SciMedCentral

JSM Environmental Science & Ecology

Review Article

Research on the Impact of $PM_{2.5}$ on Human Reproductive Health in Recent Years: A Review

Zhengjiang Liu, Pengxiang Ge, and Mindong Chen*

Jiangsu Key Laboratory of Atmospheric Environment Monitoring and Pollution Control, Collaborative Innovation Center of Atmospheric Environment and Equipment Technology, School of Environmental Science and Engineering, Nanjing University of Information Science & Technology, Nanjing 210044, China

***Corresponding author**

Mindong Chen, Jiangsu Key Laboratory of Atmospheric Environment Monitoring and Pollution Control, Collaborative Innovation Center of Atmospheric Environment and Equipment Technology, School of Environmental Science and Engineering, Nanjing University of Information Science & Technology, Nanjing 210044, China. Tel.: +86-25-58731089, Email: chenmd@nuist.edu.cn

Submitted: 24 February 2022

Accepted: 10 March 2022

Published: 18 March 2022

ISSN: 2333-7141

Keywords

- $PM_{2.5}$
- Human reproduction
- Reproductive health

Abstract

$PM_{2.5}$ is still an environmental issue of global concern, closely related to human health. $PM_{2.5}$ carries a large number of chemical substances, bacteria, viruses, etc., which can enter human lungs with respiration, and even enter alveoli and blood, causing oxidative stress, inflammatory reaction and DNA damage in the human body. In addition to harming the respiratory system, digestive system and cardiovascular system, $PM_{2.5}$ can also adversely affect human reproduction and normal development. It has been confirmed that exposure to $PM_{2.5}$ can reduce the concentration and activity of male sperm, thereby interfering with sperm-egg binding. $PM_{2.5}$ exposure to women during pregnancy can increase the incidence of high blood pressure, cause significant changes in germ cells, and increase the probability of premature birth, low birth weight and birth defects in the fetus. Furthermore, there may also be negative influences during the later development, such as obesity, asthma, frail and poor brain development. This review aims to explore the impact of $PM_{2.5}$ on human reproduction, the health of pregnant women and fetuses, and the development of offspring, to provide some help for the health protection of $PM_{2.5}$ and the prevention of related diseases.

ABBREVIATIONS

$PM_{2.5}$: Fine particulate matter; **IARC**: Agency for Research on Cancer; **DNA**: DeoxyriboNucleic Acid; **Pb**: lead; **Cd**: cadmium; **Cu**: copper; **Hg**: mercury; **As**: arsenic; **MAPK:** Mitogen-activated protein kinase ;**ROS:** oxygen species ;**BTB:** blood testosterone barrier; **RNA**: Ribonucleic Acid; **CytC:** Cytochrome C; **Mn**: Manganese; **Ni**: Nickel; **Zn**: Zinc; **Caspase**: Cysteine-requiring Aspartate Protease Caspase; **NOS**: i- nitric oxide synthase; **Apaf-1** : apoptotic protease-activating factor-1; **FLIPS**: FLICE-like inhibitory proteins; **FADD:** Fas associated death domain; **PKR**: intracellular protein kinase RNA; **Eif-2**: eukaryotic translation initiation factor-2; **ATF4**: activating transcription factor-4; **CHOP**: CEBP-homologous protein; **PTB**:Preterm Birth**; HDCP**: hypertensive disorder complicating pregnancy; **PE:** Pre-eclampsia; **mtDNA:** Mitochondrial DNA; **LTL:** telomere length

INTRODUCTION

With the rapid development of modern industry and economy, the adverse effects of air pollution on human health have become increasingly obvious, which needs global attention and common governance [1]. $PM_{2.5}$ is an important air pollutant, and $PM_{2.5}$ concentration is an important index of air pollution [2-3]. It was reported that $PM_{2.5}$-dominated pollution days accounted for more than 60 percent of the total pollution days in China in 2015 [4]. The smaller the particle size, the larger the specific surface area, the more harmful substances, viruses and bacteria carried by the particles, and the greater the adverse impact on human health [5]. The 2015 Global Burden of Disease, Injury and Risk Factors study identified $PM_{2.5}$ as the fifth most important cause of abnormal deaths, 7.2% of global deaths (about 4.2 million people) are caused by exposure to $PM_{2.5}$ [6]. 90% of people living in cities and towns are exposed to $PM_{2.5}$ concentrations above 10μg/m^3, which is estimated to have reduced their life expectancy by 0.98 years [7]. In China, $PM_{2.5}$ exposure levels were positively correlated with disease risk, each 10 μg/m^3 per cent increase in ambient $PM_{2.5}$ exposure was associated with a 0.30% increase in cardiovascular and respiratory diseases and a 0.22% increase in non-accidental mortality [8].

$PM_{2.5}$ can carry a large number of chemical substances, bacteria, viruses and soon to the alveoli and deposit in the alveoli. These harmful substances reach the various organs of the body through the blood circulation, which may cause serious diseases of multiple systems [9,10]. These come from transportation sources (diesel, gasoline vehicles), industrial sources (coal, oil and biomass burning in industrial production), domestic sources (cooking, heating and tobacco smoke), as well as secondary organic aerosols and long-distance transport sources [11]. Carbon particles make up 40 to 60 percent of $PM_{2.5}$ by weight. At present, black carbon is an important urban air pollutant and has been classified as a 2B carcinogen by the International IARC. It is

associated with respiratory and cardiovascular diseases and can cause damage to the nervous system, cardiovascular system and reproductive system. Organic matter and heavy metals are also the main components of cell toxicity of particulate matter [12-15]. Most of the organic pollutants in the fine particulate matter come from combustion sources. Cytotoxicity studies have found that polycyclic aromatic hydrocarbons and their derivatives can reduce cell viability, and some of their components, which can cause DNA damage, oxidative stress and inflammatory responses, are important sources of inducing and carcinogenic chemicals under human exposure to $PM_{2.5}$ [16-18]. Heavy metals such as Pb, Cd, Cu, Hg, As etc. can cause cell death, bone and nerve damage, and even have genetic toxicity can cause bone, nerve damage, and even have genetic toxicity.

Studies on the toxicology of $PM_{2.5}$ have been focused on the respiratory system and cardiovascular system, in recent years, the research on reproductive toxicity has been gradually paid attention to and is considered as an important part of the research on human toxicity of $PM_{2.5}$ [19-21]. $PM_{2.5}$ enter the human body along with the respiratory system and breaks through the blood-testosterone barrier and blood-brain barrier [22]. Even at low concentrations, $PM_{2.5}$ still poses a public health risk [23]. $PM_{2.5}$ causes defects in the process of reproduction, leading to a decline in the reproductive capacity of exposed people. Studies have found that fertility rates in Both China and the United States have decreased with the increase of $PM_{2.5}$ concentration in the air [24,25]. Exposure to $PM_{2.5}$ during sperm production in men leads to a decrease in sperm content in semen and an increase in semen abnormalities [26]. Exposure of pregnant women to $PM_{2.5}$ can cause pathological changes in placental tissue, affecting reproductive health. Pregnant women are also at increased risk of related diseases that affect fertility [27,28]. $PM_{2.5}$ exposure causes birth defects in offspring, premature birth, low birth weight and other problems [29]. The overall environment of the world is stable, and the human population is developing rapidly with food health, social welfare and human health. It is estimated that by 2050, the world population will reach 9.6 billion [30]. China's population is also on the rise. Therefore, it is very important to ensure the safety of childbirth and the healthy growth of newborns, protect the reproductive health of the population and prevent and cure genetic diseases for the healthy and sustainable development of China's population. At present, many scientists have made research achievements on the impact of $PM_{2.5}$ on population growth in recent years. But the results are relatively sporadic and lack of systematic summary, some on premature death, some on adverse birth outcomes, and some on effects of fertility [31-33]. When $PM_{2.5}$ enters the human body, it breaks the barrier structure, induces inflammatory response, causes oxidative stress, affects hormone receptors, leads to cell apoptosis and so on. Understanding these has important reference value for treating the affected population and preventing the harm caused by $PM_{2.5}$.

Search for keywords $PM_{2.5}$, reproductive health, etc., in SCIE, AMS and Elsevier databases. Articles on male/male, female/female, fetus/infant, toxic effects of $PM_{2.5}$ exposure and reproductive health were obtained, and 136 articles were selected and screened. The relationship between $PM_{2.5}$ and fertility damage was analyzed and summarized. $PM_{2.5}$ affects the fertility of the human population as a whole by damaging the reproductive capacity of different populations. This paper discusses the effects of $PM_{2.5}$ exposure on reproductive health of male and female adults, as well as the effects of $PM_{2.5}$ exposure on fetal and infant health. Studies of each population group have been classified by damage and mechanism studies. The toxicological effects and possible mechanisms of $PM_{2.5}$ on the human population and fertility status were summarized. This review is expected to help implement some prevention and control measures, reduce the impact of specific pollution sources on fertility, and provide some reference for follow-up research on reproductive health.

IMPACT ON MEN/MALES

Sperm quality and germ cell structure

Male reproductive health is an important aspect of studying the effects of $PM_{2.5}$ exposure on fertility. A survey of 6,475 ordinary males aged 15 to 49 in Taiwan Province from 2001 to 2014 was conducted [34]. It was found that exposure at both times resulted in lower semen concentration in men. Peking University Third Hospital analyzed 8945 semen samples of young men living in Beijing for a long time from 2015 to 2018. The screened semen was collected from healthy donors free from bad habits (smoking, alcoholism, etc.). It was found that $PM_{2.5}$ concentration ninety days before collection had an impact on the concentration and activity of the collected sperm [35]. A similar study in a southern Chinese province showed that exposure to $PM_{2.5}$ may adversely affect semen quality during sperm production, with men's sperm counts significantly reduced after two weeks of exposure to high levels of $PM_{2.5}$ [36]. A growing number of studies have shown that $PM_{2.5}$ exposure adversely affects semen quality.

