Review Article

Impacts of Climate Changes on Pregnancy and Birth Outcomes: A Review

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Abstract

This study aimed to review the impact of climate change around the world on the incidence of emerging and noncommunicable diseases in sensitive and vulnerable individuals, such as pregnant women and newborns. The combination of keywords such as climate change, ambient temperature, pregnancy outcomes, spontaneous abortion, preterm birth, stillbirth, autism, orofacial cleft, cleft palate, heart disorders, and diabetes was used for comprehensive search on reputable citation databases such as Scopus, PubMed, Web of Science, and Google Scholar, throughout research conducted previously with a focus on the years from 2018 to 2020. The results of the literature cited showed that long-term exposure to high temperatures reduced birth weight. Heat has been reported to have serious adverse effect than cool weather for preterm birth. A significant association has been reported between seasonal changes and diabetes and gestational hypertension. Climate changes, by increasing infant mortality and miscarriage, have made a difference in sex ratios. Further, the development of neonatal abnormalities such as hypospadias, autism, cleft palate, and heart disorders has been significantly associated with climate change. Seasonal changes, rising temperatures, sunlight, increased ultraviolet rays, and ozone concentration have been suggested to involve in the prevalence of cleft palate. Changes in relative humidity, temperature, sunlight, oxygen pressure, and elevated environments have also contributed to the development of heart disorders. This review showed that climate change has played an important role in the incidence and prevalence of emerging diseases. Hence, climate change has adverse effects on pregnant women and neonates. This study confirms critical importance of climate change and its negative effect on susceptible people and next generation.

Keywords: Birth outcome, climate change, perinatal period, pregnancy outcome, review

Introduction

Researchers pay more attention to climate change as a new and effective contributor to disease. Hence, in recent years, with a high variety and different climatic events, different sanitary hazards have effects on the incidence and prevalence of diseases in different geographical areas. Increasing global warming and ecological changes have led to natural events, such as glacial melt, floods, earthquakes, and changes in habits and lifestyles, which play a major role in the prevalence of these diseases. Increasing ambient temperature in a period is named global warming that led to changes in climate patterns such as changes in sea level, precipitation, droughts, and floods, as well as its high impact on disease and vector development.

With the development of technology and industry and the increasing use of various artificial materials, further, natural factors have witnessed climate changes. Fossil fuels are the main source of unnatural factors that release greenhouse gases and chlorofluorocarbons compounds into the atmosphere. Destruction of the ozone layer, land destruction and reduced vegetation are the major impacts.[1] Environmental pollution related to climate change produces an unbalance in some air compound.[2] Some of the pollutant associated with climate change are greenhouse gases,[3] sulfur dioxides, particulate matters (PMs),[2] and ozone.[4] Sulfur dioxide and PMs reflect

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light when released in the atmosphere, which keeps sunlight out and creates a cooling effect. Greenhouse gases increase temperature and they have a deteriorating effect on earth's ozone layer.[2] In addition, high ambient temperatures are strongly associated with ozone exceedance days.[4] Seasonal winds and heavy rains are reported to have had a main role in the South American epidemic. Various factors in the environment such as temperature and humidity affect the physiological characteristics of the human body. There are reports that there is a direct relationship between trends in environmental temperature changes and mortality rates. Mortality directly was impacted by rising or decreasing temperatures including cardiovascular disease, respiratory problems, dysfunction of blood vessels,[1] and even abortion.[5]

Changes in rainfall and temperature patterns have impacts on human health. The impacts are vector and food borne disease, food insecurity, heat waves,[6] poor sanitation, changing disease patterns and morbidity, and lack of safeguards [7]. These cause millions new cases of patient, every year.[6] The forecasted global mean temperature is continuously increasing between 0.15 and 0.3 per decade.[7] Researches demonstrate that climate variability plays a part in the prevalence of diseases, particularly among vulnerable people such as pregnant women, the fetus,[7] people with disabilities, and elderly people.[8] There is evidence suggesting a correlation between exposure with extreme weather events including droughts, heavy downfall, heat waves and cold waves during pregnancy, and adverse birth outcomes.[9] Climate change is especially important in low-income countries because economic development relates to disease and humans health.[8] Adverse effects are more excessive for poor populations and with low access to healthcare systems.[10] Outdoor air pollution, indoor air pollution, and properties of built environmental are the environmental factors that cause fetal growth disturbance.[11] Each small alter in climate leads to a noticeable increase in the frequency of extreme heat waves. Scientists alarmed that by 2050, the number of days hotter than 35°C may be five to six times more than today with the consequential risk increase of congenital malformations.[12] Heat exposure can harm to the placenta, developing cells, and vascular system.[13] Pregnant women exposure to environmental risk factors may reduce uterine blood flow, placental fetal exchange, and eventually slow fetal growth.[14] Recently, several studies have reported associations with climate change and adverse maternal and birth outcomes such as low birth weight (LBW), premature delivery, stillbirth,[13-17] gestational diabetes, and gestational hypertension.[18] Further, there is some evidence for a relationship between hypospadias, sex ratios, autism, orofacial clefts (OFCs), and congenital heart defects (CHDs) and climate change. A research in 2012 evaluated the relationship between extreme summer temperature and the occurrence of birth defects to determine whether pregnant women and their newborns in New York State are potentially susceptible to impacts on climate change. Results showed positive and consistent associations between multiple heat indicators during pregnancy and congenital defects.[19] Some evidence shows that individual and community factors such as maternal age, maternal race, education level, and socioeconomic status have an impact on the heat-related adverse birth outcomes.[17] According to the effect of temperature and climate change on different diseases, this study aimed to review the effects of temperature and climate change on maternal and birth outcomes.

