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REVIEW

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Impact of environmental factors on human semen quality and male fertility: a narrative review

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Abstract

Background: Worldwide rising trend in infertility has been observed in the past few years with male infertility arising as a major problem. One main reason for the rise in male infertility cases is declining semen quality. It was found that any factor that affects semen quality can affect male fertility. There are several modifiable factors affecting semen quality including air pollution, use of pesticides and harmful chemicals, exposure to excessive heat, and can lead to decreased male fertility.

Main body: The present review focuses on some of these environmental factors that affect semen quality and hence, can cause male infertility. The literature from 2000 till June 2021 was searched from various English peer-reviewed journals and WHO fact sheets using the USA National Library of Medicine (PubMed) database, the regional portal of Virtual Health Library, and Scientific Electronic Library Online. The search terms used were: "Air pollution and male fertility", "Chemicals and male infertility", "Heat exposure and infertility", "heavy metals and male fertility".

Conclusion: Adverse environmental factors have a significant impact on semen quality, leading to decreased sperm concentration, total sperm count, motility, viability, and increased abnormal sperm morphology, sperm DNA fragmentation, ultimately causing male infertility. However, all these factors are modifiable and reversible, and hence, by mere changing of lifestyle, many of these risk factors can be avoided.

Keywords: Air pollution, Environment, Infertility, Pollutants, Semen, Sperm

Background

Worldwide infertility affects around 8–12% of couples, with male-factors identified as the primary cause in 50% of cases [1]. Furthermore, around 7% of all men are affected by male infertility all over the world [2]. Many factors predispose to male infertility including congenital malformations, hormonal, genetic, behavioral, iatrogenic, environmental, and lifestyle factors [3]. Environmental pollution has emerged as a major cause for the rising trend of male infertility in today's era all over the world due to the universal presence of environmental contaminants. Recent studies have revealed that air pollution has a significant impact on human fertility and sperm quality [4, 5].

Semen quality is the major predictor of male fertility outcome [6]. It was observed that environmental pollution unfavorably affects semen quality by impairing the process of spermatogenesis, steroidogenesis, Sertoli cell, and sperm functions, thereby leading to decreased male fertility [7, 8]. Furthermore, there are numerous natural and man-made chemicals that are released into the environment daily and have deleterious impacts on human fertility. Despite, the adverse impacts of environmental chemicals such as industrial waste, pesticides, insecticides, herbicides, food additives, etc. on spermatogenesis in adult men, there is very scarce data available on the

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direct impact of these chemicals in humans. The available studies are usually in an occupational setting, where the population is exposed to these substances at very high concentrations and not for the general population [9, 10].

The present review briefs the impact of various environmental factors that affect male fertility including air pollution, working environment, increased risk of exposure to chemicals, radiation, and heat. All these factors are modifiable and can hence, provide opportunities for the treatment of male infertility. Figure 1 Summarizes the effects of environmental factors on semen quality. Some of these environmental factors and their impact on semen quality, sperm, and overall male fertility are discussed in detail as under:

Environmental factors

Air pollution

Nowadays alarming rise in air pollution in many cities of the world has affected human health to a large extent and has also led to a rise in the number of diseases including respiratory [11], cardiovascular [12], skin-related [13], cancers [14] and reproductive diseases [15–17]. Furthermore, India is the second most populated country and the third most air polluted country all over the world [18].

The main sources of air pollution include motor vehicle exhaust, factories, fire, household, agriculture, waste treatment, oil refineries, natural sources, such as volcanic eruptions, wind, etc. The major air pollutants affecting human health are particulate matter, volatile organic compounds, ozone, nitrogen oxides, sulfur dioxide, carbon monoxide, polycyclic aromatic hydrocarbons (PAH), and radiations, such as X-ray exposure [15, 19]. The particulate matter present in the air in form of tiny liquid or solid droplets can be inhaled and can result in serious health effects [20] Furthermore, particles < 10 µm in diameter (PM_{10}) are very harmful and after inhalation are known to invade the lungs and can even reach the bloodstream causing numerous deleterious impacts. Finer particles, such as $PM_{2.5}$, are even more dangerous and pose a greater risk to health [21].

