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REVIEW

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Environmental and occupational factors and higher risk of couple infertility: a systematic review study

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Abstract

Background: Infertility is a global health problem that represents an increasing trend due to new lifestyles following technological advances since individuals are facing more risk factors than before. The present systematic review study aimed to investigate the impact of environmental and occupational factors on reproductive parameters and increased risk of couple infertility.

Main body: Scopus, PubMed, SID, and Web of Science databases were searched for the available observational (i.e., cohort, case-control, and cross-sectional) systematic review, meta-analysis, and clinical trial studies between 2007 and 2019. To this end, keywords such as 'Environmental exposure', 'Occupational exposure', 'Environmental pollutants', 'Environmental pollution', 'Couple infertility', 'Sterility', and 'Sub-fertility' were used. The retrieved investigations examined the impact of environmental and occupational risk factors on reproductive indices and increased infertility risk. Totally, 66 out of 9519 papers were evaluated after considering the inclusion and exclusion criteria. The reported risk factors in the reviewed studies were heavy metals, cigarette smoking, and exposure to chemicals through consumer goods, urban life, and proximity to main roads. In addition, occupational factors included heavy physical activity, prolonged sitting, exposure to a hot environment, contact with formaldehyde, pesticides, insecticides, mechanical vibration, and contact with ionizing radiation, all of which affected the reproductive parameters. However, some researchers found no significant associations in this regard.

Short conclusion: In general, individuals with known impairments in reproductive parameters were more exposed to risk factors. Nonetheless, more studies are needed to determine the risk of infertility in the population.

Keywords: Environmental pollution, Environmental exposure, Occupational exposure, Environmental pollutants, Couple infertility, Sterility, Subfertility

Background

Infertility is a common health problem in today's world and is defined as the failure to become pregnant after at least 12 months of regular and unprotected intercourse [1]. The existing reports indicate an infertility prevalence of 9–18% in the general population, so approximately 48.5 million couples experience this problem worldwide [2, 3]. According to Kazemijaliseh et al., the prevalence of infertility in Iran was higher than that at the global level [4].

The impact of environmental and occupational factors on reproductive health cannot be ignored due to the modernization of life and societies. Some studies reported the effect of occupational hazards, including the methods of pest control by agricultural pesticides [5], heat stress [6], prolonged sitting, and long working hours [7] on the rate of preterm birth and low birth weight [8], spontaneous abortion [9], and menstrual disorders [7].

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Limitless waste, use of fossil fuels, deforestation, air pollution [10], the release of hazardous gases from car exhausts and factories [11], and consumption of fast foods along with excessive consumption of canned foods [12] can be a danger alarm for couples by lowering the semen quality [13], hormonal changes, endocrine disruptions, and depletion of ovarian reserves [14]. Infertility has increased due to new lifestyles because today's people are at a higher risk compared to the people in the past [12].

Giaccio et al. found that environmental exposure to heavy metals was correlated with the poor quality of human semen [15]. Chemicals such as bisphenol A and phthalates can endanger reproductive health although their impact on the prevalence of infertility requires further discussion [16, 17]. Further, researchers reported that exposure to phthalates is associated with decreased sperm concentration, number, and motility [18].

Occupational factors also increase infertility, especially male infertility. Government jobs are an example. The high prevalence of abnormal semen in government employees can be due to their long hours of sitting or standing [19, 20]. In a study by Chia et al., the prevalence of abnormal sperm disorders such as asthenospermia and teratosthenospermia in government employees was higher compared to that in other occupations. Self-employed, driving, simple, and industrial workers had the most abnormal semen parameters after employee jobs. Lower-quality semen was found in simple and industrial workers, which may be due to prolonged standing, more contact with pollutants and environmental toxins, and the use of various paints and industrial coatings [21]. In a study conducted on urban people, the level of asthenospermia and asthenotratospermia was higher than that of other sperm disorders. This is probably due to the fact that the effects of environmental pollutants and polluted air as well as the density of factories are higher in the city, justifying the further reduction of the sperm quality in these areas [22]. Owing to the increasing prevalence of infertility in the world, it is essential to identify its causes in order to help infertile couples. Various studies reported that several factors cause infertility, including environmental and occupational factors. Accordingly, the present systematic review study sought to evaluate the impacts of environmental and occupational factors on the increased risk of infertility.

Main text

Search strategy

In the present study, PubMed, SID, Scopus, and Web of Science databases were searched to access related papers using the keywords of 'Environmental exposure' OR 'Environmental pollutants' OR 'Occupational exposure' OR 'Environmental pollution' AND 'Couple infertility' OR 'Sterility' OR 'Subfertility' as well as their Persian equivalents. Totally, 6825 studies were extracted using the advanced search features in the initial review. The titles and abstracts were then examined to determine the extent to which they met the inclusion criteria.

Inclusion criteria

The inclusion criteria were observational (i.e., cohort, cross-sectional, and case-control) systematic review, meta-analysis, and clinical trial studies examining the impact of environmental and occupational factors on reproductive parameters and the increased risk of infertility, access to full texts of studies, and papers published in Persian and English between 2007 and January 2019.

Extract data related to exposure

All the studies related to environmental and occupational factors affecting infertility were collected, and a list of abstracts of the articles was prepared after completing the search. At this point, all articles using the selected keywords in their titles were added to the initial list while removing other articles that examined other issues related to infertility. Then, a checklist of the necessary information for the study was provided, including the name of the researcher, the title of the article, the year and place of the study, the sample selection method, the number of samples, and the type of study in the subgroups, followed by reviewing the final checklist. The articles were separately evaluated by two reviewers (SZM and SA). Further, in cases of disagreement, the opinion of a third party (FK) was taken into account. Finally, articles related to the title of the study were reviewed to find the required data, and a total of 5842 papers that were not related to the topic of the study were excluded from this review, and 983 studies that were related to the topic of the present study remained. Among these, 283 studies were duplicates (studies published by one author on several databases), and 634 animal studies were excluded from the study. In line with research objectives, 66 papers met the inclusion criteria, and their full texts were obtained from the databases (Fig. 1).

Quality evaluation

The quality of observational studies was investigated based on the Newcastle and Ottawa [23] checklist, which examines the selection, comparison, and consequence items for evaluating the quality of studies (i.e., cohort, case-control, and cross-sectional types). This checklist includes items for investigating six sections: title and abstract, introduction, method, results, discussion, and other information. Accordingly, the studies were divided into good, medium, and poor-quality

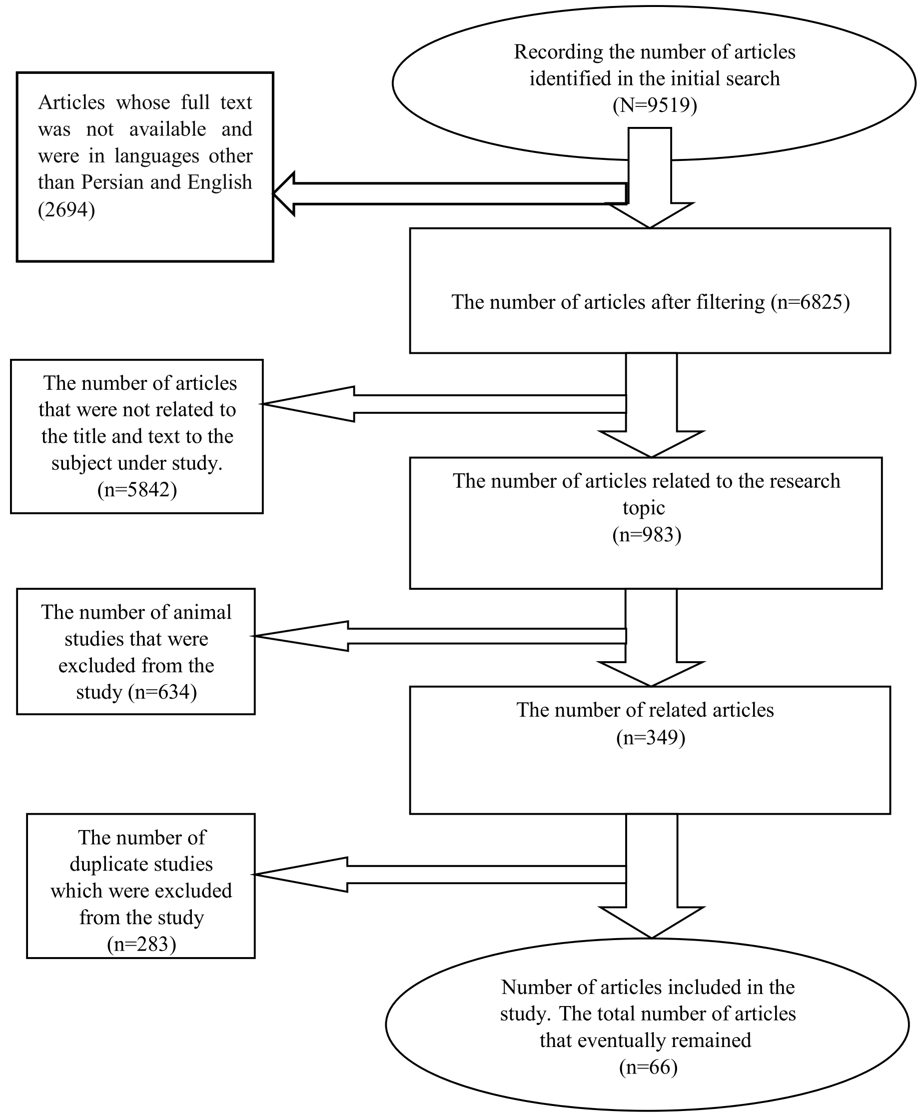

Fig. 1 Flowchart of the paper selection process

groups. Good quality studies included three or four stars in the selection section, one or two star(s) in the comparison, and two or three stars in the consequence. Medium-quality studies had two stars in the selection, one or two star(s) in the comparison, and two or three stars in the consequence. Finally, poor-quality studies were those receiving zero or one star in the selection, zero star in the comparison, and zero or one star in the consequence. Additionally, the quality of systematic review and meta-analysis studies [24] was evaluated based on the AMSTAR checklist. It contains 16 items related to the content of one systematic review and meta-analysis, consisting of the title, abstract, introduction, methods, results, discussion, and funding. Furthermore, the quality of the clinical trial study was evaluated according to Juni's study [25].