Hansen et al. [37] not only directly observed the reduction of sperm number and activity caused by $PM_{2.5}$, but also observed that under exposure to higher concentration of $PM_{2.5}$, the percentage of abnormal sperm number in total sperm significantly increased, and the risk of structural changes in germ cells increased. Cao et al., [38] studied the possible mechanism of sprem quality problems caused by $PM_{2.5}$, and found that under $PM_{2.5}$ exposure, particles enter the body with the respiratory system and break through the blood testosterone barrier, thereby increasing the risk of changes in reproductive cell tissue structure. In the study, experiments on male mice showed changes in epididymis morphology and reduced connectivity between testicular tissues. Qiu et al., [39] Similar study have been conducted that long-term exposure to $PM_{2.5}$ did not change the weight of the testis and epididymis, but its tissue structure was alienated, vacuolation of sertoli cells and dislocation of immature germ cells in seminal tubules. Long-term exposure to $PM_{2.5}$ results in structural alienation of the testis and epididymis tissues, vacuolation of sertoli cells and dislocation of immature germ cells in seminal tubules. These studies indicate that the change of germ cell structure can affect the growth and development ability of sperm.

DNA and Hormone secretion

Yang et al. [40] used $PM_{2.5}$ concentrated samples collected in Shanghai for a 125-day exposure experiment on 12 male mice. It is found that $PM_{2.5}$ exposure affects all stages of sperm

production, and has an impact on the concentration and activity of semen. The experimental group was exposed to concentrated $PM_{2.5}$, while the control group was exposed to clean filtered air. The control group found that the germ cell structure of the mice in the experimental group was damaged. The study also found that $PM_{2.5}$ exposure affected the expression of the corresponding mRNA for testosterone production, thereby reducing testosterone production. Exposure to $PM_{2.5}$ can affect the production of reproductive hormones, or the gonads' ability to secrete hormones and reduce chronic cell division by affecting the cell cycle and genetics. MAPK signal transduction pathway is the main toxic mechanism of $PM_{2.5}$ induced sperm injury, which results in significantly reduced fertility and sperm quality of male rats after exposure to $PM_{2.5}$ [41]. Liu et al. [42]'s study further explored possible toxicological mechanisms. It was found that $PM_{2.5}$ exposure caused oxidative stress and increased cellular reactive ROS in testicular germ cells. It disrupts the BTB and affects MAPK in germ cells, as well as RNA transcription and factors that regulate antioxidant responses. With the increase of $PM_{2.5}$ concentration, ROS also increases, which intensifies the oxidative stress response of germ cells and damages sperm production. Xu et al. [43] collected $PM_{2.5}$ samples from Beijing for exposure experiments on male mice and mouse spermatocytes. The changes of cell structure and abnormal apoptosis of spermatocyte were observed under $PM_{2.5}$ exposure. The above study also found that the mitochondrial function of germ cells was impaired and the gene expression of some proteins was also affected by exposure to $PM_{2.5}$. As shown in Figure 1, There are three main gene pathways involved in sperm cell apoptosis, namely external pathway, internal pathway and mitochondrial pathway.

The influence of $PM_{2.5}$ components

Huang et al. [44] collected and analyzed semen from 1081 men in Wuhan, China from 2014 to 2015, and it was found that heavy metal elements in $PM_{2.5}$ would lead to a decrease in sperm concentration and sperm activity. Although the concentration of heavy metals in $PM_{2.5}$ is generally less than 10 percent, it has strong physiological toxicity [45]. such as Cd, Pb, Mn, Ni, Zn and so on. Ingested into the body with respiration, them even passes through the respiratory barrier, enters the bloodstream and enters the circulatory system, further spread to the whole body [46]. Due to its long half-life, heavy metals can accumulate in the human body, affect the development and function of the male reproductive system, and aggravate the pathological changes of testicular tissue, including twisting of seminiferous tubules, stromal atrophy and spermatocyte apoptosis, etc. Heavy metals in $PM_{2.5}$ can lead to sperm necrosis, few or no sperm, and a decrease in the number of interstitial cells. What's more, they can affect the secretion of male hormones and destroy the growth of

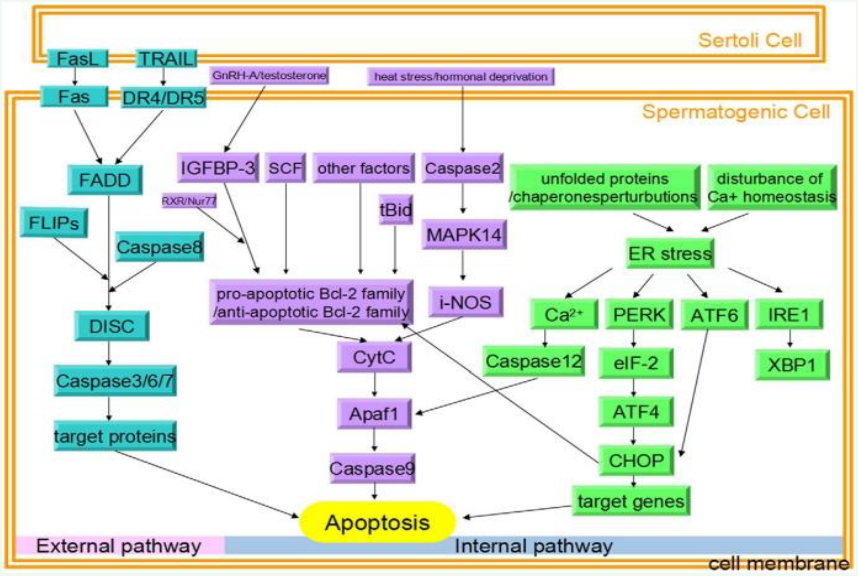

Figure 1 Signaling pathways of testicular cell survival and apoptosis. There are three main gene pathways involved in sperm cell apoptosis, namely external pathway, internal pathway and mitochondrial pathway. Mitochondria play an important role in early apoptosis of germ cells. Exposure to $PM_{2.5}$ affects hormone levels, which leads to inhibition of Cysteine-requiring Aspartate Protease Caspase (Caspase) 2 expression. It also affects the expression of MAPK, resulting in a decrease in i- Nitric Oxide Synthase (NOS) content and an increase in Cytochrome C (CytC) content. CytC can promote the effect of enzyme and enhance the oxidation effect of cells. Other interfering factors lead to changes in the content ratio of apoptotic Bcl-2 family and anti-apoptotic Bcl-2family, which also leads to increased CytC content. An increase in CytC leads to an increase in a apoptotic protease-activating factor-1Apaf-1 (Apaf-1), which stimulates caspase 3 expression and activates apoptosis. $PM_{2.5}$ expression also leads to apoptosis of external pathways. Adversely affected Sertoli cells produce cellular gene expression products that bind to Spermatogenic cells receptors. The above process can promote the absorption of FLICE-like inhibitory protein FLIPS (FLIPS) and Caspase by Fas associated death domain (FADD) to increase the content of DISC, thus activating the expression of apoptotic genes. The internal pathway of $PM_{2.5}$ exposure to germ cell apoptosis is mainly related to endoplasmic reticulum stress response. Caspase 12 lyses and thus participates in the influence of mitochondria due to changes in intracellular Ca^{2+} concentration. Except for Ca^{2+},intracellular protein kinase RNA (PKR)-like ER kinase (PERK) is affected, resulting in the production of eukaryotic translation initiation factor-2Eif-2 (Eif-2)that activate activating transcription factor-4 (ATF4) and CEBP-homologous protein CHOP (CHOP), leading to increased apoptosis levels.

spermatogenic cells, Sertoli cells and mesenchymal cells. All of these result in a loss of fertility and an increased risk of diseases such as dysfunction, impotence, cancer, obesity, metabolic syndrome, diabetes and more [47,48]. In addition, There are some organic compounds containing methyl benzene, aniline, phenol, alkyl, nitro compounds in the air belong to endocrine disruptors, these organic compounds will break through the blood testis barrier, harm to reproductive cells [49,50]. Omar et al. [49] found that part of organic matter in $PM_{2.5}$, as endocrine disruptors, affects male reproductive health and leads to reduced male hormone secretion. Mantzouki et al. [51] found that men with impaired fertility were exposed to $PM_{2.5}$, and the increase in phenolic organic matter content was significantly associated with lower sperm content, or even more serious symptoms of azoospermia. Part of the organic matter in $PM_{2.5}$, present in $PM_{2.5}$, which has been proven to be toxic at the level of the reproductive system, causing increased reactive oxygen species levels and apoptosis rates in the reproductive cells, disrupting the balance of steroids, changing the expression of sex hormones, causing fertilization failure, and causing short-term infertility [52,53]. Some organic matter can also affect genetic material and cause aneuploidy of sperm chromosomes [54].

The results of the above-mentioned animal experiments and cytotoxicity experiments show that the reproductive toxicity caused by $PM_{2.5}$ exposure will lead to a decrease in the concentration and activity of semen sperm. Oxidative and inflammatory reactions upset the balance between oxidation and anti-oxidation in cells, resulting in mitochondrial and DNA damage. It is clear that $PM_{2.5}$ exposure can lead to impaired male reproductive function, which has adverse effects on the development of a healthy and sustainable population in China. These studies also have limitations. Although $PM_{2.5}$ exposure in the environment has proven to damage the quality and production of male sperm, $PM_{2.5}$ components vary significantly in different spatio-temporal environments, which makes it difficult to draw a systematic conclusion on reproductive toxicity. There is a lack of *in vitro* data on reproductive toxicology of $PM_{2.5}$ exposure, mainly from *in vivo* data.

