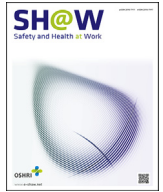




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Review Article

Occupational Exposure to Physical and Chemical Risk Factors: A Systematic Review of Reproductive Pathophysiological Effects in Women and Men



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ABSTRACT

The human reproductive system can be affected by occupational exposure to many physical and chemical risk factors. This study was carried out to review the studies conducted on the issue of the pathophysiological effects of occupational physical and chemical risk factors on the reproductive system of females and males. In this systematic review, the databases such as “Google Scholar,” “Pub-Med,” “Scopus,” and “Web of Science” were used. Following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020), the studies included in our study were published between 2000 and 2021. In order to extract the required data, all sections of the articles were reviewed. Out of 57 articles we reviewed, 34 articles were related to field studies and 23 articles to clinical studies. Among them, 43 studies dealt with the pathophysiological effects of chemical agents, six studies dealt with the pathophysiological effects of physical factors, and 8 studies dealt with the pathophysiological effects of physicochemical factors on the human reproductive system. Physical (noise, heat, and radiofrequency radiation) and chemical (such as carbamate and organophosphate pesticides, benzene, toluene, xylene, formaldehyde, NO₂, CS₂, manganese, lead, nickel, and n-hexane) risk factors had pathophysiological effects on the human reproductive system. The presence of these risk factors in the workplace caused damage to the human reproductive system. The rate of these negative pathophysiological effects can be reduced by performing appropriate managerial, technical, and engineering measures in work environments.

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1. Introduction

Occupational activities generate many various physical and chemical risk factors. The variety of these environmental risk factors has often caused most employees to be exposed to various occupational hazards [1]. Following workers' exposure to these risk factors, their health is likely to be affected, leading to various diseases and physiological disorders, including cancers and neurological and systemic abnormalities [2].

The reproductive system is one of the most sensitive systems in the human body that can be affected by these occupational exposures [3]. This system is a distinct set of organs that work together to reproduce and deliver live offspring. Despite anatomical differences in this system between men and women, their reproductive systems are complementary and created to ensure the generation's survival [4]. Female and male reproductive systems consist of various components, such as sperm, seminal fluid, and hormones,

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whose physiological parameters can be affected by occupational exposures [5].

In fact, it is possible that following exposure to many of these risk factors, the human reproductive system is affected and causes irreversible health, psychological, and social effects on workers [6,7]. Reproductive system disorders cause unintended consequences such as infertility, microscopic changes in the reproductive system, and destructive psychological effects on marital relationships [8]. Some adverse effects that may occur due to exposure to these risk factors in the human reproductive system include changes in the number of sex hormones, the emergence of abnormalities in the parameters, and the quality of semen [9,10].

Many studies have investigated the pathophysiological effect of various factors on the level of health of the human reproductive system. Many chemicals in the workplace hurt the human reproductive system [11]. Among the studies conducted on this topic, some have received contradictory answers. For example, a study showed that most of the glycol ethers used in that study did not affect the semen parameters of these individuals, while the glycol ethers used in the 1960s affected semen quality [12]. Although the possibility of some metals affecting the reproductive system has been investigated and generally confirmed, a study showed that being exposed to metal pollutants did not affect male fertility [13].

Many physical risk factors also affected this system [14]. For example, one of these risk factors is heat. A cross-sectional study involving some employees who worked in the steel industry revealed that the parameters of workers' semen were affected by heat [15]. Another example is noise. A clinical study involving men who visited an infertility clinic for diagnostic purposes showed that exposure to noise while working reduced sperm motility [16].

On the other hand, many workers are constantly exposed to these physical and chemical risk factors [16]. The work activity of many workers is such that they spend the entire work shift or a large part of their shift with many of these risk factors. So, their working conditions are such that they provide a basis for damage to many of their body systems, including the reproductive system [6]. Therefore, more studies should be done on the impact of workplace risk factors.

In addition, according to searches in authoritative scientific sources, the present study's authors did not find a systematic review study that comprehensively investigates the pathophysiological effects of physical and chemical risk factors of occupational environments on the human reproductive system. Therefore, the present research, using the keywords mentioned in the next section (Materials and methods), reviewed the studies conducted on the pathophysiological effect of physical and chemical risk factors on the reproductive system of females and males.

2. Materials and methods

2.1. Search strategy

The male reproductive system is made up of the external genitalia (a penis and bilateral testes within the scrotum) and the internal reproductive organs (prostate gland, vas deferens or ejaculatory ducts, and seminal vesicles) [17]. Ovaries, fallopian tubes, uterus, and vagina are also part of the female reproductive system [18]. Considering these definitions, the authors used the authoritative databases of "Google Scholar," "Embase," "Scopus," "PubMed," "Web of Science," "IranMedex," "IranDoc," "SID," and "Magiran" to search for relevant articles. Research articles published in Persian and English from 2000 to 2021 in these databases have been extracted. To find relevant articles in 2022 (February to March), the following English and Persian keywords were

searched: "Physical risk factors," "Chemical risk factors," "Occupational exposure," "Reproductive functions," "Sexual functions," "Reproductive hormones," "Sex hormones," "Sex organs," "Semen quality," "Reproductive disorders," "Reproductive organs," "Female Reproductive System," "Male Reproductive System," "Fertility," "Fecundity", "ریسک فاکتورهای فیزیکی", "ریسک فاکتورهای شیمیایی", "مواجهه شغلی", "عملکردهای تولید مثلی", "هورمونهای تولیدمثلی", "هورمونهای جنسی", "کیفیت مایع منی", "سیستم تولیدمثلی زنان", "سیستم تولیدمثلی مردان", "اختلالات تولیدمثلی", "اندامهای تولیدمثلی", and "باروری". The collected articles were entered into EndNote, X20 software, and duplicate articles were removed.

2.2. Study selection and data extraction

In order to select articles, five authors reviewed the search results and screened qualified articles for full-text review based on the title and abstract and two others, one as the team leader and the other as a consultant, supervised the research implementation process. Also, in order to extract data, on the one hand, all studies that specifically investigated the pathophysiological effects of occupational physical and chemical risk factors on the reproductive system of females and males were included in this study, but on the other hand, nonresearch articles such as authors' notes, editorials, popular texts, and articles not written in Persian and English were removed. These forms contained information such as the study design, country and year of publication of the article, occupational risk factor, study population (number, gender, and age of participants), confounding factors, and pathophysiological reproductive effects. The articles containing these forms' information were selected, and other articles were discarded.

2.3. Evaluation of quality of articles

In order to present this study and evaluate the quality of the articles, The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 [19] and The Joanna Briggs Institute (JBI) checklist [20] were used, respectively.

3. Results

Fifty-seven studies were finally selected for use in this article (Fig. 1). Among them, thirty-four studies were field studies (59.65%) and 23 studies were clinical studies (40.35%) (Tables 1 and 2). In field studies, 33 studies (97%) were conducted with the participation of men, and 1 study (3%) with the participation of women. In clinical studies, 19 studies (82.6%) were conducted with the participation of men, 1 study (4.4%) with the participation of women, and 3 studies (13%) with the participation of women and men.

According to Tables 1 and 2, 28 studies (49.1%) were cross-sectional, 16 studies (28.1%) were case-control, and 13 studies (22.8%) were performed according to other study designs. Out of 57 studies, 11 studies (19.3%) were conducted in China, 5 studies in Iran (8.8%), and 5 studies (8.8%) in the United States (Fig. 2). Among them, the share of Asia was 23 studies (40.35%), Europe 15 studies (26.3%), North America 10 studies (17.54%), Africa 5 studies (8.8%), and South America 4 studies (7.01%).

Forty-three studies (75.44%) investigated chemical agents, 6 studies (10.53%) investigated physical agents, and 8 studies (14.03%) investigated physicochemical agents (Fig. 3). Among them, in field studies, 30 studies (88.23%) studied chemical factors. Also, in clinical studies, 13 studies (56.5%) investigated chemical agents, 2 studies (8.7%) investigated physical factors, and 8 studies (34.8%) investigated physicochemical factors.