Methods

This review was carried out based on the evaluation of several studies between 1998 and 2020 and concentrating on studies on the impact of climate changes on obstetrical outcomes from 2017 to 2020. All scientific data related to the issue were collected from scientific databases of Google Scholar, Scopus, PubMed, and Web of Science. We used any combination of the following keywords: climate change, ambient temperature, pregnancy outcome, preterm birth, spontaneous abortion, low birth weight, diabetes, preeclampsia, hypospadias, autism, cleft palate, orofacial clefts, heart defects, etc.

Results

Impact of climate change on birth weight

Birth weight is a proxy for fetal growth and forecast baby mortality and morbidity and is related to future health problems.[11] LBW is due to immature birth or intrauterine embryo development.[9] More than 40.3% of deaths in children under 5 years of age happen in newborns.[6] Premature delivery or preterm birth (PTB) means a baby born before 37 weeks of gestation that correlates with detrimental health outcomes including morbidity, mortality, and permanent impact on cognitive functioning and behavior.[17] Exposure with temperature excess during pregnancy may induce LBW by rising oxidative stress and systemic inflammation in response to temperature alterations.[11,14] LBW is defined as weight <2500 g for an infant who delivered between 37 and 44 pregnancy weeks. Neonates with small size are vulnerable to adverse health outcomes in the adulthood such as diabetes, hypertension, coronary heart disease, and abnormal amounts of blood lipids.[20] Literature showed a relationship between LBW and coronary heart disease and stroke.[21] LBW is a pricey for individuals, families, and societies. The last research showed evidence for the effect of LBW on educational attainment and future income.[9] LBW was more common in female infants than male infants. Low educated mothers and mothers younger 25 years and older than 30 years delivered infants with lower weight.[17] Many particular risk factors remain unexplored for LBW, although air pollution exposure, smoking, alcohol and drug use during pregnancy, maternal body mass index, and weight gain during pregnancy, hypertension, and other chronic health conditions have been reported.[13] A study reported that temperature can affect fetus health by five pathways: (a) diseases that are related to changes in the temperature levels by itself (i.e., respiratory diseases); (b) exposure to extreme temperature, (c) maternal infection, (d) maternal psychological disease, and (e) food insecurity. Rising temperature variability can lead to reductions in healthcare and an increase in food insecurity during pregnancy, and probably, these factors lead to born neonates with LBW.[8] Previous studies suggested that heat exposure during pregnancy damages the placenta, developing cells, and vascular system.[13] In addition, scientists suggested that fetal health is impaired by longer exposure to high temperature levels during pregnancy. Molina *et al*. investigated the effects of temperature variability on birth outcomes in Bolivia, Colombia, and Peru. They found that one standard deviation increase in the long-term local temperature means during the first trimester of pregnancy reclined birth weight by 20 g and increased the likelihood of a child born with LBW by 10%. In addition, they reported that a 1.5 standard deviation above the historical local temperature means during 6–8 months' gestation reduced birth weight by 42.5 g.[8]

Basu *et al*. surveyed the effect of both long- and short-term temperature exposure on LBW in California from 1999 to 2013. This study evaluated LBW among 43,629 full-term LBW infants and 2,032,601 normal-weight infants. They found a significantly negative link between alter temperature during the first trimester and LBW, while the risk slightly increased in the second trimester, last month, and last 2 weeks of pregnancy. There was the highest risk for mothers who were black, older, delivered male neonate, and gave birth in hot seasons.[13] According to study of MacVicar et al., there was an association between rainfall patterns during the third trimester and birth weight, so that, reducing precipitation caused LBW. Despite other previous studies, they found with an increase in average daily temperature during the third trimester, birth weight increase. An increase of 41.8 g weight per additional Celsius degree was observed. Because of this study based on hospital birth in a rural population in Southwestern Uganda and approximately <50% of birth occurred in the hospital in this region, this result cannot be appropriately extrapolated to the general population.[10] Deschenes *et al*. studied climate change impacts on fetuses' health among 37.1 million births. They observed that exposure to extremely hot temperatures during pregnancy leads to LBW. Besides, they estimated that mean birth weights will reduce on an average by 0.22% (7.5 g) among Whites and by 0.36% (11.5 g) for Blacks by the end of the century.[22] A systematic review in 2014 probed the relationships between season and birth weight and revealed that birth weights are lower for babies who were born in winter and summer months.[23] Finally, Anderko *et al*. reported an association between climate change and low birth weight.[24] According to short- and long-term complications of fetal growth and climate change, it is important to update our data about the impact of climate change on fetal growth.