IMPACT ON WOMEN/FEMALES

Stillbirths, Miscarriages and Preterm Birth

Pregnant women are very sensitive to the environment during pregnancy. Any risk that exists during pregnancy can lead to adverse effects on the birth population [55]. Exposure to $PM_{2.5}$ will have an adverse effect on the outcome of pregnancy, and may cause miscarriage or even severe stillbirth [56-58]. Yang et al. [59] evaluated $PM_{2.5}$ exposure in 95,354 births from 2011 to 2013. They analysis determined the correlation of exposure to $PM_{2.5}$ to stillbirths with adverse pregnancy outcomes. It found that exposure to $PM_{2.5}$ increases the risk of stillbirth throughout pregnancy. Gaskins et al. [60] found that the proportion of miscarriage in the adverse pregnancy results was very large. Long-term exposure to $PM_{2.5}$ has a significant impact on abortion, but there are few studies on short-term exposure to abortion, and further research is needed. Liu et al. [61] Conducted a cohort study in Ningbo and found that the pregnant women were evaluated using $PM_{2.5}$ exposure at the corresponding time. The results showed that exposure to $PM_{2.5}$ is positively correlated with the risk of PTB throughout pregnancy. In addition to the long-term exposure to $PM_{2.5}$ that will increase the risk of PTB, short-term $PM_{2.5}$ exposure is also positively correlated with the risk of PTB. Li et al. [62] also found long-term exposure to $PM_{2.5}$ has greater harm on pregnancy outcomes and a large impact on increasing risk of chronic pregnancy disease. But there may also be a link between short-term exposure and PTB. It is important to protect the air quality of pregnant women. Exposure to $PM_{2.5}$, even at low concentration and for a short period of time, has adverse effects. Exposure to $PM_{2.5}$ from different sources has different effects on pregnant women, as does the exposure of women at different times of pregnancy. Li et al. [63] considered the difference between the results of more than half a million pregnancies in Hubei province and $pm_{2.5}$ exposure in urban and rural areas. There is still a positive correlation between $PM_{2.5}$ exposure and PTB risk in various regions, but among different regions, the risk of urban PTB is significantly higher than that in rural areas. This is related to the relatively large proportion of traffic sources and industrial sources among the sources of urban $PM_{2.5}$. Given the impact of the environment on reproductive health, pregnant women should be kept away from emission sources. Liu et al. [64] Cohort analysis found that $PM_{2.5}$ exposure was positively correlated with preterm birth, especially in the first trimester of pregnancy, the impact of $PM_{2.5}$ exposure is the most significant. Alman et al. [65] concluded exposure to $PM_{2.5}$ during the first and second trimesters was significantly associated with PTB. Wang et al. [66] conducted a study assessing $PM_{2.5}$ exposure in 469,975 singleton fetuses born in Guangzhou, China, from 2015 to 2017. It was found that exposure to $PM_{2.5}$ in the mid and late trimester of pregnancy is an important period for pregnant women to have premature delivery. Severe PTB is more correlated with $PM_{2.5}$ exposure. The sensitivity of exposure to $PM_{2.5}$ varies at different stages of pregnancy, so it is obviously an important means of prevention and treatment to avoid exposure of pregnant women to higher concentration of $PM_{2.5}$ during relatively sensitive periods.

HDCP

Pregnant women are more sensitive to the environment, and the oxidative stress response resulting from exposure to $PM_{2.5}$ leads to a higher incidence of HDCP [67]. $PM_{2.5}$ concentration is closely related to the risk of gestational diabetes, which is also often associated with HDCP. PE is a hypertensive disorder during pregnancy that, along with gestational diabetes, leads to an increased risk of adverse health outcomes for pregnant women and the fetus. Gestational diabetes also increases the risk of a birth defect. [68-73]. PE is a major contributor to maternal morbidity and mortality worldwide and has a high likelihood of adverse birth outcomes [74-76]. Sun et al. [77] evaluated $PM_{2.5}$ exposure at birth in 6297 cases in Zhejiang, China, from 2013 to 2017. It was found that long-term exposure of pregnant women to $PM_{2.5}$ during pregnancy led to an increased risk of pregnancy-induced hypertension and PTB. Xue et al. [78] conducted a relevant cohort study to analyze the relationship between maternal exposure to $PM_{2.5}$ and gestational hypertension and found the large correlation between $PM_{2.5}$ estimates and gestational hypertension. Savitz et al. [79] conducted a cohort study that also found that $PM_{2.5}$ exposure was associated with the risk of pregnancy-induced hypertension and PE. Assibey et al. [80] through the use of

winter $PM_{2.5}$ concentration studies, it is found that high-density $PM_{2.5}$ environmental exposure is correlated with HDCP. His other study analyzed the $PM_{2.5}$ concentration in each pregnancy month and before pregnancy, it was found that an increase in $PM_{2.5}$ concentration also leads to an increase in the risk of PE. All of these studies have shown a significant association between $PM_{2.5}$ exposure and increased HDCP risk. But,the concentration data of $PM_{2.5}$ exposure in the above study lacked individual differences and ignored the differences in actual $PM_{2.5}$ exposure of each individual. Xia et al. [27] Conducted a survey of 198 pregnant women living in Shanghai from 2017 to 2018. Each pregnant woman is equipped with close-fitting air sampling equipment to obtain environmental $PM_{2.5}$ exposure conditions. It was found that during the first and second trimester of pregnancy, $PM_{2.5}$ exposure would lead to changes in blood pressure parameters through inflammatory responses, and many components in $PM_{2.5}$ were found to be related to blood pressure parameters. Madhloum et al. [81] studied the results of exposure to $PM_{2.5}$ during different pregnancy periods. Through the discovery of the insulin in the fetus' plasma at birth, the change of $PM_{2.5}$ concentration will also affect the concentration of insulin. This indicates that pregnant women exposed to $PM_{2.5}$ have an increased risk of high blood pressure, which increases the risk of adverse fertility outcomes. High blood pressure in pregnant women also has a degree of heritability, which increases the adverse effects on reproduction and on future generations. After a pregnant woman suffers from pregnancy-induced hypertension, her risk of PTB will increase significantly [82]. The results of Mandakh et al. [83] showed that PE risk was significantly correlated with $PM_{2.5}$ exposure during pregnancy, and the correlation between PE risk and exposure window period was also different. In women with HDCP, their fertility is impaired, which has a negative impact on the continued health of the population.

mtDNA

The genes of mitochondria are unique and lack the corresponding repair ability. Oxidative stress can cause mtDNA damage .Therefore, through the study of changes in the content of mtDNA, It can be used to show that $PM_{2.5}$ exposure can cause the accumulation of oxidative stress in uterus [84-87]. Clemente et al. [84] analyzed the sensitivity of mtDNA in the placenta to toxic substances in the environment by using European counterparts in the two groups of Spanish and Belgian people. Analysis of mtDNA was used to investigate the physiological toxicity of $PM_{2.5}$ exposure. Grevendonk et al. [89] analyzed 293 cord blood samples from 224 pregnant women in Belgium. Exposure of pregnant women to $PM_{2.5}$ aggravates the oxidative stress of the whole body in the early pregnancy. Examination of genetic material in mitochondria revealed that oxidative stress caused DNA damage. Compared with DNA damage in the nucleus, mtDNA damage may be more serious. Rosa et al. [90] conducted $PM_{2.5}$ exposure assessments on pregnant women from 2007 to 2011. There is significant correlation between increased $PM_{2.5}$ exposure and decreased mtDNA content in cord blood. Late pregnancy is the period when mtDNA is most affected by $PM_{2.5}$ exposure. Brunst et al. [91] assessed exposure to $PM_{2.5}$ in 167 pregnant women in Israel in 2011-2012 and found similar results. The reduction of mtDNA exposure to $PM_{2.5}$ during pregnancy is related and has a cumulative effect. Long-term exposure can also cause trauma to the mother, resulting in a decrease in mtDNA in the placenta. During the $PM_{2.5}$ exposure period, there is this gender difference in the sensitive window period of mtDNA reduction. The sensitive window period for boys is mainly the late pregnancy, and the sensitive window period for girls is the early pregnancy. A study finds Leukocyte LTL as a guarantee of cell division, it can reflect the reproductive potential of cells and is sensitive to environmental exposure. $PM_{2.5}$ exposure in the first trimester is significantly related to LTL shortening, in addition, it is more obvious in girls [92].

The placenta and bone

The placenta is a very important organ for women during pregnancy. It has a biofilm that separates the fetal circulation from the mother's body, as well as a large surface area for material exchange. Exposure to $PM_{2.5}$ will lead to dysfunction of placenta, which will affect the normal growth and development of the fetus. In addition, Placental hormones also play an important role in maternal metabolism, and if placental hormone levels are unbalanced, it can lead to an increased risk of pregnancy complications such as placental abruption [93-95]. Ananth et al. [96] conducted a cohort study on the results between placental abruption and $PM_{2.5}$ in both long-term and short-term $PM_{2.5}$ exposure modes. The study showed that short-term $PM_{2.5}$ exposure was associated with the risk of acute placental abruption, while long-term exposure led to an increased risk of placental abruption. In addition to showing the adverse effects of $PM_{2.5}$ on placenta, some studies have also explained the possible toxicological mechanism of $PM_{2.5}$ exposure to placenta. Yue et al. [28] found that as for the expression of gene substances in placenta, $PM_{2.5}$ exposure compared with the control group found that gene expression was affected, and $PM_{2.5}$ exposure would also adversely affect the growth and development of blood vessels in placenta. Leptin an important hormone for fetal growth in the womb, was used to determine placenta health, the increase in Leptin methylation concentration has a great correlation with the risk of adverse outcomes during pregnancy [97]. Exposure to $PM_{2.5}$ increases oxidative stress and inflammation in placental cells, both of which are the toxic mechanisms responsible for placental abruption [98]. $PM_{2.5}$ exposure will adversely affect the bones of pregnant women. Exposure to $PM_{2.5}$ during pregnancy and postpartum has an impact on the mother's bone recovery and the fetus's bone development. Systemic inflammation and oxidative stress caused by $PM_{2.5}$ exposure can inhibit postnatal bone recovery in pregnant women [99,100]. Wu et al. [101] conducted a longitudinal cohort study of people receiving prenatal care from Mexico City. They use the spatio-temporal prediction model to evaluate the $PM_{2.5}$ exposure of these pregnant women during pregnancy, pre-pregnancy and post-natal time. Studies have found that high levels of $PM_{2.5}$ exposure are negatively correlated with bone strength. Long-term exposure to $PM_{2.5}$ increases the loss of bone strength in pregnant women. These results lead to an increased risk of fractures during pregnancy and postpartum osteoporosis.

Female germ cell

In addition to affecting women during pregnancy, $PM_{2.5}$ also adversely affects female germ cells, resulting in impaired

female fertility and affecting the overall development of the population. Gaskins et al. [102] subjected female mice to toxicological exposure to $PM_{2.5}$. It was found that the tissue structure of ovary was changed, and the expression of apoptotic protein was significantly higher than that of the control group. Meanwhile, exposure to $PM_{2.5}$ also affected hormone levels. An increase in $PM_{2.5}$ concentration reduces the number of ovarian follicles in the stomach antrum, while a decrease in ovarian reserve affects a woman's fertility. At present, the research on female germ cells is still in the stage of animal experiments, and the related epidemiological studies are relatively few. Gai et al. [103] observed in the experiment of $PM_{2.5}$ exposure in female mice that $PM_{2.5}$ exposure would not only aggravate oxidative stress response, but also aggravate the inflammatory response to ovarian cells with the increase of $PM_{2.5}$ concentration. In Figure 2, The original experimental cells were observed at a multiple of 100,000. In the control group, the mitochondria in the germ cells were intact and arranged regularly in the cells.