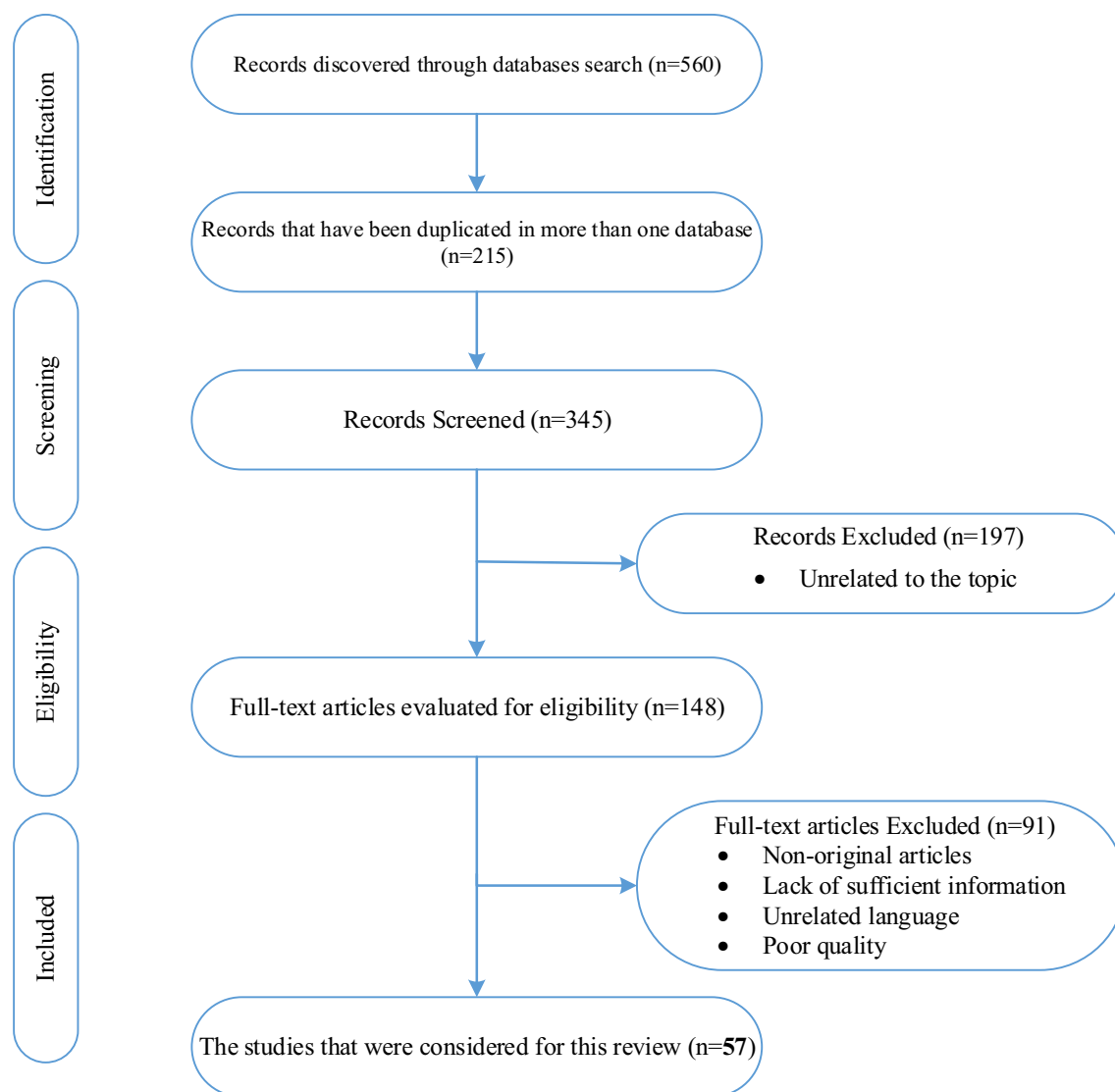


Fig. 1. The process of identifying and selecting the articles.

Among the physical risk factors of work environments, the pathophysiological effects of heat, noise, vibration, extremely low-frequency magnetic field (ELF-MF), and radio frequency (RF) radiation on the parameters of the human reproductive system were studied. According to the results, the noise reduced testosterone (T) levels [11]. Heat could also affect sperm volume, morphology, number, and motility [15]. Among the radiation rays, RF radiation affected follicle-stimulating hormone (FSH) levels and increased them, and caused harmful effects on the human reproductive system [21].

In addition, several other chemical risk factors had destructive pathophysiological effects on the human reproductive system. Semen quality could be affected by pesticides of carbamate and organophosphate, lead, cadmium, benzene, toluene, and xylene (BTXs) [31,35,39,43]. Sperm motility can also be overshadowed by being exposed to ethylbenzene, BTXs, formaldehyde, bisphenol A (BPA), NO₂, lead, CS₂, and manganese (Mn) [9,10,27,28,33,41,44].

These chemical risk factors also affected other parameters of the reproductive system. Ethylbenzene, BTXs, BPA, and lead affected the total sperm count [9,10,44]. Exposure to chromium and BPA changed sperm concentration [9,42]. Carbamate and organophosphate pesticides, n-hexane, municipal solid waste, soil and paint, CS₂, and BPA affected sex hormones [23–27,30,34,35]. In addition, pesticides

affected sperm morphology [25]. Infertility, congenital anomalies and miscarriage were reported in humans following being exposed to pesticides, n-hexane, and organic solvents [23,29,38,40].

According to Table 2, radiation, fungicides, herbicides, and electromagnetic fields (EMFs) increased fertility problems in individuals [49,60,67]. Excessive heat, noise, polyvinyl chloride (PVC), polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), and glycol ether also had detrimental effects on sperm motility [16,55,57,61,66]. Some phthalates, SO₂ and NO₂, affected the concentration and the total number of sperm [50,52]. Furthermore, sperm concentration could be affected by PVC [16]. Sperm quality could also change after being exposed to pyrethroid insecticides, phthalates, noise, polychlorinated biphenyls, and hexachlorobenzene [16,52,53,56]. Some sex hormones are also damaged by being exposed to solvents [68].

The influence of many of these work environment risk factors on the human reproductive system has made this issue always important and constantly being researched (Fig. 4). It is worth mentioning that many of these studies were conducted considering confounding factors such as age, race, BMI, education, marital status, smoking, income, abstinence time, alcohol consumption, and working age.

Table 1
Summary of field studies on the effect of physical and chemical risk factors on the human reproductive system