Impact of climate change on preterm birth

The birth of a baby earlier than 37 weeks of pregnancy is called PTB. Preterm delivery is reported in the United States, Australia, and the United Kingdom at 8%–13%. Its prevalence has increased in recent decades due to the increasing age of mothers and the increasing number of deliveries. Pregnancy <37 weeks is associated with a decline in baby health. For example, it is associated with behavioral, developmental, learning, and neurodevelopmental disorders, communication, and social interactions.[25] Several factors correlate with PTB including genetic, sociodemographic, behavioral, and environmental factors,[26] such as contaminant exposures and climate disturbances.[27] Ambient temperature was recognized as a risk factor for preterm delivery[16] and was significantly associated with PTB for all mothers, regardless of maternal racial/ethnic group, maternal age, maternal education, or sex of the baby.[28] Evidence of seasonal variation has been shown to affect PTB rates. Several studies on preterm delivery make pregnancy more likely in winter and spring, and other studies have reported maximal preterm delivery during summer or winter. Perhaps, the difference between studies about seasonal pattern refers to geographical and socioeconomic differences.[29] Ambient temperatures, whether too cold or hot, affect the rate of PTB.[25,29,30]

The short-term effects of maternal exposure to heat wave were evaluated in Australia. In this study socio-economic, demographic, and meteorological factors and also ambient air pollutants were evaluated. Environmental data including daily maximum temperature, relative humidity, and ambient barometric pressure were studied. The adjusted hazard ratios (HRs) were reported from 1.13 (95% confidence interval [CI] 1.03–1.24) to 2.00 (95% CI 1.37–2.91). The results showed that heat wave was considerably linked with PTB. This paper revealed that the threshold temperatures, rather than the duration, could be more likely to impact the evaluation of birth-related heat waves.[26]

Vicedo-Cabrera *et al*. also examined the short-term effects of elevated temperatures on the risk of prematurity in Valencia (a coastal city with a Mediterranean climate). Results revealed that exposure to elevated temperatures was associated with an increased risk of PTB.[31] Next, a study in Belgium, in temperate climates, analyzed the association between temperature and the risk of PTB among 807,835 singleton deliveries. The scientists examined moderate and extreme heat and cold. Hence, this paper suggested that ambient temperature was associated with preterm delivery and proposed pregnant women should avoid temperature extremes.[32]

Son *et al*. found that heat exposure during pregnancy especially 4 weeks and 1 week before delivery causes PTB. Age and education level of mothers and community level were risk factors for them. They found that most impacts were on neonates with low educated mothers and low socioeconomic status. In addition, the risk of premature delivery was higher in male newborns.[17]

The effect of ambient temperature on PTB was evaluated in the United States in 2019. A strong study was conducted related to heat weather and PTB in areas with cold and dry climates. Results have shown that days of extremely cold temperatures were associated with lower rather than the higher risk of PTB.[33] In another study in 2019, Mohammadi *et al*. measured the minimum and maximum daily temperatures of −11.2°C and 45.4°C, respectively. The highest risk temperature in extreme cold was estimated for the apparent temperature. The inhabitants of arid regions are not adapted to the cold temperature and are therefore more sensitive to the effect of the low temperature than high temperatures.[34]

Besides, Yu *et al*. explored that high precipitation (both intensity and frequency) and high frequency of storm and flood events can increase the risk of PTB rates. While they did not find a direct association of the lagged effect of temperature on birth outcome, they confirmed the negative effects on PTB from weather extremes.[27] For the first time, Ha *et al*. discovered that preterm premature rupture of membranes as a common precursor to preterm delivery was correlated with temperature changes. They found that a 1°C increase during warm seasons was correlated with 5% (95% CI: 3%–6%) increased, and during cold seasons, a 2% decreased preterm premature rupture of membranes risk, respectively. They reported adverse effects of both high and low ambient temperatures on the risk of premature rupture of membranes.[35] In addition, Schifano *et al*. concluded a unit increase in maximum apparent temperature, PM_{10}, NO_2, and O_3, especially in the second half of the second trimester, effectively increasing the risk of preterm and particularly early PTB.[36] The study of Ilango *et al*. revealed that acute exposure to extreme heat during the last week of gestation may trigger an earlier delivery.[37]

According to above studies, maybe is concluded that climate change has an adverse influence on PTB, but more researches are needed.

Impact of climate change on gestational diabetes

Carbohydrate intolerance at the first diagnosis during pregnancy is called gestational diabetes. In recent years, it has followed a growing trend of 1.9%–4.2%. Today, its variations range from 1% to 10%. According to an assessment in 2007 in the United States, its costs to the community are estimated at 636 million USD. Gestational diabetes is one of the important causes of diseases in pregnancy that increases the risk of hypertension disorders. Gestational diabetes also affects the health of infants, increasing its mortality and morbidity rates, because of the free transfer of glucose through the placenta and the amount of blood sugar for both the mother and the fetus increased. As a result, it will cause excessive insulin production in the fetus. Increased maternal glucose levels in pregnancy are directly related to increased PTB, birth injury, a 2.2-fold increase in neonatal hypoglycemia, and the need for neonatal intensive care. This type of diabetes is also associated with birth defects. Various risk factors are involved in the development of gestational diabetes, such as maternal overweight and obesity, race, maternal age, and family history. Nutritional and lifestyle habits, such as the use of saturated fat, Vitamin D deficiency during pregnancy, and physical activity also play an important role in the development of gestational diabetes. Besides these, recent studies have considered the effects of ambient temperature and seasonal and climate change as a risk factor for gestational diabetes.[38]

