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REPRODUCTIVE HEALTH UNDER GLOBAL WARMING

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Цитування: Медичні перспективи. 2022. Т. 27, № 4. С. 4-12

Cited: Medicni perspektivi. 2022;27(4):4-12

Key words: global warming, premature birth, reproductive health, adverse effects of pregnancy

Ключові слова: глобальне потепління, передчасні пологи, репродуктивне здоров'я, несприятливі наслідки вагітності

Abstract. Reproductive health under global warming. Tsymbalyuk V.I., Vadzyuk S.N., Tolokova T.I., Pankiv I.B. Reproductive health problems are attracting the attention of biomedical scientists in connection with changes in the environment. Climate change in the direction of rising temperatures is an urgent threat to human health with negative long-term effects. Under conditions of global warming, the number of negative consequences of pregnancy is increasing, namely idiopathic premature termination of pregnancy with the birth of premature newborns. The priority to reduce the negative health effects of climate change is to identify most sensitive risk groups to the negative impacts of climate change on health, which include pregnant women and newborns. The strategy to prevent and reduce changes in reproductive health is based on the recognition of global warming as a risk factor that contributes to the growth of premature birth and the associated adverse effects of pregnancy.

Реферат. Репродуктивне здоров'я в умовах глобального потепління. Цимбалюк В.І., Вадзюк С.Н., Толокова Т.І., Паньків І.Б. Порушення репродуктивного здоров'я населення привертає увагу науковців медико-біологічної галузі у зв'язку зі змінами навколишнього середовища. Зміна клімату в бік підвищення температури є актуальною загрозою здоров'ю людства з негативним довготривалим впливом. В умовах глобального потепління зростає кількість негативних наслідків вагітності, а саме ідіопатичного передчасного завершення вагітності з народженням недоношених новонароджених. Пріоритетним напрямком зменшення викликаних зміною клімату негативних наслідків для здоров'я населення є визначення груп ризику, найбільш вразливих до негативних наслідків зміни клімату для здоров'я, до яких належать вагітні жінки та новонароджені діти. Стратегія попередження та зменшення змін репродуктивного здоров'я ґрунтується на визнанні глобального потепління як фактора ризику, що сприяє зростанню передчасних пологів та пов'язаних з цим несприятливих наслідків вагітності.

Reproductive health of citizens is one of the most important indicators of the effectiveness of social and economic policy, a factor of national security. The decrease in indicators of the quality of somatic health and the growth of pathologies of the reproductive system on the basis of a complex demographic situation attract the special attention of state policy both at the global level and in Ukraine, which motivates the conduct of research and the formation of a strategy aimed at improving reproductive health [1].

Special attention to the importance of preserving the reproductive health of Ukrainians becomes especially important in the context of the modern tragedy

in the country, which was caused by the war and the numerous deaths of citizens of reproductive age and children as a result of military operations, which make up the gene pool of the nation [52].

The high rates of reproductive losses, perinatal morbidity and mortality of premature newborns are caused by premature birth [2, 3, 4].

Reducing the frequency of premature births is a national priority of health care organizations of Ukraine (Order of the Ministry of Health of Ukraine No. 624 dated from the 3rd of November, 2008, Clinical protocol on obstetric care "Premature births").

This can be achieved only by implementing a monitoring strategy that focuses on the study of risk factors.

In order to to achieve the goal of developing modern ideas about the prediction and prevention of reproductive health disorders, it is necessary to investigate the views on the relationship between this pathology and global warming.

Every year, according to world statistics, about 15 million children are born prematurely [5] (10.6% – North America, 5.9% – Europe). Early neonatal mortality among premature babies is 70-80% and is the cause of 65-75% of child mortality [6]. Similar trends are typical for Ukraine.

Thus, according to the data of the Kyiv Perinatal Center, the frequency of premature births in 2013 increased significantly – 915 compared to 2012 – 728, which corresponds to 14% and 10.1% of the total number of births, moreover, the increase in the number of premature births is characteristic in terms of gestation 29-31 weeks – 115 (23.2%) and in 32-34 weeks – 219 (42.9%) compared to last year – 98 (21.3) and 204 (44.7), respectively [7].