Study design	Country (year)	Risk factor(s)	Study population	Confounding factors	Pathophysiological reproductive effects
Physical risk factors					
Case study [11]	Iran (2021)	WBV and noise	Workers of automobile parts manufacturing plant: 162 men; age: 22–50 years	Age, smoking, BMI, working age, urogenital disease, marital status, reproductive health status, and medical histories	- Only the association between noise exposure (in all values (dB): <87.1, 87.1–92.69, and >92.69) and T levels ($R = -0.201$, $p = 0.013$) were statistically significant - ELF exposure had no statistically significant connection with blood levels of free T, LH, or FSH ($p = 0.08$, $p = 0.28$, and $p = 0.88$, respectively) (median exposure values in three groups: (low = $0.33 \mu\text{T}$), (moderate = $1.51 \mu\text{T}$), and (high = $14.78 \mu\text{T}$))
Cross-sectional [14]	Iran (2020)	ELF-MF	Power plant workers: 122 men; age: 20–50 years	Age, smoking, working age, BMI, urogenital disease, reproductive health status, and medical histories	- Heat had a detrimental effects on most semen parameters (volume, morphology, motility, and sperm) ($p < 0.005$). The mean \pm (SD) of the $\text{WBG}_{\text{T}_{\text{WVA}}} (\text{C}^\circ)$ index: the exposed group: $35.76 \pm (2.52)$ and the unexposed group: $20.7 \pm (0.36)$. The mean \pm (SD) of the $\text{PHS}_{\text{T}_{\text{WVA}}} (\text{W}/\text{m}^2)$ index: the exposed group: $491.56 \pm (18.75)$ and the unexposed group: $80.51 \pm (3.1)$
Cross-sectional [15]	Iran (2018)	Heat	Steel industry workers: 44 men; age: 21–50 years	Age, smoking, urogenital disease, use of antioxidant medications, reproductive health status, and medical histories	- Workers who had been exposed to RF had a higher mean FSH level than workers who had not been exposed (7.6 vs. 5.8 mIU/mL, $p = 0.05$)
Cross-sectional [21]	USA (2000)	RF radiation	RF radiation heater operators: 46 men	Working age, and some chemical substances (1,1,1-trichloroethane, toluene, decane, 2-ethyl-1-hexanol, undecane, dodecane, remaining total hydrocarbons, formaldehyde, hydrochloric acid, and sulfuric acid), reproductive health status, and medical histories	
Chemical risk factors					
Cross-sectional [3]	Iran (2019)	Lead	Welders: 165 men; age: 20–50 years	Age, marital status, drinking, smoking, working age, urogenital disease, reproductive health status, and medical histories	- Exposure to lead may cause reproductive disorders - Blood lead levels were associated inversely to T levels and directly to LH ($r = 0.72$; $p = 0.004$) and FSH ($r = 0.78$; $p = 0.001$) levels. (The average concentration of lead fumes in the blood and breathing zone were $460.28 \pm 93.65 \mu\text{g}/\text{L}$ and $0.57 \pm 0.12 \text{ mg}/\text{m}^3$, respectively)
Cross-sectional [22]	China (2019)	Manganese	workers: 260 men; age: above 18 years	Age, length of service, smoking, BMI, alcohol intake, duration of abstinence, education, and offspring's birth weight	- Mn caused the abnormal release of hormones and decreases sperm total motility ($p < 0.01$). (Urinary Mn levels in individuals exposed to Mn varied from 0.56 to $34.25 \mu\text{g}/\text{L}$, with an average of $15.92 + 8.49 \mu\text{g}/\text{L}$)
Nested case-control [23]	Mexico (2019)	N-hexane	Women working in a shoe factory: 64 women	Age, drinking, smoking, marital status, and gynecologic-obstetric histories	- Exposure to N-hexane caused menstrual cycle lengthening, a longer period to become pregnant ($p = 0.007$), and a drop in FSH ($r = -0.34$, $p = 0.028$) and LH levels ($r = -0.36$, $p = 0.033$). (The mean exposure to n-hexane was $49.2 \pm 39.6 \text{ mg}/\text{m}^3$)
Cross-sectional [24]	Egypt (2017)	Pesticides	Farmers: 51 men	Age, smoking, working age, and socioeconomic status	- Exposure to pesticides significantly increased FSH concentration ($p < 0.001$).
Cross-sectional [25]	Brazil (2017)	Pesticides	Farmers: 135 men; age: 18–23 years	Age, education, working age, drinking, smoking, BMI, reproductive health status, and medical histories	- Exposure to pesticides caused the destruction of morphology and the reduction of LH ($p = 0.01$) and prolactin ($p = 0.05$).
Cross-sectional analytical [26]	Nigeria (2017)	Municipal solid wastes, sawdust, and paint	Workers of municipal solid waste disposal, paint factory and sawmill companies: 157 men; age: 18–50 years	Age, BMI, working age, and sociodemographic characteristics	- Workers' exposure to chemical risk factors (municipal solid waste, sawdust, and paint) resulted in a drop in the average level of LH ($p < 0.05$), serum estrogen ($p < 0.05$), and T ($p < 0.05$)

Historical cohort [27]	China (2016)	CS ₂	Workers of a chemical fiber factory: 173 men	Age, BMI, education, working age, alcohol consumption, smoking, marital status, reproductive health status, and medical histories	- Exposure to CS ₂ reduced sperm viability ($r = -0.67, p < 0.005$), motility ($r = -0.64, p < 0.005$) and morphology ($r = -0.67, p < 0.007$). - The CS ₂ -exposed individuals ($9.73 \pm 2.76 \text{ mg/m}^3$) had considerably greater blood FSH and LH levels but decreased serum T levels
Case-control [28]	China (2015)	Formaldehyde	Workers: 190 men; age: 23–40 years	Age, BMI, working age, education, income, smoking, drinking, and abstinence duration	- Exposure to formaldehyde (0.22 to 2.91 mg/m^3) decreased progressive sperm motility ($\beta = -0.19, p = 0.01$) and total sperm motility ($\beta = -0.23, p = 0.004$)
Cross-sectional [29]	Iran (2014)	Pesticides	Married male farmworkers: 268 men	Age, smoking, working age, education, BMI, maternal status, alcohol and coffee use, socioeconomic class, and reproductive health status	- Farmers' families had a greater rate of primary infertility owing to exposure to pesticide than the general population ($p < 0.05$)
Cross-sectional [30]	Mexico (2013)	Organophosphate	Floriculture workers: 143 men; age: 18–53 years	Age, income, education, BMI, tobacco and alcohol consumption, working age, occupational and pesticide exposure, residential pesticide exposure, living close to industry, place of residence, PONI activity, p,p'-DDE, creatinine, and total lipids	- Exposure to organophosphate pesticides increased serum FSH and prolactin levels and decreases serum T ($p < 0.05$)
Cross-sectional [31]	Venezuela (2013)	Organophosphate and carbamate pesticides	Farmers: 99 men; age: 18–52 years	Age, smoking, history of work with pesticides, clinical characteristics, reproductive disorders, alcohol consumption, sociodemographic characteristics, BMI, reproductive health status, and medical histories	- Exposure to pesticides caused a decrease in the quality of semen quality and changes in male reproductive hormones ($p < 0.05$) - Exposure to pesticide resulted in a significant variation in certain sperm parameters, including greater semen pH ($p = 0.004$) and a decreased proportion of live sperm ($p > 0.0001$). Furthermore, there was a marginally notable relationship ($p = 0.05$) between exposure to pesticide and rapid and progressive sperm motility
Case-series [10]	Egypt (2013)	Lead (PbB)	Infertile painters: 27 men; age: 27–39 years	Age, working age, socioeconomic status, genetic disorders related to the reproductive system, reproductive disorders, reproductive health status, and medical histories	- Blood lead had a substantial negative relationship with sperm count and motility ($p < 0.05$ and $p < 0.05$, respectively) Individuals with $\text{PbB} \geq 20 \text{ } \mu\text{g dL}^{-1}$ had a substantial reduction in sperm motility and an increase in T levels
Cohort study [9]	China (2011)	BPA	Workers of factories with and without BPA: 218 men	Age, education, history of chronic disease, previous exposure to other chemicals and heavy metals, employment history, marital status, age at first intercourse, smoking, drinking, and study site	- BPA reduced sperm concentration ($\beta = -15.6, p < 0.001$), total sperm count ($\beta = -42.1, p = 0.004$), sperm vitality ($\beta = -4.6, p < 0.001$), and sperm motility ($\beta = -3.1, p < 0.001$)
Cross-sectional [32]	Taiwan (2011)	DEHP	Workers of PVC plants: 45 men	Age, coffee drinking, smoking, and working age	- DEHP concentrations in breathing air area had a positive correlation with sperm DNA denaturation ($\beta = 0.038$) and DFI ($\beta = 0.140$) but a negative correlation with sperm motility ($\beta = -0.227$) (Personal DEHP air concentrations (mg/m^3) in groups exposed to high and low DEHP were 56.3 ± 26.8 and 7.9 ± 7.1 , respectively)
Cross-sectional [33]	Italy (2009)	NO ₂	Workers employed in a motorway company: 307 men; age: 23–57 years	Age, BMI, time of abstinence, smoking, alcohol and drug consumption, working age, urogenital disease, reproductive health status, and medical histories	- Exposure to NO ₂ significantly reduced sperm motility in workers ($p < 0.001$) (NO ₂ exposures (Mean $\mu\text{g/m}^3$): Group 1: 301.1, Group 2: 297.13, Group 3: 154.78, and Group 4: 151.28)
Cross-sectional [34]	Korea (2008)	BPA	Epoxy resin painters: 25 men, mean age: 42.8 years	Age, smoking, drinking, and working age	- Exposure to BPA reduced T level ($\beta = -0.049, p = 0.754$) while increased LH ($\beta = 0.487, p = 0.040$) and ($\beta = -0.057, p = 0.855$) FSH levels (The concentration of BPA in the urine of painters = $2.61 \pm 1.08 \text{ } \mu\text{g/g creatinine}$)
Cross-sectional [12]	France (2007)	Glycol ethers	Workers of the Paris municipality: 109 men	Age, sexual abstinence, and season of semen analysis	- The glycol ether used did not affect semen quality or hormone levels ($p > 0.05$)