Similarly, Guo et al. [104] exposed mice to clean air and $PM_{2.5}$. The results showed that the oxidative stress response of the oocytes of female mice was significantly higher in mice exposed to $PM_{2.5}$ than in mice exposed to clean air. The number of oocytes in mice exposed to $PM_{2.5}$ decreased significantly. The measurement of transcription factors in oocytes found that it also affected the gene expression of germ cells. In the final production results, the number and weight of mice in the $PM_{2.5}$ exposure group were reduced. Bao et al. 's study supplement to a possible mechanism for adverse birth outcomes in mice exposed to $PM_{2.5}$. Exposure to $PM_{2.5}$ can lead to cell apoptosis, changes in the morphology of female mouse germ cells, impaired embryo quality, and finally the number of litters of female mice is reduced.

$PM_{2.5}$ exposure can lead to changes in the tissue structure of female germ cells, genetic material is affected, oxidative stress and inflammation are caused, and the risk of various pregnancy diseases in pregnant women is increased, and it can also lead to adverse pregnancy outcomes. Taking medications related to antioxidants and inflammatory responses can help treat diseases caused by $PM_{2.5}$ exposure. Reducing female reproductive injury caused by $PM_{2.5}$ can protect the healthy and sustainable growth of the population.

IMPACT ON THE FETUS/INFANT

Numerous epidemiological body provides evidence that high individual exposure to $PM_{2.5}$ may adversely affect developing fetuses, and reproductive epidemiology provides evidence that fetuses and infants may be more sensitive than adults to a variety of environmental poisons [100,105,106]. For China, the healthy birth of a fetus and the healthy growth of children are all related

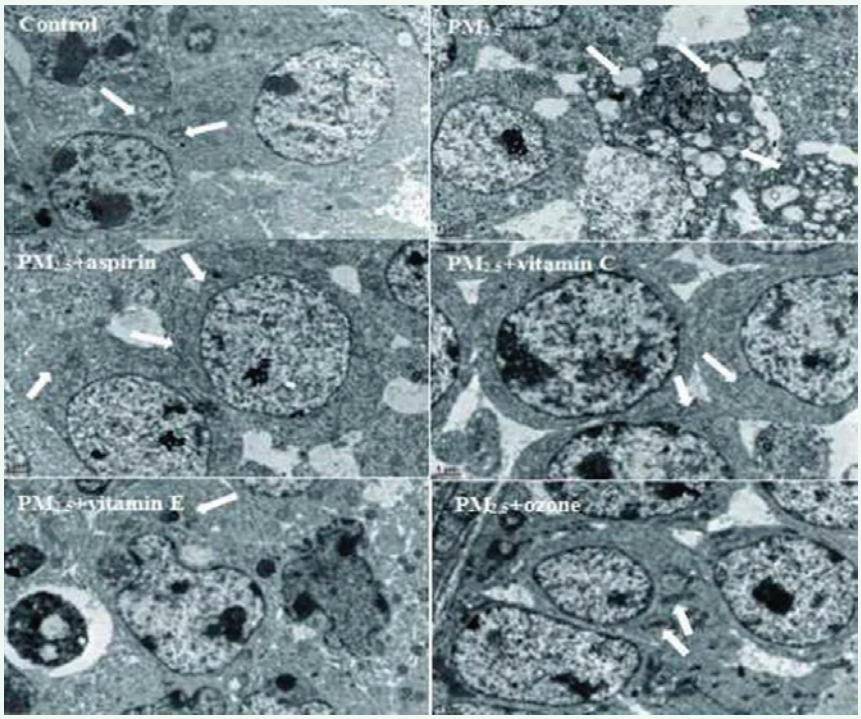

Figure 2 Comparison of the ultrastructural alterations in mitochondria in ovarian tissues in mice of different groups (original magnification ×10,000) .In the control group are the germ cells of mice that grow normally, the rest are $PM_{2.5}$ injections, and the experimental group supplemented with vitamin C, vitamin E, aspirin and Ozone. Ultra structural changes of mitochondria in ovarian tissues of different groups were compared. In the $PM_{2.5}$ exposure group, mitochondria were swollen, mitochondria membrane was damaged, linear particles were disordered and vacuolated. Combined exposure to Ozone and $PM_{2.5}$ increased the risk of ovarian cell damage, while mixed exposure to the other three substances and $PM_{2.5}$ reduced the risk. It indicates that in the actual exposure environment, $PM_{2.5}$ will interact with other environmental pollutants, resulting in a further increase in reproductive toxicity. Through the combined exposure experiment with the addition of relevant antioxidant and inflammatory drugs and $PM_{2.5}$, it was proved that oxidative stress and inflammatory response of cells exposed to $PM_{2.5}$ were the important reasons leading to the reproductive toxicity of $PM_{2.5}$.

to the country's policy of healthy birth and post-natal care. Ensuring a healthy population group is of great significance to the future development of our country. $PM_{2.5}$ exposure will affect all stages of the growth and development of the fetus in the mother. It will have an adverse effect on the growth of cells involved in the vegetative ectoderm of the fetus, as well as the cells involved in the individual development of the fetus in the future [99]. Child birth defects due to $PM_{2.5}$ exposure during pregnancy problem has aroused people's wide attention, such as fetal chromosomal abnormalities, premature birth, low birth weight, long-term complications etc. [107,108].

Obesity and Low Birth Weight

Chiu et al. [109] conducted a growth and development study on 277 full-term children. In the early and mid-trimesters of pregnancy, higher levels of $PM_{2.5}$ exposure are related to the weight change of girls, while exposure to $PM_{2.5}$ in the second trimester is associated with increased fat in boys. Kim et al. [110] indicated that $PM_{2.5}$ exposure can affect the decomposition of carbohydrates, which may be the cause of childhood obesity. The study of Lin et al. [111] found that $PM_{2.5}$ exposure is related to birth weight and obesity in the subsequent growth and development of children. Exposure to $PM_{2.5}$ not only affects children's metabolic development and leads to obesity, but also increased neonatal DNA methylation. Both contribute to childhood obesity. As shown in Figure 3, analyze the relationship between newborn birth weight and pregnant women's prenatal exposure. $PM_{2.5}$ exposure will destroy the ideal intrauterine environment, disrupt the metabolic plan of the growing fetus, increase the level of inflammatory cytokines, impair the function of insulin receptors, affect the decomposition of glucose, and increase the possibility of obesity in later childhood [112].

In addition to obesity, low birth weight can also lead to congenital deficiencies in the growth and development of babies. The reduction in birth weight is significantly correlated with $PM_{2.5}$ exposure during pregnancy [113]. A cohort study on the relationship between $PM_{2.5}$ and birth weight found After excluding the interference of personal living habits, it was found that higher $PM_{2.5}$ exposure during pregnancy is related to the reduction of birth weight. However, as the birth weight is greatly reduced, the correlation of $PM_{2.5}$ will decrease. $PM_{2.5}$ exposure has an adverse effect on birth weight, but it is not a decisive factor [114]. Guo et al. [115] Studied the relationship between $PM_{2.5}$ exposure and birth weight change at term. The study also found a link between reduced birth weight and $PM_{2.5}$ exposure. In the mixed model of all air pollutants, it was not found to be related to birth weight, but in a single $PM_{2.5}$ exposure model, $PM_{2.5}$ concentration was negatively correlated with birth weight. Early pregnancy has the greatest impact on birth weight throughout pregnancy. Fleischer et al. [31] analyzed adverse pregnancy outcomes caused by exposure to $PM_{2.5}$ during pregnancy. It was also found that the $PM_{2.5}$ concentration in the environment is negatively correlated with birth weight, and the higher the $PM_{2.5}$ exposure level, the more serious the impact. Slama et al. [116] analyzed the relationship between the birth weight of 1016 children born in the 1990s in Munich, Germany and their exposure to $PM_{2.5}$ from traffic sources. $PM_{2.5}$ concentration and absorbance were found to have adverse effects on birth weight, and $PM_{2.5}$ exposure from traffic sources led to lower birth weight. Janssen et al. [117] cohort analysis was performed on pregnancy outcomes and fetuses of pregnant women exposed to $PM_{2.5}$. The results found that thyroid hormone in cord blood decreased with increased $PM_{2.5}$ concentration. Such changes in late pregnancy may affect fetal thyroid function and lead to changes in birth weight. The research of Eliot et al. [118] further explained the possible toxicological mechanism. $PM_{2.5}$ from the traffic source cause DNA damage, adversely affect the growth and development of the fetus, and cause a decrease in birth weight. Yang et al. [119] research on the main mechanism of adverse effects of $PM_{2.5}$ exposure on fetal growth. In addition to directly affecting fetal growth and development through inflammatory response, oxidative stress and other mechanisms, $PM_{2.5}$ also indirectly affects fetal growth through affecting blood glucose level.

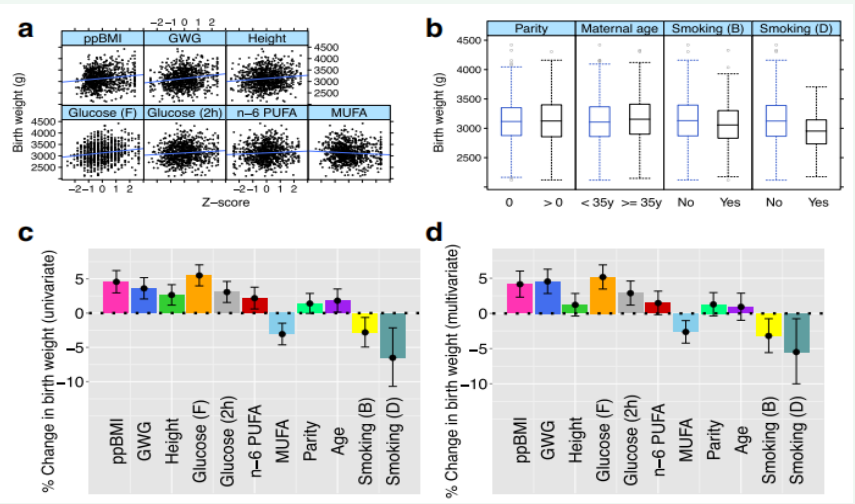

Figure 3 Prenatal environment influences on birth weight. Figure 3a and Figure 3b are both the relationship between prenatal environmental variables and body weight, and it is found that there is a significant correlation between them. Figure 3c and Figure 3d deal with the interference factors, and the percentage change of birth weight with the prenatal environment change is significantly related to the environment. A mother's weight, blood sugar levels, and environmental exposure are all related to a child's weight.