Results

In the present study, 66 papers met the inclusion criteria, the findings of which are presented in Tables 1, 2, and 3.

Some studies compared living conditions and the prevalence of risk factors in two groups of fertile and infertile individuals. Other studies focused on the role of environmental and occupational factors in reproductive ability through in vitro examinations. The present study investigated the impacts of heavy metals, cigarette smoking, exposure to chemicals through consumer goods, urban living, and proximity to main roads on reproductive

Table 1 Papers assessing the impact of various conditions on reproductive and infertility indices

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
Chemicals and environmental pollutants	Kumar et al. (2014) [26]	Cross-sectional	Questionnaire-Measurement	240 men (India)	Exposure to environmental toxins (cigarette smoke, pesticides) increases infertility in men by affecting the spermatogenesis, hormonal balance, semen quality, and oxidative stress. The occurrence of asthenozoospermia and azoospermia was significantly ($P<0.05$) higher among the exposed subjects as compared to the non-exposed subjects. Total progressive motility ($P<0.05$) and percentage of normal morphology ($P<0.001$) were significantly lower among chewers in comparison to non-chewers among the oligozoospermic subjects.
	Ji et al. (2013) [27]	Cross-sectional	Questionnaire-Measurement	433 men (China)	Environmental pollutants including aromatic hydrocarbons are associated with decreased sperm concentration, motility and count by creating covalent bonding with sperm DNA and damage to it. Compared with men who had the lowest sperm PAH-DNA adducts category, men with the highest sperm PAH-DNA adducts level had a suggestive decline in sperm concentration, sperm count, sperm motility, and VCL. Trend *P* values of sperm concentration, sperm count, sperm motility, and curvilinear velocity were <0.001, <0.001, 0.004, and <0.001, respectively
	Jurewicz et al. (2013) [28]	Cross-sectional	Interview- Measurement-	277 men (Poland)	Contact with aromatic hydrocarbon metabolites was associated with reduced semen volume and a low percentage of motile sperm. ($P = 0.014$, $P = 0.0001$, respectively)

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Petersen et al. (2015) [29]	Cross-sectional	Questionnaire-Measurement Physical examination	266 fertile men (Denmark)	Environmental chemicals like polychlorinatedbiphenyls may adversely affect fertility by increasing the ratio of androgen to estrogen (P=0.04) but their serum levels are not correlated with semen quality.
	Vestergaard et al. (2012) [30]	Prospective cohort	Questionnaire-Measurement	222 women (Denmark)	The entry of perfluorinated compounds into the body through foods and drinking water can have a negative impact on the reproduction and length of time to become pregnant. Odds ratio for a longer time to pregnancy>6 cycles for those with PFC concentrations above the median were 0.96 [95% confidence interval (CI): 0.54–1.64] for perfluorooctane sulfonic acid (PFOS).
	Xia et al. (2009) [31]	Case-control	Questionnaire-Measurement-Physical examination	513 idiopathic infertile male subjects and 273 fertile males as controls (China)	Urinary concentrations of aromatic hydrocarbon metabolites in men with idiopathic infertility were higher than the control group. 1-hydroxypyrene and 2-hydroxyfluorene and Sum PAH metabolites (polycyclic aromatic hydrocarbons): (P value for trend = 0.034, 0.022, and 0.022, respectively). Exposure to polycyclic aromatic hydrocarbons in the environment may increase the risk of infertility in men.
	Gennings et al. (2013) [32]	Cohort	Questionnaire-Measurement	289 daughters (Oakland, California area)	Exposure to environmental Polychlorinated biphenyl pollutants is associated with increased time needed to become pregnant. (average weight, 89%)
	Nishihama et al. (2017) [33]	Cross-sectional	Questionnaire-Measurement	($n = 42$) (Tokyo)	Exposure to paraben chemicals does not affect semen quality.

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Du et al. (2018) [34]	Retrospective cohort	Questionnaire-Measurement	415 women (China)	There was an insufficient correlation between the urinary concentration of phthalate and the level of anti-Mullerian hormone. However, exposure to phthalate was associated with reduced antral follicle growth. Further studies should be conducted to investigate its effect on ovarian function and fertility.
	Meeker et al. (2008) [35]	Cross-sectional	Questionnaire-Measurement	207 men (Massachusetts)	Contact with pyrethroid insecticides is associated with lower quality of semen (concentration, motility, and morphology) and damage to sperm DNA and may threaten reproductive health.
	Velez et al. (2015) [36]	Cohort	Questionnaire-Measurement	1743 (Canada)	The cumulative probabilities of pregnancy at 1, 6, and 12 months were 0.42 (95% confidence interval (CI) 0.40–0.45), 0.81 (95% CI 0.79–0.83), and 0.90 (95% CI 0.89–0.92), respectively. Increased serum levels of Perfluorinated compounds is associated with a decline in women's ability to become pregnant.
	Yang et al. (2008) [37]	Cohort study	Questionnaire- Interview- Measurement	412 women (Taiwan)	Contact with polychlorinated biphenyls and dibenzofurans is associated with the prolongation of time needed to become pregnant. the infertility odds ratio was 2.34 (95% CI, 1.23–4.59) for Yucheng women compared with the reference group.
	Chen et al. (2018) [38]	Cross-sectional	Questionnaire-Measurement	68 pregnant women (Taiwan)	Exposure to organochlorine pesticides in the environment and through eating habits can cause infertility by disturbing the endocrine glands.

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Ji et al. (2010) [39]	Cross-sectional	Questionnaire-Measurement	n= 465 (China)	Improper dietary habits and increased industrial production can have an adverse effect on the fertility and damage sperm DNA by exposing people to polycyclic aromatic hydrocarbons.
	Harville et al. (2017) [40]	Cross-sectional	Questionnaire-Measurement	1524 women (southeastern Louisiana)	There was no conclusive evidence of the impact of environmental exposure to oil spills and reproductive failure.
	Bastos et al. (2013) [41]	Cross-sectional	Questionnaire-Measurement	Fertile ($n = 21$), infertile ($n = 15$) (Brazil)	pp'DDE was detected in 100% of infertile women, at higher mean levels than in pregnant women (3.02 mcg/L vs. 0.88 mcg/L; P= 0.001; the power of 69%) Canned foods and exposure to organochlorine chemicals may affect fertility in women.
	Smith et al. (2013) [42]	Prospective cohort	Measurement of patients' medical record	192 women (USA)	There were no correlations between the urinary concentration of butylparaben or methylparaben and antral follicle count and follicle-stimulating hormone levels. However, exposure to propylparaben chemicals may affect fertility by disrobing the endocrine system and reducing ovarian reserves.
	Meeker et al. (2011) [43]	Cross-sectional	Measurement	Serum hormone levels ($n = 167$), semen quality parameters ($n =$ 190), and sperm DNA damage measures ($n = 132$) (USA)	There was no correlation between paraben concentration in urine and low semen quality, but there was a direct correlation between Urinary concentration of butylparaben, bisphenol A and damage to sperm DNA. (p for trend = 0.03)

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Meeker et al. (2010) [44]	Cross-sectional	Measurement	167 men)Massachusetts(	Exposure to bisphenol A chemicals is associated with impaired hormone levels (estradiol, testosterone, and thyroid-stimulating hormone) in men. There was a positive trend between urinary BPA quartiles and FSH to inhibin *B* ratio (p for trend = 0.01) and a suggestive inverse trend between urinary BPA quartiles and E2:T ratio (p for trend = 0.06). There was a positive dose-response trend between urinary BPA concentration quartiles and serum FSH levels (p for trend = 0.002) and an inverse trend between urinary BPA quartiles and inhibin B (p for trend = 0.04)
	Cohn et al. (2011) [45]	Prospective	Questionnaire-Measurement	289 daughters (Oakland, California area(	Probability of pregnancy fell by 38% (95% CI 17–53%) and infertility was higher (30% not pregnant after 13 cycles vs.11% not pregnant after 13 cycles). Mothers, who had serum levels of polychlorinatedbiphenyl, their daughters were facing an extended time to be pregnant. Therefore, mothers' exposure to Polychlorinatedbiphenyl chemicals reduces pregnancy power in their daughters.

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Crawford et al. (2017) [46]	Cohort	Measurement	99 women (North Carolina)	Measuring the antimalarial hormone, the present study indicated that exposure to perfluorinated chemicals through consumer goods, pesticides, etc. affected thyroid hormone levels (Thyroid hormones were weakly correlated with PFCs. Specifically, PFOA and PFNA were positively correlated with T3 (r=0.23, p=0.03) PFNA was positively correlated with free T4 (r=0.24, p=0.02) but there was no correlation with TSH.) but did not affect the ovarian reserve and fertility.
	Thurston et al. (2016) [47]	Cross-sectional	Measurement	420 men (USA)	Exposure to environmental pollutants, phthalate, did not affect semen parameters, but monobenzyl phthalate was associated with decreased sperm motility. ($\beta = -1.47$, 95% CI -2.61, -0.33)
	Guo et al. (2014) [48]	Prospective cohort	Measurement	469 couples from Michigan and Texas	Exposure to phthalates because of increased oxidative stress can have a harmful effect on fertility.
	Jurewicz et al. (2018) [49]	Cross-sectional	Questionnaire-Measurement	315 men (Poland)	High urinary concentration of triclosan 50th–75th percentile and $\geq$ 50 percentile was associated with increasing the abnormal morphology of sperm. ($p = 0.016$ and $p = 0.002$, respectively). The exposure to triclosan can endanger fertility in men by reducing semen quality.
	Conti et al. (2017) [50]	Cross-sectional	Questionnaire-Measurement	86 males (Catania, Italy)	Exposure to dangerous pollutants, Benzo(a)pyrene, through cigarette smoke, frozen foods, incomplete combustion of fossil fuels, etc. adversely affects male fertility by bonding with sperm DNA.