(continued on next page)

Table 1 (continued)

Study design	Country (year)	Risk factor(s)	Study population	Confounding factors	Pathophysiological reproductive effects
Cross-sectional [35]	Peru (2006)	Organophosphorus pesticides	Organophosphorus pesticides applicators: 111 men; age: 20–60 years	Age, BMI, smoking, drinking, and coffee consumption	- Use of pesticide had a negative impact on the quality of sperm (seminal volume ($\beta = -0.60, p = 0.009$), seminal PH ($\beta = 0.52, p < 0.0001$), time of liquefaction ($\beta = 2.64, p = 0.04$), and normal sperm morphology ($\beta = -9.74, p < 0.0001$)) and sex hormones (T ($\beta = -0.947, p = 0.009$) and LH ($\beta = -0.48, p < 0.0001$)) - Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Case-control [36]	China (2006)	Buprofezin	Workers of a pesticide factory: 86 men	Age, BMI, smoking, drinking, and sexual abstinence	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Case-control [37]	China (2006)	Fenvalerate	Workers of a pesticide factory: 122 men; age: 18–45 years	Age, length of service, smoking, and drinking.	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Case-control [38]	Netherlands (2006)	Organic solvents	Painters: 700 men; age: 31–56 years	Maternal age, parental smoking and alcohol use, maternal use of prescribed medication, and maternal occupational exposures	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Cross-sectional [39]	Peru (2005)	Lead	Traffic police officers: 43 men; age: 20–55 years	Age, working age, and zinc concentration in serum	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Historical cohort [40]	Mexico (2004)	DDT	Malaria control workers: 2033 men; age: 28–82 years	Parents' age at each child's birth, exposure to other pesticides, exposure to chemical substances in other jobs, smoking, and alcohol consumption	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Cross-sectional [41]	Taiwan (2004)	Lead (PbB)	Male lead workers: 163 men; age: 18–38 years	For men: Age at the beginning of TTP, use of tea or coffee, use of alcohol, and smoking. For women: Age at the beginning of TTP, use of tea, use of alcohol, smoking, contraceptive use before TTP, age at menarche, shift work, calendar year of pregnancy, and pregnancy sequence	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Case-control [42]	India (2003)	Nickel and chromium	Workers of a welding plant: 114 men	Age, smoking, duration of exposure, medicine usage, medical histories, and alcohol abuse	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Case-control [43]	China (2001)	BTXs	Workers who were exposed to BTXs: 61 men; age: 26–41 years	Age, smoking, working history, reproductive history, tobacco and alcohol use, and detailed past and present occupational and medical histories	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Comparative [44]	Mexico (2000)	Ethylbenzene and BTX	Workers of a rubber factory: 90 men; age: 20–40 years	Age, smoking, working age, alcohol abuse, medical histories, exposure to other gonadotoxic agents, and genetic factors	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Cross-sectional [45]	Denmark (2000)	Pesticides	Green house workers: 122 men; age: 18–45 years	Age, working age, urogenital disease, fever, spillage, time of abstinence, tobacco and alcohol use, and use of tea or coffee	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]
Cross-sectional [46]	Italy (2000)	Pesticides	Pesticide applicators: 83 men; age: 20–55 years	The age of the woman at the first pregnancy, working age, smoking, and status of men and women before pregnancy	- Exposure to buprofezin increased the two parameters of sperm progress and motion ($p < 0.05$) - Fenvalerate reduced sperm motility parameters ($p < 0.05$) (Fenvalerate concentrations in exposed areas and individual samplings in exposed areas were 21.55×10^{-4} mg/m ³ and 0.11 mg/m ³ , respectively) - Exposure to organic solvents increased the chances of congenital malformations (odds ratio 6.2, 95% CI: 1.4 to 27.9) - Exposure to lead (between the 40 µg/dL and >40 µg/dL categories) reduced the quality of semen, especially sperm motility ($p = 0.03$) and viability ($p < 0.01$) - Exposure to high levels of DDT had increased the risk of birth defects - When comparing pregnancies after and before the first exposure, the odds ratio for birth defects was 3.77 [95% confidence interval (95% CI), 1.19–9.52]

Cross-sectional [47] Croatia (2000) Lead, cadmium, zinc, and copper
 Workers of a machine tool factory: 149 men; age: 20–43 years
 Age, smoking, working age, alcohol consumption, professional and medical histories, marital status, sexual history, and andrology physical status
 - Exposure to mild Pb (PbB < 400 µg/L) and Cd (CdB < 10 µg/L) can greatly decrease human sperm quality without indication of male reproductive endocrine function impairment ($p < 0.05$)

Abbreviations: BMI, body mass index; BPA, bisphenol A; BTX, benzene, toluene, xylene; CdB, blood cadmium; DDT, dichlorodiphenyltrichloroethane; DEHP, di (2-Ethylhexyl) phthalate; DNA, deoxyribonucleic acid; ELF-MF, extremely low-frequency magnetic field; FSH, follicle-stimulating hormone; LH, luteinizing hormone; PbB, blood lead; PHS, predicted heat strain; PVC, polyvinyl chloride; RF, radio frequency; SD, standard deviation; T, testosterone; TTP, time to pregnancy; WBGT, wet bulb globe temperature; WBV, whole body vibration.

4. Discussion

Occupational exposure to physical and chemical risk factors could have different pathophysiological effects on the reproductive system of men and women. According to the investigations, these risk factors could affect some parameters of the reproductive system, including parameters related to sperm (such as volume, morphology, and motility) [15,25,27,35,54], semen quality [12,15,31,39,45], sex hormones (such as T and LH) [3,14,21,23,24], and fertility status [13,29,49,60,65].

The mentioned pathophysiological effects of these risk factors in many industries, including process industries (such as power plant and steel industries), manufacturing (such as rubber, shoe, and automobile parts manufacturing plants), and services (such as traffic police officers and painters) have been investigated [10,11,14,15,23,38,39,44,47]. The results of the studies showed the variable extent of the pathophysiological effects of these risk factors on the human reproductive system according to their nature and exposure level.

4.1. Exposure to physical risk factors

4.1.1. Radiation

Many industrial workers are inadvertently and significantly exposed to ionizing radiation during their work shifts [6]. These radiations had harmful effects on the human reproductive system. When being exposed to this radiation, abnormalities occur due to chromosomal changes caused by exposure, leading to adverse effects such as congenital disabilities [69]. A retrospective case-control study showed that occupational exposure to radiation caused adverse effects on fertility [67]. Furthermore, a study demonstrated that the human reproductive system was affected by exposure to this radiation, so the quality of semen and reproductive hormones was altered [21].