Global warming causal aspects

Climate change towards global warming is today an extremely important scientific and political issue with a certain multifacetedness regarding the causal context. It has been established that the average annual temperature of atmospheric air is reliably increasing in all regions of the world. The main cause of global warming is considered to be the greenhouse effect, due to the active absorption of pollution components (water vapor, carbon dioxide, methane, nitrogen oxide, etc.) in the layers of the Earth's atmosphere, which must be transported into space [8, 9].

The concern of all circles of society about the problem of climate change was embodied in the adoption of a number of international agreements. In 1992, 154 countries signed the UN Framework Convention on Climate Change, in 1997 the Kyoto Protocol was adopted [10]. Both documents have been ratified in Ukraine. The 2021 Climate Conference in Glasgow (UK) predicts a 2.7°C rise in temperature this century. Experts have recognized that due to climate changes, the health of the female population becomes more vulnerable during pregnancy and motherhood [11].

The World Meteorological Organization and the United Nations Environment Program established the Intergovernmental Panel on Climate Change (IPCC) in 1988 to carry out a scientific, technical and socio-economic analysis of global climate change and the problems triggered by these phenomena.

The IPCC's significant contribution to the understanding of the extremely important problem for all mankind, the need to mitigate the negative

consequences of global warming, was recognized by the awarding of the Nobel Peace Prize to the Intergovernmental Panel on Climate Change in 2007 [12].

The search for ways to save the world from catastrophic global warming is recognized as extremely important by the scientific community. The 2021 Nobel Prize in Physics was awarded "for ground-breaking contributions to our understanding of complex systems" to pioneering scientists in the study of the devastating anthropogenic impact on ecology, to Syukuro Manabe and Klaus Hasselmann for "physical modeling of Earth's climate, quantification of variability and reliable prediction of global warming" [thirteen].

The global average annual air temperature in the surface layer is an integral characteristic of the global climate system, which is used to judge the intensity of changes in temperature patterns. During the period 1907-2006, the average global air temperature increased by 0.74°C, a linear temperature trend over the past 50 years (0.13°C per ten years) and exceeded the corresponding value for the century period by almost twice [14].

As a result of modeling natural processes and assessing the potential negative impact of human activities, the IPCC analyzed the main climate system change forecasts for the period until the end of the 21st century, taking into account the likely growth of the Earth's population, the introduction or inhibition of the implementation of new technologies, the use of organic fuels for energy production or using alternative sources. In accordance with these conditions, the most significant increase in the global surface temperature of the globe by 2099 is predicted by 1.8°-4.0° (with possible limits of changes from 1.1° to 6.4°) [15].

In 1996, Ukraine undertook the systematic monitoring and research of the climate on its territory after the ratification of the UN Framework Convention on Climate Change, as specified in Article 5 of the Convention. This is the range of tasks of the national hydrometeorological service. The Hydrometeorological Service carries out scientific research and monitors the main climate-forming factors in Ukraine, analyzes the specifics of the main meteorological parameters of the climate of the country's regions through instrumental observations, systematizes and coordinates changes in the current climate period. The linear trend of the surface regional temperature in terms of its growth rate coincides with the parameters of the global temperature. Over the past 35 years (1972-2006), the average increase in surface air temperature was more than 1°C. The most positive temperature trends have been observed in recent years. It has been established

that the climate of Ukraine, like that of the entire planet, changed in the direction of warming during the period of instrumental observations, changes in the climate of Ukraine are largely synchronous with the global climate [16].

The urgency of solving the problem in the field of climate change is due to insufficient awareness of society and state authorities with all aspects of the climate change problem. Development and further implementation of a coherent national state policy in the field of global warming, harmonized with international legislation, is a difficult task due to the multidisciplinary nature of the problem. Politically, economically and scientifically sound decisions on climate change must be made for the health sector to adapt people to climate change.

