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# Association Between Fine Particulate Matter ($PM_{2.5}$) and the Reproductive System: A Narrative Review

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**Abstract:** In the last two decades, the issue on exposure to air pollution, especially fine particulate matter ($PM_{2.5}$), and its health effects has been a global concern. $PM_{2.5}$ can enter the bronchi, lung cells, and subsequently the body, thus causing adverse health effects. One of these health effects include damage to the reproductive system. However, this has not gained much attention. In addition, $PM_{2.5}$ contain toxic compounds, such as heavy metals or PAHs, which can cross various barriers, including epithelial barrier and blood-testis barrier, causing hormonal disorders in both, men and women, thus resulting in infertility. In this review, an attempt was made to provide useful information about effects of $PM_{2.5}$ on the reproductive system.

**Keywords:** $PM_{2.5}$; Dust; Air pollution; Pathological effects; Reproductive system

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## 1. Introduction

Global attention has been drawn to the issue of air pollution with the gradual worsening of haze, which has undoubtedly become a considerable health problem [1,2]. Haze mainly contains fine particulate matter ($PM_{2.5}$), which is defined as particulate matter with an aerodynamic diameter of less than 2.5 μm and is associated with global disease burden (GBD) [3-5]. According to the GBD report, $PM_{2.5}$ exposure led to 5 million deaths worldwide in 2017, with 1.2 million in China. $PM_{2.5}$ has a small size and large area, and it can be suspended in the air for a long time and over long distances; hence, it is difficult to be eliminated [6]. $PM_{2.5}$ is mainly produced via fuel combustion in vehicles and various industrial and dust storms in China, where the concentration of $PM_{2.5}$ is mostly higher than the air quality standards [7,8]. Its major constituents are complex, and they include heavy metals, minerals, ammonium salt, sulfate, nitrate, as well as elemental and organic carbon particles [9-11].

When $PM_{2.5}$ enters the lungs through the blood-air barrier, it enters the blood and reaches other tissues and organs, causing damage to the circulatory system, central nervous system, respiratory system, and reproductive system. Hence, clinicians must investigate the harm caused by $PM_{2.5}$ [12-14].

Reproductive toxicity is becoming more well recognized as a significant aspect of human health.

Despite conducting various studies in this field, the association between $PM_{2.5}$ and the reproductive system is unclear. The most widely discussed mechanisms include inflammation, barrier structure destruction, oxidative stress, and apoptosis induction, all of which can lead to reproductive toxicity [15-18].

Reproductive physiology entails several intricate physiological systems that are susceptible to chemical contaminants. Based on current research, testicular dysplasia and testicular cancer have increased over time [19,20]. Exposure to environmental contaminants may be associated with an increase in the occurrence of male reproductive disorders. Furthermore, as a result of air pollution, women are at an increased risk of infertility and preterm delivery. Therefore, this study was conducted to investigate the results of several studies on the association between $PM_{2.5}$ and the reproductive system.

## 2. Materials and methods

A search was conducted on PubMed and Scopus from the year 2000 up to November 30, 2021, to retrieve papers on PM2.5 exposure and its effects on the reproductive system in both, men and women. The following keywords were included: "air pollution" OR "$PM_{2.5}$" OR "fine particulate matter" OR "toxic elements" OR "dust" OR "haze" AND "reproductive system" OR "infertility" OR "sterile."

## 3. Results and discussion

### 3.1. Function of the male reproductive system

The internal and external genitalia make up the male reproductive system. The internal genitalia include the conduits, testis, and accessory glands. The major function of the testis is to produce male hormones and sperm. The reproductive conduits that transport sperms include the epididymis, ejaculatory canal, vas deferens, and urethra. In addition to storing sperm temporarily, the epididymis also feeds and promotes the maturation of sperms [21].

### 3.2. Function of the female reproductive system

The female reproductive system consists of associated tissues as well as internal and external genitalia. The external genitalia include the mons pubis, labia majora, labia minora, vaginal vestibule, and clitoris, whereas the internal genitalia include the fallopian tubes, vagina, uterus, and ovaries. The ovaries are made up of two gonads that produce and release steroid hormones in addition to ovum. The oviduct is where the fertilized ovum is transported after the sperm and ovum have met. The uterus is responsible for menstruation as well as carrying pregnancies and embryos. The fetus is born, and menstrual blood is discharged through the vaginal canal [22].

### 3.3. Exposure to $PM_{2.5}$ and the reproductive system

Reproductive dysfunction has become a global major health concern worldwide. The international health committee estimates that about 45 million people suffer from infertility in China. Two hundred and forty million couples encounter infertility with a rate of 15-20% in China. In recent years, studies have shown that increasing the concentration of $PM_{2.5}$ can affect the reproductive system [23]. Air pollution has been proven in animal and epidemiological studies to affect sperm quality, including its concentrations, vitality, morphology, and ejaculation volume.

Exposure to $PM_{2.5}$ can increase the risk of premature delivery and low birth weight [24,25]. In addition, both, long and short exposure to $PM_{2.5}$ can affect the blastocyst stage in female and subsequently disrupt embryo development [26].