Two years ago, many studies have focused on the prevalence of diabetes during pregnancy that they had a high prevalence in summer as compared to winter, especially in the geographical areas of Australia, Canada, Sweden, Italy, and Greece. Researchers believed that these seasonal changes in glucose may be due to ambient air temperature. However, the mechanism of the effect of temperature and glucose metabolism in pregnant women is unclear. In 2018, in Canada, in the 29 weeks of pregnancy among 1464 pregnant women, the relationship between blood glucose and pancreatic beta cell function and insulin sensitivity at 18 different temperatures was studied. The results showed that changes in blood glucose levels were more noticeable in the months of the year that the average daily temperature increased. Hence, the rising environmental temperature during gestation may be related to beta cell dysfunction and increased risk of gestational diabetes mellitus (GDM).[39]

In Australia, according to a study in 2016, gestational diabetes between 2007 and 2011 was surveyed among 3632 women. Its values increased from 4.9% to 7.2%, respectively. Using the seasonal modeling method, a significant relationship ($P < 0.001$) was found between gestational diabetes and seasonal and temperature changes so that maximum values of glucose were reported in winter and minimum in summer.[38]

In another study in 2016, pregnancy glucose test data were collected from 7369 women over 3 years at different seasons. Their 1-h diagnostic level of blood glucose was 29% higher in summer and 27% lower in winter than in the overall state. Moreover, the 2-h diagnostic level of glucose was 28% higher in summer and 31% lower in winter than in the overall. As a result, the prevalence of gestational diabetes varies according to the seasons, with higher detection rates in summer and lower in winter.[40] In 2018, the effects of different temperatures on the activity of pancreatic and insulin-producing cells were examined by modeling. The results have shown that different temperatures with different degrees can change the dynamic state of the pancreatic cell system.[41] Some researchers expressed that most likely due to redistribution of blood between the arterial and venous systems with changes in core temperature, the ambient temperature can affect glucose tolerance.[40] The interpretation of the studies is complicated, but the evidence suggests causality of the effect of climate change on gestational diabetes. A study in Sweden examined seasonal patterns in glucose tolerance and the diagnosis of GDM. Results showed that the seasonal frequency of GDM ranged from 3.3% in spring to 5.5% in summer. Further, mean 2-h glucose concentrations followed the seasonal trend and this value increased by 0.009 mmol/L for every degree increase in the temperature. On the other hand, gestational diabetes increased with temperature increasing.[42] Booth *et al*. investigated the relationship between outdoor air temperature and the risk of GDM. Among 396,828 women from 2002 to 2014 who have taken place in the study, the prevalence of

GDM was 4.6% among women exposed to extremely cold mean ambient temperature (≤–10°C) in the 30 days before the screening and increased to 7.7% among those exposed to hot mean 30-day temperature (≥24°C). Results revealed a direct relation between ambient temperature and the risk of GDM.[43] Finally, we inferred evidence for causality are sufficient. Table 1 shows some studies that investigated climate change and gestational diabetes relationship.

Impact of climate change on the hypertensive disorders of pregnancy

It is important to know the factors that regulate blood pressure in the body. One of these factors is the temperature. Many studies have paid to the relationship between blood pressure and seasonal and ambient temperatures.[44] Hypertension is a common disorder among pregnant women. According to research in the USA, 18.2% of a major contributor to fetal mortality is related to hypertension. Hypertension, preeclampsia, and eclampsia are common types of pressure disorders. Blood pressure of 140/90 mmHg or more is called pregnancy blood pressure. If there is a protein in the urine of a pregnant woman and her hypertension is or not associated with edema, this condition is called preeclampsia and if it is accompanied by seizures and coma is eclampsia. It can lead to placental abruption, organ failure, high liver enzymes, and hemolysis, which can lead to maternal and fetal death if untreated. Many risk factors, such as environmental factors, cardiovascular disease, early or late pregnancy, temperature, humidity, and seasonal variations have a major impact on the prevalence of hypertension during pregnancy.[45]

Preeclampsia is assessed when the pregnancy is during the warm months of the year and delivery occurs during the cold months. According to studies, there is a strong relationship between preeclampsia and pregnancy hypertension. High temperature can affect pregnancy blood pressure by affecting the vessels in the placenta after conception or by increasing stress at the end of pregnancy. One study has shown that since the body temperature changes during pregnancy and the temperature at the beginning of pregnancy differ with the temperature at the delivery, as a result in this study after adjusted the baseline maternal condition, the risk of preeclampsia during the beginning of gestation in higher temperatures and at the end of pregnancy in lower and colder temperature has happened.[46]

A cross-sectional study in 2017 in Iran between 2011 and 2013 collected data from 8000 pregnant women by using a questionnaire to assess the relationship between blood pressure and months of the year. The results showed that the prevalence rates of gestational hypertension in summer and winter were highest and lowest, respectively.