Adaptation of anthropogenic and natural elements of interaction to climate change, increase of resistance with reduction of risks that are realized during climate change, is carried out by developing and carrying out effective measures for adaptation to climate change and increasing resistance to factors related to climate risks in the field of health care. self and life activities of people [17].

Scientists in the medical and biological field draw the attention of the world public to alarming conclusions based on the results of scientific research. On November 28, 2019, the European Parliament declared a climate emergency in the European Union [18].

According to the Intergovernmental Panel on Climate Change, rising temperatures on the planet, heat waves will become more frequent in the future, and their duration and intensity will probably increase in the coming years [19].

With the gradual increase in global warming, the health effects of extreme temperatures are becoming the subject of scientific attention, but its correlation with preterm birth remains completely unclear.

In the direction of studying the negative consequences of changing the temperature regime, scientists are focusing their main efforts on tracking the impact on people's health of the sources of the degree of air pollution, the growth of the greenhouse effect and extreme hyperthermic phenomena.

Climate change affects the health of the planet's inhabitants, the quality and length of their lives. Life expectancy since the beginning and during the industrial period is parallel to a decrease in human fertility, a decrease in sperm quality, an increase in premature ovarian failure, and a decrease in the reserve of germ cells in the gonads [20].

Premature birth under conditions of global warming

Childbirth, which begins spontaneously in the period of pregnancy from 22 to 36 weeks and six days

with the progression of labor activity and the birth of a fetus weighing more than 500 g, is the leading cause of child morbidity and mortality in the world. The level of indicators of premature birth is from 4 to 15%, there is a clear trend towards the growth of this indicator. The number of premature newborns in the structure of perinatal losses is within 48-58%. In fact, one in 10 children in the world is born prematurely [21, 22].

According to Alan Barrek, an employee of the Institute of Environment and Sustainable Development of the University of California, the cause of premature birth is hot weather, which increases the level of oxytocin in women, a hormone that regulates the birth process. It is also suggested that heat causes stress and prompts the woman's body to adapt in this situation [23].

With support from the National Health and Medical Research Council of Australia, scientists conducted a study and established the relationship between ambient temperature, preterm birth and stillbirth in Brisbane, Australia, between 2005 and 2009 (n=101,870). The Cox proportional hazards model (Cox, 1972) was used for birth and stillbirth as competing risks. The authors also studied the relationship between pregnancy periods and the effect of exposure to high temperatures. Higher ambient temperature during the last 4 weeks of pregnancy increased the risk of stillbirth [24].

An important role is played by the pathogenetic mechanism of premature labor along with the biological reactions of anti-inflammatory action, the final result of which is the active formation of prostaglandins, as well as the cytokine reaction of the organism of the pregnant woman and the fetus [25].

In addition, it is known that in the hypothalamus of pregnant women, which provides integrative modulation of the physiological stimulation of all autonomous functions of the body, in functional and morphological proximity to the center of thermoregulation, there are periventricular nuclei of the anterior group – the place of synthesis of oxytocin, the kinetic effect of which is the ability to trigger the contractile activity of the myometrium. as an effector organ and initiate contraction of the uterus prematurely for delivery. Afferent signals, including those to thermoregulation centers, enter the hypothalamus via polysynaptic pathways, which have not yet been identified. Integrated complex reactions of stimulation of hypothalamus thermoreceptors, which provide resistance to heat loads, by physico-chemical destructive effects of suboptimal environmental temperature on the homeostasis of the body, probably have an induction effect on the strengthening of blood circulation and stimulation of thinly connected adjacent

zones and probably serve as a biological motivation for its prolonged excitement [26, 27].