4.1.2. Magnetic fields (MFs)

EMFs are also one of the physical risk factors affecting individuals' reproductive systems. However, the effects of exposure to EMFs on the reproductive performance of individuals vary according to frequency and wave, power (energy), and length of exposure [70]. One of the reproductive parameters that artificial EMFs may alter is sperm quality. According to the findings of a clinical study, increasing exposure to MFs reduced sperm quality. In addition, this increase in exposure was statistically significantly related to sperm density, vitality, and motility [71].

4.1.3. Noise

Occupational and epidemiological evidence indicated the destructive effect of ambient noise on the reproductive system [72]. Given that noise stress interferes with the endocrine glands, this risk factor was assumed to affect fertility. Studies have confirmed this in animals and humans in noise pollution caused by excessive standard exposures [73]. In a subjective study based on the comments of people referred to a clinic in Poland, it was found that exposure to noise and standing for more than 6 hours in workplaces with lower semen quality were directly related [16].

4.1.4. Vibration

Workers in various industries are vulnerable to the vibrations of their machinery [74]. This component is an environmental stressor that could directly affect the reproductive system [11]. One study showed that whole body vibration had a high effect on men's T hormone as the primary hormone. However, the correlation test results in this study only confirmed the relationship

Table 2
Summary of clinical studies on the effects of physical and chemical risk factors

Study design	Country (year)	Risk factor(s)	Study population	Confounding factors	Pathophysiological reproductive effects
Physical risk factors					
Case-control [48]	Iraq (2016)	Occupational and mobile phone towers hazards	200 men	Age, education, smoking, duration of exposure, medical and surgical examinations	<ul style="list-style-type: none"> Occupational risks exacerbated oligozoospermia (OR = 1.8, 95% CI: 0.569–5.527) Teratospermia was enhanced by occupational (OR = 5.23, 95% CI: 0.524–52.204) and environmental (OR = 2.6, 95% CI: 0.342–19.070) risks, as well as smoking (OR = 1.7, 95% CI: 0.225–12.353) EMFs and high workloads in particular businesses, such as service and office employees, may contribute to infertility
Case-control [49]	Singapore (2001)	Highly workload and ionization	640 men	Age, occupational groupings, alcohol consumption, smoking, drinking, and medical histories	<ul style="list-style-type: none"> Exposure to SO₂ with a latency of 0–90 days were linked with lower sperm concentration ($\beta = -1.362$; 95% CI: $-1.844, -0.879$), sperm count ($\beta = -2.979$; 95% CI: $-4.267, -1.691$), and PR ($\beta = -0.551$; 95% CI: $-0.710, -0.393$) Exposure to NO₂ with a latency of 0–90 days were linked with lower sperm concentration ($\beta = -0.517$; 95% CI: $-1.006, -0.027$), sperm count ($\beta = -1.914$; 95% CI: $-3.214, -0.615$), and PR ($\beta = -0.264$; 95% CI: $-0.425, -0.102$) Gaseous contaminants significantly negatively impacted sperm quality outcomes during development ($p < 0.05$)
Chemical risk factors					
Cross-sectional [50]	China (2020)	SO ₂ , NO ₂ , and PM _{2.5}	Women and men	Age, smoking, time of sexual abstinence, education, and BMI	<ul style="list-style-type: none"> There were positive correlations between serum mPAE molar concentrations and sperm concentration ($\beta = 0.084$; 95% CI: 0.013, 0.154; $p = 0.020$), PR ($\beta = 0.057$; 95% CI: 0.002, 0.112; $p = 0.041$), and sperm motility ($\beta = 0.019$; 95% CI: 0.001, 0.038; $p = 0.040$) MECPP had a positive relationship with sperm volume ($\beta = 0.027$; 95% CI: 0.003, 0.051; $p = 0.029$) and total sperm number ($\beta = 0.069$; 95% CI: 0.007, 0.132; $p = 0.031$) MCMHP and PR were revealed to have positive correlations ($\beta = 0.027$; 95% CI: 0.009, 0.046; $p = 0.004$) (the mean of MCMHP = 4.14 ± 0.57 ng/mL) MEOHP and PR were revealed to have a negative relationship ($\beta = -0.025$; 95% CI: $-0.050, 0.000$; $p = 0.046$) (the mean of MEOHP = 0.643 ± 0.088 ng/mL) MBP concentration (The urinary quartile levels ($\mu\text{g/g creatinine}$) = 35.61, 68.23, 133.08) was related to declining trends in sperm concentration ($p < 0.05$) and total sperm count ($p < 0.05$) Exposure to DBP and DEHP in the environment may contribute to a decrease in sperm quality
Cross-sectional [52]	China (2015)	Phthalates	1040 men	Age, BMI, smoking, education, race, alcohol consumption, income, and abstinence time	<ul style="list-style-type: none"> Patients with testicular cancer who had detectable amounts of organochlorines (14.4%) exhibited poorer mean sperm parameters than those who did not (1.0%) ($p < 0.0001$) PCBs and hexachlorobenzene disturbed sperm quality ($p < 0.05$) Urinary pyrethroid metabolites levels (the mean \pm SD ($\mu\text{g/L}$): CDCCA = 0.25 ± 0.29, TDCCA = 0.34 ± 0.15, 3PBA = 0.32 ± 0.17, and DBCA = 0.30 ± 0.52) were shown to be substantially related to an increase in the percentage of sperm with defective morphology ($p < 0.05$) and a reduction in sperm concentration ($p < 0.05$) and the level of T ($p < 0.05$) The amount of 1-OHP in urine was related to sperm neck defects and the percentage of static sperm cells ($p = 0.001$, $p = 0.018$, respectively) (the level of 1-OHP in urine = 0.33 ± 0.31 $\mu\text{g/L}$) Exposure to PAHs in urine reduced sperm volume and the percentage of motile sperm cells ($p = 0.014$, $p = 0.0001$, respectively)
Case-control [53]	Italy (2015)	PCBs and hexachlorobenzene	228 men	Age, BMI, medical history, smoking, and perinatal and congenital characteristics	
Cross-sectional [54]	Poland (2014)	Pyrethroids	344 men	Age, education, sexual abstinence, past diseases, alcohol consumption, and smoking	
Cohort [55]	Poland (2013)	PAHs (1-OHP)	277 men	Age, smoking, season of the year, past diseases, education, and sexual abstinence	

