were decreased testosterone levels in smoking patients, albeit insignificantly, with a mean difference of -9.60 [-42.55, 23.36] and a moderate heterogeneity as seen in Fig. 8. Although insignificantly, the FSH and LH levels were increased in smoker patients with mean differences of 0.35 [-1.20, 1.89] and 0.27 [0.05, 0.48], respectively. However, a study by Al-Turki et al. (2015) showed that smoking significantly reduced LH levels (p-value = 0.04). As shown in Figs 9, 10.

Table 6. Morphology defect of spermatozoa.

Abnormal form			
Study	**Smokers (%)**	**Non- smokers (%)**	**p value**
Jain et al. (2012)	72 ± 7.51	56 ± 6.45	0.001
Meri et al (2013)	73.0%	69.7%	<0.005
Head defect			
Study	**Smokers (%)**	**Non- smokers (%)**	**p value**
Cui et al. (2016)	88.38 ± 15.11	82.5 ± 11.66	>0.05
Mitra et al. (2013)	16.3%	9.52%	0.000
Zhang et al. (2013)	88.32 ± 4.3	87.81 ± 3.78	0.016
Keskin et al. (2016)	44.61 ± 3.02	42.50 ± 3.05	>0.05
Neck defect			
Study	**Smokers (%)**	**Non- smokers (%)**	**p value**
Cui et al. (2016)	49.32 ± 14.43	41.38 ± 8.58	>0.05
Zhang et al. (2013)	2.15 ± 2.02	2.34 ± 2.29	0.222
Keskin et al. (2016)	4.87 ± 0.36	5.43 ± 0.41	>0.05
Tail defect			
Study	**Smokers (%)**	**Non- smokers (%)**	**p value**
Cui et al. (2016)	11.64 ± 12.77	6.23 ± 7.19	>0.05
Mitra et al. (2013)	8.98%	8.7%	0.000
Zhang et al. (2013)	2.3 ± 2.21	2.24 ± 1.71	0.114
Keskin et al. (2016)	3.54 ± 0.27	3.80 ± 0.31	>0.05

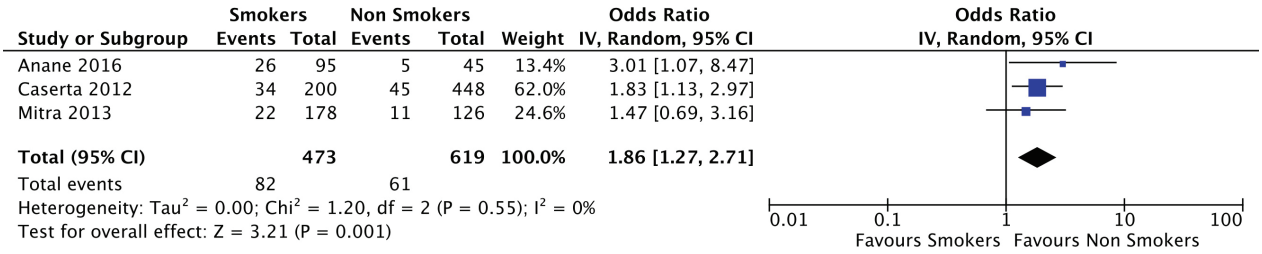

Figure 2. Forest plot oligozoospermia.

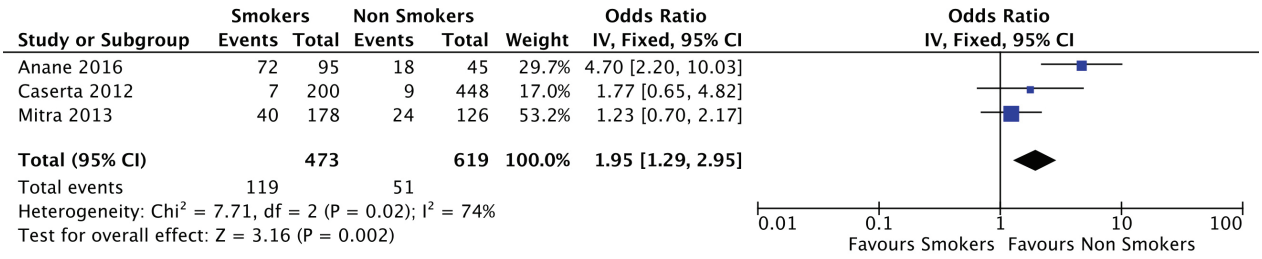

Figure 3. Forest plot teratozoospermia.

