

V.I. Tsymbaliuk¹,
S.N. Vadziuk²,
T.I. Tolokova²,
P.S. Tabas²

PREVALENCE OF PREMATURE BIRTH IN CONDITIONS OF GLOBAL WARMING

National Academy of Medical Sciences of Ukraine¹

Herzen str., 12, Kyiv, 04050, Ukraine

I. Horbachevsky Ternopil National Medical University Ministry of Health of Ukraine²

Voli Square, 1, Ternopil, 46002, Ukraine

Національна академія медичних наук України¹

вул. Герцена 12, Київ, 04050, Україна

Тернопільський національний університет імені І.Я.Горбачевського МОЗ України²

Майдан Волі, 1, Тернопіль, 46002, Україна

e-mail: tolokova@tdmu.edu.ua

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Ключевые слова: глобальное потепление, преждевременные роды, детская смертность, неблагоприятные последствия беременности

Abstract. Prevalence of premature birth in conditions of global warming. Tsymbaliuk V.I., Vadziuk S.N., Tolokova T.I., Tabas P.S. The dynamics and likely associative link between global warming and the prevalence of preterm births in Ukraine over the years 2009-2018 was studied. to form modern ideas about the prognosis and prevention of this pathology. Data on medical care for pregnant women, mothers and parturients and adverse effects of pregnancy on preterm birth (form 21) for the period 2009-2018 were obtained from the municipal non-profit enterprise "Ternopil Regional Center of Public Health of Ternopil Regional Council". The correlation between the number of premature births per 100 births according to the average annual air temperature according to the Global Historical Climatology Network from the US Department of Ocean and Atmospheric Research in the climatically homogeneous regions of Ukraine was estimated. Predictive analysis of time series was performed by the method of integrated auto-regression of the moving average (ARIMA). The model error was estimated by calculating the absolute percentage error of the mean (MAPE). Statistical processing of materials was performed using programs Statistica 6.0 (StatSoft, USA) and open statistical package "R". The study meets modern requirements of moral and ethical standards regarding the provisions of legislative acts of Ukraine. Analysis of these reports of women's counseling shows an increase in the average number of preterm births from 2.88 per 100 births in the total number of births in Ukraine – 491445 in 2009 to 3.33, per 100 births in the total number of 309191 in 2018, which testifies to a significant increase in premature births in our country. Since 2009, there has been an annual, varying degree of increase in average annual air temperature in Ukraine. As a result of the correlation analysis, a significant strong direct correlation was established between the average level of premature birth and the average annual air temperature in Ukraine ($r=0.84$, $p<0.05$). Regression analysis revealed a significant increase in the number of premature births (per 100 births) in 1, 2, 5, 6, 7, 8 and 10 climatically homogeneous regions and a tendency to increase in, respectively, 3, 4, 9, 11 and 12 climatically homogeneous regions of Ukraine. Based on the analysis of data on the average annual air temperature in Ukraine for 2009-2018, the average annual air temperature in Ukraine is projected to increase by 0.3 ° C in 3 years (MAPE <10%, $p<0.05$). The annual number of premature births is expected to increase (cases per 100 births) in 3 years by 0.4 cases per 100 births (MAPE <10%, $p <0.05$). In the context of global warming, the number of negative consequences of pregnancy is increasing, namely idiopathic premature termination of pregnancy with the birth of premature infants. Strong correlations have been established between the annual number of premature births and the average annual air temperature in Ukraine. Regression models of preterm birth showed a significant increase in 1, 2, 5, 6, 7, 8, and 10 climatically homogeneous regions and a tendency to increase in 3, 4, 9, 11 and 12 climatically homogeneous regions. The annual number of premature births in Ukraine is projected to increase by 2023 by 20 cases per 100 births compared to 2018. The strategy for preventing premature births and related adverse effects of pregnancy should include the identification of global warming as a risk factor for increasing level of this pathology.