According to modern research by experts in the field of reproductive medicine, almost 10% of all births are premature, and 2.2% are stillbirths. Recent studies have shown that environmental factors may be responsible for these adverse birth outcomes. The researchers found an association between ambient temperature and preterm births and stillbirths in Brisbane, Australia, between 2005 and 2009 (n ¼ 101,870). They applied a Cox proportional hazards model with birth and stillbirth as competing risks. They also investigated whether there were periods of pregnancy in which exposure to high temperatures had a more pronounced effect. An increase in ambient temperature during the final 4 weeks of pregnancy increased the risk of stillbirth. The hazard ratio for stillbirths was 0.3 at 12°C relative to a reference temperature of 21°C. The temperature effect was greatest on the course of pregnancy at 36 weeks. There was an association between higher temperature and premature termination of pregnancy, as the hazard ratio for stillbirth was 0.96 at 15°C and 1.2 at 27°C. This effect was greatest in the later stages of pregnancy, 28-36 weeks of gestation. Such results provide strong evidence of the relationship between elevated temperature and increased risk of stillbirth and shortening of pregnancy [28].

Multivariate regression analysis makes it possible to determine the numerical risk factors of premature birth, the dependence of their level on the increase in ambient temperature is the subject of research [29]. Among the established prognostic markers of the spontaneous development of premature birth, the most informative is a comprehensive assessment of age, body mass index, and hormonal profile. The established data showed that the dependent risk factors of premature birth include progesterone level less than 139.5 ng/ml, cortisol less than 577.9 ng/ml, BMI less than 24 kg/m² and pregnant woman's age more than 25 years. Independent factors include the age of pregnant women over 35 years old, the level of insulin more than 31.36 µIU/ml and the level of progesterone less than 247.8 ng/ml [30].

Researchers from the National Research Institute of Family Planning, Peking Union Medical College Graduate School and the Environmental and Spatial Epidemiology Research Center, National Center for Human Genetic Resources (Beijing, China) conducted a study of the relationship between exposure to extreme temperatures and premature birth. based on data on temperature exposure and birth outcomes of 1,020,471 pregnant women from 132 cities in China, of which 73,240 (7.2%) were premature births.

The pregnancy process was divided into different periods of pregnancy. The study areas were divided into three categories (cold, medium and hot zones) according to the local average temperature through cluster analysis. The mean temperature data for each province used in the cluster analysis were obtained from the China Statistical Yearbook 2013. Logistic regression was used to compare the effects of exposure to hot and cold conditions on pregnancy outcomes in different periods and regions. Compared with moderate temperatures, exposure to increased temperatures during different periods of pregnancy increased the risk of preterm birth in regions with hot climates. The most obvious increase in preterm birth occurred 3 months before the end of gestation (confidence interval (CI): 1.166-1.295). Unlike exposure to heat, exposure to cooling in hot regions reduces the risk of preterm birth; the protective effect was most pronounced 3 months before the end of the gestation period (CI confidence interval: 0.734-0.832). In areas with medium and low ambient temperatures, a reduction in the risk of premature birth was also found. The effect of acute and chronic exposure to extreme temperatures throughout pregnancy, according to comprehensive scientific analysis, can affect the premature termination of pregnancy. Extreme heat is a risk factor for preterm birth, and a decrease in temperature has been shown to be a protective factor [31].

Consequences of reproductive health disorders under conditions of global warming

Based on the study and analysis of 36 identified original epidemiological studies on the adverse effects of pregnancy, namely premature birth, birth of children with low birth weight and stillbirth, which were carried out and published in the period up to 2017, the biostatisticians of the University of Wuhan (China) found the current evidence of adverse effects of warm temperature waves on pregnancy termination outcomes [32].

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proven increase in the rate of premature births (per 100 births) and a tendency towards its increase in climatically homogeneous regions of Ukraine were revealed. The number of premature births during the year and the average annual air temperature in Ukraine have been found to be correlated. The increase in the level of premature births per year in the territory of Ukraine until 2025 by 0.4 cases per 100 births in comparison with the data of 2018 [33].

The spectrum of reproductive problems associated with obesity in the female population encompasses a wide range of disorders, including infertility problems, miscarriage, and pregnancy complications [35].

Global warming and the obesity epidemic are unprecedented challenges today. PubMed, Web of Science, EBSCO, and Scopus were searched for articles published up to July 2017 that report data on the link between global warming and the obesity epidemic. Fifty studies were identified. Thematically, the articles were classified into four relationships – global warming and the obesity epidemic are related through common factors (n=21); global warming affects the obesity epidemic (n=13). Policies that support the use of clean and sustainable energy sources and urban projects that promote active lifestyles are likely to alleviate the societal burden of global warming and obesity [34].