Congenital defect disease

Fetal growth restriction is mainly caused by uterine placental dysfunction, resulting in an inadequate supply of nutrients and oxygen, affecting the normal growth of the fetus. Related research has shown that $PM_{2.5}$ exposure is associated with placental inflammatory response, abnormal trophoblast invasion and reduced placental angiogenesis, which may lead to impaired fetal growth [120-122]. Exposure to $PM_{2.5}$ causes changes in the arterial wall of young children, thereby increasing the risk of cardiovascular disease, oxidative stress and inflammation are believed to be important links between air pollution and cardiovascular risk caused by atherosclerosis [123,124]. Ntarladima et al. [125] measured carotid intima media thickness, carotid artery opening, elastic modulus, diastolic and systolic blood pressure, and the results showed that the carotid artery density in children exposed to $PM_{2.5}$ decreased by standard deviation. In further research, Hwang et al. [126] conducted a comparative analysis of the birth environment exposure of 1087 children with heart defects and More than 10000 normal children in Taiwan Province. It is found that babies born prematurely are at greater risk than full-term babies. The greater the concentration of air pollution in the environment, the greater the risk of heart defects. Except for the cardiovascular birth defects, Adel et al. [127] evaluated 216,730 infants from 1997 to 2004, using data from air monitoring stations to assess their pollution exposure. Research results show that exposure to air pollution significantly increases the risk of congenital malformations, especially the special malformations in the reproductive organs and circulatory system. Jordan et al. [128] assessed the relationship between partial congenital defects and $PM_{2.5}$ exposure. Analysis of spina bifida, critical congenital heart defects and orofacial clefts, found that exposure to $PM_{2.5}$ is related to these birth defects. Interestingly, Schembari et al. [129] used $PM_{2.5}$ exposure from traffic sources to compare 2247 children with chromosomal abnormalities in Barcelona from 1994 to 2006 and 2991 normal children in a comparative study. Traffic source $PM_{2.5}$ exposure does not have an obvious relationship with every congenital defects, but there is a clear correlation between cardiovascular-related congenital diseases and $PM_{2.5}$ concentration. Stingone et al. [130] conducted $PM_{2.5}$ exposure assessments on congenital anomalies in nine states of America. The current high levels of $PM_{2.5}$ exposure are significantly related to a variety of congenital defects. In the sensitive window period of fetal heart development, the oxidative stress response caused by $PM_{2.5}$ exposure is the main potential mechanism for cardiovascular congenital diseases. Embryonic exposure affects the maternal and/or intrauterine environment and leads to impaired fetal development. During rapid fetal growth, the developing cardiovascular system is particularly susceptible to its environment, fetal exposure can cause changes in epigenetic characteristics that lead to permanent changes in gene expression [131]. The increased risk of congenital defects in children is also detrimental to the healthy development of the population.

Nervous system and other diseases

Perinatal exposure to $PM_{2.5}$ has been shown to have negative effects on children's neuropsychological development. Emam et al. [132] analyzed the effects of $PM_{2.5}$ exposure to the nervous system during prenatal and pregnancy in female mice. Found that $PM_{2.5}$ exposure can affect the secretion of hypothalamic neurohormones, thereby affecting children's social behavior and nervous system, which may be the cause of children's autism. McGuinn et al. [133] conducted a comparative analysis of 855 people with early tendency and 647 children with autism from 2003 to 2004. $PM_{2.5}$ exposure was assessed before and throughout pregnancy, and in the first year of life. An association was observed between $PM_{2.5}$ exposure and autism in the first year of life, with higher concentrations increasing the risk. Bose et al. [134] studied the effects of 375 pregnant women and single-born children in Mexico from 2007 to 2011 and the effects of $PM_{2.5}$ exposure on children's sleep quality and nervous system. It find that the development of the nervous system of the fetus in the womb will affect the sleep structure after birth, and Exposure to $PM_{2.5}$ can lead to less sleep in young children, possibly because of damage to their neuron-development. The sensitive window of influence is mainly concentrated in the early and third trimesters. This may be because $PM_{2.5}$ will break through the blood-brain barrier and affect the construction of the cerebral nervous system.

Seeni et al. [135] analyzed the results of 223,385 births with only one child born in the United States from 2002 to 2008, and used a model to evaluate $PM_{2.5}$ exposure during pregnancy. It was found that exposure to $PM_{2.5}$ in the latter part of pregnancy leads to an increased risk of temporary dyspnea. There is a significant correlation between $PM_{2.5}$ exposure and the risk of suffocation during the entire pregnancy. As the $PM_{2.5}$ concentration increases, the possibility of suffocation also increases. Exposure to high levels of $PM_{2.5}$ in the second trimester also increased the risk of respiratory distress syndrome. Clinical experience has shown that the incidence of neonatal jaundice increases when air quality degrades. A study of 25,782 newborns reported an increase in neonatal bilirubin levels. Bilirubin levels increase linearly with exposure time from 0 to 48h. Improving air quality may be the key to reducing the risk of jaundice in newborns [136].

All of the above studies have shown that $PM_{2.5}$ exposure can lead to an increased risk of congenital diseases and affect the quality of the birth population. Reducing $PM_{2.5}$ concentration can reduce the negative impact of environmental exposure on the population policy of healthy birth and nurturing. Research also has certain limitations. The main toxicological mechanisms currently discussed are inflammatory factors, stress response, which destroys the barrier structure as the blood enters the body, affects hormone receptors and cell apoptosis. However, reproductive toxicology involves very complex physiological processes, and the composition of $PM_{2.5}$ is also complex and diverse, which leads to challenges in the study of specific molecular mechanisms. Long-term Chronic Toxicology Experimental Research and the toxicological study of complex $PM_{2.5}$ components on the growth and development of young children is still a difficult and important point.

CONCLUSION

$PM_{2.5}$ exposure causes oxidative stress in testicular tissue, oxidative damage in testicular cells, increased apoptosis of Sertoli cells, spermatogenic cells and mesenchymal cells, damage to the microbiological environment, and decrease of sperm quality,

leading to male infertility. Exposure to air pollutants can disrupt hormones in the body, destroy OS balance, damage embryo and placental tissue, and affect normal embryo implantation. Women preparing for pregnancy should do a good job of air pollution protection before conception, early protection will improve the clinical pregnancy rate, reduce the occurrence of spontaneous abortion. Have immediate and long-term effects on the influence of the child during pregnancy, such as congenital deformity inflammation, premature birth, low birth weight, long-term complications hypertension and obesity, etc. Oxidative stress, DNA methylation, changes in mitochondrial DNA content, endocrine disorders and so on Maybe the mechanism of $PM_{2.5}$'s effect on offspring. $PM_{2.5}$ affects the fertility of men and women of the right age, endangers the growth and development of fetuses and adversely affects the growth of children, thus causing adverse effects on human fertility. Understanding the impact of $PM_{2.5}$ on human fertility is necessary for the long-term and scientific development of human beings, as well as for the current global population problem and the policy of good birth and postnatal care.

In our review report, many countries and regions are involved, and the influence of spatial factors is comprehensively considered. However, in the study of the impact of $PM_{2.5}$ on human fertility, the single $PM_{2.5}$ factor may not be the main factor, and other complex environmental factors around it are also important to influence fertility. In addition, different components of $PM_{2.5}$ in different regions and different periods have different influences on fertility. A more detailed and comprehensive consideration of the impact of $PM_{2.5}$ on fertility is still a problem waiting to be solved. In toxicity studies, there are differences between in vitro experiments and the real environment of the human body. It is closer to the specific toxicological mechanism of the human body, which will help us better understand the harm of $PM_{2.5}$ to fertility.

ACKNOWLEDGEMENTS

This research was funded by the National Natural Science Foundation of China (grant number 21976094, 22176100); and the National Key Research and Development Project 9(grant number 2018YFC0213802)