Реферат. Поширеність передчасних пологів в умовах глобального потепління. Цимбалюк В.І., Вадзюк С.Н., Толокова Т.І., Табас П.С. Досліджено динаміку та ймовірний асоціативний зв'язок глобального потепління із поширенням передчасних пологів в Україні за 2009-2018 рр. з метою формування сучасних уявлень щодо прогнозування та профілактики цієї патології. Дані про медичну допомогу вагітним, матерям та

породіллям та несприятливі наслідки вагітності стосовно передчасних пологів (форма 21) за період 2009-2018 рр. отримані в комунальному некомерційному підприємстві «Тернопільський обласний центр громадського здоров'я Тернопільської обласної ради». Проведено оцінку кореляційного зв'язку за методом Пірсона між кількістю передчасних пологів на 100 пологів та рівнем середньорічної температури повітря за даними «Global Historical Climatology Network» від Національного управління океанічних й атмосферних досліджень США на території кліматично однорідних регіонів України. Прогностичний аналіз часових рядів здійснювали методом інтегрованої моделі авторегресії ковзної середньої (ARIMA). Похибку моделі оцінювали за допомогою обрахунку абсолютної відсоткової похибки середньої (MAPE). Статистичну обробку матеріалів проведено з використанням пакетних програм Statistica 6,0 (StatSoft, США) і відкритим статистичним пакетом «R». Дослідження відповідає сучасним вимогам морального та етичного стандарту стосовно положень законодавчих актів України. Аналіз даних звітів роботи жіночих консультацій показує збільшення середньої кількості передчасних родорозрішень з 2,88 на 100 пологів при загальній кількості пологів в Україні 491445 у 2009 році до 3,33 на 100 родорозрішень у загальній кількості 309191 у 2018 році, що достовірно свідчить про зростання кількості передчасних пологів у нашій державі. Починаючи з 2009 року, спостерігається щорічне, різного ступеня зростання середньорічної температури повітря на території України. У результаті проведеного кореляційного аналізу встановлено достовірний сильний прямий кореляційний зв'язок між усередненим рівнем передчасних пологів та середньорічною температурою повітря на території України ($r=0,84$, $p<0,05$). Регресійний аналіз виявив достовірне зростання кількості передчасних пологів (на 100 пологів) у 1, 2, 5, 6, 7, 8 і 10 кліматично однорідних регіонах та тенденцію до збільшення у відповідно 3, 4, 9, 11 і 12 кліматично однорідних регіонах України. На підставі аналізу даних середньорічної температури повітря на території України за 2009-2018 рр. прогнозується зростання середньорічної температури повітря на території України через 3 роки на 0,3 °C (MAPE <10%, $p<0,05$). Прогнозується зростання річної кількості передчасних пологів (випадків на 100 пологів) через 3 роки на 0,4 випадка на 100 пологів (MAPE <10%, $p<0,05$). В умовах глобального потепління зростає кількість негативних наслідків вагітності, а саме ідіопатичного передчасного завершення вагітності з народженням недоношених новонароджених. Між річною кількістю передчасних пологів та середньорічною температурою повітря в Україні встановлено сильні кореляційні зв'язки. Регресійні моделі реєстрації передчасних пологів засвідчили їх достовірне зростання в 1, 2, 5, 6, 7, 8, і 10 кліматично однорідних регіонах та тенденцію до збільшення в 3, 4, 9, 11 і 12 кліматично однорідних регіонах. Прогнозується зростання річної кількості передчасних пологів на території України до 2023 р. на 0,4 випадка на 100 пологів порівняно з 2018 р. Стратегія попередження передчасних пологів та пов'язаних з цим несприятливих наслідків вагітності повинна включати ідентифікацію глобального потепління як фактора ризику, що сприяє зростанню рівня цієї патології.

It is established that the average annual air temperature is rising in all regions of the world, which is an evidence of global warming. The main reason is considered to be the greenhouse effect, due to the active delay of infrared rays with thermal energy, which must be transferred into space by pollutants (water vapor, carbon dioxide, methane, nitrogen oxides, etc.) in the Earth's atmosphere. Forecasting climate change in the future attracts special attention of scientists about the consequences of these changes [4, 7, 9, 11].

Global warming affects all components of the biosphere and affects human health, both directly and indirectly. Modern knowledge of scientists in the medical and biological field, allows us to identify the categories and systemic relationships most vulnerable to the negative effects of global temperature rise [21].

Conditions created by global warming also affect reproductive efficiency [6, 22, 24]. Italian scientists have analyzed all natural births that took place in Rome in 2001-2010. Moreover, the share of premature births was almost 6% of the total. An increase in preterm births by + 19% (95% CI 7.91-31.69) was observed during heat waves [12]. The journal Environ Health Perspect published the results of studies (1990-2010) in the state of Alabama (USA),

which show a correlation between the general increase in temperature and the number of premature births [19].