Numerous recent researches have shown the adverse effect of air pollution on reproductive outcomes in both males and females. It seriously affects the semen quality in males. It was observed that air pollution causes increased sperm Deoxyribonucleic acid (DNA) fragmentation, sperm morphological changes, and reduced sperm motility [22]. A systematic meta-analysis reported that the level of air pollution was significantly associated with decreased semen volume, sperm concentration,

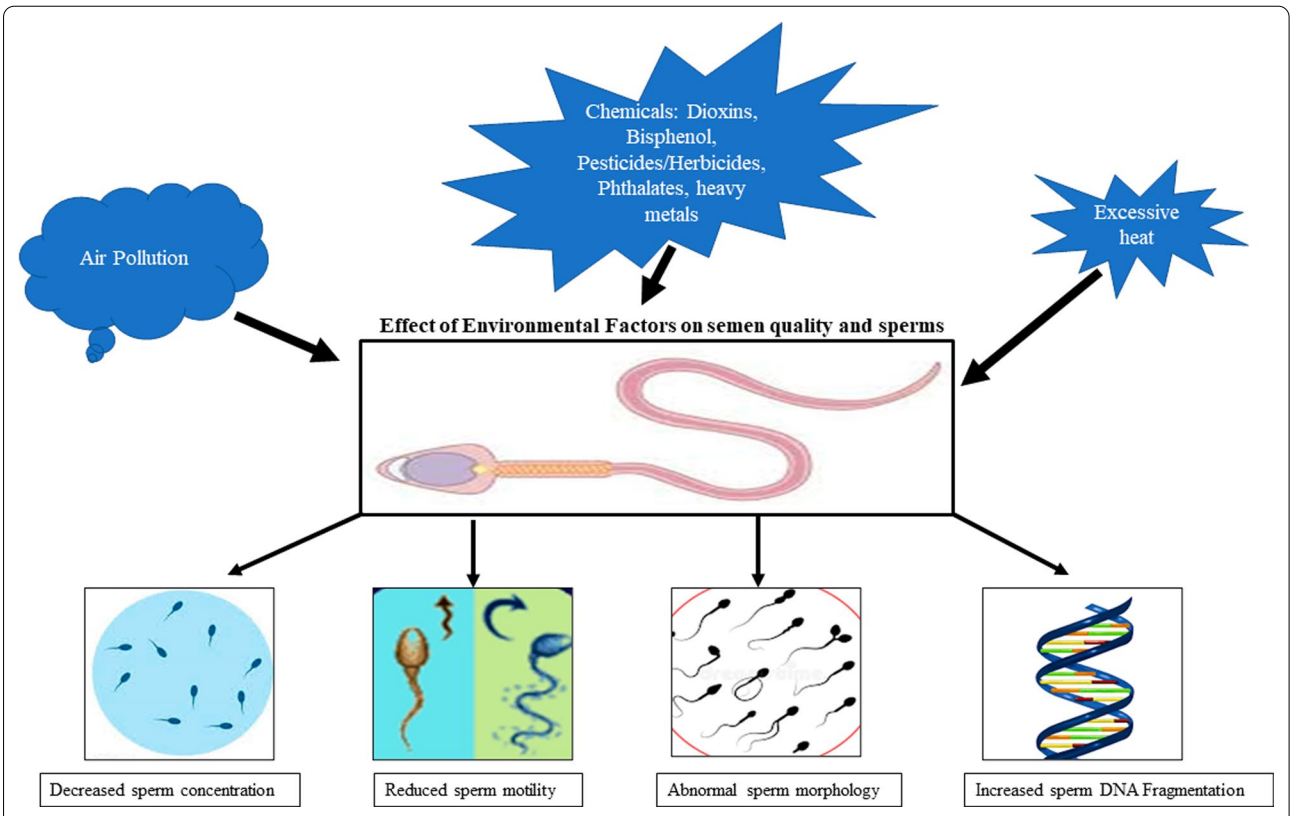

Fig. 1 Impact of environmental and lifestyle factors on semen quality and male fertility

progressive and total sperm motility, and normal sperm morphology rate. It also results in increased sperm DNA fragmentation index, further leading to decreased fertility in males [23]. A recent study evaluated the association between various gaseous pollutants and semen quality and reported that Sulfur dioxide (SO_2) exposure has significant negative impacts on sperm parameters during all exposure windows. They also observed that both SO_2 and nitrogen dioxide (NO_2) had significant adverse impacts on sperm concentration and motility which was found to be more aggressive in the initial phase of spermatogenesis. Hence, concluding that gaseous pollutants have a significant adverse impact on semen quality especially during the sperm development period [24]. Findings of original research reported that in motorway tollgate workers the total sperm motility, forward progression, and sperm kinetics were significantly lesser as compared to other men living in that area. It was found that the nitrogen oxide and lead released from automobile exhaust severely affected the overall semen quality in these men as compared to their controls [25]. A study reported that tollgate workers who are exposed to large amounts of automobile exhaust had an increased quantity of damaged sperm chromatin and fragmented DNA as compared to their unexposed healthy men, and hence, concluded that car exhaust exposure can lead to a significant genotoxic effect on human spermatozoa [26].