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Messerlian et al. (2018) [51]	Prospective cohort	Questionnaire-Measurement	)$N = 799$ women, $N = 487$ men((Massachusetts ,USA)	The high urinary concentration of phthalate metabolites in women was associated with a decrease in oocytes and a decrease in live births in men. The chemicals had a negative effect on fertility.
	Aneck-Hahn et al. (2007) [52]	Cross-sectional	Questionnaire-Measurement	311 males (South Africa)	Exposure to DDT pesticide was associated with decreased ejaculation volume ($b = -0.0003$; $P = .024$) as well as serum concentration of DDT in people with asthenozoospermia, oligozoospermia, and teratozoospermia. There was a significant positive association between participants with asthenozoospermia (32%) and p,p9-DDT (OR 1.003, $P = .006$) and p,p9-DDE (OR 1.001, $P = .02$).
	Wang et al. (2016) [53]	Systematic review and meta-analysis	Electronic databases	9 studies (7 cross-sectional, 1 case-control, and 1 pilot study) were analyzed for classic EDCs (5 studies for phthalate esters and 4 studies for organochlorines).	Organochlorine and phthalate ester were associated with poor sperm quality. Risk of abnormal sperm quality was found in the phthalate ester group (OR=1.52; 95% CI: 1.09–1.95) and organochlorine group (OR=1.98; 95% CI: 1.34–2.62).
	Hipwell et al. (2019) [54]	Systematic review	Electronic databases	The search returned 3456 articles. There were 15 papers from 12 studies which met inclusion criteria, of which eight included biomarkers of chemical exposure.	Although there is a link between exposure to chemicals (phthalates, BPA, TCS, TCC, benzophenones, parabens, and glycol ethers) and reduced fertility in men and women, more studies are being done
	Bonde et al. (2017) [55]	Systematic review and meta-analysis	Electronic databases	Papers included in qualitative synthesis ($n = 33$)	Exposure to environmental pollutants can adversely affect the male reproductive system. The overall odds ratio (OR) across all exposures and outcomes was 1.11 (95% CI 0.91–1.35). exposure to one of the four compounds, p,p′-DDE, was related to an elevated risk: OR 1.35 (95% CI 1.04–1.74).

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Caserta et al. (2011) [56]	Systematic review	Electronic databases	---	Studies have shown that environmental pollutants that disrupt the endocrine glands affect the reproductive system.
	Martenies and Perry (2013) [57]	Systematic review	Electronic databases	17 studies	Contact with pesticides was associated with decreased sperm concentration and motility. In two studies, the relationship between pesticides and sperm morphology was reported.
	Machtinger et al. (2013) [58]	Randomized trial	Measurement	352 GV-stage oocytes from 121 patients (Brigham)	The higher the dose of bisphenol-A, oocytes the lower the progression in metaphase 2 ($P = 0.002$) also the higher the percentage of degeneration ($P = 0.01$).
Cigarette smoking	Schuh-Huerta et al. (2011) [59]	Cohort	Questionnaire measurement	232 Caucasian and 200 African American (California) women (USA)	Smoking adversely affects the ovarian reserve and levels of reproductive hormones and subsequently the fertility.
	Shin et al. (2017) [60]	Cross-sectional	Questionnaire	785 women (Korea)	Prevalence of current, secondhand, past, and never smokers were 12.7%, 45.7%, 0.9%, and 40.6%, respectively. Primary infertility was more frequent in secondhand smokers. Cigarette smoke did not affect menstruation and reproductive hormones, but the rate of smoking was higher in infertile people.
	Axelsson et al. (2013) [61]	Cross-sectional	Register-based data, Questionnaire-Measurement, physical examination	295 adolescents (Sweden)	Paternal smoking was associated with 46% lower total sperm count (95%CI 21%, 64%) during the adulthood and affects fertility. Both paternal and maternal smoking were associated with a lower sperm concentration (mean differences: 35%; 95%CI 8.1%, 55% and 36%; 95%CI 3.9%, 57%, respectively

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Keshavarzi et al. (2016) [62]	Analytical - cross-sectional	Questionnaire measurement	514 individuals who were divided into two groups of infertile men, and those with children and no history of infertility (Iran - Kermanshah)	142 infertile men smoked, while 112 once smoked in a group of men with children. It can be concluded that smoking can be an effective factor in causing the infertility. *P*<0/05
Air pollution	Mahalingaiah et al. (2015) [63]	Prospective cohort	Questionnaire	36,294 women (USA)	Proximity to main roads due to air pollution is associated with an increased incidence of primary and secondary infertility. For women living closer to compared to farther from a major road, for primary infertility hazard ratios = 1.05 (CI 0.94–1.17) while for secondary infertility hazard ratios = 1.21 (CI 1.07–1.36)
	Vecoli (2017) [64]	A Pilot Study	Measurement	Normospermic men (n= 57, high group) (n= 55, low group) (Grouping is based on the environmental pressure) (Italy)	High levels of environmental pollution can adversely affect reproductive health by increasing sperm telomere length.
	Joffe et al. (2008) [65]	Retrospective	Questionnaire	('unexposed' group, n=400), ('exposed' group, n=200) (UK)	Environmental pollution sources in two study groups (pregnant local residents living within 3 km of a landfill site or elsewhere in the Rhondda valleys) had no effect on the time needed for female pregnancy.
	Najafi et al. (2015) [66]	Meta-analysis	Electronic databases	11 articles	The CI for pooled means were as follows: 2.68 ± 0.32 for ejaculation volume (mL) 62.1 ± 15.88 for sperm concentration (million per milliliter) 39.4 ± 5.52 for sperm motility (%) 23.91 ± 13.43 for sperm morphology (%) and 49.53 ± 11.08 for sperm count. Air pollution was associated with decreased sperm motility but did not affect other sperm parameters.
	Carré et al. (2017) [67]	Systematic review	Electronic databases	61 articles	Air pollution affects the reproductive capacity of men and women by affecting gametogenesis.

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
Ionizing radiation	Sharma et al. (2017) [68]	Experimental study	Measurement	Group I: normal, control males of proven fertility (n=40) Group II: males with oligoasthenozoospermia (OAT) (n=36) Group III: Males with unexplained infertility (MUI) (n=42) (India)	Groups 2 and 3 exposed to ultra-violet radiation showed a higher percentage of immature sperm than group 1; hence, exposure to UV adversely affected the fertility by damaging the sperm DNA.
	Moghbeli-Nejad et al. (2012) [69]	Experimental study	Questionnaire-measurement	Oligospermia with mean sperm count (15 × 106±2.4) n=10, azoospermia with no sperm in semen n=10, and normal males with mean sperm count (50× 106±3.1) n=10 (Tehran, Iran)	Exposure to ionizing radiation reduces male reproductive capacity by causing anomalies and mutations in sperm DNA (genomic instability). Although the high background frequency of micronucleus in oligospermia and azoospermia samples is statistically different compared to normal control (P<0.05). the difference between oligospermia and azoospermia groups is not significant (P>0.05).
	Stone et al. (2013) [70]	Prospective cohort	Interview questionnaire—physical examination	1466 (USA)	Childhood thyroid radiation dose was possibly associated with infertility [adjusted odds ratio (AOR) = 1.17; 95% CI 0.82, 1.67 and AOR = 1.35; 95% CI 0.96, 1.90 for the middle and upper tertiles vs. the first tertile of exposure, respectively]. Exposure to radioactive substances (iodine therapy) in childhood to treat thyroid diseases can be associated with infertility in the adulthood.
	Adams et al. (2014) [71]	Systematic review and meta-analysis	Electronic databases	10 studies	Exposure to mobile phones was associated with reduced sperm motility (mean difference −8.1% (95% CI −13.1, −3.2)) and viability (mean difference −9.1% (95% CI −18.4, 0.2)), but the effects on concentration were more equivocal.

Table 1 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
Ambient temperature	ShaiShefi et al (2007) [72]	Cohort	Questionnaire-measurement	11 infertile men (USA)	Decrease in ambient temperature was associated with increased sperm count and motility. (This increase was largely the result of a statistically significant increase in sperm motility from a mean of 12% at baseline to 34% post-intervention ($p = 0.02$)). As a result, high-temperature environments such as Jacuzzi, and hot baths endanger male fertility by affecting semen quality and spermatogenesis.

Table 2 Papers assessing the impact of heavy metals on reproductive and infertility indices

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
Heavy metals	Moran-Martinez et al. (2013) [73]	Cross-sectional	Questionnaire-measurement	Exposed group N=20 Non-exposed group N=27 (Torreon Coahuila, Mexico)	Exposure to lead in the environment and workplace is associated with decreased sperm concentration and motility and increased abnormal sperm forms. there were significant differences in the spermatic concentration [EG=43.98±6.26 and NEG=68.78±8.51 × 10^6 cell mL^{-1} ((p<0.01), motility [EG=49±7 and NEG=67±4% (p=0.029)], viability [EG=36.32±3.59 and NEG=72.12±1.91% (p<0.01)], and abnormal morphology [EG=67±18 and NEG=32±12% (p<0.01)].
	Xu et al. (2012) [74]	Cross-sectional	Questionnaire-measurement	96 males (China)	Arsenic entry into the body through a contaminated environment, water, and food may be associated with reduced semen quality and infertility. (DMA concentrations above the median were significantly associated with below-reference sperm concentrations (P =0.02))
	Wu et al. (2012) [75]	Prospective	Questionnaire-measurement	341 males (Taiwan)	High concentration of lead in semen was associated with reduced sperm count, but did not affect its volume, motility, and morphology. (the sperm count was negatively associated with semen lead concentration (r=0.130, P=0.0165).) Consequently, it can be concluded that heavy metals such as lead entry into the body through the environment and food have negative effects on human fertility by affecting the semen quality and count.
	He et al. (2016) [76]	Experimental study	Measurement	20 males (China)	Environmental exposure to lead affects sperm function, which can subsequently reduce reproductive capacity in men, by reducing CAMP, calcium, and tyrosine phosphorylation.
	Lei et al. (2015) [77]	Cross-sectional	Questionnaire-measurement	Infertile women (N=310) Pregnant women (N=57) (Taiwan)	Serum levels of lead and arsenic were higher in infertile women than in pregnant women. A significant difference was observed in the categorized frequencies of Chinese herbal medicine use between the groups ($p < 0.01$). In particular, an obvious difference was noted in infertile women taking Chinese herbal medicine 1–6 times per week compared with pregnant women (30.9 % versus 10.5 %). The blood Pb and As levels were also significantly higher in the infertile women than in the pregnant women ($p < 0.01$).