Case-control [13]	Lebanon (2008)	Heavy metals	150 men	Age, salary, education, years of marriage, tobacco and alcohol consumption, consanguinity, family history of infertility, history of reproductive illness, and exposure to war	<ul style="list-style-type: none"> - Despite Lebanon's dismal environmental and occupational stewardship records, exposure to metal pollutants (mean concentration in fertile and infertile subjects (respectively) ($\mu\text{g/L}$): arsenic: 1.13 ± 1.4 and 0.93 ± 0.9); (manganese = 8.06 ± 3.4 and 7.53 ± 2.6); (copper = 715.5 ± 206 and 701.7 ± 160); (cadmium = 0.47 ± 0.47 and 0.51 ± 0.66); (lead = 49.2 ± 20.2 and 49.5 ± 19.7); (zinc = 6295.9 ± 1853 and 6405.6 ± 1472); and (selenium = 109.3 ± 33.9 and 104.4 ± 24.1)) was not a substantial risk factor for male infertility (arsenic: OR = 0.66, 95% CI: 0.36–1.2, manganese: OR = 0.63, 95% CI: 0.32–1.2, copper: OR = 0.84, 95% CI: 0.58–1.2, cadmium: OR = 0.46, 95% CI: 0.21–1.007, lead: OR = 1.02, 95% CI: 0.49–2.1, zinc: OR = 0.86, 95% CI: 0.50–1.5, and selenium: OR = 0.60, 95% CI: 0.33–1.1) - There was a possible link between higher creatinine-adjusted 3-PBA quartiles and sperm concentration (quartile 1: OR = 1.00), (quartile 2: OR = 1.31; 95% CI: 0.65–2.64), (quartile 3: OR = 1.73; 95% CI: 0.87–3.45), (quartile 4: OR = 2.04; 95% CI: 1.02–4.09)) ($p = 0.027$) (The median concentration of 3-PBA = 0.879 $\mu\text{g/g}$ of creatinine) - There were relationships between 3-PBA levels and some changed sperm quality, indicating that exposure to pyrethroid had reproductive effects on adult men
Retrospective case-control [56]	China (2008)	Pyrethroid insecticides	376 men	Age, abstinence time, smoking and drinking status, BMI, physical activity, reproductive health status, and medical histories	<ul style="list-style-type: none"> - Exposure to glycol ether was directly related to poor motile sperm count in men who referred to reproductive clinics (moderate exposure: OR = 1.70; 95% CI: 1.11–2.61, and high exposure: OR = 2.54; 95% CI: 1.24–5.21)
Case-control [57]	UK (2008)	Glycol ether	2118 men	Age, surgical examinations, previous conception, wearing boxer shorts, drinking alcohol, and being employed in manual work	<ul style="list-style-type: none"> - Exposure to glycol ether was directly related to poor motile sperm count in men who referred to reproductive clinics (moderate exposure: OR = 1.70; 95% CI: 1.11–2.61, and high exposure: OR = 2.54; 95% CI: 1.24–5.21)
Pilot [58]	USA (2008)	Phthalates	45 men	Age, race, education, income, BMI, smoking, drinking, abstinence time, reproductive health status, and medical histories	<ul style="list-style-type: none"> - Low sperm concentration was related to above-median MEP concentrations (geometric mean concentration = $121.9 \mu\text{g/L}$) (OR = 6.5, 95% CI: 1.0–43.6), and low morphology was significantly related to above-median mono-3-carboxypropyl phthalate concentrations (OR = 7.6, 95% CI: 1.7–33.3)
Nested case-control [59]	Spain (2007)	Organochlorine pesticides	162 men	Parents' age, BMI, residence, education, and occupation of mother and father	<ul style="list-style-type: none"> - Mothers' involvement in agriculture (OR = 3.47; 95% CI, 1.33–9.03; $p = 0.01$), fathers' occupational exposure to xenoestrogens (OR = 2.98; 95% CI, 1.11–8.01), and a history of past stillbirths (OR = 4.20; 95% CI, 1.11–16.66) were linked to higher abnormalities - The combined action of environmental estrogens in the placenta increases the incidence of male urogenital abnormalities
Case-control [60]	Canada (2003)	Herbicides and fungicides	644 women	Education, income, smoking, alcohol consumption, time spent reviewing exposure lists, weight pattern during adult life, male partner's age, woman's age at menarche, and number of sexual partners	<ul style="list-style-type: none"> - Exposure to herbicide increases the chance of infertility in women (OR = 26.9; 95% CI, 1.9–384.8) - Each couple's exposure to fungicides was linked to an elevated chance of female infertility (OR = 3.3; 95% CI, 0.8–13.2)
Pilot [61]	USA (2002)	PCBs and p,p'-DDE	29 men	Age, medical history, abstinence time, smoking, and medicine usage	<ul style="list-style-type: none"> - PCBs (the mean \pm SD of the ΣPCB = $203 \pm 78.1 \text{ ng/g}$ lipids) had adverse effects on sperm motility ($p < 0.05$), concentration ($p < 0.05$), and morphology ($p < 0.05$) - There was a link between p,p'-DDE (The mean \pm SD = $255 \pm 192 \text{ ng/g}$ lipids) and improper motility ($p < 0.05$), sperm concentration ($p < 0.05$), and morphology ($p < 0.05$)
Physicochemical risk factors					
Cross-sectional [62]	Tunisia (2017)	Excess heat, mechanical vibrations, cement, pesticides, solvents	Men	Age, medical history, and working age	<ul style="list-style-type: none"> - Exposure to pesticide was linked to a considerably increased risk of asthenozoospermia (OR = 1.6; 95% CI, 1.0–2.4) and necrozoospermia (OR = 2.6; 95% CI, 1.4–4.7). - Exposure to cement was associated with an increased incidence of oligozoospermia (OR = 1.1; 95% CI, 0.9–1.4)
Cohort [63]	USA (2015)	Some workplace risk factors	Women and men	Age, race, BMI, smoking, reproductive health status, and medical histories	<ul style="list-style-type: none"> - Compared to normotensive men, individuals with high blood pressure exhibited lower tight morphology ratings (17% vs. 21%) - There was a negative relationship between the number of drugs used and sperm count ($p < 0.05$)

(continued on next page)

Table 2 (continued)

Study design	Country (year)	Risk factor(s)	Study population	Confounding factors	Pathophysiological reproductive effects
Cross-sectional [64]	Poland (2015)	Some workplace risk factors	212 men	Age, sexual abstinence, socioeconomic status, medical history, smoking, BMI, alcohol consumption, and past diseases	- A link was discovered between disomy XY18, 18, sex chromosomal disomy and exposure to mechanical vibrations ($p = 0.03$, $p = 0.04$, and $p = 0.03$, respectively) - Exposure to noise during activities reduced sperm motility and increased DNA damage ($p = 0.005$ and $p = 0.02$, respectively) - Exposure to PVC decreased sperm concentration and motility ($p = 0.02$ and $p = 0.03$, respectively)
Cross-sectional [16]	Poland (2014)	Some workplace risk factors	336 men	Age, smoking, BMI, past diseases, time of sexual abstinence, alcohol consumption, occupational stress, cell phone use, boxer short use, coffee drinking, and physical activity	- Solvents and painting materials (OR: 3.88, 95% CI: 1.50–10.03), lead (OR: 5.43, 95% CI: 1.28–23.13), VDTs and computers (OR: 8.01, 95% CI: 4.03–15.87), shift work (OR: 3.60, 95% CI: 1.12–11.57), and job-related stress (fairly present: OR: 3.11, 95% CI: 1.85–5.24; often present: OR: 3.76, 95% CI: 1.96–7.52) significantly enhanced the incidence of male infertility - There was a strong association between sperm impairment and occupational risk factors such as exposure to heavy metals (OR = 5.4; 95% CI, 1.6–18.1), fumes (OR = 1.9; 95% CI, 1.1–3.4), solvents (OR = 2.5; 95% CI, 1.4–4.4), and PAHs (OR = 1.9; 95% CI, 1.1–3.5) - Mechanical vibrations were found to be linked to oligospermia (OR = 1.9; 95% CI, 1.2–3.1; $p = 0.011$) and teratospermia (OR = 2.0; 95% CI, 1.3–3.2; $p = 0.040$) - Excessive heat (OR = 3.3; 95% CI, 1.1–9.5; $p = .032$) and lengthy duration of sitting (>20 h/wk; $p = 0.047$) were linked to decreased sperm motility
Case-control [65]	Egypt (2010)	Some workplace risk factors	522 men	Age, residence, education, income, smoking, BMI, working age, reproductive health status, and medical histories	- Exposure to radiation (OR = 0.21; 95% CI, 0.06, 0.77) and VDTs (OR = 0.30; 95% CI, 0.13, 0.68) were found to have a protective relationship with infertility
Retrospective case-control [67]	USA (2005)	Some workplace risk factors	Women and men	Woman's age (in 5-year intervals), race, education, employment, smoking, drinking, marijuana use, heat exposure, and consumption of caffeinated beverages	- Serum estradiol concentrations (mean \pm (SD): 36.8 \pm (25.7) Pg/mL) were greater in pesticide-exposed men ($p = 0.002$) - Men exposed to solvents had lower LH concentrations (mean \pm (SD): 2.6 \pm (0.9) IU/l) ($p = 0.004$)
Case-control [68]	France (2001)	Heat and pesticides and solvents and mixed	225 men	Age, smoking, drinking, BMI, income, health center, length of abstinence, reproductive health status, and medical histories	- DBCA, <i>cis</i> -2,2-dibromovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid; DBP, di-n-butyl phthalate; DEHP, di-(2-Ethylhexyl)- Phthalate; DNA, deoxyribonucleic acid; EMFs, electromagnetic fields; LH, luteinizing hormone; MBP, monobutyl phthalate; MCMHP, mono [(2-carboxymethyl) hexyl] phthalate; mDEHP, metabolites of di-(2-Ethylhexyl) phthalate; MECPP, mono (2-ethyl-5-carboxypentyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MEP, mono ethyl phthalate; mPAE, phthalate metabolites; 1-OHP, 1-hydroxypyrene; OR, odds ratio; PAHs, polycyclic aromatic hydrocarbons; 3-PBA, 3-phenoxybenzoic acid; PCBs, polychlorinated biphenyls; PM 2.5, particulate matter 2.5; PR, progressive motility; PVC, poly vinyl chloride; SD, standard deviation; T, testosterone; TDCCA, <i>trans</i> -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid; VDTs, video display terminals; WBV, whole body vibration.