Studying the consequences of global warming for the health of vulnerable population groups, such as expectant mothers, and predicting changes in the health of future generations is relevant in the field of human health.

Numerical studies demonstrate the evolutionary substitution of dominant causes in the genesis of polyetiological complications of pregnancy, namely premature birth [36].

Premature birth, in turn, is an important cause of perinatal morbidity and mortality and increases the risk of neurological complications and impaired development of newborns [37].

In a study by scientists from the USA and Great Britain, the results of which were published in Springer Nature, Science Alert talks about the acquisition of special etiological significance of initiating premature termination of pregnancy and, as a consequence of the birth of premature children, the factor of general increase in temperature, which characterizes climate changes on the planet [38].

Global warming will lead to the birth of premature newborns as a result of stimulating premature births with negative disorders in the health and cognitive functions of children. This is according to a general analysis of information on 56 million births in Britain and the United States. As a result of temperature anomalies, 25,000 more premature babies were born

per year than during the period 1969-1988. according to scientists. Thermal effects led to a total loss of more than 150,000 gestational days per year due to shortening the pregnancy period by several days. The study was published in the journal Nature Climate Change [39].

Data from the State Program "Reproductive Health of the Nation" in Ukraine for the period up to 2015 show that direct reproductive losses from miscarriage annually reach 36-40 thousand unborn children who are lost during a desired pregnancy, and there is no tendency to decrease. despite the recognized potential of the domestic health care system [40].

Conducted research by Greek scientists to study the influence of the season of birth on fetal development using two independent databases of all citizens who were born (total: 516,874) or died (total: 554,101) between 1999 and 2003 in the autumn and winter seasons of the year. In addition, it was found that an increase in temperature at birth is associated with adverse consequences for the development of the fetus. Results show a strong effect of season of birth on fetal development, mediated, at least in part, by ambient temperature at birth [41].

The results of a national study by Taiwanese scientists, which analyzed more than 2 million births between 2001 and 2010, were correlated with the average daily outdoor temperatures at birth. A log-binomial model was used to estimate the risk of adverse birth outcomes due to environmental temperature at birth after adjusting for possible errors. A significant correlation of rising ambient temperature with premature birth and low birth weight was revealed [42].

The increase in the number of premature births during the period of certain global warming leads to reliable economic costs caused by the medical care of premature babies and the probability of health disorders in the future life, as well as a significant part of disability due to neurological and somatic complications in later life [43].

According to scientists in Great Britain and Northern Ireland, during the period of general increase in environmental temperature, statistical consequences for children born prematurely in the period of pregnancy up to 26 weeks have been proven: 22% of children had a severe disability, 24% of children were born with special needs (average degree of disability), 34% of children - with slightly expressed disorders (IQ, visual disorders) and only 20% of children with no disorders [44].

Californian scientists evaluated the relationship between warmth and humidity, measured by apparent temperature, and preterm birth. They performed a

binary analysis of nearly 60,000 births in California between May and September 1999 to 2006. The authors identified cases of preterm births from the state birth registry, which were combined with meteorological and air pollution monitoring data based on the residential zip code. High ambient temperature was significantly associated with preterm birth for all mothers, regardless of race and ethnicity, age, maternal education, or infant sex. Results showed that an 8.6% (95% CI: 6.0, 11.3) increase in preterm births was associated with a 10°F (5.6°C) increase in weekly mean (lag 06) apparent temperature [45].

Italian scientists analyzed all natural singleton births that took place in Rome in 2001-2010. The effects of minimum temperature, maximum visible temperature, heat waves, particulate matter with an aerodynamic diameter of 10 µm or less (PM10), ozone, and nitrogen dioxide were evaluated using a time series approach; the analysis was conducted separately for cold and warm seasons, subject to interaction with socio-demographic and clinical risk factors. The established share of premature births was almost 6% of the total number. A 1.9% (95% confidence interval (CI) 0.86-2.87) increase in preterm birth per 1°C increase in maximum apparent temperature in the 2 days preceding birth was estimated in the warm season. An increase in preterm births by +19% (95% CI 7.91-31.69) was observed during heat waves [46].