AUTHOR CONTRIBUTIONS

Conceptualization, M.C. and Z.L.; formal analysis, P.G.; investigation, Z.L.; resources, M.C; data curation, P.G. and Z.J.; writing—original draft preparation, Z.L.; writing—review and editing, Z.L.; funding acquisition, M.C. All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Li M, Hu M, Guo Q, Tan T, Du B, Huang X, et al. Seasonal Source Apportionment of PM2.5 in Ningbo, a Coastal City in Southeast China. Aerosol Air Qual Res. 2018; 18: 2741-2752.
2. Ehsan E, Zainab K, Zhang Z. Understanding farmers' intention and willingness to install renewable energy technology: A solution to reduce the environmental emissions of agriculture. Appl Energy. 2022; 309: 118459.
3. Ehsan E, Zhang Z, Zainab K, Xu H. Application of an artificial neural network to optimise energy inputs: An energy-and cost-saving strategy for commercial poultry farms. Energy. 2022; 244: 123169.
4. Wu W, Zhang M, Ding Y. Exploring the effect of economic and environment factors on PM2.5 concentration: A case study of the Beijing-Tianjin-Hebei region. J Environ Manage. 2020; 268: 110703.
5. Xu G, Ren X, Xiong K, Li L, Bi X, Wu Q. Analysis of the driving factors of PM2.5 concentration in the air: A case study of the Yangtze River Delta, China. Ecological Indicators. 2020; 110.
6. Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. Lancet. 2017; 389: 1907-1918.
7. Yangs L, Li C, Tang X. The Impact of $PM_{2.5}$ on the Host Defense of Respiratory System. Front Cell Dev Biol. 2020; 8: 91.
8. Renjie Chen PY, Meng X, Liu C, Wang L, Xu X, Ross JA, et al. Fine Particulate Air Pollution and Daily Mortality: A Nationwide Analysis in 272 Chinese Cities. Am J Respir Crit Care Med. 2017; 196: 73-81.
9. Georgakakou S, Gourgoulianis K, Daniil Z, Bontozoglou V. Prediction of particle deposition in the lungs based on simple modeling of alveolar mixing. Respir Physiol Neurobiol. 2016; 225: 8-18.
10. Wang ZJ, Han LH, Chen XF, Cheng SY, Yue LI, Tian C, et al. Characteristics and sources of PM_(2.5) in typical atmospheric pollution episodes in Beijing. Journal of Safety and Environment. 2012; 10: 1007/s11783-011-0280-z.
11. Lewtas, J. Air pollution combustion emissions: characterization of causative agents and mechanisms associated with cancer, reproductive, and cardiovascular effects. Mutat Res. 2007; 636: 95-133.
12. Grahame TJ, Klemm R, Schlesinger RB. Public health and components of particulate matter: The changing assessment of black carbon. J Air Waste Manag Assoc. 2014; 64: 620-660.
13. Mikołajczyk U, Bujak-Pietrek S, kowska-Stańczyk I. Worker exposure to ultrafine particles during carbon black treatment. Med Pr. 2015; 66: 317-326.
14. Rong W. Global Emissions of Black Carbon from 1960 to 2007; Global Emission Inventory and Atmospheric Transport of Black Carbon: 2015.
15. Li Y, Liu X, Liu M, Xiaofei M, Meng F, Wang J. Investigation into atmospheric $PM_{2.5}$-borne PAHs in Eastern cities of China: concentration, source diagnosis and health risk assessment. Environ Sci Process Impacts.2016; 18: 529-537.
16. Chen XC, Chuang HC, Ward TJ, Tian L, Cao JJ, Ho SS, et al. Indoor, outdoor, and personal exposure to $PM_{2.5}$ and their bioreactivity among healthy residents of Hong Kong. Environ Res. 2020; 188: 109780.
17. Kamal A, Qamar K, Gulfraz M, Anwar MA, Malik RN. PAH exposure and oxidative stress indicators of human cohorts exposed to traffic pollution in Lahore city (Pakistan). Chemosphere. 2015; 120: 59-67.
18. Totlandsdal AI, Lg M, Lilleaas E, Cassee F, Schwarze P. Differential Proinflammatory Responses Induced by Diesel Exhaust Particles with Contrasting PAH and Metal Content. Environ Toxicol. 2015; 30: 188-196.
19. Gu H, Yan W, Ehsan E, Cao Y. Air pollution risks human mental health: An implication of two-stages least squares estimation of interaction effects. Environ Sci Pollut Res Int, 2019; 27: 2036-2043.
20. Gu H, Cao Y, Ehsan E, Jha SK. Human health damages related to air pollution in China. Environ Sci Pollut Res Int. 2019; 26: 13115-13125.
21. Uski O, Jalava PI, Happo MS, Torvela T, Leskinen J, Maeki-Paakkanen J, et al. Effect of fuel zinc content on toxicological responses of particulate matter from pellet combustion in vitro. Sci Total Environ. 2015; 511: 331-340.

22. Traboulsi H, Guerrina N, Iu M, Maysinger D, Baglole CJ. Inhaled Pollutants: The Molecular Scene behind Respiratory and Systemic Diseases Associated with Ultrafine Particulate Matter. Int J Mol Sci. 2017; 18: 243.

23. Feng S, Gao D, Liao F, Zhou F, Wang X. The health effects of ambient $PM_{2.5}$ and potential mechanisms. Ecotoxicol Environ Saf. 2016; 128: 67-74.

24. Xue T, Zhang Q. Associating ambient exposure to fine particles and human fertility rates in China. Environ Pollut. 2018; 235: 497-504.

25. Xue T, Zhu T. Association between fertility rate reduction and pre-gestational exposure to ambient fine particles in the United States, 2003-2011. Environ Int. 2018; 121: 955-962.

26. Wei Y, Cao XN, Tang XL, Shen LJ, Lin T, He DW, et al. Urban fine particulate matter (PM2.5) exposure destroys blood-testis barrier (BTB) integrity through excessive ROS-mediated autophagy. Toxicol Mech Methods. 2018; 28: 302-319.

27. Xia B, Zhou Y, Zhu Q, Zhao Y, Wang Y, Ge W, et al. Personal exposure to $PM_{2.5}$ constituents associated with gestational blood pressure and endothelial dysfunction. Environ Pollut. 2019;250: 346-356.

28. Gu H, Bian F, Ehsan E. Effect of Air Pollution on Female Labor Supply: An Empirical Analysis Based on Data of Labor Force Dynamic Survey of China. Soc Work Public Health. 2020; 35: 4.

29. Li Z, Tang Y, Song X, Lazar L, Lie Z, Zhao J. Impact of ambient $PM_{2.5}$ on adverse birth outcome and potential molecular mechanism. Ecotoxicol Environ Saf. 2019; 169: 248-254.

30. Sutovsky P, Cupp AS, Thompson W, Baker M. Reproductive systems biology tackles global issues of population growth, food safety and reproductive health. Cell Tissue Res.2016; 363: 1-5.

31. Fleischer NL, Merialdi M, van Donkelaar A, Vadillo-Ortega F, Martin RV, Betran AP, et al. Outdoor air pollution, preterm birth, and low birth weight: analysis of the world health organization global survey on maternal and perinatal health. Environ Health Perspect. 2014; 122: 425-430.

32. Madaniyazi L, Guo Y, Yu W, Tong S. Projecting future air pollution-related mortality under a changing climate: progress, uncertainties and research needs. Environ Int. 2015; 75: 21-32.

33. Wang L, Luo D, Liu X, Zhu J, Wang F, Li Bet al. Effects of PM2.5 exposure on reproductive system and its mechanisms. Chemosphere. 2021; 264: 128436.

34. Lao XQ, Zhang Z, Lau AKH, Chan TC, Chuang YC, Chan J, et al. Exposure to ambient fine particulate matter and semen quality in Taiwan. Occup Environ Med. 2018; 75: 148-154.

35. Zhang HT, Zhang Z, Cao J, Tang WH, Zhang HL, Hong K, et al. Ambient ozone pollution is associated with decreased semen quality: longitudinal analysis of 8945 semen samples from 2015 to 2018 and during pollution-control period in Beijing, China. Asian J Androl. 2019; 21: 501-507.

36. Huang G, Zhang Q, Wu H, Wang Q, Chen Y, Guo P, et al. Sperm quality and ambient air pollution exposure: A retrospective, cohort study in a Southern province of China. Environ Res. 2020;188: 109756.

37. Hansen C, Luben TJ, Sacks JD, Olshan A, Jeffay S, Strader L, et al. The effect of ambient air pollution on sperm quality. Environ Health Perspect. 2010; 118: 203-209.

38. Cao XN, Shen LJ, Wu SD, Yan C, Zhou Y, Xiong G, et al. Urban fine particulate matter exposure causes male reproductive injury through destroying blood-testis barrier (BTB) integrity. Toxicol Lett. 2017; 266: 1-12.

39. Qiu L, Chen M, Wang X, Qin X, Chen S, Qian Y, et al. Exposure to Concentrated Ambient PM2.5 Compromises Spermatogenesis in a Mouse Model: Role of Suppression of Hypothalamus-Pituitary-Gonads Axis. Toxicol Sci. 2018; 162: 318-326.

40. Yang Y, Yang T, Liu S, Cao Z, Zhao Y, Su X, et al. Concentrated ambient PM2.5 exposure affects mice sperm quality and testosterone biosynthesis. Peer J. 2019; 7: e8109.

41. Liu B, Shen LJ, Zhao TX, Sun M, Wang JK, Long CI, et al. Automobile exhaust-derived PM2.5 induces blood-testis barrier damage through ROS-MAPK-Nrf2 pathway in sertoli cells of rats. Ecotoxicol Environ Saf. 2020; 189.

42. Liu B, Wu SD, Shen LJ, Zhao TX, Wei Y, Tang XL, et al. Spermatogenesis dysfunction induced by PM2.5 from automobile exhaust via the ROS-mediated MAPK signaling pathway. Ecotoxicol Environ Saf. 2019; 167: 161-168.

43. Xu YR, Dong HS, Yang WX. Regulators in the apoptotic pathway during spermatogenesis: Killers or guards? Gene. 2016; 582: 97-111.

44. Huang X, Zhang B, Wu L, Zhou Y, Li Y, Mao X, et al. Association of Exposure to Ambient Fine Particulate Matter Constituents With Semen Quality Among Men Attending a Fertility Center in China. Environ Sci Technol. 2019; 53: 5957-5965.

45. Wang F, Wang J, Han M, Jia C, Zhou Y. Heavy metal characteristics and health risk assessment of PM2.5 in students' dormitories in a u'iversity in Nanjing, China. Building and Environment. 2019; 160.

46. He X, Wu J, Yuan L, Lin F, Yi J, Li J, et al. Lead induces apoptosis in mouse TM3 Leydig cells through the Fas/FasL death receptor pathway. Environ Toxicol Pharmacol. 2017; 56: 99-105.

47. Radwan M, Jurewicz J, Sobala W, Brze Nicki S, Radwan P, Jakubowski L, et al. Human sperm aneuploidy after exposure to polycyclic aromatic hydrocarbons. Reprod Fertil Dev. 2016; 28: 1376.

48. Yuanlong Hou XW, Lei Z, Ping J, Liu J, Ma Z, Zhang Z, et al. Heat-stress-induced metabolic changes and altered male reproductive function. J Proteome Res. 2015; 14: 1495-1503.

49. Omar Quintana-Belmares R, Krais AM, Kourangi Esfahani B, Rosas-Perez I, Mucs D, Lopez-Marure R, et al. Phthalate esters on urban airborne particles: Levels in PM10 and PM2.5 from Mexico City and theoretical assessment of lung exposure. Environ Res. 2018; 161: 439-445.

50. Zhou Q, Chen J, Zhang J, Zhou F, Zhao J, Wei X, et al. Toxicity and endocrine-disrupting potential of $PM_{2.5}$: Association with particulate polycyclic aromatic hydrocarbons, phthalate esters, and heavy metals. Environ Pollut. 2021; 292: 118349.

51. Mantzouki C, Bliatka D, Iliadou PK, Margeli A, Papassotiriou I, Mastorakos G, et al. Serum Bisphenol A concentrations in men with idiopathic infertility. Food Chem Toxicol. 2019; 125: 562-565.

52. Jurewicz J, Dziewirska E, Radwan M, Hanke W. Air pollution from natural and anthropic sources and male fertility. Reprod Biol Endocrinol. 2018; 16: 109.

53. Miao Y, Zhou C, Bai Q, Cui Z, ShiYang X, Lu Y, et al. The protective role of melatonin in porcine oocyte meiotic failure caused by the exposure to benzo(a)pyrene. Hum Reprod. 2018; 33: 116-127.