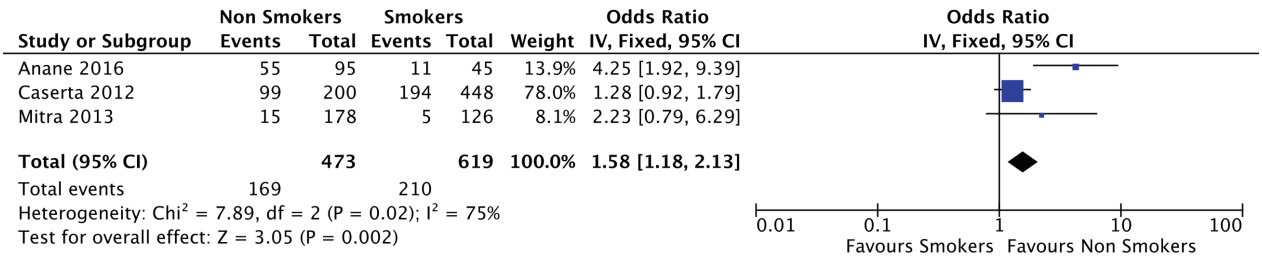

Figure 4. Forest plot asthenozoospermia.

Table 7. Hormon Reproductive Levels in smokers and non-smokers.

Testosterone			
Study	**Smokers**	**Non- smokers**	**p value**
Al-Turki et al. (2015)	383.8 ± 239.5	422.5 ± 139.2	0.009
Brucker et al. (2012)	4.37 ± 1.79	4.25 ± 1.60	>0.05
FSH			
Study	**Smokers**	**Non- smokers**	**p value**
Al-Turki et al. (2016)	5.39 ± 5.32	5.98 ± 5.93	0.34
Brucker et al. (2012)	6.44 ± 6.72	5.43 ± 5.37	<0.001
LH			
Study	**Smokers**	**Non- smokers**	**p value**
Al-Turki et al. (2016)	4.07 ± 4.35	4.77 ± 3.27	0.04
Brucker et al. (2012)	4.90 ± 2.64	4.59 ± 1.60	>0.05

Semen volume in alcoholics

Table 8 presents our exploration of the connection between alcohol consumption and a range of semen parameters. In our comprehensive meta-analysis, we determined that the link between alcohol use and semen volume was statistically inconclusive, as indicated by a mean difference of -0.24 [-0.80, 0.32] (Fig. 11). Anifandis et al. (2014) established that alcohol significantly influenced the overall semen quality, notably the percentage of spermatozoa with small halos ($r = 0.21$, $p < 0.05$). They also detected a correlation between smoking and alcohol use ($r = 0.16$, $p < 0.05$), hinting at a tendency to combine these behaviors

Sperm concentration in alcoholics

Our meta-analysis found that alcohol use was insignificantly related to a decrease in sperm concentration with a mean difference of -2.51 [-3.86, -1.15] (Fig. 12). Keskin et al. (Keskin et al. 2016) observed that there were no statistically significant differences in any of the parameters (including volume, concentration, total motility, progressive motility, normal morphology, head anomaly, neck anomaly, tail anomaly) among various groups of patients with varying amounts of alcohol consumption compared to a control group consisting of patients who did not use alcohol.

Sperm DNA fragmentation in alcoholics

Komiya et al. (2014) found that alcohol consumption was related to increased sperm DNA fragmentation (Table 8). However, our meta-analysis revealed that the relationship between alcohol use and increased Sperm DNA fragmentation was insignificant. Komiya et al. (2014) discovered that the SDFI was linked to diminished semen quality, assessed through traditional semen parameters, computer-assisted semen analysis of sperm motility characteristics, serum FSH levels, and the habit of chronic alcohol consumption. A multivariate linear regression analysis pinpointed sperm progressive motility ($P = 0.0008$) and chronic alcohol use ($P = 0.0394$) as the prominent predictive factors for sperm DNA fragmentation. Anifandis et al. (2014) highlighted that those labeled "no smokers and no alcoholics" had notably lower sperm DNA fragmentation (SDF) values (35.23% ± 1.52, n = 73) than the "smokers (moderate and heavy) and alcohol consumers (moderate and heavy)" group, which had higher SDF percentages (38.21% ± 1.56, n = 60) ($p < 0.05$). Comparing sperm volume and the percentage of degenerated spermatozoa between these groups revealed significant disparities (3.75 ± 0.1 vs. 2.94 ± 0.1 ml, $p < 0.05$ and 12.11% ± 0.8 vs. 14.67% ± 0.9, $p < 0.05$, respectively). As shown in Fig. 13. Thus in overall result from our analytical study revealed that alcohol consumption does not correlate to sperm DNA fragmentation.

Table 8. Semen parameters in alcoholics and non-alcoholics.