One major air pollutant is ozone. Ozone can result in decreased percentages of sperm with normal sperm morphology and hence, can explain the rising trend of males reporting to infertility clinics with abnormal sperm morphology [27]. Recent studies have proposed the role of particulate matter 2.5 ($PM_{2.5}$), a fine particulate matter that is the main component of haze and an important indicator of air pollution in causing male infertility [28, 29]. It was observed that exposure to $PM_{2.5}$ results in an increased number of sperm cells with cytoplasmic drop and morphological abnormalities in sperm heads [30]. Other similar studies have also found a significant inverse relationship between $PM_{2.5}$ and sperm motility, sperm concentration, total sperm count, sperm head morphology, and overall semen quality [31, 32].

The exact mechanism by which air pollutants result in male infertility is not clear, but it can be explained to some extent by the facts that air pollution leads to: a). Hormonal disruption: The heavy metals such as lead, zinc, copper, and PAH present in the exhaust of automobiles have estrogenic, antiestrogenic, and antiandrogenic actions, which in turn can result in abnormal gonadal steroidogenesis and gametogenesis, thereby leading to infertility [33, 34]. Another recently studied particulate matter $PM_{2.5}$ gets accumulated in the reproductive organs through blood-testis, epithelial, or placental barrier and can disrupt hormone levels, leading to infertility [28]; b). Increased production of reactive oxygen species due to oxidative stress, leading to lipid peroxidation, sperm DNA fragmentation, and infertility [33, 35]; c). Sperm DNA alteration due to the formation of DNA adducts especially with PAH results in changes in gene expression and DNA methylation causing male infertility [33, 36]. Hence, air pollution is one major factor in today's era resulting in defective spermatogenesis, increased sperm DNA fragmentation, reduced motility, and abnormal morphological changes, leading to a rise in male infertility.

Exposure to harmful chemicals

Human beings all over the world are exposed to a wide variety of chemicals in their day-to-day life. Many of these chemicals have serious ill effects on the functioning of the human body, especially reproductive organs. Recent studies have shown that male reproductive organs are one of the major sites for insults resulting from exposure to environmental chemicals leading to male infertility [37]. A recent large cross-sectional study on maternal occupational exposure to potential endocrine-disrupting chemicals during pregnancy, especially to pesticides, phthalates, and heavy metals on the semen quality of their sons in adulthood reported a significant correlation between maternal occupational exposure with low semen volume and total sperm count in their sons. Furthermore, a significant association was found between maternal heavy metal exposure and low sperm concentration. Hence, they concluded that there is need to inform pregnant women about the potential hazards of chemicals during pregnancy that can impair their child's fertility, though further studies are needed to confirm the impact of endocrine disrupting chemicals on fertility [38]. Some of the chemicals that significantly affects male fertility are summarized as under:

Dioxins Dioxins are a group of highly persistent lipophilic chemicals produced as a by-product to several industrial and natural processes including smelting, chlorine bleaching of paper and pulp, in production of some pesticides, biomedical and plastic waste incineration [39–41]. Chemically it is 2,3,7,8- tetrachlorodibenzo para dioxin (TCDD) and is considered a "dirty dozen" that is a cluster of hazardous chemicals also known as persistent organic pollutants (POPs) as they resist biological and environmental degradation. They are of concern because of their highly toxic nature and ability to get absorbed by fat tissue and stored in the body for long periods (7–11 years) [36]. They are known to cause serious reproductive, developmental, and cancer problems [42]. Dioxins act as endocrine disruptors and mediate their effects by binding to

the aryl hydrocarbon receptor (AHR)/aryl hydrocarbon receptor nuclear translocator (ARNT) receptor complex present over human testicular cells to mediate their toxic effects [43]. The exact mechanism by which it affects the reproductive functions in humans is not clear. A recent study in male Zebrafish proposed DNA methylation as a possible mechanism of reproductive effects of dioxins [44]. Since DNA methylation pattern in zebrafish is carried down paternally through the sperm [45], inheritance of epimutations in the DNA methylome is a promising mechanism of transgenerational male-mediated reproductive defects resulting from TCDD exposure. Furthermore, early disruption of DNA methylation during gonad development can result in reproductive and epigenetic gene changes leading to impaired reproductive functions [46]. A study on 135 human males exposed to dioxin at three age groups (prepuberty, puberty, and adulthood), and 184 healthy males as control reported that exposure to dioxin in prepubertal males was significantly associated with reduced sperm concentration and motility [47]. Only available human study on dioxin exposure during the developmental stage reported that male babies fed on breast milk of women exposed to high concentrations of dioxins at the time of conception had significantly decreased sperm concentration, total sperm count, and total sperm motility [48]. Another retrospective study also reported that the dioxin and furan content was 2.2–2.3 times higher in the ejaculate of infertile males as compared to the fertile ones [49]. A recent study in male mice reported a significant fall in sperm motility and count, in mice exposed to dioxin. Furthermore, on testicular histopathology, they observed necrotic degeneration and reduced epithelium thickness in mice exposed to dioxin as compared to the controls [50]. Furthermore, supporting the fact that dioxin exposure seriously affects the sperm functions in males resulting in poor quality semen and hence, male infertility.