However, the scientific literature does not show the dependence of premature birth on the increase in average annual air temperature in Ukraine.

The aim – to investigate the dynamics and likely associative link between global warming and the increase in premature births in Ukraine over the years 2009-2018 to form modern ideas about the prognosis and prevention of pathology.

MATERIALS AND METHODS OF RESEARCH

Data on medical care for pregnant women, mothers and parturients and adverse (form 21) for the period 2009-2018 were obtained from the municipal non-profit enterprise "Ternopil Regional Center of Public Health of Ternopil Regional Council".

The correlation between the number of premature births per 100 births according to the average annual air temperature according to the Global Historical Climatology Network from the US Department of Ocean and Atmospheric Research in the climatically homogeneous regions of Ukraine was estimated, that is regularly updated online [15].

Predictive analysis of time series was performed by the method of integrated auto-regression of the

moving average (ARIMA) [20]. The model error was estimated by calculating the absolute percentage error of the mean (MAPE).

Statistical processing of materials was performed using programs Statistica 6.0 (StatSoft, USA) and open statistical package "R" [26].

The study meets modern requirements of moral and ethical standards in relation to the provisions of legislative acts of Ukraine (Minutes of the meeting of the Commission on Bioethics of I. Horbachevsky Ternopil National Medical University No. 6 dated 17.05.2021) and was conducted in accordance with the principles of bioethics set out in the WMA Declaration of Helsinki – “Ethical principles for medical research involving human subjects” and “Universal Declaration on Bioethics and Human Rights” (UNESCO).

RESULTS AND DISCUSSION

Analysis of these reports of women's counseling shows an increase in the average number of preterm births from 2.88 per 100 births in the total number of births in Ukraine – 491445 in 2009 to 3.33, per 100 births in the total number of 309191 in 2018, which testifies to a significant increase in premature births in our country.

Thus, in over a ten-year period, we found an overall increase in the number of preterm births, as illustrated in Figure 1.

As a result of the conducted statistical analysis, a significant strong direct correlation was found between the level of premature birth in conditions of increase in the average annual air temperature in Ukraine ($r=0.84, p<0.05$) (Fig. 1).

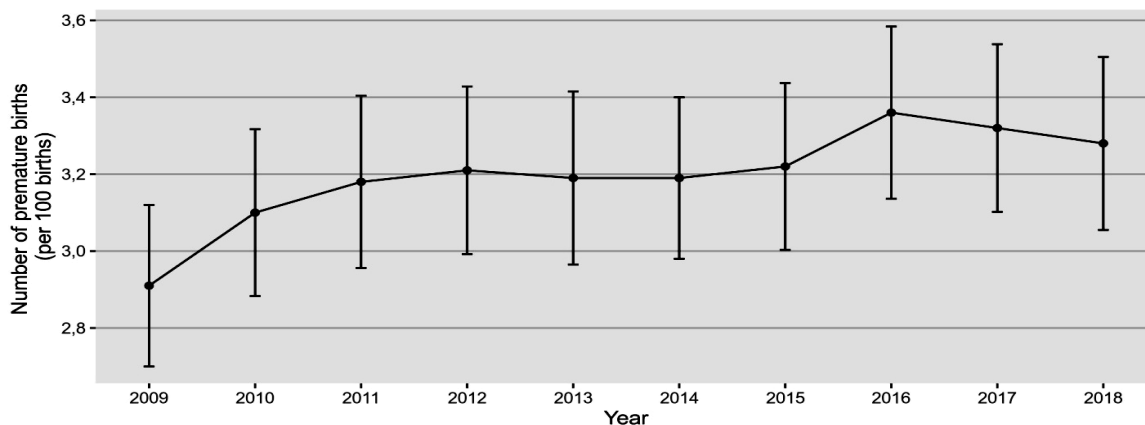


Fig. 1. Number of premature births (per 100 births) in Ukraine from 2009 to 2018

A regression model of the average annual air temperature in Ukraine is presented in Figure 2. The temperature trend line shows that since 2009 there has

been an annual, varying degree of growth, which is in line with the conclusions of an international group of experts on climate change on global warming [8, 18].