Volume			
Study	**Alcoholics**	**Non-alcoholics**	**p value**
Anifandis et al. (2014)	3.07 ± 0.19	3.57 ± 0.1	<0.05
Keskin et al. (2016)	3.016 ± 1.59	2.94 ± 1.51	>0.05
Concentration			
Study	**Alcoholics**	**Non-alcoholics**	**p value**
Anifandis et al. (2014)	37.63 ± 5.77	40.06 ± 3.4	>0.05
Keskin et al. (2016)	32.56 ± 31.84	37.51 ± 38.68	>0.05
Sperm DNA Fragmentation			
Study	**Alcoholics**	**Non-alcoholics**	**p value**
Anifandis et al. (2014)	38.13 ± 1.97	37.51 ± 1.1	>0.05
Komiya et al. (2014)	49.6 ± 23.3	33.9 ± 18.0	0.0084

Discussion

Infertility can be influenced by a multitude of factors, encompassing congenital or acquired anomalies in the urogenital system, urogenital tract infections, conditions raising scrotal temperature (such as varicocele), endocrine irregularities, genetic variations, immunological aspects, and lifestyle choices. Interestingly, in 30–40% of instances, the cause of male infertility remains unidentified, termed idiopathic male infertility (Bundhun et al. 2019). Nevertheless, semen analysis may uncover irregularities in the spermogram. Various lifestyle elements, including occupational, environmental, and behavioral factors such as tobacco use and alcohol consumption, have been recognized as potential contributors to male infertility.(Meri et al. 2013)

We found that conventional semen parameters were adversely affected by tobacco smoking. Smokers had a significantly higher prevalence of oligozoospermia, teratozoospermia, and asthenozoospermia than non-smokers. This is consistent with the study by Anane et al. (2016), who reported that the proportions of oligozoospermia (27.8% vs 11.1%, $p = 0.00047$) and teratozoospermia (76.0% vs 39.8%, $p = 0.0010$) were higher in smokers than non-smokers. Tobacco smoking also impaired sperm motility (asthenozoospermia) and we observed a significant difference between the two groups. A previous meta-analysis by Bundhun et al. (2019) showed a similar effect of tobacco smoking on oligozoospermia (RR: 1.29, 95% CI: 1.05–1.59; $p = 0.02$), but not on teratozoospermia (RR: 1.22, 95% CI: 0.96–1.56; $P = 0.10$) or asthenozoospermia (RR: 1.42, 95% CI: 0.97–2.09; $p = 0.07$).

Smoking can affect the morphology of spermatozoa, causing defects in the head, neck, and tail regions. In this study, smokers had significantly higher head defects with a mean difference of 2.66 [0.57, 4.74], neck defects with a mean difference of 1.95 [0.46, 3.45], and tail defects with

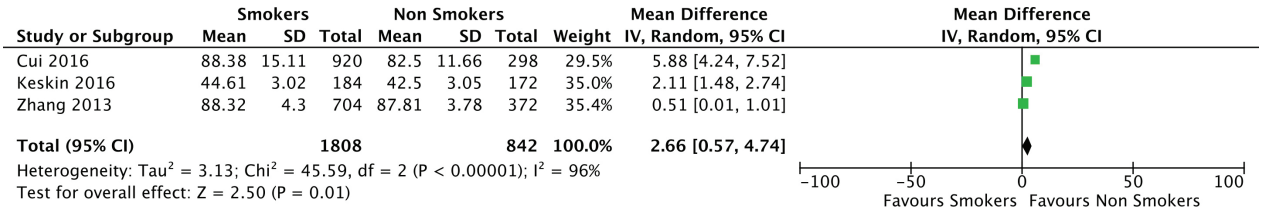

Figure 5. Forest plot head defect.

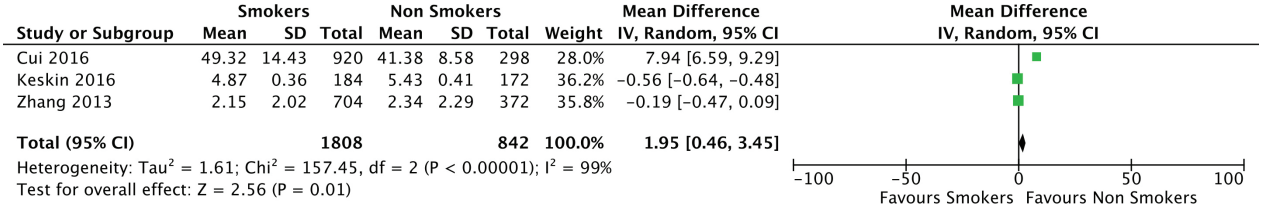

Figure 6. Forest plot neck defect.

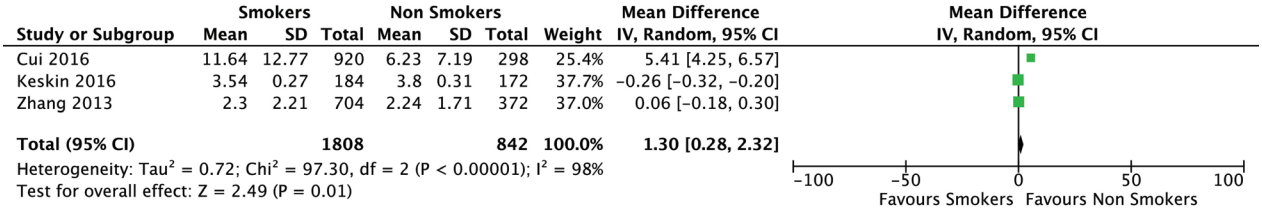

Figure 7. Forest plot tail defect.