Plastic contaminants (Bisphenols): Plastic use has become indispensable in our daily lives, but being non-biodegradable, it has now become a major cause of concern all over the world. Bisphenol A (BPA) a major component of plastic is released into the environment during the process of production, use, or disposal of plastics and from break-down of industrial plastic-related wastes [51]. In a recent study in the United States, adults and children reported that Bisphenols substitutes such as Bisphenol F, bisphenol S, and bisphenol A are almost universal [52]. It is nowadays considered hazardous to human health, because of its universal presence, prolonged persistence in the environment, and as an endocrine disruptor. It has been linked to numerous health problems including cardiovascular diseases, metabolic disorders, infertility, and cancers [53–55]. It was found that BPA has estrogenic, antiandrogenic, and antithyroid activities and hence, can disrupt the hypothalamic–pituitary–gonadal axis, resulting in altered reproductive system functions [54]. Increased exposure to BPA results in sperm DNA damage, mitochondrial dysfunction, and degeneration, decreased sperm motility, sperm count, and increased risk of aneuploidies in sperm [54, 56]. Numerous studies on rodents have shown that BPA exposure in male rodents results in a significant decrease in sperm motility, count, normal sperm morphology, increased sperm DNA damage, and adversely affects the spermatogenesis process resulting in male infertility [53, 57–59]. Another recent study reported that excessive exposure to BPA results in impaired sperm motility by reducing the sperm Adenosine Triphosphate (ATP) levels and premature acrosome reaction resulting in poor fertilization and embryonic developmental problems [60]. Other studies have also found a close association between increased BPA exposure and poor semen quality and parameters including sperm quality and motility [61–63]. The exact mechanism by which BPA affects human sperm quality is still under research but it was found that BPA is an endocrine disruptor that results in inhibition of anti-apoptotic pathways such as Bcl-2 and causes activation of pro-apoptotic signaling pathways including mitogen-activated protein kinase (*MAPK*), Fas/FasL, Caspase 3 and 9, Bax leading to diminished proliferation, increased reactive oxygen species-mediated damage and enhanced apoptosis of male gametes [64]. It acts as an Androgen receptor (AR) antagonist resulting in reduced AR translocation and increases AR transcriptional corepressors thereby resulting in suppression of Sertoli cell proliferation [65]. A study in mice reported that BPA inhibits testosterone synthesis in male pups [66]. This decreased testosterone levels in plasma results in reduced expressions of steroidogenic enzymes, cholesterol carrier protein in Leydig cells, and plasma Luteinizing hormone (LH) levels. BPA also results in decreased Leydig cell numbers in the testis [67]. All leading to male reproductive dysfunction. Hence, prolonged exposure to BPA in excessive concentrations can affect male fertility.

Pesticides and herbicides Pesticides especially dibromochloropropane, ethylene dibromide which has been extensively studied is known to cause direct spermatozoa damage, Sertoli or Leydig cell function alteration, disordered endocrine function during hormonal regulation of processes, such as synthesis, release, storage, transport, and clearance of hormones; binding of hormones to their receptors, thyroid function, etc. leading to male infertility [68]. Organochlorine pesticides which are widely used, including DDT and its metabolites, act as endocrine-disrupting chemicals [69]. The main metabolite of DDT,