Abbreviations: BMI, body mass index; CDCCA, *cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid; CI, confidence interval; DBCA, *cis*-2,2-dibromovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid; DBP, di-n-butyl phthalate; DEHP, di-(2-Ethylhexyl)- Phthalate; DNA, deoxyribonucleic acid; EMFs, electromagnetic fields; LH, luteinizing hormone; MBP, monobutyl phthalate; MCMHP, mono [(2-carboxymethyl) hexyl] phthalate; mDEHP, metabolites of di-(2-Ethylhexyl) phthalate; MECPP, mono (2-ethyl-5-carboxypentyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MEP, mono ethyl phthalate; mPAE, phthalate metabolites; 1-OHP, 1-hydroxypyrene; OR, odds ratio; PAHs, polycyclic aromatic hydrocarbons; 3-PBA, 3-phenoxybenzoic acid; PCBs, polychlorinated biphenyls; PM 2.5, particulate matter 2.5; PR, progressive motility; PVC, poly vinyl chloride; SD, standard deviation; T, testosterone; TDCCA, *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid; VDTs, video display terminals; WBV, whole body vibration.

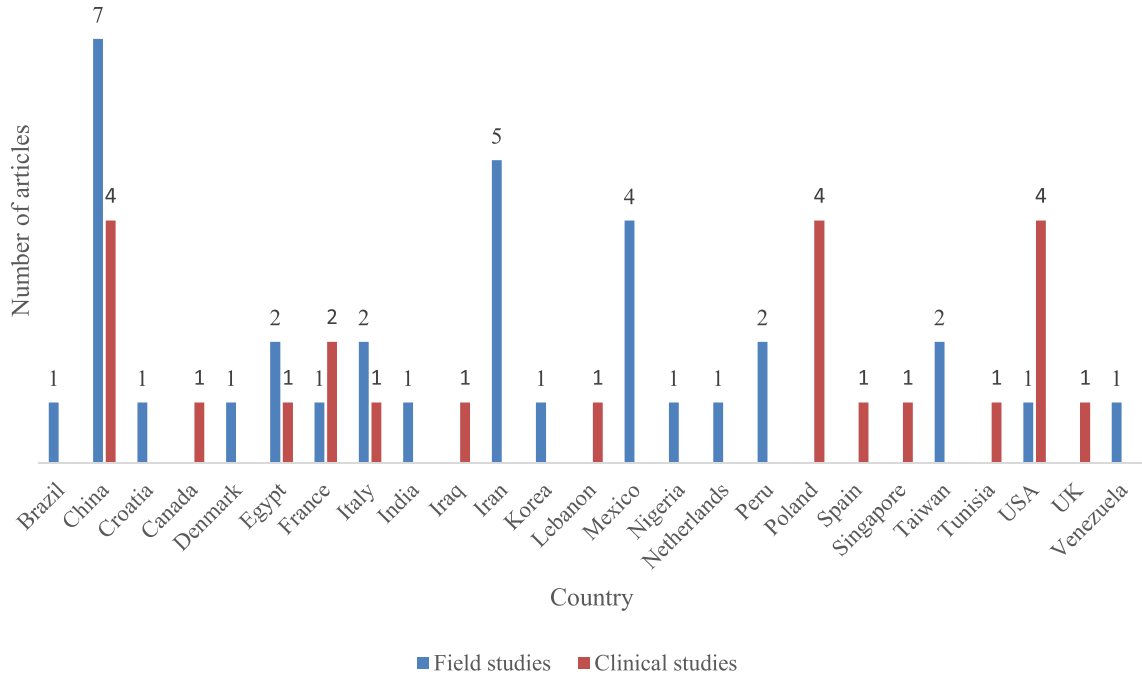


Fig. 2. Distribution of field and clinical studies by country (2000–2021).

between noise exposure and T levels [11]. A cross-sectional clinical study also showed a significant relationship between mechanical vibrations, oligospermia and teratospermia [66].

4.1.5. High temperature

Several occupations like baking, making ceramics, and welding create very high temperatures that can seriously damage the proper functioning of the human reproductive system [69]. If workers are exposed to heat stress, their thermal homeostasis is disrupted due to rising temperatures in the workplace. A study revealed a negative relationship between some physiological and most sperm parameters [15]. Among clinical trials, a study showed that exposure to excessive heat reduced sperm motility [66]. In

addition, sperm volume changed due to exposure to high temperatures. Exposure to the working environment’s general heat caused endocrine disorders, exacerbated them over time, and reduced sperm volume [75].

4.2. Exposure to chemical risk factors

4.2.1. Pesticides

Almost all pesticides have endocrine-disrupting properties [76]. When men are exposed to endocrine disrupting compounds (EDCs), many fertility parameters, such as undescended testes, hypospadias, declined semen quality, and testicular cancer, change negatively [76]. A study found that the herbicides alachlor and

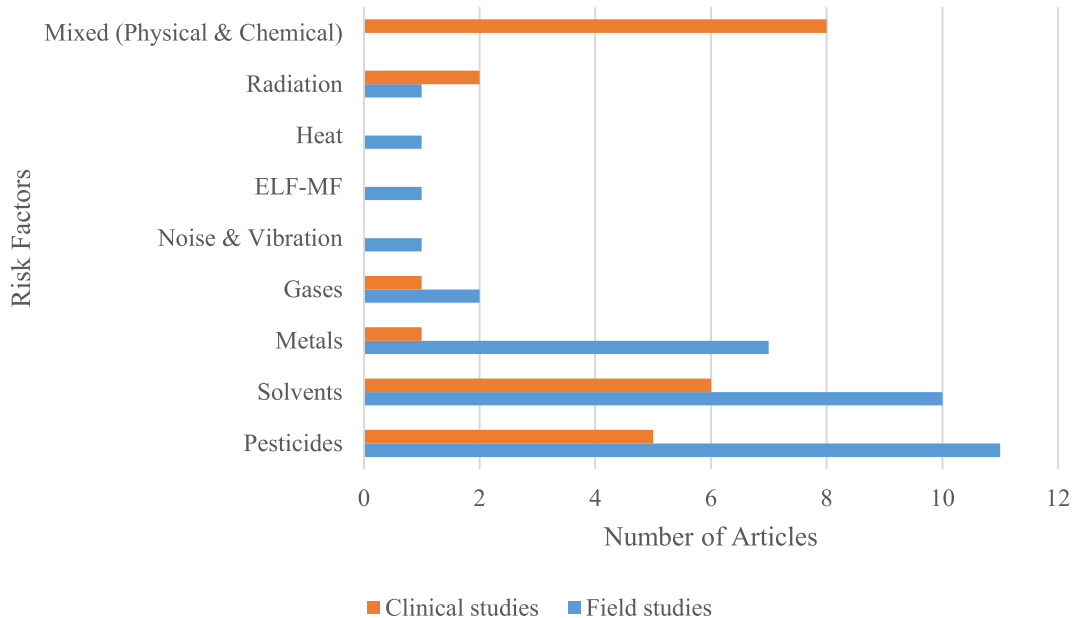


Fig. 3. Distribution of field and clinical studies based on risk factors (2000–2021).