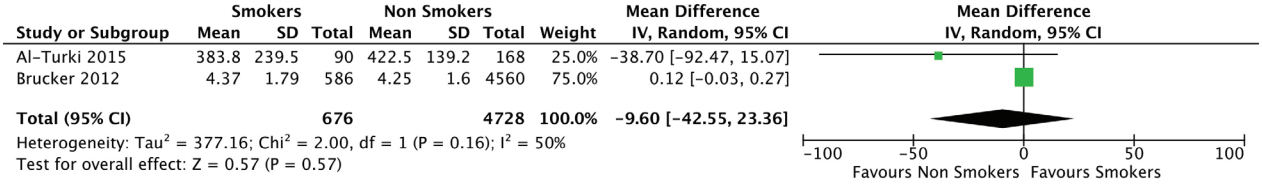

Figure 8. Forest plot testosterone.

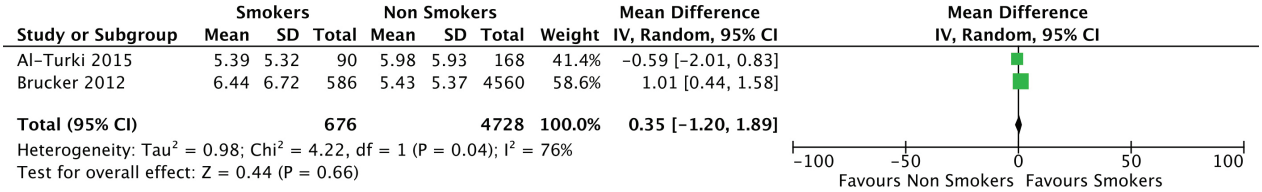

Figure 9. Forest plot FSH.

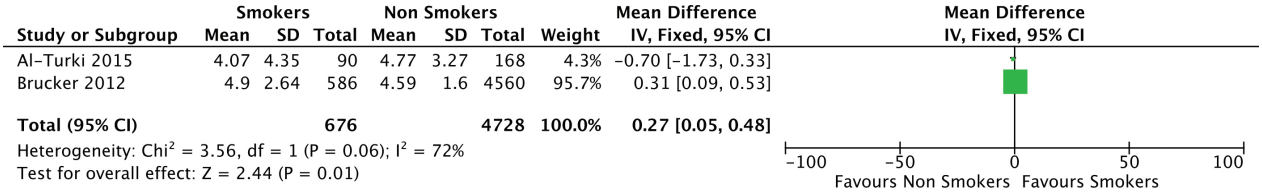

Figure 10. Forest plot LH.

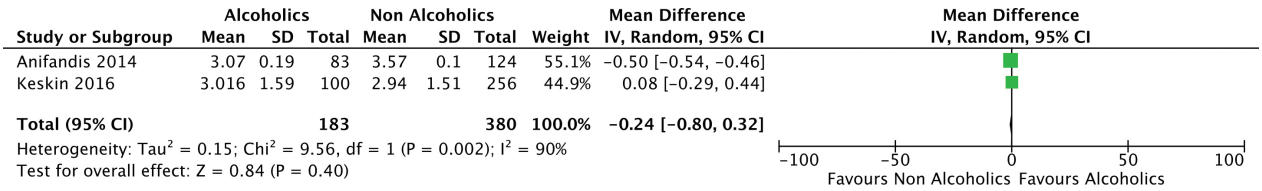

Figure 11. Forest plot volume.

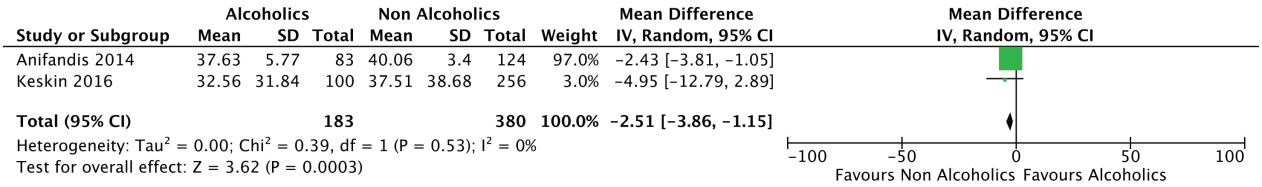

Figure 12. Forest plot concentration.