p,p′-Dichlorodiphenyl-dichloroethylene (*p,p′*-DDE), is an anti-androgenic and binds to androgen receptors and hence, inhibits the action of testosterone [70]. Furthermore, it was observed that *p,p′*-DDE may have an additive or multiplicative effect with other endocrine-disrupting environmental pollutants leading to adverse impacts on reproductive functions [69]. Pesticide exposure can result in defective spermatogenesis leading to reduced sperm concentration, sperm motility, an increased number of morphologically abnormal sperms, causing poor semen quality and reduced male fertility [71]. A recent study on the in-vitro impact of Herbicide Roundup on human sperm motility and sperm mitochondria reported that the direct exposure of semen samples to the active component of this herbicide even at a very low concentration of 1 mg/L can result in adverse effects on sperm motility and in sperm mitochondrial dysfunction [72]. At low doses, Roundup herbicide also induces oxidative stress and causes Sertoli cell death [73]. Another commonly used pesticide is DDT. Its main metabolite is 1,1-dichloro-2,2-bis(4-chlorophenyl) ethylene and direct exposure to this metabolite was found to be strongly associated with sperm immobility and mitochondrial dysfunction in a concentration-dependent manner [74, 75]. Furthermore, it's been 49 years, since organochlorine chemicals such as DDT and polychlorinated biphenyls (PCB) have been banned in the USA, but that doesn't mean that they are gone. They persist in the environment for years after use and are known as 'legacy pesticide' and still can produce deleterious impacts on male fertility. Organochlorine chemicals show resistance to breakdown, can bioaccumulate, enter the food chain, and can be transported over long distances [76, 77]. The use of DDT has been restricted in many nations across the world as a result of the Stockholm Convention, 2004 as a measure to protect human and environmental health from the side effects of exposure to specific persistent organic pollutants. Although its use in South Africa continued for malaria vector control and a cross-sectional study from this area reported a statistically significant positive correlation between the percentage of sperm with cytoplasmic droplets, teratozoospermia, asthenospermia, and oligospermia with blood plasma concentration of DDT and an inverse correlation with semen volume. Hence, they concluded that nonoccupational exposure to DDT results in impaired seminal parameters in healthy men [78]. A recent study observed that pesticide exposure also results in erectile dysfunctions in males, by causing apoptosis of Leydig cells, thereby decreasing the overall concentration of circulating testosterone in the body [79]. Many environmental pollutants including pesticides, polybrominated diphenyl ethers, BPA, phthalates act as endocrine-disrupting compounds. These chemicals are known to induce the *MAPK* signaling pathway in the testis. Three *MAPK* signaling pathways are known to be involved in pesticides related testicular injury. The testicular Erk1/2, p38 *MAPK* result in disruption of the blood testes barrier by blocking gap junction communications leading to germ cell depletion from the seminiferous epithelium [80]. Hence, prolonged, and excessive exposure to various pesticides and herbicides in our daily life can be a cause of compromised male fertility.

Phthalates Phthalates, also known as Phthalic acid diesters are a group of man-made chemicals that are used in several consumer and industrial goods [81]. They are universally present environmental chemicals commonly found in many consumer products such as toys, pharmaceuticals, cosmetic products, building and construction materials, scent retainers, some medications, personal care products, etc. [82] and are known for their anti-androgenic activity. Phthalate gets easily absorbed in the human body through ingestion, skin, or inhalation of contaminated air. It causes a wide array of male reproductive organ dysfunction known as "phthalate syndrome" comprising of diminished anogenital distance, infertility, low sperm count, undescended testes, hypospadias, and many other reproductive-tract anomalies [83]. Phthalates, especially mono-(2-ethyl-hexyl) phthalate (MEHP), an active metabolite of Di-2-ethylhexyl phthalate (DEHP) causes activation of both PPAR (peroxisome proliferator-activated receptor) α and γ pathways [84], which in turn stimulates PPAR: RXR (retinoid X receptor) heterodimers that compete for DNA binding sites required for gene transcription, thus stopping the transcription of aromatase enzyme involved in sexual development. Furthermore, MEHP decreases the production of steroidogenic proteins including steroidogenic acute regulatory (StAR), and cytochrome P450 side-chain cleavage (P450scc), thereby adversely affecting male reproductive health. At high levels, it inhibits the activity of 3β-hydroxysteroid dehydrogenases (3β-HSD) and 17β-hydroxysteroid dehydrogenases (17β-HSD) specific to Leydig cell function in addition to the steroidogenic proteins by causing increased oxidative stress in Leydig cells, and hence, decreases testosterone synthesis [85]. A recent study conducted on male partners of infertile couples found that males who were exposed to ortho-phthalate drugs had poor semen quality as compared to unexposed ones [86]. Several other studies have also reported that phthalate exposure in humans has a significant adverse impact on overall semen quality [87, 88]. It causes reduced semen volume, total sperm counts, sperm concentration, morphological abnormalities of sperm head including large sperm head sizes, and other variations [61, 87]. Furthermore, it was observed that exposure to mono-methyl phthalate (MMP) and mono-