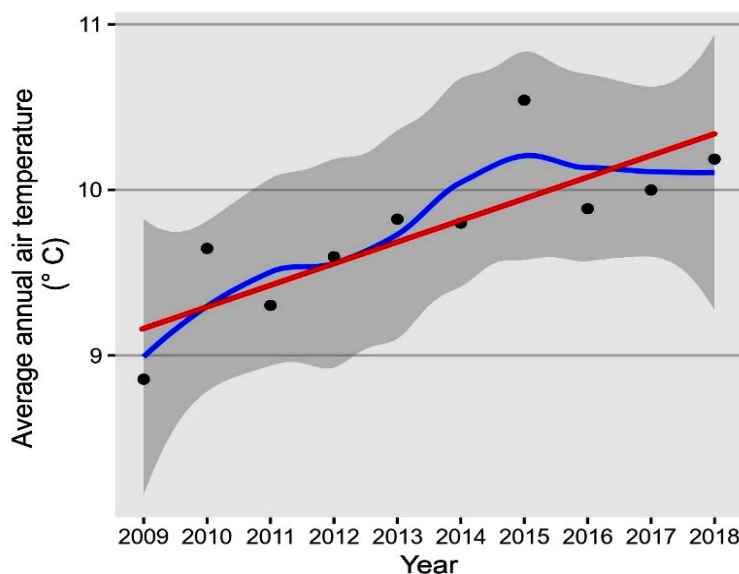


Fig. 2. Dynamics of average annual air temperature for the period from 2009 to 2018 in Ukraine (°C)

Based on the analysis of the data of the average annual air temperature on the territory of Ukraine for 2009-2018, its growth is projected by 0.3°C (MAPE <10%, p<0.05) by 2023.

The prognostic analysis of the results of the number of premature births on the territory of Ukraine for 2009-2018 showed their growth by 0.4 cases per 100 births (MAPE <10%, p<0.05) by 2032.

Climatologists of the Central Geophysical Observatory, according to one hundred and fifty years of analysis of the main climatic characteristics obtained at 187 meteorological stations from the Climate Cadastre of Ukraine and the World Climate Center CRU (Climate Research Unit, University of East

Anglia, Norwich), identified twelve climatically homogeneous regions in Ukraine [2].

Data on preterm births in climatically homogeneous regions (Statistical and analytical directories: The state of the female population of Ukraine for the period 2009-2018.

<https://moz.gov.ua/article/statistic/centr-medichnoi-statistiki-moz-ukraini>) are presented in Table 1.

Statistical indicators of the seventh and eleventh climatically homogeneous regions, which include Donetsk, Luhansk regions and Crimea, are presented until the year 2013 as a result of the lack of the following statistics.

Table 1

Premature births per 100 births in climatically homogeneous regions (CHR) in 2009-2018

No. CHR	Region	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
1	Rivne, Zhytomyr, Volyn	2.69	2.90	3.01	3.02	3.01	3.13	3.23	3.11	3.14	3.25
2	Ternopil, Lviv, Khmelnytsky	2.42	2.44	2.63	2.66	2.57	2.54	2.85	2.76	3.38	2.93
3	Kyiv, Chernihiv	2.86	3.02	2.93	3.17	3.05	3.29	3.44	3.27	3.33	3.25
4	Sumy	2.53	2.74	2.59	2.90	3.06	3.12	3.41	3.62	3.25	3.12
5	Vinnitsia, Cherkasy	2.87	2.98	3.08	3.28	2.89	3.07	3.51	3.44	3.68	3.59
6	Poltava, Kirovograd, Dnipro	3.25	3.50	3.52	3.53	3.75	4.04	4.18	4.16	4.06	4.58
7	Donetsk, Luhansk	3.36	3.62	3.54	3.58	3.76	-	-	-	-	-
8	Zaporizhia, Mykolaiv, Kharkiv	3.02	3.25	3.31	3.34	3.23	3.19	3.26	3.55	3.47	3.59
9	Odessa	2.54	2.73	2.85	2.67	2.63	2.41	2.35	2.40	2.71	2.77
10	Kherson	3.10	3.15	3.32	3.04	3.22	3.11	3.34	3.75	3.92	3.96
11	Crimea	3.46	3.57	3.81	3.7	3.78	-	-	-	-	-
12	Chernivtsi, Zakarpattia	2.85	3.29	3.59	3.57	3.37	3.46	3.23	3.44	3.12	2.96

The regression analysis showed a significant increase in the number of premature births (per 100 births) in 1, 2, 5, 6, 7, 8 and 10 climatically homogeneous regions and a tendency to increase in 3, 4, 9, 11 and 12, respectively. regression models of preterm birth in 1 and 3 climatically homogeneous regions (see Fig. 3 and Fig. 4).