In the journal *Environ Health Perspect*, the results of heat wave studies in the state of Alabama, USA (1990-2010) in relation to preterm birth using a cross-sectional time analysis of prematurity and heat wave days suggest a correlation between an overall increase temperature and number of premature births and proves the strategic usefulness of developing effective heat wave prevention systems [47].

In modern health care, pregnancy prevention is increasingly becoming not the main goal of family planning for couples, since current changes in the environment affect reproductive health in a destructive way, and in men there is clearly a constant decrease in the quality of spermatogenesis (Skakkebaek et al., 2016; Skakkebaek et al., 2006), women have an increased prevalence of polycystic changes and a reduced ovarian germ cell reserve (Grindler et al., 2015; Smith et al., 2013), adverse pregnancy outcomes, including miscarriage and premature birth.

The need to develop and apply a set of preventive measures based on the results of research on the impact of global warming as an etio-pathogenetic factor of fertility disorders and will allow to reduce the frequency of negative reproductive consequences

and increase the number of pregnancies with the birth of full-term healthy children.

There was a need to forecast and assess risks related to reproductive health disorders associated with changes in the temperature regime in dynamics with continuous monitoring and detailed clarification of the degree, determination of previous impacts and the level of probable realization, until the risk transitions to a higher level. The strategy that the state will choose to ensure the population depends significantly on the capabilities, tolerance to climate risks, the level of responsibility, which is based on comprehensive awareness of the prevention of foreseeable negative consequences.

Prevention of reproductive disorders is considered a public health priority because of its potential to preserve human health.

In addition to the traditionally more vulnerable populations that have the hardest time adapting to environmental changes, namely pregnant women, children, patients with chronic diseases and the elderly, scientists are finding a correlation between global warming and male reproductive health.

Decreased fertility in men is no longer a subject of debate, which is reflected in a decrease in sperm volume, total sperm count, and sperm motility with normal morphology. Global trends in male reproductive health problems and their potential impact on male fertility were analyzed, as well as the possible etiological roles of environmental, epigenetic, and genetic factors in these trends [48].

Epidemiological data from a cohort analysis support the idea of an increase in the intrauterine origin of germ cell cancer, since men born in later calendar years have a higher rate of oncological morbidity of the reproductive system, which makes it possible to link warming with an increase in cancer risks of the reproductive system for the male population [49].

There is an increase in the demand for assisted reproductive technologies of married couples of reproductive age associated with disorders in male reproductive health. A marker of fertility problems is the time it takes for pregnancy to occur after cessation of contraception in married life (Buck Louis et al., 2013, 2014).

The insufficiently studied relationship between environmental changes and the successful implementation of reproductive plans by spouses deserves special attention [50], which is recorded through research on reproductive health in periods of life of women and men sensitive to reproductive toxic effects [51].

CONCLUSIONS

1. Looking at the association between global warming and reproductive health disorders found in scientific research, a larger and more detailed study of the revealed relationship becomes relevant. It is necessary to investigate the possibilities of protecting the birth rate of future generations through urgent management and minimization of destructive effects on the environment, to develop a strategy to protect future generations from environmental disasters.

2. Taking into account the results of scientific research, the high specificity and sensitivity of the proposed multivariate models, it would be appropriate to develop comprehensive advice on the prevention of reproductive health disorders and the implementation of timely prevention.

Contributors:

Tsybalyuk V.I. – project administration, methodology, conceptualization, writing – review & editing;

Vadzyuk S.N. – project administration, conceptualization, data analysis and interpretation, writing – review & editing;

Tolokova T.I. – visualization, writing – original draft, resources, investigation, data analysis and interpretation;

Pankiv I.B. – writing – review & editing.

Funding. This research received no external funding.

Conflict of interests. The authors declare no conflict of interest.

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Стаття надійшла до редакції
07.07.2022