cyclohexyl phthalate (MCPP) results in reduced sperm motility [87, 89]. Another recent study on the impact of eight phthalate metabolites measured in urine samples of 599 men attending an in-vitro fertilization clinic on the male reproductive functions and semen parameters reported an inverse correlation between serum testosterone and mono-isobutyl phthalate, FSH, and mono-(2-ethyl-5-hydroxyhexyl) phthalate, and prolactin and mono-(2-ethyl-5-oxohexyl) phthalate. Furthermore, they reported a positive correlation between sperm concentration and mono-(2-ethyl-5-carboxypentyl) phthalate, mono-(2-ethyl-5-hydroxyhexyl) phthalate, mono-(2-ethyl-5-oxohexyl) phthalate, and DHEP, but a negative correlation with the percentage of MEHP to molar sum of DHEP metabolites, hence indicating the need for further studies on the role of phthalates in male fertility [90]. Several mechanisms have been proposed for how phthalates affect male fertility by causing testicular damage, impairing normal testicular tissue structure, decreasing levels of circulating testosterone and other reproductive hormones, increasing sperm abnormalities, and by decreasing Sertoli cell viability [61, 91, 92]. A study reported that fetal exposure of male rats to di (*n*-butyl) phthalate results in testicular changes that are very similar to testicular dysgenesis syndrome observed in humans, characterized by focal areas of dysgenetic tubules in normal testes. di (*n*-butyl) phthalate exposure leads to abnormal accumulation of significantly small Leydig cells centrally in the fetal testis. The testosterone levels were also reduced. These Leydig cell collections did not exhibit features of focal proliferation as observed normally and have trapped isolated Sertoli cells within them resulting in the formation of dysgenetic tubules. These centrally located dysgenetic tubules have germ cells in early puberty, but have only Sertoli cells by adulthood, indicating that the presence of intratubular Leydig cells adversely affects spermatogenesis [93]. Hence, exposure to phthalates, a common component of many products used in daily life can affect male fertility.

Heavy metals Another widespread environmental pollutant that can affect male fertility are non-essential heavy metals, such as lead, cadmium, arsenic, mercury, barium, etc. These heavy metals can adversely affect the semen and sperm quality in men. It was observed that the presence of Cadmium and Barium in blood, and Lead, Cadmium, Barium, and Uranium in seminal plasma were closely linked with increased risk for reduced sperm viability and normal sperm morphology [94]. Heavy metals affect male fertility by inducing reactive oxygen species generation, which in turn cause lipid peroxidation, sperm DNA damage, leading to infertility [95]. Lead and cadmium are known reproductive toxicants and are suspected endocrine disruptor compounds, which can alter hormonal levels in men and cause impaired semen quality and male infertility [96]. A study reported that exposure to high concentrations of copper sulphate ($CuSO_4$—250 µg/ml) and Cadmium chloride ($CdCl_2$—500 µg/ml) was associated with significantly reduced sperm motility parameters [97]. This was supported by the findings of another study which reported the association of heavy metals, such as lead, cadmium, mercury, zinc with oligospermia and male infertility [98]. Many other studies have also proposed the role of heavy metals in male infertility [99, 100].

Heat exposure

Another major factor that may contribute to male infertility is exposure to excessive heat at the workplace or due to climate change. Temperature plays a crucial role in maintaining normal spermatogenesis in testes. The scrotal temperature is 2–4 °C lower than the core body temperature [101, 102] and any factor that causes a rise in scrotal temperature will affect the spermatogenesis process resulting in male infertility [103]. Furthermore, it was observed that 1–1.5 °C elevation in scrotal temperature can result in impaired sperm production (oligozoospermia, azoospermia, teratozoospermia), and sperm morphological abnormalities [104]. Environmental stresses, such as a temperature rise, resulting in the activation of heat shock protein (HSP). Of these the most important is HSP70s, one of the major classes of proteins induced by elevated temperatures. They are responsible for the folding, assembly, and disassembly of other proteins [105] and are known to play a crucial role in spermatogenesis [106]. Hence, any factor that perturbs their normal expression and regulation results in an adverse impact on male fertility [107]. A study on 37 infertile men (cases) and 13 fertile men (controls) reported that HSP 70 levels were significantly increased in the infertile group as compared to fertile males, thereby concluding that HSP 70 expression increases in spermatozoa of infertile men as a protective mechanism against apoptosis [108]. Constant exposure to high temperatures as seen in cases of occupational exposure to radiant heat in people working in furnaces, bakeries, welding or ceramic factories, those working for long hours in kitchens, laundries, dry cleaning shops, or drivers can result in loss of thermoregulatory function of scrotum affecting one or more component of semen quality in males [103, 109]. This fact was further supported by a study that revealed that tight undergarments in men also lead to a rise in scrotal temperature resulting in decreased sperm concentration, total sperm count, motility, and hence, male infertility [110]. It was observed that higher scrotal temperatures result in a rise in testicular metabolism without the surge in blood supply, leading to local tissue hypoxia