Table 2 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Mendiola et al. (2011) [78]	Case-control	Questionnaire-measurement	Exposed group ($n = 30$) Non-exposed group ($n = 31$) (Spain)	That association remained statistically significant after adjustment for age, BMI, and number of cigarettes per day (*b*= 1.5; 95% CI, 0.37, 1.9, and *b*= 4.9; 95% CI, 0.84, 9.1, respectively). An inter-quartile increase in seminal plasma concentrations of Pb (5.0 μg/L) and Cd (0.3 μg/ L) for a 33.5-year-old with a BMI of 23 kg/m^2 would be predicted to increase immotile sperms 21.6% and 24.3%, respectively. Heavy metals (lead and cadmium) endanger reproductive health in men by affecting semen plasma levels and sperm motility.
	Hsi et al. (2016) [79]	Cross-sectional	Questionnaire-measurement	*N*= 224 (Taiwan)	The concentration of methylmercury in the hair of infertile women (1.82 ± 0.14 mg/kg) was significantly higher than the of pregnant women (1.24 ± 0.18 mg/kg). As a result, exposure to mercury while consuming fish can reduce the fertility.
	Meeker et al. (2008) [80]	Cross-sectional	Measurement	219 men) Michigan, USA(	There was a direct correlation between the serum level of molybdenum and a decrease in sperm concentration and normal morphology. As a result, it can be concluded that exposure to heavy metals (zinc, mercury, copper, cadmium, arsenic, etc.) endangers reproductive health in men by reducing the semen quality and damage to sperm DNA. [adjusted odds ratios (ORs) for below-reference semen quality parameters in the low, medium, and high Mo groups were 1.0 (reference) 1.4 [95% confidence interval (CI) 0.5–3.7], and 3.5 (95% CI, 1.1–11) for sperm concentration and 1.0 (reference), 0.8 (95% CI, 0.3–1.9), and 2.6 (95% CI, 1.0–7.0) for morphology]

Table 3 Papers assessing the impact of occupational factors on reproductive and infertility indices

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
Occupational factors	Iepecka-Klusek et al. (2011) [81]	Prospective	Questionnaire - physical Examination - measurement	224 males (Poland)	Living conditions, occupational hazards, and difficult tasks were not associated with semen quality.
	Minguez-Alarcon et al. (2017) [82]	Prospective cohort	Questionnaire- measurement	(n=473 and n=313 for ovarian reserve and ovarian response analysis, respectively) USA	Women who moved heavy objects and worked longer every day had fewer oocytes (p value=0.08) mature oocytes (p value=0.007) and antral follicles (p value=0.06) than others. Consequently, occupational factors such as heavy physical activity may be associated with decreased fertility.
	Gaskins et al. (2015) [83]	Cohort	Questionnaire	1739 women (USA)	Women, who worked more than 40 hours a week (95% CI 7 to 35%) or moved heavy objects, became pregnant later than those who worked 21 to 40 h per week. (p trend=0.005).
	Wang et al. (2015) [84]	Cross-sectional	Questionnaire, physical examination, measurement	Exposed group (N=114) Non-exposed group (N=76) (China)	There was no significant difference in semen volume, sperm concentration, and total count in both groups (a group exposed to formaldehyde (FA) and a control group) but a number of motile sperm in the group exposed to formaldehyde was lower than the control group. (OR=3.21; 95%CI 1.24–8.28). A significant elevated risk of abnormal sperm progressive motility was found in the low-FA-exposed group (OR= 2.58; 95%CI 1.11–5.97) and high-FA-exposed group (OR= 3.41; 95%CI 1.45–7.92, respectively) compared with the reference group.
	Wijesekara et al. (2015) [85]	Cross-sectional	Questionnaire, measurement	300 men (Colombo- Sri Lanka)	People in polluted regions and exposed to industrial chemicals had higher percentages of lead and cadmium in seminal plasma Pb (r=0.06, p>0.05) and Cd (r=0.26, p<0.05) and less alive, motile, and normal sperms. In the exposed, mean lead concentration was 17.7 (95% CI 15.0–20.4) μg/dl and 13.5 (95% CI 11.2–15.7) μg/dl in non-exposed and cadmium concentration in exposed was 1.2 (95% CI 1.1–1.4) μg/dl and 1.1 (0.9–1.3) μg/dl in non-exposed.

Table 3 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	de Fleurian et al. (2009) [86]	Cross-sectional	Interview, questionnaire, measurement	Total (n = 402) Exposed group (n = 314) Non-exposed group (n = 88) (France)	Various physical and chemical occupational factors, including mechanical vibration, heat, prolonged sitting, exposure to chemicals, and heavy metals can affect semen quality. (adjusted odds ratio [OR] = 5.4; 95% confidence interval [CI], 1.6–18.1) solvents (OR = 2.5; 95% CI, 1.4–4.4) fumes (OR = 1.9; 95% CI, 1.1–3.4), and polycyclic aromatic hydrocarbons (OR = 1.9; 95% CI, 1.1–3.5). Exposure to pesticides or cement was nearly significant (OR = 3.6; 95% CI, 0.8–15.8, and OR = 2.5; 95% CI, 0.95–6.5, respectively) (mechanical vibration was associated with oligospermia and teratospermia, exposure to high temperature; and prolonged sitting was associated with lower mobility) but exposure to ionizing radiation and electromagnetic fields was not associated with lower semen quality.
	Daoud et al. (2017) [87]	Cross-sectional	Questionnaire, measurement	2122 men (Sfax, Tunisia)	Occupational exposure to pesticides and substances such as cement was correlated with asthenozoospermia, necrozoospermia, and oligozoospermia. pesticides: (adjusted odds ratio [OR] = 1.6; 95% CI, 1.0–2.4) and necrozoospermia (OR = 2.6; 95% CI, 1.4–4.7). Cement: (OR = 1.1; 95% CI, 0.9–1.4). While there was no relationship between the presence in very hot environments and mechanical vibrations with sperm abnormalities.
	Mahboubi et al. (2014) [88]	Case-control	Questionnaire, measurement	Infertile men (n: 108) Fertile men (n: 161) (Shiraz, Iran)	Workers with heavy physical activity are more prone to infertility due to damage to testicles and a decrease in semen quality. Smoking is also associated with decreased sperm motility.

Table 3 (continued)

Effective factor	First author (year)	Type of study	Research instrument	Sample size and research place	Result
	Kumar et al. (2013) [89]	Cross-sectional	Questionnaire, measurement	134 males ((‘unexposed’ group, n=51), (‘exposed’ group, n=83)) (India)	Occupational exposure to ionizing radiation is associated with decreased motility and normal morphology of sperm by the creation of malformations and mutations in sperm DNA (P<0.05–0.0001) but further studies should be conducted to investigate fertility.
	Jeng et al. (2016) [90]	Cross-sectional	Questionnaire, measurement	(Nonexposed’ group N=35 Exposed group (N= 52) (Taiwan)	Coal furnace workers experienced a greater reduction in sperm motility and normal morphology than the control group, but it was not statistically significant. For DNA integrity, the coke oven workers had significantly higher concentrations of bulky DNA adducts and 8-oxo-7,8-dihydro-2′-deoxyguanosine than the control subjects ($p = 0.009$ and $p = 0.048$, respectively) The workers’ occupational exposure to aromatic hydrocarbons endangers the reproductive health by damaging the sperm DNA and decreasing its integrity.
	Kim et al. (2016) [91]	Meta-analysis	electronic databases	19 articles	The meta-analysis revealed a significantly increased risk of infertility (OR 1.15, 95 % CI 1.03–1.28), fetal death (OR 1.14, 95 % CI 1.04–1.24), and preterm delivery (OR 1.04, 95 % CI 1.00– 1.07) among hairdressers and cosmetologists.

parameters. It also explored the effects of occupational factors such as heavy physical activity, prolonged sitting, presence in a hot environment, and exposure to formaldehyde, pesticides, insecticides, mechanical vibration, and ionizing radiation on reproductive indices.

Table 1 provides data regarding articles evaluating the impact of chemicals and environmental pollutants (n=33), air pollution (n=5), smoking (n=4), ambient temperature (n=1), and ionizing radiation (n=4) on reproductive and infertility indices.

It was found that exposure to chemicals and environmental pollutants is associated with decreased sperm concentration, motility, and count [27], increased androgen-estrogen ratios [29], decreased semen volumes [28], decreased antral follicle growth [34], endocrine disruption [38], and increased oxidative stress [26, 48]. The effect of smoking on spermatogenesis, ovarian reserve, hormonal balance, semen quality, and oxidative stress was also discussed in the reviewed investigations [26, 59]. In addition, two studies comparing infertile people and those with children reported a higher rate of smoking in the infertile group [60, 62].

One cohort study revealed that proximity to major roads was associated with an increased incidence of primary and secondary infertility due to a high rate of air pollution [63]. Environmental contamination with sperm DNA damage can also affect fertility in an individual [64]. Contact with ionizing radiation is also associated with mutations in sperm genetic material [68, 69]. Moreover, one study pointed to the impact of iodine therapy in childhood on infertility in adulthood [70]. In addition, high-temperature environments may affect fertility in men by affecting semen quality and spermatogenesis [72] as illustrated in Table 1.

Table 2 summarizes the literature (eight articles) evaluating the impact of heavy metals on reproductive indices and the increased risk of infertility. Exposure to heavy metals through the environment and food was associated with decreased sperm concentration, motility, and morphology [73, 74, 78, 80]. The serum levels of heavy metals were found to be higher in infertile women compared to those in fertile women [77].

Table 3 provides data related to studies on the effect of occupational factors on reproductive parameters and the risk of infertility (11 articles). Based on the findings, performing heavy and long-term physical activity was correlated with a decrease in the number of antral follicles [82]. Workers with heavy physical activity are also more prone to infertility due to damage to the testicles and a decrease in semen quality [88]. Moreover, coal furnace workers experienced greater reductions in sperm motility and normal morphology in comparison with the control group [90]. Further, people exposed to contaminated areas and industrial chemicals had higher percentages of lead and cadmium in their semen plasma [85] (Tables 4, 5 and 6).

Discussion

The present study reviewed the effects of environmental and occupational factors on reproductive parameters after collecting 66 papers according to the inclusion criteria. However, the risk of infertility was somewhat unclear in the studied populations.