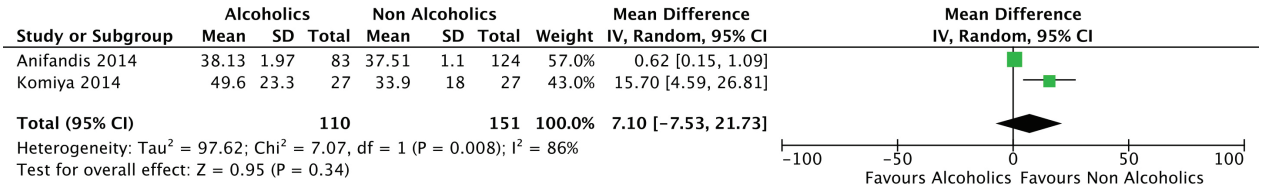

Figure 13. Forest plot sperm DNA fragmentation.

a mean difference of 1.30 [0.28, 2.32] than non-smokers. Bundhun et al. (2019) also found significant increases there is a significant difference of 2.44 (with a 95% confidence interval between 0.99 and 3.89) when comparing smokers to non-smokers. This difference is observed in various aspects of sperm morphology, including the head (with a mean difference of 1.76 and a 95% confidence interval between 0.32 and 3.20, with a significance level of p = 0.02), the neck (with a mean difference of 1.97 and a 95% confidence interval between 0.75 and 3.18, with a significance level of p = 0.002), and the tail (with a mean difference of 1.29 and a 95% confidence interval between 0.35 and 2.22, with a significance level of p = 0.007), when comparing smokers and non-smokers.(Bundhun et al. 2019) The association between smoking and sex-hormone-binding globulin was not independent, as Wang et al. demonstrated, and the number of cigarette packets correlated with sex-hormone binding globulin. A Taiwanese study also found no significant difference in LH and FSH levels among smokers and non-smokers (Bundhun et al. 2019).

How smoking affects semen parameters is not fully elucidated, but cigarette-derived chemical compounds have detrimental effects on the maturation of male germ cells, Leydig cells, and Sertoli cells. Nicotine adversely affected sperm morphology and sperm count, and seminal cotinine impaired sperm motility (Sharma et al. 2016). The reduced sperm volume observed in heavy smokers could be attributed to the disruption of the hypothalamus–pituitary–gonadal axis due to heightened nicotine levels and other harmful substances present in cigarettes, or potentially due to an escalated apoptotic process during spermatogenesis. Although the precise mechanisms underlying the detrimental effects of smoking on semen parameters remain partially elusive, a plausible explanation lies in the direct toxic influence of accumulated nicotine (or other chemical constituents) on the epithelium of the male germ line. (Harlev et al. 2015) Cigarette smoke can mutate and damage cells, and some of its components can interfere with the function of male and female gametes prominent constituents like lead, cadmium, nicotine, and benzopyrene have a significant impact on semen characteristics and sperm functionality. This research has noted a correlation between smoking and diminished sperm concentration and motility. (Mitra et al. 2012 and Sharma et al. 2016) In Fig. 2, potential mechanisms by which smoking influences sperm parameters and overall quality are illustrated. Nicotine predominantly exerts detrimental impacts on male reproductive function by promoting the overproduction of reactive oxygen species (ROS). Smoking leads to irreversible DNA damage in sperm. Additionally, elevated levels of active caspases have been identified within spermatozoa of men experiencing infertility, suggesting that an intensified apoptotic process in spermatozoa contributes to diminished semen motility and an increased proportion of deteriorated spermatozoa post-ejaculation (Komiya et al. 2014). The oxidative effects of nicotine on spermatogenesis damages the membrane structure of the sperm cells, causing reduced motility of sperm. Another possible mechanism is the interference of nicotine with the nicotinic acetylcholine receptor of sperm cells, which affects the intracellular Ca+2 dynamics and reduces motility (Mitra et al. 2012 and Harlev et al. 2015). Smoking may also impair motility by altering the expression of eight nAChR subunits and different proteins (Aldoa, ATP5a1, Gpx4, Cs) in human sperm cells, causing smoking-related sperm damage. Moreover, smoking may decrease the activity of Ca2+ ATPase in sperm cells, which is involved in motility regulation. Creatine kinase is an enzyme that provides energy for cells with high energy demand, such as sperm cells. It participates in the metabolism of adenosine triphosphate (ATP) and adenosine diphosphate. Ghaffari and Rostami et al. found that smoking reduced creatine kinase activity in sperm cells, which affected sperm motility and fertility (Harlev et al. 2015).

Smokers had low-quality sperm shape in the study. Heavy metals in cigarettes lead to high levels of oxidative stress. This can damage the membrane and cause shape defects. Heavy metals can also harm DNA during sperm formation, which can affect the normal development of sperm structure. Previous studies found that DNA damage was higher in regular smokers. Previous studies also have shown that heavy metals can cause DNA damage and prevent DNA repair. When DNA is damaged, the Chk1 is activated and stops or delays the cell cycle at S and G2 phases, and it may help the cells survive when agents damage DNA. The Chk1 activates other

molecules to start a cellular response that involves changing gene expression, energy use, cell cycle or DNA repair, or killing the cell if the damage is too much to fix (Mitra et al. 2012; Harlev et al. 2015; Cui et al. 2016).