and oxidative stress [111]. Human spermatozoa are very susceptible to oxidative stress-induced lipid peroxidation because of high levels of polyunsaturated fatty acids (PUFAs) in their plasma membrane [112]. This in turn causes increased production of reactive oxygen species (ROS) which causes increased sperm DNA fragmentation and male infertility [113, 114]. It was demonstrated recently that excessive heat exposure causes decreased sperm motility by downregulating mitochondrial activity and reducing ATP levels [115]. Furthermore, a transient rise in scrotal temperature results in a reversible drop in proteins essential for the spermatogenesis process, gamete interaction, and sperm motility [116]. A recent study on male rats reported that exertional heatstroke can cause erectile dysfunctions, disruption of testicular temperature, poorly differentiated seminiferous tubules, diminished sperm quality, loss of interstitial Leydig cells, Sertoli cells, leading to azoospermia and infertility [117]. Another similar study conducted on bovine sperm also reported that heat stress in bulls induces seminal plasma oxidative stress thereby affecting the sperm mitochondrial function, motility, plasma membrane integrity, and DNA fragmentation, ultimately leading to infertility [118]. Another study observed the impact of wet heat exposure in the forms of hot tubs, Jacuzzi or hot baths in infertile male partners and concluded that the toxic effects of wet heat exposure are reversible, and withdrawal of hyperthermia resulted in increased sperm motility and quality in these patients, further supporting the fact that excessive heat exposure affects sperm parameters and can cause infertility in males [119]. A large longitudinal study including 10,802 Chinese men in Wuhan was conducted to quantitatively evaluate the exposure–response relationship between ambient temperature exposure and semen quality and observed that exposure to extremes of temperature, both high and low was found to be associated with decreased semen quality including reduced sperm concentration, total sperm count, total motility, progressive motility [120]. Another similar study reported that seasonal and monthly temperature variation has a significant impact on the human semen parameters. It was observed in their study that sperm concentration and total amount per ejaculate was significantly lower in summer and higher in winter, whereas the sperm progressive and total motility was found to be higher in spring and summer and lower in autumn and winter [121]. A large data analysis study in Northern Italy to evaluate the impact of environmental temperature and air pollution on semen parameters also reported that total sperm number was significantly lower in summer/autumn and was found to be inversely related with the duration of daylight [122]. Hence, though the data related to the impact of season or climate change on human semen quality is very little, pieces of evidence have been found to link extreme changes of temperature with poor semen quality. Other studies have also reported the impact of seasonal and environmental temperature variation on sperm quality [123–125]. Furthermore, many animal studies have also shown that a rise in testicular temperature results in reduced testicular size, decreased sperm production, increased abnormal sperm forms, and reduced motility leading to male infertility [115, 126, 127]. Hence, exposure to high temperatures both due to occupation or environmental factors has a deleterious impact on overall semen quality and can cause male infertility.

Table 1 depicts the impact of various environmental factors on male fertility in human and animal studies.

Conclusion

Hence, the environment plays a crucial role in male fertility. Adverse environmental factors can result in poor semen quality with decreased sperm concentration, sperm motility, viability, normal morphological forms, and increased sperm DNA fragmentation index, mitochondrial dysfunction, all leading to male infertility. However, all these factors can be prevented or modified, allowing us to decrease the risk associated with them. Decreasing air, chemical pollution, heat exposure and bringing positive changes in our daily lifestyle can prevent these adverse impacts on semen quality to a large extent, thereby reducing the overall incidence of male infertility.

Table 1 Effect of Environmental Factors on Semen Quality and Male Fertility: A Comparison of Human and Animal Studies