#### 3.3.1. $PM_{2.5}$ and the male reproductive system

Cadmium can accumulate in the testis and epididymis. Alike other heavy metals, cadmium in $PM_{2.5}$ can cause reproductive toxicity [27]. Various components in $PM_{2.5}$ causes damage to the epididymis and testis in male mice [28].

#### 3.3.1.1. Male infertility

Female infertility is related to 50% of male infertility factors [29]. The factors mainly include the decrease in sperm quality. Exposure to $PM_{2.5}$ may be a factor in blood-testis barrier disturbance and abnormal spermatogenesis [30]. Exposure to $PM_{2.5}$ has an effect on testicular spermatogenic tubules, causing a decrease in sperm count and the shedding of spermatogenic cells [31,32]. In addition, studies have shown that the sperm count in male mice and the malformation rate significantly decreased compared to the control group after exposure to $PM_{2.5}$ [33,34].

In addition, the exposure to $PM_{2.5}$ directly affects reproductive parameters. Moreover, toxic elements bound to $PM_{2.5}$ can affect the quality of semen and break down the DNA of sperms [35]. Exposure to $PM_{2.5}$ can decrease spermatogonia markers and the protein expression in the tight junction, thus resulting in low sperm quality and spermatogenic ability [36]. People with certain occupations that are more exposed to air pollution, such as coal burning and road traffic, have lower sperm counts and sperm motility [37,38]. In addition, the presence of lead and cadmium at low levels in semen is associated with low quality of sperms [39,40].

#### 3.3.1.2. Hormonal disorders in male

Polycyclic aromatic hydrocarbons (PAHs) in $PM_{2.5}$ have destructive endocrine effects, which can cause hypothalamic gonadal dysfunction, thus slowing down follicular development and spermatogenesis [41].

Studies have shown that the exposure to $PM_{2.5}$ can reduce germ cells and sperm count along with testosterone, follicle-stimulating hormone, and gonadotropin-releasing hormone [33,42]. The integrity of spermatogonia is dependent on testosterones. The loss of specific androgen receptors in Leydig and Sertoli cells can result in a reduction in testis weight [43]. It has been found that increased $PM_{2.5}$ concentrations lowered testosterone and luteinizing hormone levels in rats [31]. The above studies justify that the exposure to $PM_{2.5}$ can increase the risk of male infertility.

### 3.3.2. $PM_{2.5}$ and the female reproductive system

Given that heavy metals and PAHs can bind to $PM_{2.5}$, its toxicity to the female reproductive system cannot be disregarded [44]. Persistent lipophile pollutants, such as polychlorinated biphenyls, polychlorinated dibenzofurans, and polychlorinated dibenzo-p-dioxins, can cause a dysfunction in the reproductive endocrine system and miscarriage, a decrease in pregnancy rate, ovulation failure, and infertility [45]. Several studies have revealed that toxic elements, such as lead, mercury, and cadmium, have obviously embryonic and reproductive toxicity [46,47].

#### 3.3.2.1. Diminished ovarian reserve

Heavy metals (cadmium and lead) and PAHs in $PM_{2.5}$ have destructive effects on estrogen in the ovaries. These toxic compounds interfere with estrogen synthesis mainly by disrupting endocrine environments [48]. According to studies, cadmium chloride can accumulate in ovaries and have destructive effects in chickens (150 mg/kg) and mice (100 mg/l) [27,49]. Cadmium is known as one of the major endocrine disruptors with estrogen-like functions. It has the potential to harm the reproductive system by direct toxicity to the gonads or indirect toxicity to the hypothalamus [50].

In fact, Cd can activate estrogen receptors by binding to estrogen receptors and subsequently blocking them [48,51].

A study has shown that cadmium can be effective in the expression of estrogen genes [48,51]. A study carried out on 632 women in Massachusetts General Hospital Fertility Center showed that the exposure to $PM_{2.5}$ can significantly reduce the quality and quantity of ovum [52].

#### 3.3.2.2. Hormonal disorders in female

Estrogen is produced by follicular cells and plays a main role in regulating the secondary sexual characteristics in women, and it aids in preventing follicular atresia. Estradiol is the most important and powerful hormone in estrogen, which can simulate follicle maturation [53].

In an animal study, the expression of estrogen receptor alpha (ERα) in the uterine tissue after exposure to $PM_{2.5}$ was significantly lower than that of the control group; in addition, the weight of the rats also reduced [38].

Progesterone has a significant role in maintaining the function of the reproductive system. LH and FSH are the main gonadotropin secretions and have considerable role in ovulation, follicular formation, and follicular maturation. In relation to $PM_{2.5}$ exposure, it increases FSH levels and decreases estradiol [34].

## 4. Conclusion

This paper attempted to investigate several studies on the association between $PM_{2.5}$ with the reproductive system. Exposure to $PM_{2.5}$ has destructive effects on the reproductive system. Despite various studies in this field, a full understanding of the relationship between $PM_{2.5}$ and the reproductive system has yet to be established. Therefore, further studies may help us better understand the effects of $PM_{2.5}$ on the reproductive system.

## Disclosure statement

The author declares no conflict of interest.

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