54. Bolden AL, Rochester JR, Schultz K, Kwiatkowski CF. Polycyclic aromatic hydrocarbons and female reproductive health: A scoping review. Reprod Toxicol. 2017; 73: 61-74.

55. Li Z, Tang Y, Song X, Lazar L, Li Z, Zhao J. Impact of ambient PM2.5 on adverse birth outcome and potential molecular mechanism. Ecotoxicol Environ Saf. 2019; 169: 248-254.

56. Grippo A, Zhang J, Chu L, Guo Y, Qiao L, Zhang J. et al. Air pollution exposure during pregnancy and spontaneous abortion and stillbirth.

Rev Environ Health. 2018; 33: 247-264.

57. Hyland A, Piazza KM, Hovey KM, Ockene JK, Andrews CA, Rivard C, et al. Associations of lifetime active and passive smoking with spontaneous abortion, stillbirth and tubal ectopic pregnancy: a cross-sectional analysis of historical data from the Women's Health Initiative. Tob Control. 2015; 24: 328.

58. Siddika N, Balogun HA, Amegah AK, Jaakkola J. Prenatal ambient air pollution exposure and the risk of stillbirth: systematic review and meta-analysis of the empirical evidence. Occup Environ Med. 2016; 73: 573.

59. Yang S, Tan Y, Mei H, Wang F, Li N, Zhao J, et al. Ambient air pollution the risk of stillbirth: A prospective birth cohort study in Wuhan, China. Int J Hyg Environ Health. 2018; 221: 502-509.

60. Gaskins AJ, Minguez-Alarcon L, Williams PL, Chavarro JE, Schwartz JD, Kloog I, et al. Ambient air pollution and risk of pregnancy loss among women undergoing assisted reproduction. Environ Res. 2020: 191.

61. Liu WY, Yu ZB, Qiu HY, Wang JB, Chen XY, Chen K. Association between ambient air pollutants and preterm birth in Ningbo, China: a time-series study. Bmc Pediatrics. 2018; 18.

62. Li, X, Liu Y, Liu F, Wang Y, Yang X, Yu J. et al. Analysis of short-term and sub-chronic effects of ambient air pollution on preterm birth in central China. Environ Sci Pollut Res Int. 2018; 25: 19028-19039.

63. Li L, Ma J, Cheng Y, Feng L, Wang S, Yun X, et al. Urban-rural disparity in the relationship between ambient air pollution and preterm birth. Int J Health Geogr. 2020; 19: 23.

64. Liu C, Sun J, Liu Y, Liang H, Wang M, Wang C, et al. Different exposure levels of fine particulate matter and preterm birth: a meta-analysis based on cohort studies. Environ Sci Pollut Res Int. 2017; 24: 17976-17984.

65. Alman BL, Stingone JA, Yazdy M, Botto LD, Desrosiers TA, Pruitt S. et al. Associations between PM2.5 and risk of preterm birth among liveborn infants. Ann Epidemiol. 2019; 39: 46-53.

66. Wang Q, Benmarhnia T, Zhang H, Knibbs LD, Sheridan P, Li C, et al. Identifying windows of susceptibility for maternal exposure to ambient air pollution and preterm birth. Environ Int. 2018; 121: 317-324.

67. Shin D, Song WO. Prepregnancy body mass index is an independent risk factor for gestational hypertension, gestational diabetes, preterm labor, and small- and large-for-gestational-age infants. J Matern Fetal Neonatal Med. 2015; 28: 1679-1686.

68. Chen L, Mayo R, Chatry A, Hu G. Gestational Diabetes Mellitus: Its Epidemiology and Implication beyond Pregnancy. Current Epidemiology Reports. 2016; 3: 1-11.

69. Gadgil M, Oza-Frank R, Kandula NR, Kanaya AM. Type 2 diabetes after gestational diabetes mellitus in South Asian women in the United States. Diabetes Metab Res Rev. 2017; e2891.

70. Inocêncio G, Braga A, Lima T, Vieira B, Zulmira R, Carinhas M, et al. Which Factors Influence the Type of Delivery and Cesarean Section Rate in Women with Gestational Diabetes? J Reprod Med. 2015; 60: 529.

71. Meo SA, Memon AN, Sheikh SA, Rouq FA, Arain SA. Effect of environmental air pollution on type 2 diabetes mellitus. Eur Rev Med Pharmacol Sci. 2015; 19: 123-128.

72. Shostrom D, Sun Y. Oleson JJ, Snetselaar LG, Wei B. History of Gestational Diabetes Mellitus in Relation to Cardiovascular Disease and Cardiovascular Risk Factors in US Women. Front Endocrinol. 2017; 8: 144.

73. Zhao E, Zhang Y, Zeng X, Liu B. Association between maternal diabetes mellitus and the risk of congenital malformations: A meta-analysis of cohort studies. Drug Discov Ther. 2015; 9: 274-281.

74. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. Bmj. 2013; 347: f6564.

75. Auger N, Luo ZC, Nuyt AM, Kaufman JS, Fraser WD. Secular Trends in Preeclampsia Incidence and Outcomes in a Large Canada Database: A Longitudinal Study Over 24 Years. Can J Cardiol. 2015; 32.

76. Pur De MT, Baumann M, Wiedemann U, Nydegger UE, Risch M. Incidence of preeclampsia in pregnant Swiss women. Swiss Med Wkly. 2015; 145: w14175.

77. Sun Z, Yang L, Bai X, Du W, Shen G, Fei J, et al. Maternal ambient air pollution exposure with spatial-temporal variations and preterm birth risk assessment during 2013-2017 in Zhejiang Province, China. Environment International. 2019; 133.

78. Xue T, Zhu T, Lin W, Talbott EO. Association Between Hypertensive Disorders in Pregnancy and Particulate Matter in the Contiguous United States, 1999-2004. Hypertension. 2018; 7: 77-84.

79. Savitz DA, Elston B, Bobb JF, Clougherty JE, Dominici F, Ito K, et al. Ambient Fine Particulate Matter, Nitrogen Dioxide, and Hypertensive Disorders of Pregnancy in New York City. Epidemiology 2015; 26: 748-757.

80. Assibey-Mensah V, Glantz JC, Hopke PK, Jusko TA, Thevenet-Morrison K, Chalupa D, et al. Ambient wintertime particulate air pollution and hypertensive disorders of pregnancy in Monroe County, New York. Environ Res. 2019; 168: 25-31.

81. Madhloum N, Janssenv BG, Martens DS, Saenen ND, Bijnens E, Gyselaers W, et al. Cord plasma insulin and in utero exposure to ambient air pollution. Environ Int. 2017; 105: 126-132.

82. Malmqvist E, Larsson HE, Joensson I, Rignell-Hydbom A, Ivarsson SA, Tinnerberg H, et al. Maternal exposure to air pollution and type 1 diabetes-Accounting for genetic factors. Environ Int. 2015; 140: 268-274.

83. Mandakh Y, Rittner R, Flanagan E, Oudin A, Isaxon C, Familari M, et al. Maternal Exposure to Ambient Air Pollution and Risk of Preeclampsia: A Population-Based Cohort Study in Scania, Sweden. Int J Environ Res Public Health. 2020; 17: 1744.

84. Menon R, Behnia F, Polettini J, Saade GR, Velarde M. Placental membrane aging and HMGB1 signaling associated with human parturition. Aging. 2016; 8: 216-229.

85. Pieters N, Janssen BG, Dewitte H, Cox B, Cuypers A, Lefebvre W, et al. Biomolecular Markers within the Core Axis of Aging and Particulate Air Pollution Exposure in the Elderly: A Cross-Sectional Study. Environ Health Perspect. 2016; 124: 943-950.

86. Shaughnessy DT, Kimberly M, Leroy W, Haugen AC, Meyer JN, Domann FE et al. Mitochondria, Energetics, Epigenetics, and Cellular Responses to Stress. Environ Health Perspect. 2014; 122: 1271.

87. Yang L, Hou XY, Wei Y, Thai P, Chai F. Biomarkers of the health outcomes associated with ambient particulate matter exposure. Sci Total Environ. 2016; 1446-1459.

88. Clemente DBP, Casas M, Vilahur N, Be Giristain H, Bustamante M, Carsin AE, et al. Prenatal Ambient Air Pollution, Placental Mitochondrial DNA Content, and Birth Weight in the INMA (Spain) and ENVIRONAGE (Belgium) Birth Cohorts. Environ Health Perspect. 2016; 124: 659-665.

89. Grevendonk L, Janssen BG, Vanpoucke C, Lefebvre W, Hoxha M, Bollati V, et al. Mitochondrial oxidative DNA damage and exposure to particulate air pollution in mother-newborn pairs. Environmental Health. 2016; 15: 10.

90. Rosa MJ, Just AC, Guerra MS, Kloog I, Hsu H.-H.L, Brennan KJ, et al. Identifying sensitive windows for prenatal particulate air pollution exposure and mitochondrial DNA content in cord blood. Environ Int. 2017; 98: 198-203.

91. Brunst KJ, Sanchez-Guerra M, Chiu YM, Wilson A, Coull BA, Kloog I, et al. Prenatal particulate matter exposure and mitochondrial dysfunction at the maternal-fetal interface: Effect modification by maternal lifetime trauma and child sex. Environ Int. 2018; 112: 49-58.

92. Rosa MJ, Hsu HL, Just AC, Brennan KJ, Bloomquist T, Kloog I, et al. Association between prenatal particulate air pollution exposure and telomere length in cord blood: Effect modification by fetal sex. Environ Res. 2019; 172: 495-501.

93. Ananth CV, Hansen AV, Williams MA, Andersen AN. Cardiovascular Disease in Relation to Placental Abruption: APopulation-Based Cohort Study from Denmark. Paediatr Perinat Epidemiol. 2017; 31: 209-218.

94. Burton GJ, Fowden AL. The placenta: a multifaceted, transient organ. Philos Trans R Soc Lond B Biol Sci. 2015; 370: 20140066.

95. Downes KL, Shenassa ED, Grantz KL. Neonatal Outcomes Associated With Placental Abruption. Am J Epidemiol. 2017; 186: 1319-1328.

96. Ananth CV, Kioumourtzoglou MA, Huang Y, Ross Z, Friedman AM, Williams MA, et al. Exposures to Air Pollution and Risk of Acute-onset Placental Abruption: A Case-crossover Study. Epidemiology. 2018; 29: 631-638.