One of the sources of reactive oxygen species (ROS) such as hydroxyl radical (HO), superoxide radical (O_2), or hydrogen peroxide (H_2O_2) is cigarette smoke, which contains heavy metals like lead and cadmium. When the ROS levels surpass the antioxidant capacity of the cells, oxidative stress occurs (18). The sperm membrane and the sperm DNA are susceptible to oxidative stress damage. The seminal plasma may have low antioxidant levels or high oxidant levels from the smoke, resulting in oxidative stress. Additionally, smoking may cause inflammation in the male genital tract, which can generate more ROS from leukocytes. (Harlev et al. 2015)

A positive association between tobacco smoking and seminal OS markers has been demonstrated, as evidenced by a significant rise in ROS levels and reduced ROS-TAC values. Spermatozoa are especially vulnerable to excessive ROS-induced damage due to the high amount of polyunsaturated fatty acids in the plasma membrane that are targets for ROS and the low amounts of scavenging enzymes in their cytoplasm. The sources of heightened levels of reactive oxygen species (ROS) in the seminal fluid of smokers can originate from either internal or external sources. External factors like smoking, alcohol consumption, and exposure to air pollutants represent the external origins of ROS, while the primary internal sources of ROS are white blood cells, specifically neutrophils and macrophages, along with contributions from immature spermatozoa (Harlev et al. 2015).

This study also investigates FSH, LH, and testosterone levels in patients with infertility due to tobacco smoking. The result shows that the testosterone level lower in smokers than non-smokers, while the FSH and LH levels are higher in smokers than non-smokers, albeit insignificantly. Bundhun et al. (1) reported no significant differences in the levels of testosterone (MD: 0.18, 95% CI: -1.26 – 1.63; P = 0.80), LH (MD: 0.18, 95% CI: -0.47 – 0.83; P = 0.58), or FSH (MD: 0.12, 95% CI: -0.41 – 0.64; P = 0.66) among smokers and non-smokers. This contrasts with the study conducted by Mitra et al. (2012). The study revealed that FSH, LH, and testosterone levels were higher, lower, and lower respectively with increased smoking. This conflicts with earlier research that identified positive links between smoking and testosterone and LH levels, along with elevated LH/free testosterone ratios associated with heightened smoking or increased smoking and testosterone. Nicotine, a toxic substance in cigarette smoke, may be responsible for the reduced testosterone in heavy smokers by impairing androgen production and Leydig-cell development. Primary testicular failure, a condition where the testes' seminiferous tubules are damaged and cannot produce sperm normally, is usually indicated by a high FSH level (Mitra et al. 2012 and Harlev et al. 2015).

Some articles in this study investigate infertility with the total number of cigarettes smoked daily and the number of years of smoking. The study conducted by Cui et al. (2016) showed that progressive motility of the sperm is significantly decreased in moderate and heavy smokers than non-smokers. No association was found between male infertility and the duration or chronicity of smoking in other investigations (Bundhun et al. 2019).

Our study also found the complexity in alcohol's impact on sperm. Anifandis et al. (2014) identified a positive association between alcohol intake and sperm abnormalities, emphasizing the importance of moderation when it comes to alcohol consumption. Komiya et al. (2014) research delved into the detrimental effects of chronic alcohol use on sperm DNA fragmentation. Their results demonstrated that continuous alcohol consumption could increase Sperm DNA Fragmentation Index (SDFI), contributing to compromised semen quality. This highlights the need for individuals, particularly those of reproductive age, to be aware of the potential consequences of heavy alcohol consumption on their fertility. These findings are in line with the study conducted by Joo et al. (Joo et al. 2012), which found that individuals with high alcohol consumption had fewer morphologically normal sperm cells than those with moderate alcohol consumption. Moderate and high alcohol consumption were associated with fewer normally shaped nuclei compared to very low alcohol consumption. Furthermore, the low alcohol consumption group had fewer sperm cells with normal plasma membranes than the very low alcohol group ($p < 0.05$). On the other hand, Keskin et al. (2016) found no substantial differences in semen parameters among groups with varying alcohol consumption levels when compared to a control group of non-drinkers. This suggests that moderate alcohol use may not have a significant impact on semen quality, although it's crucial to remember that individual factors can vary. Additionally, it has been observed to cause damage to sperm morphology, particularly in the sperm head. Hence, it can be observed that there exists a positive correlation between the amount of alcohol use and the decline in sperm quality. The impact of both moderate and heavy smoking on spermmotility is evident, leading to a decline in sperm quality (Amor et al. 2022).