Table 1: Summary of some studies on climate change and gestational diabetes relationship

Author, year	Title	Finding	Reference
Booth *et al*., 2017	Influence of environmental temperature on the risk of gestational diabetes	Prevalence of GDM was 4.6% among women exposed to extremely cold mean ambient temperatures (≤–10°C) and increased to 7.7% among those exposed to hot mean 30-day temperatures (≥24°C). There was a direct relation between ambient temperature and the risk of GDM	[43]
Retnakaran *et al*., 2018	Impact of daily incremental change in environmental temperature on beta-cell function and the risk of gestational diabetes in pregnant women	In the 29 weeks of pregnancy among 1464 pregnant women in Canada, the relation between blood glucose and pancreatic beta cell function and insulin sensitivity at 18 different temperatures was studied. The results showed that changes in blood glucose levels were more noticeable in the months of the year that the average daily temperature increased. Moreover, rising environmental temperature during pregnancy may be related to beta-cell dysfunction and an increased risk of GDM	[39]
Verburg *et al*., 2016	Seasonality of GDM: A South Australian population study	Gestational diabetes between 2007 and 2011 surveyed and diagnosis among 3632 women was studied. Its values increased from 4.9% to 7.2%, respectively. A significant relationship ($P < 0.001$) was found between gestational diabetes and seasonal and temperature changes. The maximum values of glucose were reported in winter and minimum in summer	[38]
Moses *et al*., 2016	Seasonal changes in the prevalence of GDM	The pregnancy glucose test data were collected from 7369 women over 3 years at different seasons. Their 1-h diagnostic level of blood glucose was 29% higher in summer and 27% lower in winter than in the overall state. Moreover, the 2-h diagnostic level of glucose was 28% higher in summer and 31% lower in winter than in the overall. The prevalence of gestational diabetes varies according to the seasons, with higher detection rates in summer and lower detection in winter	[40]
Farashi *et al*., 2018	Computational modeling of the effect of temperature variations on the human pancreatic β-cell activity	The effects of different temperatures on the activity of pancreatic and insulin-producing cells were examined by modeling. Different temperatures with different degrees can change the dynamic state of the pancreatic cell system	[41]

GDM: Gestational diabetes mellitus

Moreover, it seems that changes in humidity and temperature (increasing temperature and decreasing humidity) are affecting preeclampsia.[45] Therefore, climate change affects on eclampsia and preeclampsia.[18] Summary of some studies on climate change and the hypertensive disorders of pregnancy is illustrated in Table 2.

Impact of climate change on spontaneous abortion

Past studies have shown that one of the harmful effects of climate change and environmental heat is the detrimental effects on human health. Although maternal exposure to environmental factors does not directly cause adverse effects, it is influenced by genetics, epigenetics, and social and demographic information.

The largest source of heat generation in the human body is through metabolism. Furthermore, heat can be gained from the environment. The effects of heat on pregnant women are unclear, but with increase in temperature the hormone levels will change. Then, the amounts of blood circulate needed for the fetus from the mother increases. It leads to heat disorders in the fetus. Moreover, even excessive maternal heat due to a particular illness can lead to fetal malformations. Environmental factors can create defects in structure, function, growth restriction, and death in the fetus and eventually to abortion that leads to delivery.[5] Furthermore, environmental shocks may increase maternal stress levels during conception that is correlated with higher rates of stillbirth and miscarriage. When climate change leads to scarcity of crops and food, intrahousehold food consumption patterns may be altered. Parents reduce food intake of themselves to save it for their children and effects that may have had ramifications on future pregnancy outcomes. Hence, parents who experience nutritional shortage, resulting from climate-related crop losses and who experience stress as a repercussion of the economic and social consequences of climate shocks, may be more likely to lose their fetus *in utero*.[51] On the other hand, maternal infectious diseases in the 7th to 16th week of pregnancy that cause fever can lead to severe fetal malformations due to maternal hyperthermia. Many studies have shown that these disorders generally occur in the first trimester of pregnancy.[5] In addition, increasing environmental heat can cause congenital defects such as miscarriage among mammals. There is no widespread research to prove this in humans. In 2017, a study examined heat exposure during pregnancy in hot areas and increased the probability of spontaneous abortion. In this study, data of 1136 pregnant women was used between 2004 and 2007. Among them, 141 women had aborted pregnancies. Some parameters such as air temperature, humidity, thermal radiation, and air movement through wind were studied. Mean annual exposure and mean monthly exposure were evaluated. The results showed that an increase in temperature at any degree was associated with an increase in abortion.[5] In a study by Dadvand *et al*., a significant relationship was found between exposure to stress and heat with decreasing pregnancy duration[52] that is very important on abortion. It has also been reported in more

Table 2: Summary of recent studies on climate change and the hypertensive disorders of pregnancy