Premature births is one of the major obstetric syndromes with numerous risk factors, however, in the context of global warming there are etiologically caused changes in extragenital organs and systems [1].

The mechanism of development of premature births caused by global warming can now be obviously be explained as follows. Afferent information enters the centers of thermoregulation in the hypothalamus by polysynaptic pathways, which are not yet all identified [24]. Integrated complex responses to stimulate the thermoreceptors of the hypothalamus, which provide resistance to heat stress, are likely to induce blood circulation and stimulate adjacent areas, which probably serves as a biological motivation for their prolonged excitation.

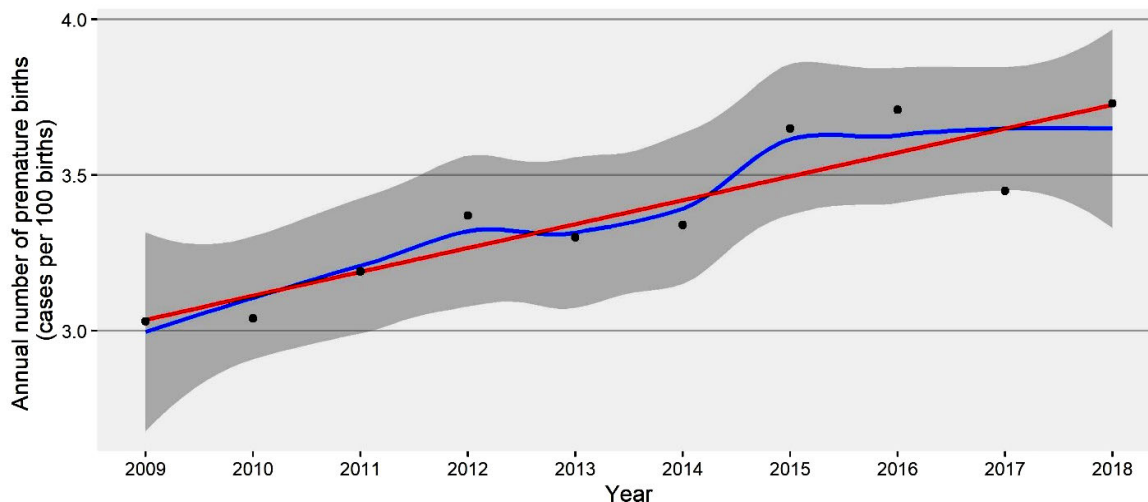


Fig. 3. Regression model of preterm births per 100 births in the 1st climatically homogeneous region

Equation for regression model of preterm births per 100 births in the 1st climatically homogeneous region:

$$Y = -150.987 + 0.07667 * X,$$

where X is year (p<0.01).

As a result, according to Alan Barreck of the University of California's Institute for Environment and Sustainable Development, hot weather leads to an increase in levels of oxytocin in women, a hormone that enhances childbirth [10].

Cytokine response of the pregnant woman and fetus plays an important role in the pathogenetic mechanism of premature birth simultaneously with

biological reactions, the end result of which is the active prostaglandins [9].

Every year, about 15 million children are born prematurely in the world [25] (10.6% – North America, 5.9% – Europe). Premature infants account for 70-80% of early neonatal mortality and 65-75% of infant mortality.