While reversible changes in morphology may occur, heavy alcohol use is associated with decreased sperm volume and concentration. (Boeri et al. 2019) Even short-term alcohol consumption can impact semen quality due to the hormonal imbalance affecting the reproductive axis. Some studies found no impact on sperm parameters, but chronic alcohol consumption may increase DNA fragmentation and apoptosis. Apart from differences in sperm volume (between moderate and non-alcohol consumers) and the percentage of small halos (between heavy and moderate alcohol consumers), no other significant distinctions were identified among the groups. Variations in sperm volume could relate to hypo-testosteronemia in heavy alcohol users. Elevated alcohol consumption may promote apoptosis during spermatogenesis.(Anifandis et al. 2014; Keskin et al. 2016; Joo et al. 2012).

Combining smoking and alcohol amplifies their negative impact on sperm parameters. Despite separate actions, substantial DNA fragmentation differences were seen. Reduced semen volume in combined users points to synergistic impact.

The mechanisms remain unclear, but the study by Anifandis et al.(2014) suggests that alcohol may hinder the reproductive axis, impacting LH and FSH secretion, while smoking may trigger apoptosis. These results align with Martini et al.'s observations, indicating that dual exposure of tobacco smoking and alcohol consumption impairs sperm quality, especially the sperm's volume and concentration. (Martini et al. 2004). We believe our study would be very beneficial for the importance of other proffesional practices and education purposes as it clearly highlight the relevances of smoking and alcohol consumption in the impact of sperm quality.

Conclusion

On average, smoking has a detrimental impact on conventional semen characteristics. Increased risk of oligozoospermia, teratozoospermia, asthenozoospermia, and sperm morphological defects were all linked to tobacco use. Alcohol consumption may harm the sperm's quality. Combining smoking and alcohol amplifies their negative impact on sperm parameters. Due to the harmful effects of both factors, men seeking reproduction should be advised to avoid these habits.

References

Al-Turki HA (2015) Effect of smoking on reproductive hormones and semen parameters of infertile Saudi Arabians. Urology Annals 7(1): 63–66. https://doi.org/10.4103/0974-7796.148621

Amor H, Hammadeh ME, Mohd I, Jankowski PM (2022) Impact of heavy alcohol consumption and cigarette smoking on sperm DNA integrity. Andrologia 54(7): e14434. https://doi.org/10.1111/and.14434

Anifandis G, Bounartzi T, Messini CI, Dafopoulos K, Sotiriou S, Messinis IE (2014) The impact of cigarette smoking and alcohol consumption on sperm parameters and sperm DNA fragmentation (SDF) measured by Halosperm. Archives of Gynecology and Obstetrics 290: 777–782. https://doi.org/10.1007/s00404-014-3281-x

Asare-Anane H, Bannison SB, Ofori EK, Ateko RO, Bawah AT, Amanquah SD, Oppong, Gandau BBN, Ziem JB (2016) Tobacco smoking is associated with decreased semen quality. Reproductive Health 13(1): 90. https://doi.org/10.1186/s12978-016-0207-z

Boeri L, Capogrosso P, Ventimiglia E, Pederzoli F, Cazzaniga W, Chierigo F, Dehò F, Montanari E, Montorsi F, Salonia A (2019) Heavy cigarette smoking and alcohol consumption are associated with impaired sperm parameters in primary infertile men. Asian Journal of Andrology 21(5): 478–485. https://doi.org/10.4103/aja.aja_110_18

Bundhun PK, Janoo G, Bhurtu A, Teeluck AR, Soogund MZS, Pursun M, Huang F (2019) Tobacco smoking and semen quality in infertile males: a systematic review and meta-analysis. BMC Public Health 19(1): 36. https://doi.org/10.1186/s12889-018-6319-3

Caserta D, Bordi G, Di Segni N, D'Ambrosio A, Mallozzi M, Moscarini M (2013) The influence of cigarette smoking on a population of infertile men and women. Archives of Gynecology and Obstetrics 287(4): 813–818. https://doi.org/10.1007/s00404-012-2643-5

Chitta S, Tambe MK, Kherde PM, Aggarwal SS, Nandedkar PDG, Atram G (2016) Effect of cigarette smoking on semen quality parameters in male partners of infertile couple: A cross sectional study. IOSR Journal of Dental and Medical Sciences 15(09): 112–116. https://doi.org/10.9790/0853-150905112116

Cui X, Jing X, Wu X, Wang Z, Li Q (2016) Potential effect of smoking on semen quality through DNA damage and the downregulation of Chk1 in sperm. Molecular Medicine Reports 14(1): 753–761. https://doi.org/10.3892/mmr.2016.5318

Davar R, Sekhavat L, Naserzadeh N (2012) Semen parameters of non-infertile smoker and non-smoker men. Journal of Medicine and Life Science 5(4): 465–468.