In a prospective study by Minguez-Alarcon et al. women working longer and moving heavier objects had a lower number of antral follicles and mature oocytes [82]. In a cohort study by Gaskins et al. on 1739 women, those working more than 40 h per week became pregnant later than those who worked 21–40 h per week [83]. Similarly, Mahboubi et al. found that workers who worked hard were more likely to have lower fertility because of damage to testicles, which reduced semen quality [88]. However, Celina Lepecka-Klusek et al. studied 224 men and reported that difficult activity was not significantly correlated with a semen quality decline [81]. Dangerous physical conditions (e.g., carrying heavy loads, bending over, and straightening while working) may have a negative effect on pregnancy and fertility efficiency in women, especially when they are threatened by other hazards such as a history of miscarriage or other hazardous conditions at work. The mechanism of the action of these factors is unknown, and their negative effect may be due to reduced oxygen and nutrient supply or hormonal system disruption [93]. Prolonged physical activity with an increase in body temperature and the testis may adversely affect the process of spermatogenesis. Previous research demonstrated that the mean scrotal temperature in infertile men with varicocele was higher than normal, and high testicular temperature changes the integrity of sperm DNA [94].

In the field of exposure to pesticides and insecticides, Aneck-Hahn et al. conducted a study in South Africa and found that men using pesticides to control malaria have a lower ejaculatory volume [52]. In their cross-sectional study, Daoud et al. observed that occupational exposure to pesticides was associated with asthenozoospermia, necrozoospermia, and oligozoospermia [87]. Occupational toxins such as organochlorine, organophosphate, carbamate, pyrethroids, and other pesticides directly impair sperm structure by damaging testicular cells or indirectly by disrupting the hormonal regulation of spermatogenesis. These disorders occur as decreased sperm production, incomplete sperm production, and androgen production disorders [95].

Hai-xu Wang examined the impact of occupational exposure to formaldehyde in two groups of men with

Table 4 Quality assessment of studies (cohort, case-control, and cross-sectional) (Newcastle and Ottawa checklist)

Quality	Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcome (max 3 stars)	NOS score
Good Quality	Jurewicz et al. [28]	***	**	**	7
	Petersen et al. [29]	***	**	***	8
	Vestergaard et al. [30]	****	**	***	9
	Xia et al. [31]	***	**	***	8
	Gennings et al. [32]	****	**	***	9
	Du et al. [34]	****	**	***	9
	Meeker et al. [35]	***	**	***	8
	Velez et al. [36]	****	**	***	9
	Yang et al. [92]	**	**	***	7
	Guixiang et al. [39]	****	**	**	8
	Harville et al. [40]	****	**	**	8
	Bastos et al. [41]	***	**	**	7
	Smith et al. [42]	****	**	***	9
	Meeker et al. [43]	***	**	***	8
	Meeker et al. [44]	***	**	***	8
	Cohn et al. [45]	**	**	***	7
	Crawford et al. [46]	****	**	***	9
	Thurston et al. [47]	***	**	**	7
	Guo et al. [48]	***	**	***	8
	Jurewicz et al. [49]	**	**	***	7
	Messerlian et al. [51]	****	**	***	9
	Aneck-Hahn et al. [52]	***	**	***	8
	Schuh-Huerta et al. [59]	****	**	***	9
	Shin et al. [60]	**	**	***	7
	Axelsson et al. [61]	***	**	***	8
	Mahalingaiah et al. [63]	****	**	***	9
	Cecilia Vecoli [64]	****	**	**	8
	Mike Joffe et al. [65]	****	**	**	8
	Sharma et al. [68]	***	**	**	7
	Moghbeli-Nejad et al. [69]	****	**	**	8
	Stone et al. [70]	****	**	***	9
	ShaiShefi et al [72]	****	**	***	9
	Moran-Martinez et al. [73]	****	**	**	8
	Xu et al. [74]	***	**	**	7
	Wu et al. [75]	***	**	***	8
	He et al. [76]	**	**	***	7
	Lei et al. [77]	**	**	***	7
	Mendiola et al. [78]	***	**	***	8

Table 4 (continued)

Quality	Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcome (max 3 stars)	NOS score
	Hsi et al. [79]	**	**	***	7
	Meeker et al. [80]	***	**	***	8
	lepecka-Klusek et al. [81]	***	**	**	7
	Minguez-Alarcon et al. [82]	****	**	***	9
	Gaskins et al. [83]	****	**	***	9
	Wang et al. [84]	***	**	***	8
	Wijesekara et al. [85]	**	**	***	7
	de Fleurian et al. [86]	****	**	**	8
	Daoud et al. [87]	**	**	***	7
	Mahboubi et al. [88]	***	**	***	8
	Kumar et al. (2013) [89]	***	**	***	8
	Jeng et al. (2016) [90]	***	**	***	8
Medium quality	Kumar et al. [26]	**	**	**	6
	Ji et al. [27]	**	**	**	6
	Nishihama et al. [33]	**	**	**	6
	Chen et al. [38]	***	*	**	6
	Conti et al. [50]	**	**	**	6
	Keshavarzi et al. [62]	**	**	**	6

and without exposure to formaldehyde. Based on their results, there were no statistically significant differences in the semen volume, concentration, and total count in both groups although the total number of the motile sperm was lower in the formaldehyde-exposed group compared to control men [84]. De Fleurian concluded that various physical and chemical occupational factors such as mechanical vibration, heat, prolonged sitting, exposure to chemicals, and heavy metals could affect semen quality. More precisely, mechanical vibration was associated with oligospermia and teratospermia, while exposure to high temperatures and prolonged sitting was related to lower mobility. However, no association was found between exposure to ionizing radiation and electromagnetic fields with lower semen quality [86], and oxidative stress caused by heavy metals was reported in abnormal sperm function and male infertility [96].

Toxic metals have been studied for centuries. These pollutants affect human health through the food chain, water pollution, and inhalation of air pollutants. To rehabilitate land damaged by heavy metals, some low-cost efficiencies and approaches need to be widely promoted. Research has demonstrated that there is a direct link between high concentrations of heavy metals in the blood and urine and abnormal spermograms. Part of the toxic effects of heavy metals on the sperm is due to impaired motility and cessation of sperm motility [74]. In another study, Moran-Martinez et al. determined the effects of heavy metals on the performance of reproductive indices and indicated that exposure to lead in the environment was associated with decreased sperm concentrations and motility and increased sperm abnormalities [73]. Furthermore, Meeker analyzed the serum levels of 219 males, reporting that high-serum levels of molybdenum were associated with lower sperm concentrations and normal morphology [80]. Likewise, Wu conducted a prospective study and found that a high concentration of lead in the semen was correlated with lower sperm counts; however, it had no effects on sperm volume, motility, and morphology [97].

Some studies reported the effects of chemicals and environmental pollutants on reproductive parameters. Ji et al. conducted a cross-sectional study on 433 men and detected that environmental pollutants (e.g., aromatic hydrocarbons) were associated with lower sperm concentrations, motility, and counts through damaging sperm DNA [27]. Moreover, Xia et al. studied 513 men with idiopathic infertility and 273 men with fertility as the control group, finding that the urinary concentrations of aromatic hydrocarbon metabolites were higher in men with idiopathic infertility compared to those in the control group. Exposure to polycyclic aromatic

Table 5 Quality assessment of systematic review and meta-analysis studies (AMSTAR checklist)

First author (year)	Title	Abstract	Introduction	Methods	Results	Discussion	Funding	Total score
ChaoWang et al. (2016) [53]	1	1	2	11	7	3	1	26
Hipwell et al. (2019) [54]	1	1	2	11	7	3	1	26
Bonde et al. (2017) [55]	1	1	2	12	7	2	1	26
Caserta et al. (2011) [56]	1	1	2	10	7	3	1	25
Martenies and Perry (2013) [57]	1	1	2	12	6	2	1	25
Najafi et al. (2015) [66]	1	1	2	10	5	2	1	22
Carré et al. (2017) [67]	1	1	2	12	7	3	1	27
Kim et al. (2016) [91]	1	1	2	11	7	3	1	26
Adams et al. (2014) [71]	1	1	2	11	7	3	**1**	26

Table 6 Quality assessment of clinical trial study (according to Juni's study)

First author (year)	Title and abstract	Introduction	Methods	Results	Discussion	Registration	Protocol	Funding	Total score
Machtinger et al. (2013) [58]	1	2	16	9	3	1	1	1	34

hydrocarbons in the environment may increase the risk of infertility in men [31]. Petersen et al. investigated 226 men who were exposed to polychlorinated biphenyls and found that environmental chemicals (e.g., polychlorinated biphenyls) might adversely affect fertility by increasing the androgen-estrogen ratio although the serum levels of substances were not correlated with semen quality [29]. Similarly, Gennings et al. reported that exposure to polychlorinated biphenyls is related to prolonged pregnancy [32]. In their study, Smith et al. determined the urinary concentrations of paraben metabolites in 192 women who visited the infertility center, observing that the urinary concentrations of butylparaben or methylparaben were not related to antral follicle counts and follicle-stimulating hormone levels. However, exposure to propylparaben might affect fertility by disrobing the endocrine system and reducing ovarian reserves [42]. Furthermore, Meeker et al. indicated no association between paraben concentrations in the urine and lower semen quality, but a direct relationship was found between the urinary concentrations of butylparaben and damage to sperm DNA [43].

Du et al. examined urinary concentrations of phthalate metabolites in 415 women and reported that there is an insufficient correlation between the urinary concentration of phthalate and anti-Mullerin hormone levels, but exposure to phthalates was associated with decreased antral follicle growth [34].