S. no	Predisposing factor	Source/cause	Human studies	Animal studies
1	Air Pollution	Motor vehicles exhaust, factories, fire, household, agriculture, waste treatment, oil refineries, natural sources, such as volcanic eruptions, wind, etc.	$PM_{2.5}$ in the air is directly associated with total sperm number and concentration [25, 128] PM_{10} is related to semen volume and typical forms and inversely related to atypical forms [25, 129] SO_2 exposure at the time of sperm development causes oxidative damage to sperm [5] Air pollution negatively affects testosterone levels [129]	$PM_{2.5}$ exposure in mice causes a significant fall in sperm concentration, motility, serum testosterone levels, an increased percentage of morphological abnormalities in sperms [130] •$PM_{2.5}$ causes severe testicular damage on histopathology [131]
2	Chemicals			
	i. Dioxins/Furans	Produced as a by-product of industrial and natural processes, such as smelting, chlorine bleaching of paper and pulp, production of pesticides, biomedical and plastic waste incineration	Reduced sperm concentration and motility [47] Ejaculate of infertile men had 2.2–2.3 times higher content of dioxins and furans as compared to their fertile counterparts [49]	Reduced daily sperm production, epididymis sperm counts, and dose-dependent histological changes in the testes [132] Fall in plasma concentrations of testosterone, and LH [132]
	ii. Bisphenol A (BPA)	A major component of plastic and released during production, use, or disposal of plastics and breakdown of industrial plastic-related wastes	Pro-oxidative/apoptotic mitochondrial dysfunction [56] Inverse correlation between sperm concentration and urinary BPA levels [67]	Reduced sperm production, motility, increased sperm abnormalities, acrosomal and sperm plasma membrane damage, decreased mitochondrial activity and, increased defective spermatozoa [58, 133] Reduced serum concentrations of testosterone, LH [58]
	iii. Pesticides/ Herbicides	Used in agriculture, to control insects	Reduced sperm motility, sperm count, concentration, and increased sperm morphological abnormalities [134, 135]	Reduced sperm motility, motion kinematic parameters, sperm ATP levels, and increased morphological modifications [136, 137]
	iv. Phthalates	Found in numerous consumer products, such as toys, pharmaceuticals, cosmetic products, building and construction materials, scent retainers, some medications, and personal care products	Reduced total sperm counts, sperm concentration, larger sperm head sizes, an increased number of morphologically abnormal sperm lead to reduced semen quality [86, 87]	Reduced sperm motility, capacitation, and acrosome reaction, leading to poor fertilization in mice [138] Increased DNA fragmentation and decreased sperm motility in dogs [139]
	v. Heavy Metals	Volcanic eruptions, Weathering of metal-bearing rocks, mining, and industrial and agricultural activities	Increased blood Cadmium and Barium levels and higher seminal lead, Cadmium, Barium, and Uranium result in low sperm viability and increased immotile sperm [94, 96] Uranium levels correlate with decreased sperm motility and abnormal sperm morphology [94] Exposure to high $CuSO_4$ (250 µg/ml) and $CdCl_2$ (500 µg/ml) results in reduced sperm motility [97]	Acute and chronic cadmium exposure causes reduced sperm motility, viability, and acrosome reaction both in vivo and in vitro [140] Heavy metals adversely affect testicular morphology, sperm production, and quality [141]
3	Heat Exposure	Occupational exposure in people working in furnaces, bakeries, welding, ceramic factories, laundries, dry cleaning shops, or drivers, hot climate, excessive use of hot tubs, Jacuzzi, or hot baths	Extremes of temperature result in decreased semen quality including reduced sperm concentration, total sperm count, total motility, progressive motility [120] Reduced sperm concentration and total amount per ejaculate in summers as compared to winters [121]	Heat stress causes a rise in sperm abnormalities, lipid peroxidation, altered mitochondrial function, decreased sperm motility, plasma membrane integrity, increased DNA fragmentation, and reduced sperm quality [118, 142, 143] Heatwave conditions (5–7 °C above the optimum temperature for 5 days) adversely affect male reproductive potential, halve male fertility, and severely affect sperm competitive ability [144]

Abbreviations
AR: Androgen receptor; AHR: Aryl hydrocarbon receptor; ARNT: Aryl hydrocarbon receptor nuclear translocator; ATP: Adenosine triphosphate; BPA: Bisphenol A; $CdCl_2$: Cadmium chloride; $CuSO_4$: Copper sulphate; DDT: Dichlorodiphenyltrichloroethane; *p,p* DDE: *p,p′*-Dichlorodiphenyl-dichloroethylene; DEHP: Di-2-ethylhexyl phthalate; DNA: Deoxyribonucleic acid; FSH: Follicle stimulating hormone; HSD: Hydroxysteroid dehydrogenases; HSP: Heat shock proteins; LH: Luteinizing hormone; MAPK: Mitogen-activated protein kinase; MCPP: Mono-cyclohexyl phthalate; MEHP: Mono-(2-ethylhexyl) phthalate; MMP: Mono-methyl phthalate; MnBP: Mono *n*-butylphthalate; NO_2: Nitrogen dioxide; PAH: Polycyclic aromatic hydrocarbons; PCB: Polychlorinated biphenyls; PM: Particulate matter; POP: Persistent organic pollutants; PPAR: Peroxisome proliferator-activated receptor; PUFAs: Polyunsaturated fatty acids; P450scc: Cytochrome P450 side-chain cleavage; ROS: Reactive oxygen species; RXR: Retinoid X receptor; SO_2: Sulfur dioxide; StAR: Steroidogenic acute regulatory; TCDD: Tetrachlorodibenzo para dioxin; WHO: World Health Organization.

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Authors' contributions
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