97. Saenen ND, Vrijens K, Janssen BG, Roels HA, Neven KY, Vanden Berghe W, et al. Lower Placental Leptin Promoter Methylation in Association with Fine Particulate Matter Air Pollution during Pregnancy and Placental Nitrosative Stress at Birth in the ENVIRONAGE Cohort. Environ Health Perspect. 2017; 125: 262-268.

98. Saenen NDV, Janssen K, Bram G, Narjes M, Martien P, Wilfried G, et al. Placental Nitrosative Stress and Exposure to Ambient Air Pollution During Gestation: A Population Study. Am J Epidemiol. 2016; 184: 442-449.

99. Carre J, Gatimel N, Moreau J, Parinaud J, Leandri R. Does air pollution play a role in infertility?: a systematic review. Environ Health. 2017: 16: 82.

100. Dadvand P, Parker J, Bell ML, Bonzini M, Brauer M, Darrow LA, et al. Maternal exposure to particulate air pollution and term birth weight: a multi-country evaluation of effect and heterogeneity. Environ Health Perspect. 2013; 121: 267-373.

101. Wu H, Kioumourtzoglou MA, Just AC, Kloog I, Sanders A, Svensson K, et al. Association of ambient PM2•5 exposure with maternal bone strength in pregnant women from Mexico City: a longitudinal cohort study. The Lancet Planetary Health. 2020; 4: e530-e537.

102. Gaskins AJ, Minguez-Alarcon L, Fong KC, Abdelmessih S, Coull BA, Chavarro JE, et al. Exposure to Fine Particulate Matter and Ovarian Reserve Among Women from a Fertility Clinic. Epidemiology. 2019; 30: 486-491.

103. Gai H F, An JX, Qian XY, Wei YJ, Williams JP, Gao GL. Ovarian Damages Produced by Aerosolized Fine Particulate Matter (PM2.5) Pollution in Mice: Possible Protective Medications and Mechanisms. Chin Med J. 2017; 130: 1400-1410.

104. Guo Y, Cao Z, Jiao X, Bai D, Zhang Y, Hua J, et al. Pre-pregnancy exposure to fine particulate matter (PM2.5) increases reactive oxygen species production in oocytes and decrease litter size and weight in mice. Environ Pollut. 2021: 268: 115858.

105. Li X, Huang S, Jiao A, Yang X, Yun J, Wang Y, et al. Association between ambient fine particulate matter and preterm birth or term low birth weight: An updated systematic review and meta-analysis. Environ Pollut. 2017; 227: 596-605.

106. Tan Y, Rong Y, Zhao J, Cao Z, Zhang B. The Associations Between Air Pollution and Adverse Pregnancy Outcomes in China. Adv Exp Med Biol. 2017; 1017: 181-214.

107. Li M, Qian Z, Vaughn M, Boutwell B, Ward P, Lu T, et al. Sex-specific difference of the association between ambient air pollution and the prevalence of obesity in Chinese adults from a high pollution range area: 33 Communities Chinese Health Study. Atmospheric Environment. 2015; 117: 227-233.

108. Pennington AF, Strickland MJ, Klein M, Zhai X, Russell AG, Hansen C, et al. Measurement error in mobile source air pollution exposure estimates due to residential mobility during pregnancy. J Expo Sci Environ Epidemiol. 2017; 27: 513-520.

109. Chiu YM, Hsu HL, Wilson A, Coull BA, Pendo MP, Baccarelli A, et al. Prenatal particulate air pollution exposure and body composition in urban preschool children: Examining sensitive windows and sex-specific associations. Environ Res. 2017;158: 798-805.

110. Kim JS, Chen Z, Alderete TL, Toledo-Corral C, Lurmann F, et al. Associations of air pollution, obesity and cardiometabolic health in young adults: The Meta-AIR study. Environ Int 2019; 133: 105180.

111. Lin X, Lim IY, Wu Y, The AL, Chen L, Aris IM, et al. Developmental pathways to adiposity begin before birth and are influenced by genotype, prenatal environment and epigenome. BMC Med. 2017; 15: 50.

112. Ponticiello BG, Capozzella A, Di Giorgio V, Casale T, Giubilati R, Tomei G, et al. Overweight and urban pollution: preliminary results. Sci Total Environ. 2015: 518-519: 61-64.

113. Stieb DM, Chen L, Eshoul M, Judek S. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. Environ Res. 2012; 117: 100-111.

114. Fong KC, Kosheleva A, Kloog I, Koutrakis P, Laden F, Coull BA, et al. Fine Particulate Air Pollution and Birthweight: Differences in Associations Along the Birthweight Distribution. Epidemiology. 2019; 30: 617-623.

115. Guo P, Chen Y, Wu H, Zeng J, Zeng Z, Li W, et al. Ambient air pollution and markers of fetal growth: A retrospective population-based cohort study of 2.57 million term singleton births in China. Environ Int. 2020; 135.

116. Slama R, Morgenstern V, Cyrys J, Zutavern A, Herbarth O, Wichmann HE, et al. Traffic-related atmospheric pollutants levels during pregnancy and offspring's term birth weight: a study relying on a land-use regression exposure model. Environ Health Perspect. 2007; 115: 1283-1292.

117. Janssen BG, Saenen ND, Roels HA, Madhloum N, Gyselaers W, Lefebvre W, et al. Fetal Thyroid Function, Birth Weight, and in Utero Exposure to Fine Particle Air Pollution: A Birth Cohort Study. Environ Health Perspect. 2017; 125: 699-705.

118. Kingsley SL, Eliot MN, Whitsel EA, Huang Y-T, Kelsey KT, Marsit CJ, et al. Maternal residential proximity to major roadways, birth weight, and placental DNA methylation. Environ Int. 2016; 92-93: 43-49.

119. Yang Y, Lin Q, Liang Y, Ruan Z, Qian Z, Syberg KM, et al. The mediation effect of maternal glucose on the association between ambient air pollution and birth weight in Foshan, China. Environ Pollut. 2020; 266: 115128.

120. Choe SA, Jang J, Kim MJ, Jun YB, Kim SY. Association between ambient particulate matter concentration and fetal growth restriction stratified by maternal employment. BMC Pregnancy Childbirth. 2019; 19: 246.

121. Melo JD, Soto SF, Katayama IA, Wenceslau CF, Pires AG, Veras MM, et al. Inhalation of fine particulate matter during pregnancy increased

IL-4 cytokine levels in the fetal portion of the placenta. Toxicol Lett. 2015; 232: 475-480.

122. Soto S, Melo J, Marchesi GD, Lopes KL, Heimann JC. Exposure to fine particulate matter in the air alters placental structure and the renin-angiotensin system. Plos One. 2017; 12: e0183314.

123. Chin MT. Basic mechanisms for adverse cardiovascular events associated with air pollution. Heart. 2015; 101: 253-256.

124. Sun X, Hao H, Han Q, Song X, Liu J, Dong L, et al. Human umbilical cord-derived mesenchymal stem cells ameliorate insulin resistance by suppressing NLRP3 inflammasome-mediated inflammation in type 2 diabetes rats. Stem Cell Res Ther. 2017; 8: 241.

125. Ntarladima AM, Vaartjes I, Grobbee DE, Dijst M, Schmitz O, Uiterwaal C, et al. Relations between air pollution and vascular development in 5-year old children: a cross-sectional study in the Netherlands. Environ Health. 2019; 18: 50.

126. Hwang BF, Lee YL, Jaakkola J. Air Pollution and the Risk of Cardiac Defects: A Population-Based Case-Control Study. Medicine. 2015; 94: e1883.

127. Farhi A, Boyko V, Almagor J, Benenson I, Segre E, Rudich Y, et al. The possible association between exposure to air pollution and the risk for congenital malformations. Environ Res. 2014; 135: 173-180.

128. Jordan M, M.; hia, C.c.; P.; Watkins; S.; M.; Stuart; A. Associations between Exposure to Ambient Benzene and PM2.5 during Pregnancy and the Risk of Selected Birth Defects in Offspring. Environ Res. 2015; 142: 345-353.

129. Schembari A, Nieuwenhuijsen MJ, Salvador J, Nazelle AD, Vrijheid M. Traffic-Related Air Pollution and Congenital Anomalies in Barcelona. Environ Health Perspect. 2013; 122: 317-323.

130. Stingone JA, Luben TJ, Daniels JL, Fuentes M, Richardson DB, Aylsworth A, Set al. Maternal Exposure to Criteria Air Pollutants and Congenital Heart Defects in Offspring: Results from the National Birth Defects Prevention Study. Environ Health Perspect. 2014; 12: 863-872.

131. Ma N, Nicholson CJ, Wong M, Holloway A, Hardy DB. Fetal and neonatal exposure to nicotine leads to augmented hepatic and circulating triglycerides in adult male offspring due to increased expression of fatty acid synthase. Toxicol Appl Pharmacol. 2014; 275: 1-11.

132. Emam B, Shahsavani A, Khodagholi F, Zarandi SM, Hopke PK, Hadei M, et al. Effects of PM2.5 and gases exposure during prenatal and early-life on autism-like phenotypes in male rat offspring. Part Fibre Toxicol. 2020; 17: 8.

133. McGuinn LA, Windham GC, Kalkbrenner AE, Bradley C, Di Q, Croen LA, et al. Early Life Exposure to Air Pollution and Autism Spectrum Disorder: Findings from a Multisite Case-Control Study. Epidemiology. 2020; 31: 103-114.

134. Bose S, Ross KR, Rosa MJ, Chiu YM, Just A, Kloog I, et al. Prenatal particulate air pollution exposure and sleep disruption in preschoolers: Windows of susceptibility. Environ Int. 2019; 124: 329-335.

135. Seeni I, Ha S, Nobles C, Liu D, Sherman S, Mendola P. Air pollution exposure during pregnancy: maternal asthma and neonatal respiratory outcomes. Ann Epidemiol. 2018; 28: 612-618 e614.

136. Zhang L, Liu W, Hou K, Lin J, Song C, Zhou C, et al. Air pollution exposure associates with increased risk of neonatal jaundice. Nat Commun. 2019; 10: 3741.

Cite this article

Liu Z, Ge P, Chen M (2022) Research on the Impact of PM2.5 on Human Reproductive Health in Recent Years: A Review. JSM Environ Sci Ecol 10(1): 1078.