Cigarette smoke contains harmful chemicals, many of which are mutagenic and affect sperm production and function. However, in addition to the effect of smoking on fertility decline, there are factors that can lead to inconsistent findings between studies, including medical diseases, use of other drugs along with smoking, as well as social and economic status. However, despite these issues, every man and woman who intends to become pregnant should be warned to quit smoking. It can also be difficult to examine people who are indirectly exposed to smoking [61]. According to Schuh-Huerta et al., smoking negatively affected ovarian reserves and reproductive hormone levels, and subsequently, fertilization [59]. On the contrary, Shin et al. concluded that cigarette smoke did not affect menstruation and reproductive hormones and reported that the overall smoking rates are higher in infertile people when compared with other people [60]. These agents include natural or synthetic chemicals. The prevalence of testicular cancer and some congenital anomalies (e.g., cryptorchidism or hypospadias), along with the apparent decrease in sperm production and its quality in the male population, is closely related to the widespread use of chemicals with hormonal properties. Nonetheless, there is no definite consensus on this issue, and these changes probably occur during the embryonic period [98]. Most studies indicated that environmental and occupational pathogens can negatively affect fertility, while many studies did not find this relationship since many factors affect a couple's fertility, including socio-economic factors, medical problems, and psychological issues. In addition, methodological review of studies can also affect the results such as sample selection method, sample size, statistical analysis, and the type of used questionnaires and checklists. In sum, all the abovementioned factors have caused the results of some studies to be inconsistent with other studies.

Strengths of the study

In this study, an attempt was made to discuss all the environmental factors that lead to a decrease in fertility and subsequent infertility. Further, by taking the systematic review, observational studies, and clinical trials into account as the criteria for entering the study, a large number of studies have been examined so that the obtained results are close to certainty.

Strengths and limitations of the study

One of the strengths of this study is the investigation of databases by the search strategy. All databases were carefully examined. One of the limitations of this study is that because the role of environmental and occupational factors in causing infertility is more or less accepted, the investigation of these factors may not be among the priorities of researchers in the world. At the same time, parallel to the advancement of technology, the role of the above factors in causing infertility will be more effective. Furthermore, meta-analysis was not possible due to severe heterogeneity in the independent variables, different measurement methods, variation in the studied outcomes, and the small number of similar studies to perform subgroup analysis.

Conclusions

In general, this systematic review study examined the environmental and occupational factors affecting infertility. According to the results, chemicals and environmental pollutants, cigarette smoking, air pollution, ionizing radiation, ambient temperature, and heavy metals are effective on male and female infertility. Environmental and occupational factors cause disorders in the quality and quantity of semen and natural forms, movements, and the number of sperms, along with ovulation disorders and hormonal imbalances in women. Therefore, identifying and eliminating the affecting factors are effective in reducing the prevalence of infertility worldwide. Accordingly, it is suggested to conduct prospective studies with a larger sample size so that the obtained results are close to certainty.

Abbreviations

AMH: Anti-Mullerian hormone; AMSTAR: A Measurement Tool to Assess Systematic Reviews; BMI: Body mass index; FSH: Follicle-stimulating hormone; NOS: Newcastle and Ottawa; CONSORT: Consolidated Standards of Reporting Trials; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses.

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Authors' contributions

SZM and SA conceived the study, developed the study protocol, conducted the study, and reviewed the articles. FK analyzed the data and drafted the manuscript. SGh reviewed the articles. The authors read and approved the final manuscript.

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Availability of data and materials

The produced data set during this study is available from the corresponding author.

Declarations

Ethics approval and consent to participate

The study procedures were approved by the Research Ethics Review Board, Hamadan University of Medical Sciences, School of Nursing and Midwifery (Grant No: 9712077581, Hamadan University of Medical Sciences Ethics Committee ID: IR.UMSHA.REC.1397.908).

Consent for publication

Hamadan University of Medical Sciences was allowed to publish and print the article.

Competing interests

The authors declare that they have no competing interests.

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References

1. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HWG, Behre HM, Haugen TB, Kruger T, Wang C, Mbizvo MT, Vogelsong KM (2009) World Health Organization reference values for human semen characteristics. Hum Reprod Update 16:231–245. https://doi.org/10.1093/humupd/dmp048
2. Aghajanova L, Hoffman J, Mok-Lin E, Herndon CN (2017) Obstetrics and gynecology residency and fertility needs: national survey results. Reprod Sci 24:428–434. https://doi.org/10.1177/1933719116657193
3. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA (2012) National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med 9:e1001356. https://doi.org/10.1371/journal.pmed.1001356
4. Kazemijaliseh H, Ramezani Tehrani F, Behboudi-Gandevani S, Hosseinpanah F, Khalili D, Azizi F (2015) The prevalence and causes of primary infertility in Iran: a population-based study. Glob J Health Sci 7:226–232. https://doi.org/10.5539/gjhs.v7n6p226
5. Mehrpour O, Karrari P, Zamani N, Tsatsakis AM, Abdollahi M (2014) Occupational exposure to pesticides and consequences on male semen and fertility: a review. Toxicol Lett 230:146–156. https://doi.org/10.1016/j.toxlet.2014.01.029
6. du Plessis SS, Agarwal A, Sabanegh ES. Male infertility: a complete guide to lifestyle and environmental factors. Springer New York; 2014.

7. Lawson CC, Johnson CY, Chavarro JE, Hibert ENL, Whelan EA, Rocheleau CM, Grajewski B, Schernhammer ES, Rich-Edwards JW (2015) Work schedule and physically demanding work in relation to menstrual function: the nurses' health study 3. Scand J Work Environ Heal 41:194–203. https://doi.org/10.5271/sjweh.3482
8. Palmer KT, Bonzini M, Harris EC, Linaker C, Bonde JP (2013) Work activities and risk of prematurity, low birth weight and pre-eclampsia: an updated review with meta-analysis. Occup Environ Med 70:213–222. https://doi.org/10.1136/oemed-2012-101032
9. Bonde JP, Jørgensen KT, Bonzini M, Palmer KT (2013) Miscarriage and occupational activity: a systematic review and meta-analysis regarding shift work, working hours, lifting, standing, and physical workload. Scand J Work Environ Heal 39:325–334. https://doi.org/10.5271/sjweh.3337
10. Giudice LC (2016) Environmental toxicants: hidden players on the reproductive stage. Fertil Steril 106:791–794. https://doi.org/10.1016/j.fertnstert.2016.08.019
11. Rengaraj D, Kwon WS, Pang MG (2015) Effects of motor vehicle exhaust on male reproductive function and associated proteins. J Proteome Res 14:22–37. https://doi.org/10.1021/pr500939c
12. Ziv-Gal A, Flaws JA (2016) Evidence for bisphenol A-induced female infertility: a review (2007–2016). Fertil Steril 106:827–856. https://doi.org/10.1016/j.fertnstert.2016.06.027
13. Jurewicz J, Radwan M, Sobala W, Radwan P, Bochenek M, Hanke W (2014) Effects of occupational exposure - is there a link between exposure based on an occupational questionnaire and semen quality. Syst Biol Reprod Med 60:227–233. https://doi.org/10.3109/19396368.2014.907837
14. Sengupta P, Banerjee R, Nath S, Das S, Banerjee S (2015) Metals and female reproductive toxicity. Hum Exp Toxicol 34:679–697. https://doi.org/10.1177/0960327114559611
15. Giaccio L, Cicchella D, De Vivo B, Lombardi G, De Rosa M (2012) Does heavy metals pollution affects semen quality in men? A case of study in the metropolitan area of Naples (Italy). J Geochemical Explor 112:218–225. https://doi.org/10.1016/j.gexplo.2011.08.009
16. Jenardhanan P, Panneerselvam M, Mathur PP (2016) Effect of environmental contaminants on spermatogenesis. Semin Cell Dev Biol 59:126–40. https://doi.org/10.1016/j.semcdb.2016.03.024Get
17. Mínguez-Alarcón L, Hauser R, Gaskins AJ (2016) Effects of bisphenol A on male and couple reproductive health: a review. Fertil Steril 106:864–870. https://doi.org/10.1016/j.fertnstert.2016.07.1118
18. Lenters V, Portengen L, Smit LAM, Jönsson BAG, Giwercman A, Rylander L, Lindh CH, Spanò M, Pedersen HS, Ludwicki JK, Chumak L, Piersma AH, Toft G, Bonde JP, Heederik D, Vermeulen R (2015) Phthalates, perfluoroalkyl acids, metals and organochlorines and reproductive function: a multipollutant assessment in Greenlandic, Polish and Ukrainian men. Occup Environ Med 72:385–393. https://doi.org/10.1136/oemed-2014-102264
19. Weber RFA, Dohle GR, Romijn JC (2005) Clinical laboratory evaluation of male subfertility. Adv Clin Chem 40:317–364. https://doi.org/10.1016/s0065-2423(05)40008-6
20. Kurzawa R, Kozanecka A, Głabowski W, Malinowska D, Rózewicki S (1998) The analysis of the sperm parameters in view of its concentration and motility in relation to men's age and occupation. Ginekol Pol 69:460–465
21. Chia SE, Lim ST, Tay SK (2000) Factors associated with male infertility: sperm characteristics, strict criteria sperm morphology analysis and hypoosmotic swelling test. BJOG 107:55–61
22. Saremi AT, Zamanian M, Pooladi A (2017) Male infertility effective factors and failure type determination in iranian infertile men. Sarem J Reprod Med 2:3–8. https://doi.org/10.29252/sjrm.2.1.3
23. Wells G, Shea B, O'Connell D, Peterson J (2009) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hosp. Res. Inst, Ottawa
24. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA (2017) AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 358:j4008
25. Jüni P, Altman DG, Egger M (2001) Assessing the quality of controlled clinical trials. BMJ 323(7303):42–46
26. Kumar S, Murarka S, Mishra VV, Gautam AK (2014) Environmental & lifestyle factors in deterioration of male reproductive health. Indian J Med Res 140:29–35
27. Ji GX, Wu SM, Liu JN, Shi LL (2013) Bulky DNA adducts in human sperm correlate with semen parameters and sperm apoptosis. Zhonghua Nan Ke Xue 19:902–906
28. Jurewicz J, Radwan M, Sobala W, Brzeảnicki S, Ligocka D, Radwan P, Bochenek M, Hanke W (2013) Association between a biomarker of exposure to polycyclic aromatic hydrocarbons and semen quality. Int J Occup Med Environ Health 26:790–801. https://doi.org/10.2478/s13382-013-0152-9
29. Petersen MS, Halling J, Weihe P, Jensen TK, Grandjean P, Nielsen F, Jørgensen N (2015) Spermatogenic capacity in fertile men with elevated exposure to polychlorinated biphenyls. Environ Res 138:345–351. https://doi.org/10.1016/j.envres.2015.02.030
30. Vestergaard S, Nielsen F, Andersson AM, Hjøllund NH, Grandjean P, Andersen HR, Jensen TK (2012) Association between perfluorinated compounds and time to pregnancy in a prospective cohort of Danish couples attempting to conceive. Hum Reprod 27:873–880. https://doi.org/10.1093/humrep/der450
31. Xia Y, Zhu P, Han Y, Lu C, Wang S, Gu A, Fu G, Zhao R, Song L, Wang X (2009) Urinary metabolites of polycyclic aromatic hydrocarbons in relation to idiopathic male infertility. Hum Reprod 24:1067–1074. https://doi.org/10.1093/humrep/dep006
32. Gennings C, Carrico C, Factor-Litvak P, Krigbaum N, Cirillo PM, Cohn BA (2013) A Cohort study evaluation of maternal PCB exposure related to time to pregnancy in daughters. Environ Heal A Glob Access Sci Source 12:1–12. https://doi.org/10.1186/1476-069X-12-66
33. Nishihama Y, Toshima H, Yoshinaga J, Mizumoto Y, Yoneyama M, Nakajima D, Shiraishi H, Tokuoka S (2017) Paraben exposure and semen quality of Japanese male partners of subfertile couples. Environ Health Prev Med 22:1–5. https://doi.org/10.1186/s12199-017-0618-7
34. Du YY, Guo N, Wang YX, Hua X, Deng TR, Teng XM, Yao YC, Li YF (2018) Urinary phthalate metabolites in relation to serum anti-Müllerian hormone and inhibin B levels among women from a fertility center: a retrospective analysis. Reprod Health 15:1–12. https://doi.org/10.1186/s12978-018-0469-8
35. Meeker JD, Barr DB, Hauser R (2008) Human semen quality and sperm DNA damage in relation to urinary metabolites of pyrethroid insecticides. Hum Reprod 23:1932–1940. https://doi.org/10.1093/humrep/den242
36. Vélez MP, Arbuckle TE, Fraser WD (2015) Maternal exposure to perfluorinated chemicals and reduced fecundity: The MIREC study. Hum Reprod 30:701–709. https://doi.org/10.1093/humrep/deu350
37. Yang CY, Wang YJ, Chen PC, Tsai SJ, Guo YL (2008) Exposure to a mixture of Polychlorinated biphenyls and polychlorinated dibenzofurans resulted in a prolonged time to pregnancy in women. Environ Health Perspect 116:599–604. https://doi.org/10.1289/ehp.10715
38. Chen MW, Santos HM, Que DE, Gou YY, Tayo LL, Hsu YC, Chen YB, Chen FA, Chao HR, Huang KL (2018) Association between organochlorine pesticide levels in breast milk and their effects on female reproduction in a Taiwanese population. Int J Environ Res Public Health 15:931. https://doi.org/10.3390/ijerph15050931
39. Ji G, Gu A, Zhou Y, Shi X, Xia Y, Long Y, Song L, Wang S, Wang X (2010) Interactions between exposure to environmental polycyclic aromatic hydrocarbons and DNA repair gene polymorphisms on bulky DNA adducts in human sperm. PLoS One 5:e13145. https://doi.org/10.1371/journal.pone.0013145
40. Harville EW, Shankar A, Zilversmit L, Buekens P (2018) The Gulf oil spill, miscarriage, and infertility: the GROWH study. Int Arch Occup Environ Health 91:47–56. https://doi.org/10.1007/s00420-017-1257-4
41. Bastos AMX, Souza MCB d, Almeida Filho GL d, Krauss TM, Pavesi T, Silva LE d (2013) Organochlorine compound levels in fertile and infertile women from Rio de Janeiro, Brazil. Arq Bras Endocrinol Metabol 57:346–353. https://doi.org/10.1590/s0004-27302013000500003
42. Smith KW, Souter I, Dimitriadis I, Ehrlich S, Williams PL, Calafat AM, Hauser R (2013) Urinary paraben concentrations and ovarian aging among women from a fertility center. Environ Health Perspect 121:1299–1305. https://doi.org/10.1289/ehp.1205350
43. Meeker JD, Yang T, Ye X, Calafat AM, Hauser R (2011) Urinary concentrations of parabens and serum hormone levels, semen quality parameters, and sperm DNA damage. Environ Health Perspect 119:252–257. https://doi.org/10.1289/ehp.1002238
44. Meeker JD, Ehrlich S, Toth TL, Wright DL, Calafat AM, Trisini AT, Ye X, Hauser R (2010) Semen quality and sperm DNA damage in relation to