Author, year	Title	Finding	Reference
Beltran *et al*., 2014	Associations of meteorology with adverse pregnancy outcomes: a systematic review of preeclampsia, PTB, and birth weight	Pregnant women during the warmest months have a higher risk of preeclampsia. Delivery in the coldest months is correlated with a higher eclampsia risk	[23]
Poursafa *et al*., 2015	A systematic review of adverse birth outcomes of climate change	Prevalence of eclampsia and preeclampsia were more in cold and humid seasons. Exposure to heat extent, different seasons of the year, sunlight intensity, and season of fertilization were associated with higher rates of PTB, hypertension, eclampsia, preeclampsia	[18]
Janani and Changaee, 2017	Seasonal variation in the prevalence of preeclampsia	Changes in temperature and humidity in different seasons can affect preeclampsia, and preeclampsia increases with increasing frequency temperature	[47]
Subramaniam, 2007	Seasonal variation in the incidence of preeclampsia and eclampsia in tropical climatic conditions	In the tropical climate of Mumbai, the incidence of eclampsia is significantly higher in monsoon, when the weather is cooler and humid with a lower barometric pressure than the rest of the year. This strengthens the association of low temperature and high humidity with triggering of eclampsia	[48]
Mandakh *et al*., 2020	Maternal exposure to ambient air pollution and risk of preeclampsia: A population-based cohort study in Scania, Sweden	Maternal exposure to ambient air pollutants during gestation is an important factor that may contribute to the development of preeclampsia	[49]
Wang *et al*., 2018	Effects of prenatal exposure to air pollution on preeclampsia in Shenzhen, China	There is a positive gradient in associations between PM10, SO_2 exposures, and preeclampsia, in the first trimester, second trimester, and entire pregnancy. The effects of PM10 and SO_2 exposures increased markedly under relatively humid (>95th percentile of dew point temperature) conditions	[50]

PTB: Preterm birth

studies that there is a relationship between air temperature and central nervous system sensitivity and defects.[53-56]

Impact of climate change on sex ratios

The male: female birth ratios have been steadily reported in the world, although it is slightly higher in boys than in girls. This ratio has been evaluated in several countries, such as the USA, Japan, Germany, Denmark, Canada, the UK, and the Netherlands. The mechanisms of the birth rate of males compared to females due to different environmental conditions are not well understood. However, nowadays, researchers attribute this ratio to some conditions, tobacco smoke toxicities, natural disasters such as earthquakes,[57] wars, and economic crises.[58] Experts believe that in Europe and Asia, by increasing geographical latitude, the number of births of boys decreases compared to female births. Recent studies have found a significant relationship between sex ratio and mean temperature, seasons, and climate change because, in recent years, more changes have occurred in temperature.[57]

A study in Japan in 2014 found a positive and statistically significant relationship between the annual temperature difference and the sex ratio caused by fatal death. There was also a negative relationship between temperature difference and sex ratios in newborns. According to the study, the sex ratio due to fatal death increased with temperature differences, while the sex ratio of newborn infants decreased. The results of two different climates of very hot summers and very cold winters in 2010 and 2011, respectively, showed that there was a significant decrease in the sex ratios of newborns and a great increase in sex ratios due to fetal death.[57]

According to another study in Finland in 2009, the effect of various parameters such as climate change, war, economic situation, and famine on sex ratio was measured. The findings showed that births of male infants increased in warm climates and the World War II, while economic development, famine, civil wars, and death were not determinants of birth rate.[58] Catalano *et al*. investigated the association between ambient temperature and sex ratio in a cohort population which started between 1878 and 1914. The theory that women exposed to environmental stressors abort frail male embryos thus implied that climate change may affect sex ratio at birth and male longevity. Results revealed that cold ambient temperatures during gestation were associated with an increase in the sex ratio and life duration of male sex in the 1st year. Cold weather might produce these effects through different mechanisms, such as direct thermal effects, nutritional shortage, and higher exposure to internal contaminants.[59] However, studies about the relationship between climate change and sex ratio are limited and further investigations are justified.

Impact of climate change on hypospadias

Hypospadias is a congenital malformation that the urethral opening is not correctly located at the tip of the penis. It is one of the most common congenital disorders in newborn males and affects one in 200–300 boys. This disease is an important health issue because of frequency and on-going concepts.[60] Furthermore, hypospadias has been increasing over the past decades.[61] Many patients suffer from cosmetic or functional problems that can impact on urinary and sexual function. Researchers believe that compounds of environmental influences and genetic susceptibility cause this anomaly. Yu *et al*. investigated prevalence trends of hypospadias in 27 birth defect surveillance programs (27 countries including the USA, Australia, Argentina, Germany, and Iran) during 1980–2010. The international total prevalence of hypospadias for all years was reported by 20.9/10 000 births, and this increased 1.6 times during the study period, by 0.25 cases per 10 000 births/year. They found that the prevalence and trends of hypospadias among 27 birth defect surveillance system continue to increase internationally.[62] It seems that worldwide increasing of this malformation during the last decades to be related to climate change.[61] A study in Turkey explored the association between ambient temperature that a mother is exposed during pregnancy and hypospadias between January 2000 and November 2015. The results revealed that high ambient temperatures that mother and fetus are exposed at 8–14 weeks of gestation (this period was risky for the development of hypospadias) increased the risk of hypospadias in infants. In this research, the most number of patients was observed in summer ($P = 0.01$).[63] In addition, the incidence of hypospadias in countries with hot summers such as Spain, Italy, Australia, Puerto Rico, and some African countries was high; however, this value is pretty low in countries with less hot summer seasons such as Norway and Japan.[63] Nevertheless, Mamoulakis *et al*. surveyed the seasonality of hypospadias in Greece between 1991 and 1998. Their results showed that the coincidence of pregnancy with winter may result in the phenotypic expression of hypospadias.[64] At present, the evidence is inadequate to infer causality and needs further studies.