Finelli R, Mottola F, Agarwal A(2021) Impact of alcohol consumption on male fertility potential: A narrative review. International Journal of Environmental Research and Public Health 19(1): 328. https://doi.org/10.3390/ijerph19010328

Harlev A, Agarwal A, Gunes SO, Shetty A, du Plessis SS (2015) Smoking and male infertility: An evidence-based review. World Journal of Men's Health 33(3): 143–160. https://doi.org/10.5534/wjmh.2015.33.3.143

JBI (2023) The Joanna Briggs Institute Critical Appraisal tools for use in JBI systematic reviews: checklist for cohort & cross sectional studies. http://joannabriggs.org/research/critical-appraisal-tools.html

Jensen TK, Gottschau M, Madsen JO, Andersson AM, Lassen TH, Skakkebæk NE, Swan SH, Priskorn L, Juul A, Jørgensen N (2014) Habitual alcohol consumption associated with reduced semen quality and changes in reproductive hormones; a cross-sectional study among 1221 young Danish men. BMJ Open 4(9): e005462. https://doi.org/10.1136/bmjopen-2014-005462

Joo KJ, Kwon YW, Myung SC, Kim TH (2012) The effects of smoking and alcohol intake on sperm quality: light and transmission electron microscopy findings. Journal of International Medical Research 40(6): 2327–2335. https://doi.org/10.1177/030006051204000631

Keskin MZ, Budak S, Gubari S, Durmaz K, Yoldas M, Celik O, Aksoy EE, Ilbey YO (2016) Do cigarette and alcohol affect semen analysis?. Archivio Italiano di Urologia e Andrologia 88(1): 56–59. https://doi.org/10.4081/aiua.2016.1.56

Komiya A, Kato T, Kawauchi Y, Watanabe A, Fuse H (2014) Clinical factors associated with sperm DNA fragmentation in male patients with infertility. The Scientific World Journal 2014: 868303. https://doi.org/10.1155/2014/868303

Martini AC, Molina RI, Estofán D, Senestrari D, de Cuneo MF, Ruiz RD (2004) Effects of alcohol and cigarette consumption on human seminal quality. Fertility and Sterility 82(2): 374–377. https://doi.org/10.1016/j.fertnstert.2004.03.022

Meri ZB, Irshid IB, Migdadi M, Irshid AB, Mhanna SA (2013) Does cigarette smoking affect seminal fluid parameters? A comparative study. Oman Medical Journal 28(1): 12. https://doi.org/10.5001/omj.2013.03

Mitra A, Chakraborty B, Mukhopadhay D, Pal M, Mukherjee S, Banerjee S, Chaudhuri K (2012) Effect of smoking on semen quality, FSH, testosterone level, and CAG repeat length in androgen receptor gene of infertile men in an Indian city. Systems Biology in Reproductive Medicine 58(5): 255–262. https://doi.org/10.3109/19396368.2012.684195

Moher D, Liberati A, Tetzlaff J, Altman DG, The PG (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Medicine 6(7): e1000097. https://doi.org/10.1371/journal.pmed.1000097

Mokhtari GR, Esmaeili S, Zeinali Moghaddam MM, Ghanbari A (2020) Effect of cigarette smoking on sperm parameters in men with idiopathic infertility. Journal of the Guilan University of Medical Sciences 29(3): 14–21. https://doi.org/10.32598/JGUMS.29.3.1422.1

Mostafa RM, Nasrallah YS, Hassan MM, Farrag AF, Majzoub A, Agarwal A (2018) The effect of cigarette smoking on human seminal parameters, sperm chromatin structure and condensation. Andrologia 50(3): e12910. https://doi.org/10.1111/and.12910

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372: n71. https://doi.org/10.1136/bmj.n71

Rehman R, Zahid N, Amjad S, Baig M, Gazzaz ZJ (2019) Relationship between smoking habit and sperm parameters among patients attending an infertility clinic. Frontiers in Physiology 10: 1356. https://doi.org/10.3389/fphys.2019.01356

Rowe PJ, Comhaire FH, Hargreave TB, Mahmoud AM (2000) WHO Manual for the Standardized Investigation and Diagnosis of the Infertile Male. Cambridge University Press, 102 pp.

Sharma R, Harlev A, Agarwal A, Esteves SC (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. https://doi.org/10.1016/j.eururo.2016.04.010

Tang Q, Pan F, Wu X, Nichols CE, Wang X, Xia Y, London SJ, Wu W (2019) Semen quality and cigarette smoking in a cohort of healthy fertile men. Environmental Epidemiology 3(4): e055. https://doi.org/10.1097/EE9.0000000000000055

Zhang M, Zhang Q-S, Zheng H-S, Wang X-Y, Feng S-Q, Tian W-J, Fan HT (2016) Clinical, demographic and psychological characteristics of infertile male smokers in Northeast China. Journal of International Medical Research 44(1): 75–80. https://doi.org/10.1177/0300060515606285