urinary bisphenol A among men from an infertility clinic. Reprod Toxicol 30:532–539. https://doi.org/10.1016/j.reprotox.2010.07.005

45. Cohn BA, Cirillo PM, Sholtz RI, Ferrara A, Park JS, Schwingl PJ (2011) Polychlorinated biphenyl (PCB) exposure in mothers and time to pregnancy in daughters. Reprod Toxicol 31:290–296. https://doi.org/10.1016/j.reprotox.2011.01.004
46. Crawford NM, Fenton SE, Strynar M, Hines EP, Pritchard DA, Steiner AZ (2017) Effects of perfluorinated chemicals on thyroid function, markers of ovarian reserve, and natural fertility. Reprod Toxicol 69:53–59. https://doi.org/10.1016/j.reprotox.2017.01.006
47. Thurston SW, Mendiola J, Bellamy AR, Levine H, Wang C, Sparks A, Redmon JB, Drobnis EZ, Swan SH (2016) Phthalate exposure and semen quality in fertile US men. Andrology 4:632–638. https://doi.org/10.1111/andr.12124
48. Guo Y, Weck J, Sundaram R, Goldstone AE, Buck Louis G, Kannan K (2014) Urinary concentrations of phthalates in couples planning pregnancy and its association with 8-hydroxy-2′-deoxyguanosine, a biomarker of oxidative stress: longitudinal investigation of fertility and the environment study. Environ Sci Technol 48:9804–9811. https://doi.org/10.1021/es5024898
49. Jurewicz J, Radwan M, Wielgomas B, Kałużny P, Klimowska A, Radwan P, Hanke W (2018) Environmental levels of triclosan and male fertility. Environ Sci Pollut Res 25:5484–5490. https://doi.org/10.1007/s11356-017-0866-5
50. Conti GO, Calogero AE, Giacone F, Fiore M, Barchitta M, Agodi A, Ferrante M (2017) B(a)P adduct levels and fertility: a cross-sectional study in a Sicilian population. Mol Med Rep 15:3398–3404. https://doi.org/10.3892/mmr.2017.6396
51. Messerlian C, Williams PL, Ford JB, Chavarro JE, Mínguez-Alarcón L, Dadd R, Braun JM, Gaskins AJ, Meeker JD, James-Todd T, Chiu Y-H, Nassan FL, Souter I, Petrozza J, Keller M, Toth TL, Calafat AM, Hauser R (2018) The Environment and Reproductive Health (EARTH) Study: a prospective preconception cohort. Hum Reprod Open 2018:hoy001. https://doi.org/10.1093/hropen/hoy001
52. Aneck-Hahn NH, Schulenburg GW, Bornman MS, Farias P, De Jager C (2007) Impaired semen quality associated with environmental DDT exposure in young men living in a malaria area in the Province, South Africa. J Androl 28:423–434. https://doi.org/10.2164/jandrol.106.001701
53. Wang C, Yang L, Wang S, Zhang Z, Yu Y, Wang M, Cromie M, Gao W, Wang SL (2016) The classic EDCs, phthalate esters and organochlorines, in relation to abnormal sperm quality: a systematic review with meta-analysis. Sci Rep 6:1–11. https://doi.org/10.1038/srep19982
54. Hipwell AE, Kahn LG, Factor-Litvak P, Porucznik CA, Siegel EL, Fichorova RN, Hamman RF, Klein-Fedyshin M, Harley KG (2019) Exposure to non-persistent chemicals in consumer products and fecundability: a systematic review. Hum Reprod Update 25:51–71. https://doi.org/10.1093/humupd/dmy032
55. Bonde JP, Flachs EM, Rimborg S, Glazer CH, Giwercman A, Ramlau-Hansen CH, Hougaard KS, Høyer BB, Hærvig KK, Petersen SB, Rylander L, Specht IO, Toft G, Bräuner EV (2016) The epidemiologic evidence linking prenatal and postnatal exposure to endocrine disrupting chemicals with male reproductive disorders: a systematic review and meta-analysis. Hum Reprod Update 23:104–125. https://doi.org/10.1093/HUMUPD/DMW036
56. Caserta D, Mantovani A, Marci R, Fazi A, Ciardo F, La Rocca C, Maranghi F, Moscarini M (2011) Environment and women's reproductive health. Hum Reprod Update 17:418–433. https://doi.org/10.1093/humupd/dmq061
57. Martenies SE, Perry MJ (2013) Environmental and occupational pesticide exposure and human sperm parameters: a systematic review. Toxicology 307:66–73
58. Machtinger R, Combelles CMH, Missmer SA, Correia KF, Williams P, Hauser R, Racowsky C (2013) Bisphenol-A and human oocyte maturation in vitro. Hum Reprod 28:2735–2745. https://doi.org/10.1093/humrep/det312
59. Schuh-Huerta SM, Johnson NA, Rosen MP, Sternfeld B, Cedars MI, Reijo Pera RA (2012) Genetic variants and environmental factors associated with hormonal markers of ovarian reserve in Caucasian and African American women. Hum Reprod 27:594–608. https://doi.org/10.1093/humrep/der391
60. Shin JJ, Jee BC, Kim H, Kim SH (2017) Major disease prevalence and menstrual characteristics in infertile female Korean smokers. J Korean Med Sci 32:321–328. https://doi.org/10.3346/jkms.2017.32.2.321
61. Axelsson J, Rylander L, Rignell-Hydbom A, Silfver KÅ, Stenqvist A, Giwercman A (2013) The impact of paternal and maternal smoking on semen quality of adolescent men. PLoS One 8:e66766. https://doi.org/10.1371/journal.pone.0066766
62. Keshavarzi F, Omidvar BMH, Bakhtiari F (2016) The survey of infertility risk factors in admitted men to infertility center of Mo'tazedi hospital in Kermanshah, 2012-2013
63. Mahalingaiah S, Hart JE, Laden F, Farland LV, Hewlett MM, Chavarro J, Aschengrau A, Missmer SA (2016) Adult air pollution exposure and risk of infertility in the Nurses' Health Study II. Hum Reprod 31:638–647
64. Vecoli C, Montano L, Borghini A, Notari T, Guglielmino A, Mercuri A, Turchi S, Andreassi MG (2017) Effects of highly polluted environment on sperm telomere length: a pilot study. Int J Mol Sci 18:1703. https://doi.org/10.3390/ijms18081703
65. Joffe M, Paranjothy S, Fielder H, Lyons R, Palmer S (2008) Use of time to pregnancy in environmental epidemiology and surveillance. J Public Health (Bangkok) 30:178–185. https://doi.org/10.1093/pubmed/fdn005
66. Najafi TF, Roudsari RL, Namvar F, Ghanbarabadi VG, Talasaz ZH, Esmaeli M (2015) Air pollution and quality of sperm: a meta-analysis. Iran Red Crescent Med J 17. https://doi.org/10.5812/ircmj.17(4)2015.26930
67. Carré J, Gatimel N, Moreau J, Parinaud J, Léandri R (2017) Does air pollution play a role in infertility?: a systematic review. Environ Heal A Glob Access Sci Source 16:1–16. https://doi.org/10.1186/s12940-017-0291-8
68. Sharma R, Rajput N, Bansal K, Highland H (2017) Effect of low level, short wavelength ultraviolet radiation on sperm chromatin. Asian Pacific J Reprod 6:252–256. https://doi.org/10.4103/2305-0500.217336
69. Moghbeli-Nejad S, Mozdarani H, Aleyasin A (2012) Increased frequency of micronuclei in lymphocytes of infertile males after exposure to gamma irradiation: a possible sign of genomic instability. J Assist Reprod Genet 29:89–94. https://doi.org/10.1007/s10815-011-9550-8
70. Stone MB, Stanford JB, Lyon JL, van der Slice JA, Alder SC (2013) Childhood thyroid radioiodine exposure and subsequent infertility in the intermountain fallout cohort. Environ Health Perspect 121:79–84. https://doi.org/10.1289/ehp.1104231
71. Adams JA, Galloway TS, Mondal D, Esteves SC, Mathews F (2014) Effect of mobile telephones on sperm quality: a systematic review and meta-analysis. Environ Int 70:106–112. https://doi.org/10.1016/j.envint.2014.04.015
72. Hassun Filho PA (2007) Re: Wet heat exposure: a potentially reversible cause of low semen quality in infertile men [6]. Int Braz J Urol 33:269–270. https://doi.org/10.1590/s1677-55382007000200023
73. Morán-Martínez J, Carranza-Rosales P, Morales-Vallarta M, Heredia-Rojas JA, Bassol-Mayagoitia S, Betancourt-Martínez ND, Cerda-Flores RM (2013) Chronic environmental exposure to lead affects semen quality in a Mexican men population. Iran J Reprod Med 11:267–274
74. Xu W, Bao H, Liu F, Liu L, Zhu YG, She J, Dong S, Cai M, Li L, Li C, Shen H (2012) Environmental exposure to arsenic may reduce human semen quality: associations derived from a Chinese cross-sectional study. Environ Heal A Glob Access Sci Source 11:1–9. https://doi.org/10.1186/1476-069X-11-46
75. Wu H-M, Lin-Tan D-T, Wang M-L, Huang H-Y, Lee C-L, Wang H-S, Soong Y-K, Lin J-L (2012) Lead level in seminal plasma may affect semen quality for men without occupational exposure to lead. Reprod Biol Endocrinol 10:1–5
76. He YQ, Zou QX, Chen H, Weng SQ, Luo T, Zeng XH (2016) Lead inhibits human sperm functions by reducing the levels of intracellular calcium, cAMP, and tyrosine phosphorylation. Tohoku J Exp Med 238:295–303. https://doi.org/10.1620/tjem.238.295
77. Lei HL, Wei HJ, Ho HY, Liao KW, Chien LC (2015) Relationship between risk factors for infertility in women and lead, cadmium, and arsenic blood levels: a cross-sectional study from Taiwan. BMC Public Health 15:1–11. https://doi.org/10.1186/s12889-015-2564-x
78. Mendiola J, Moreno JM, Roca M, Vergara-Jurez N, Martínez-García MJ, García-Snchez A, Elvira-Rendueles B, Moreno-Grau S, Lápez-Espín JJ, Ten J, Bernabeu R, Torres-Cantero AM (2011) Relationships between heavy metal concentrations in three different body fluids and male reproductive parameters: a pilot study. Environ Heal A Glob Access Sci Source 10:1–7. https://doi.org/10.1186/1476-069X-10-6
79. Hsi HC, Hsu YW, Chang TC, Chien LC (2016) Methylmercury concentration in fish and risk-benefit assessment of fish intake among pregnant