Impact of climate change on autism

Autism is a multifactorial neurodevelopmental disorder and belongs to autism spectrum disorders (ASDs), consisting of autism, Asperger syndrome, Rett syndrome, unidentified pervasive developmental disorders, and childhood disintegrative disorder. The prevalence of autism had increased from 4–5 cases per 10,000 children in the 1980s to 1 in 88 children in 2012,[65] and the prevalence of it has increased worldwide in recent decades. This disorder is 4–5 times more common among boys than girls. Autism is caused by genetic and environmental factors.[66,67] The interactions between vulnerable genes and environmental factors have been suggested as the major mechanism of autism etiology. Environmental factors can influence the quality and quantity of gene expression without altering DNA sequences through epigenetic mechanisms.[65] None of the environmental factors is sufficient to yield autism, but a set of them can be contributed to the incidence of autism.[2] Exposure to air pollutants,[68] pesticides, heavy metals, living in crowded and polluted cities,[66] and seasonal variations are some of the environmental risk factors for Autism.[65,69] Prera *et al*. in their cohort studies in New York City and Krakow, Poland, reported that prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) was correlated with developmental delay, reduced IQ, symptoms of anxiety, and depression in children. Further, they found that there is some emerging evidence that prenatal exposure to traffic-related air pollutants and $PM_{2.5}$ (as clime change agents) may be a risk factor for ASDs.[70]

There is the strongest evidence for an association with autism risk with summer birth (relative risk [RR]: 1.14, *P* = 0.02).[69] Maybe, it can be said that heat exposure which caused by climate change leads to autism. However, Maimburg *et al*. showed that winter birth increases the risk of autism (HR: 2.21 [95% CI: 1.24–3.94]).[71] Anyway, due to the increasing prevalence of autism in the last decades, and enhancing the trend of climate change in recent years, perhaps, climate change can affect on more incidence and prevalence of autism all over the world. Furthermore, scientists reported strongly correlation between autism and LBW (<2500 g; RR: 1.63, *P* = 0.002), very LBW (<1500 g; RR: 3.00, *P* < 0.001), and small for gestational age (RR: 1.35, *P* =0.001).[69] This result was confirmed by Larsson *et al*.'s study for gestational age at birth <35 weeks (RR = 2.45, 95% CI: 1.55, 3.86).[72] As mentioned above, these factors (LBW and small gestational age) are affected by climate change, so climate change may influence ASDs both directly and indirectly. Nevertheless, there is insufficient evidence to improve the influence of climate change on ASDs.

Impact of climate change on orofacial clefts

OFCs can occur on the lip only (CL), on the alveolar (CA), involve both lip and alveolar (CLA), affect only the palate (CP), or involve both lip and palate (CLP).[73] Cleft lip and/or palate (CL/P) are one among the most common birth defects, with a global prevalence of 1 in 700 births.[74] The defects in the primary fusion of the craniofacial processes that form the primary and secondary palate between the 5th and 12th weeks of pregnancy cause CLP.[75] The main complications of CLP are feeding difficulties, hearing loss, speech and language problems, dental irregularities, and psychosocial issues.[76,77] Etiology and pathogenesis of this anomaly are poorly understood and involve both genetic and environmental factors. Geographical location, racial, sex, ethnic group,[75] alcohol,[78] family history, tobacco, poor nutrition, maternal age,[79] viral infections, and drugs have been identified as possible risk factors for CLP.[80] Bekele *et al*. studied the prevalence of CLP in Ethiopia. The prevalence of cleft deformities was reported 3.11 per 1000 live births, and they showed that the prevalence of CLP was higher than that reported in Addis Ababa and some other African countries. This high prevalence of CLP may reflect an environmental impact.[75]