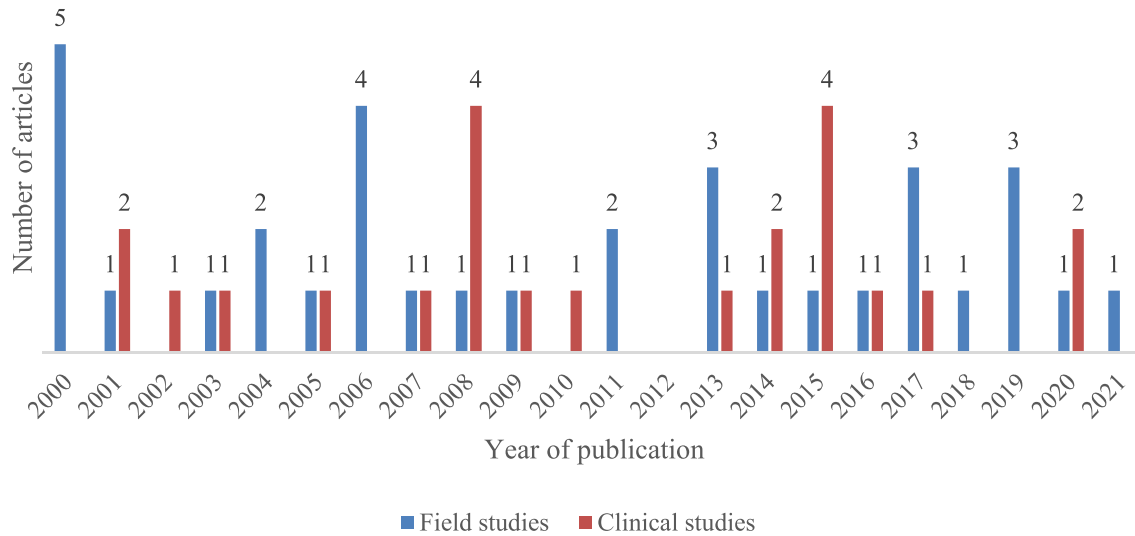


Fig. 4. Distribution of studies by year of publication (2000–2021).

atrazine, and the insecticide diazinon were more common in people with poor sperm quality [77]. Furthermore, a cross-sectional study of fruit growers and their spouses in the Netherlands showed that the time to pregnancy (TTP) was longer during the spraying season [78]. Another TTP and sperm quality study was conducted among Danish male farmers and greenhouse workers. This study also showed that sperm density and motility in greenhouse workers decreased with increasing working hours in greenhouses [45]. Another study suggested that exposure to occupational pesticides may cause a significant increase in FSH levels while not affecting the luteinizing hormone (LH) or T in the sprays studied [24]. Garduno et al also found that exposure of male flower growers to organophosphate pesticides increased serum levels of FSH and prolactin while decreasing T [30].

4.2.2. Metals

Many heavy metals expose workers to reproductive dysfunction. Mn is one of these metals that has been shown to affect some reproductive parameters, including sperm quality and infertility. A study showed that high serum Mn levels significantly affected sperm morphology and motility [79]. In addition to Mn, zinc (Zn) had destructive effects on the reproductive system. Semen Zn was associated with sperm count and length of abstinence in men with delayed fertility. Along with Mn and Zn metals, nickel (Ni) had negative reproductive effects. Ni could impair male and female fertility and cause abortion, abnormalities, and birth defects [42]. Lead and cadmium are also heavy metals that affected the reproductive system. A study showed that exposure to these metals reduced sperm quality without affecting the function of the male endocrine glands [47].

4.2.3. Solvents

Some studies have been done on the harmful consequences of reproduction (spontaneous abortion, congenital disabilities, and childhood cancers) of workers exposed to organic solvents [38,62,80,81]. A clinical study showed a negative relationship between exposure to solvents and sperm motility in infertile patients in Canada [66]. According to the findings of another clinical study, infertile men worked with solvents 1.73 times more than fertile groups [82].

Among solvents, formaldehyde is one of the most widely used substances affecting the reproductive system. A study showed that

formaldehyde affected the quality of semen, especially its excitatory parameters [28]. In addition to formaldehyde, PAHs also had detrimental effects on the reproductive system. Exposure to PAHs before and after birth was associated with reproductive toxicity and growth. Jurewicz et al found that exposure to environmental PAHs impaired sperm quality in men [55].

Phthalates are also another solvents that adversely affected the workers' reproductive system. These substances affected the concentration and quality of sperm. A study demonstrated that the concentration of monobutyl phthalate significantly affected the process of decreasing sperm concentration and exposure to dibutyl phthalate and di-(2-ethylhexyl)-phthalate (DEHP) could reduce sperm quality [52]. Another study showed that DEHP in the air adversely affected sperm motility and chromatin DNA integrity [32]. DEHP and dibutyl phthalate (DBP) have also reduced semen quality [52].

4.2.4. Gases

Gases are another chemical risk factor that can threaten human health. A cross-sectional study showed that exposure to NO₂ gas reduced the overall motility of sperm [33]. Another cross-sectional study suggested that exposure to CS₂ reduced sperm viability and motility and altered FSH, LH, and T hormone levels [27]. In clinical studies, a study showed that exposure to SO₂ and NO₂ gases reduced the concentration, number, and increased motility of sperm [50].

4.3. Limitations

The reviewed studies had some limitations that should be considered for future studies. One of these limitations was the difficulty in sperm and seminal fluid sampling due to cultural and religious reasons in some studies [3,11]. These studies tried to solve this limitation by designing and using a questionnaire. Despite removing this limitation, considering that questionnaires have inherent limitations and bias is probable in their results, another limitation was unintentionally added to these studies. It is worth noting that, in some studies, questionnaires were used instead of sampling environmental and occupational parameters [13,16,25,29,38,64–66]. This causes an accurate assessment of individual exposures to be not made, and the results are expressed and interpreted more cautiously.

Another limitations was the small sample size studied in most of the studies [3,10,12,22,25,27,34,37,39,45,46,57,58,64]. Usually, participation rates are low in studies that require semen collection [67]. This causes the probability of bias in the selection of people. In addition, the results of the studies could not effectively represent the real results in the studied population [16,52,54,64]. It is worth mentioning that in clinical studies, bias is probable in the selection of subjects and the results presented due to the clinical nature of these studies [13,52,63].

Like other studies, this systematic review has some strengths and limitations. One of the strong points of this study is examining the reproductive pathophysiological effects of occupational physical and chemical risk factors. For this purpose, the present study examined nine databases and performed a comprehensive analysis of a large number of variables. In addition, this article reviews all the studies conducted around the world and is not limited to one continent or place. Despite these cases, this systematic review also has some limitations. This study reviews only articles published in Persian and English from 2000 to 2021. In addition, the lack of access to some information and articles due to Iran sanctions is another limitation of this study.

5. Conclusion

The results of field and clinical studies showed the emergence or intensification of the pathophysiological effects on the human reproductive system following being exposed to many physical and chemical hazardous factors such as noise, heat, BTXs, NO₂, and CS₂. The results indicated the weakening of many parameters of the reproductive system, such as the characteristics of sperm and sex hormones, after occupational exposure to these risk factors. However, limited information is available regarding the influencing process and possible effects of many occupational parameters on the human reproductive system individually or in combination, as well as the mechanism of detoxification of the reproductive system in relation to these risk factors because of the small number of articles. Therefore, considering the intervening factors and existing study limitations, it is recommended to conduct more research on this topic.

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Conflicts of interest

Authors have no conflict of interest to declare.

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