versus infertile women in Taiwan. PLoS One 11:e0155704. https://doi.org/10.1371/journal.pone.0155704
80. Meeker JD, Rossano MG, Protas B, Diamond MP, Puscheck E, Daly D, Paneth N, Wirth JJ (2008) Cadmium, lead, and other metals in relation to semen quality: Human evidence for molybdenum as a male reproductive toxicant. Environ Health Perspect 116:1473–1479. https://doi.org/10.1289/ehp.11490
81. Łepecka-Klusek C, Wdowiak A, Pilewska-Kozak AB, Syty K, Jakiel G (2011) The role of age, environmental and occupational factors on semen density. Ann Agric Environ Med 18:437–440
82. Mínguez-Alarcón L, Souter I, Williams PL, Ford JB, Hauser R, Chavarro JE, Gaskins AJ (2017) Occupational factors and markers of ovarian reserve and response among women at a fertility centre. Occup Environ Med 74:426–431. https://doi.org/10.1136/oemed-2016-103953
83. Gaskins AJ, Rich-Edwards JW, Lawson CC, Schernhammer ES, Missmer SA, Chavarro JE (2015) Work schedule and physical factors in relation to fecundity in nurses. Occup Environ Med 72:777–783. https://doi.org/10.1136/oemed-2015-103026
84. Wang HX, Li HC, Lv MQ, Zhou DX, Bai LZ, Du LZ, Xue X, Lin P, Qiu SD (2015) Associations between occupation exposure to formaldehyde and semen quality, a primary study. Sci Rep 5:1–10. https://doi.org/10.1038/srep15874
85. Wijesekara GUS, Fernando DMS, Wijerathna S, Bandara N (2015) Environmental and occupational exposures as a cause of male infertility. Ceylon Med J 60:52–56. https://doi.org/10.4038/cmj.v60i2.7090
86. De Fleurian G, Perrin J, Ecochard R, Dantony E, Lanteaume A, Achard V, Grillo JM, Guichaoua MR, Botta A, Sari-Minodier I (2009) Occupational exposures obtained by questionnaire in clinical practice and their association with semen quality. J Androl 30:566–579. https://doi.org/10.2164/jandrol.108.005918
87. Daoud S, Sellami A, Bouassida M, Kebaili S, Ammar Keskes L, Rebai T, Chakroun Feki N (2017) Routine assessment of occupational exposure and its relation to semen quality in infertile men: a cross-sectional study. Turkish J Med Sci 47:902–907. https://doi.org/10.3906/sag-1605-47
88. Mahboubi M, Foroughi F, Ghahramani F, Shahandeh H, Moradi S, Shirzadian T (2014) A case-control study of the factors affecting male infertility. Turkish J Med Sci 44:862–865. https://doi.org/10.3906/sag-1304-35
89. Kumar D, Salian SR, Kalthur G, Uppangala S, Kumari S, Challapalli S, Chandraguthi SG, Krishnamurthy H, Jain N, Kumar P, Adiga SK (2013) Semen abnormalities, sperm DNA damage and global hypermethylation in health workers occupationally exposed to ionizing radiation. PLoS One 8:e69927. https://doi.org/10.1371/journal.pone.0069927
90. Jeng HA, Pan CH, Chao MR, Chiu CC, Zhou G, Chou CK, Lin WY (2016) Sperm quality and DNA integrity of coke oven workers exposed to polycyclic aromatic hydrocarbons. Int J Occup Med Environ Health 29:915–926. https://doi.org/10.13075/ijomeh.1896.00598
91. Kim D, Kang MY, Choi S, Park J, Lee HJ, Kim EA (2016) Reproductive disorders among cosmetologists and hairdressers: a meta-analysis. Int Arch Occup Environ Health 89:739–753. https://doi.org/10.1007/s00420-016-1112-z
92. Xuan L, Meng XY, Sun B, Wang Q, Liu C, Cong Y, Liu JN, Wu SK (2019) Clinical observation of docetaxel combination with bevacizumab in the multiline rescue treatment of metastatic breast cancer. Chinese J Cancer Prev Treat 26:316–319
93. Sarvari A, Naderi MM, Heidari M, Zarnani AH (2010) Review article effect of environmental risk factors on human fertility. J Reprod Infretil 11:2010
94. Figà-Talamanca I (2006) Occupational risk factors and reproductive health of women. Occup Med (Chic Ill) 56:521–531. https://doi.org/10.1093/occmed/kql114
95. He Y, Zou Q, Chen H, Weng S, Luo T, Zeng X (2016) Lead inhibits human sperm functions by reducing the levels of intracellular calcium, cAMP, and tyrosine phosphorylation. Tohoku J Exp Med 238(4):295–303.
96. Chinyere Nsonwu-Anyanwu A, Raymond Ekong E, Jeremiah Offor S, Francis Awusha O, Chukwuma Orji O, Idiongo Umoh E, Aleruchim Owhorji J, Rowland Emetonjor F, Adanna Opara Usoro C (2019) Heavy metals, biomarkers of oxidative stress and changes in sperm function: A case-control study. Int J Reprod Biomed 17(3):163–74. https://doi.org/10.18502/ijrm.v17i3.4515.
97. Niederberger C (2013) Re: Lead level in seminal plasma may affect semen quality for men without occupational exposure to lead. J Urol 190:211. https://doi.org/10.1016/j.juro.2013.04.012
98. Oliva A, Spira A, Multigner L (2001) Contribution of environmental factors to the risk of male infertility. Hum Reprod 16:1768–1776. https://doi.org/10.1093/humrep/16.8.1768

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