Seasonal variation is an environmental risk factor for CLP that has attracted the attention of scientists. Seasonal variation in the incidence of OFCs has been related to temperature changes, according to climatic regions. Birth seasonality is a complex phenomenon that is affected by rhythmical environmental factors such as photoperiods,[81] the intensity of ultraviolet (UV) light exposure,[82] and seasonally high temperatures, which decrease spermatogenesis, ovulation, and early fetus survival and/or the availability of nutrition.[81] There are some studies that investigated the influence of seasonality on the etiology of clefts.[82-87] According to a systematic review which investigated the prevalence and risk factors of OFCs from 2000 to 2016 in Iran, seasonal factors (*P* = 0.03) contributed to the development of this disorder.[77] Vega *et al*. reported the lowest incidence of CL/P in fall and winter and the highest during spring and summer (*P* = 00.2). The seasons with more incidence correspond to the time when the least numbers of conceptions are occurring. These findings reflected seasonal dietary and malnutrition of mothers.[88] Moreover, a study in Zambia showed seasonal variations in the month of birth of clefts patients, with a peak in the April–May period, and more cleft births in March through August (57.2%) than in September through February (42.8%). The highest incidence of CLP was explained by maternal malnutrition due to weather fluctuations and seasonality variation, such as seasonal waterborne and vector-spread diseases (malaria), especially during years with heavy flooding.[83] Significant seasonal variation was observed in babies born in winter versus summer, with more children born with a CL/P in winter months in South Africa. Sunlight exposure and Vitamin D levels were mentioned as a reason for this finding.[89] Recently, the association between weather□related extreme heat events (EHEs) and OFCs was explored by Soim *et al*. It was inferred from the results that extended time of EHEs may increase the risk of OFCs in some study sites located in the Southeast climate region.[90] Furthermore, Peterka *et al*. found significant differences from controls in the frequency of neonate girls with CL and boys with CP whose dates of birth correspond to conception from April to August. Further, the results demonstrated that pregnancy in warm season (from May to October) that is mainly characterized by high temperatures, sunshine and increased levels of UV radiation, and ozone concentrations, increase risk of clefts. Hence, seasonal variation in the number of clefts babies may be reflected to maternal exposure to climate change.[81] Nevertheless, future studies are necessary to investigate the impact of climate change on clefts.

Impact of climate change on congenital heart defects

CHD is a general term for a structural or functional defect of the heart that occurs at birth.[91] CHDs are the most common type of all congenital anomalies, with an estimated average birth prevalence of 9/1000 births.[92] The prevalence of congenital heart diseases has increased by 18.7% from 1990 to 2017. Moreover, congenital heart malformations are the main cause of infant mortality.[93] The etiology of most CHDs is unknown.[94] Only one-third of CHD cases have been shown to have a simple genetic cause so far because CHD can also be caused by oligogenic factors, environmental factors, and/or gene–environment interaction.[91] Malnutrition of mother and fetal,[95] maternal alcohol consumption, some therapeutic drugs,[91] radiation exposure,[96] cigarette consumption, and air pollution[97] are some of the external and environmental factors that influence CHDs. Furthermore, Mulder reported that climatological factors can play a role in CHDs incidence and mortality.[98] However, how climate affects CHDs is still unclear.[96] Recently, researchers have observed communication between CHDs and exposure to ambient air pollution and high temperature. Several studies surveyed the association between fine PM2.5 and specific types of CHDs.[99-101] Furthermore, associations with exposure to carbon monoxide, nitrogen dioxide, and sulfur dioxide have been suggested for selected CHD.[101] Ambient temperature is an exposure factor for CHDs during pregnancy. A significant relationship has been found between the maternal exposure to higher ambient temperature during pregnancy and the prevalence of CHDs.[96,102] Besides, a systematic review and meta-analysis showed that an increase in temperature of the mother's body (maternal fever) in the first trimester is a risk factor of congenital heart diseases in babies.[103]

Ma *et al*. evaluated the prevalence of congenital heart diseases in children aged 4–18 years in a city with the high-altitude environment, lower inspiratory oxygen pressure, relative humidity, and temperature, and higher solar radiation. They found that land surface temperature was negatively correlated with the prevalence of total CHDs and a subtype of CHD.[96] Lin *et al*. studied the effect of extreme heat during the fetal development period on CHDs in the US. Results showed that EHEs, the 95th percentile of daily maximum temperature (EHE95) in spring, was significantly associated with conotruncal defects (CTDs) and ventricular septal defects (VSDs) in the South of US (odds ratios: 1.23–1.78) and 3–11 days of EHE90 during summer and spring was significantly related with VSDs. Generally, they found that long-term unseasonable heat was associated with the increased risks for VSDs and atrial septal defects (ASDs), mainly in the South and Northeast of the US.[104]

Moreover, another study in the United States showed relationships between PM2.5, EHEs, and CHDs, particularly among women whose early pregnancy occurs in the spring and summer months and the South and Southeast climate regions of the US.[92] Finally, Zhang *et al*. evaluated the association between CHDs and maternal heat exposure during early pregnancy in summer and spring throughout the United States. Authors forecasted nationwide increases in maternal heat exposure during early pregnancy across the United States by 2030 and the burden of CHDs across the US may increase due to climate change.[105] Nonetheless, future studies are needed to confirm the content, and we are just at the start of trying to understand the effects of climate-related environmental exposures on pregnancy.

Conclusion

The studies included in this review indicated climate change may effect on birth weight, PTB, gestational diabetes, eclampsia and preeclampsia, and abortion.

Because climate change results from human actions by fossil fuel combustion, industrial processes, and anthropogenic greenhouse gas emissions, necessary actions should be taken to reduce the emissions. On the other hand, women's health clinicians and pregnant women should be educated about health threats of climate change, and education is also needed within public health, policy, medicine, and general education. Furthermore, the adverse impacts of climate change on pregnancy should be considered in policies related to health.

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Conflicts of interest

There are no conflicts of interest.

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