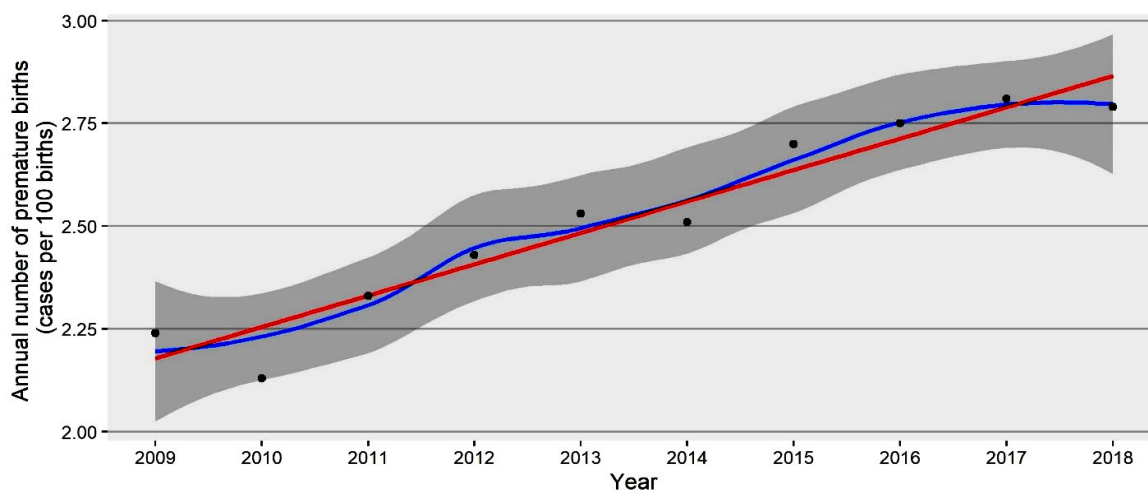


Fig. 4. Regression model of preterm births per 100 births in the 3rd climatically homogeneous region

Equation for regression model of preterm births per 100 births in the 1st climatically homogeneous region:

$$Y = -151.2 + 0.07636 * X,$$

where X is year (p<0.01).

Data from the State Program "Reproductive Health of the Nation" for the period before 2015 show that direct reproductive losses from miscarriage annually amount to 36-40 thousand of unborn children and do not tend to decrease, despite the significant potential of the domestic health care system [5].

The mortality of premature infants in Ukraine is significantly higher than the mortality of those born in physiological terms (Table 2).

According to the report on medical care for pregnant women, mothers and parturients (form 21), despite the increase in the quality of medical care for pregnant women, in 2018 the stillbirth rate as a

result of premature birth reaches 5.92% per 18,726 born children weighing up to 2,499 grams. The overall reduction in neonatal mortality confirms an increase in the efficiency of obstetric care, but the ratio between premature infants who died in the first 168 hours of life and premature infants died in 2018 proves that in 2018 perinatal infant mortality rate is 53.8 times higher than full-term against this increase by 43.7 times in 2009 and confirms an increase in mortality of premature infants by 10% during the dynamic growth of the average annual temperature in Ukraine.

Table 2

Infant mortality in Ukraine (form 21)

Year	Full-term infants (P±m; %, 95% CI)	Premature infants (P±m; %, 95% CI)	Reliability between indicators **
2009	544±12.5 95% CI [531.5; 556.5]	1069±18.7 95% CI [1050.3; 1087.7]	p<0.05
2010	528±10.1 95% CI [517.9; 538.1]	1082±17.9 95% CI [1064.1; 1099.9]	p<0.05
2011	434±9.3 95% CI [424.7; 443.3]	1090±18.2 95% CI [1071.8; 1108.2]	p<0.05
2012	422±9.8 95% CI [412.2; 431.8]	1085±16.7 95% CI [1068.3; 1101.7]	p<0.05
2013*	374±8.8 95% [365.2; 382.8]	916±16.3 95% CI [899. 7; 932.3]	p<0.05
2014	280±8.5 95% CI [271.5; 288.5]	621±14.9 95% CI [606.1; 635.9]	p<0.05
2015	246±7.9 95% CI [238.1; 253.9]	589±13.4 95% CI [575.6; 602.4]	p<0.05
2016	236±7.2 95% CI [228.8; 243.2]	537±12.8 95% CI [524.2; 549.8]	p<0.05
2017	183±6.5 95% CI [176.5; 189.5]	623±13.7 95% CI [609.3; 636.7]	p<0.05
2018	168±6.3 95% CI [161.7; 174.3]	493±9.5 95% CI [483.5; 502.5]	p<0.05

Notes: * – Statistical indicators upto 2013 contain data from Donetsk, Luhansk regions and Crimea since 2014 statistical data from these regions have not been provided; ** – Reliability between indicators full-term and premature infants.

It should be noted that the overall incidence of newborns during the period from 2009 to 2018 in Ukraine tended to increase during the last five-year period (2014-2018) after declining over the first five-year period, from 2009 to 2013. Fig. 5).

High rates of perinatal mortality and morbidity encourage the search for cause and effect in order to increase the effectiveness of preventing the adverse effects of pregnancy and maintaining the health of the nation.

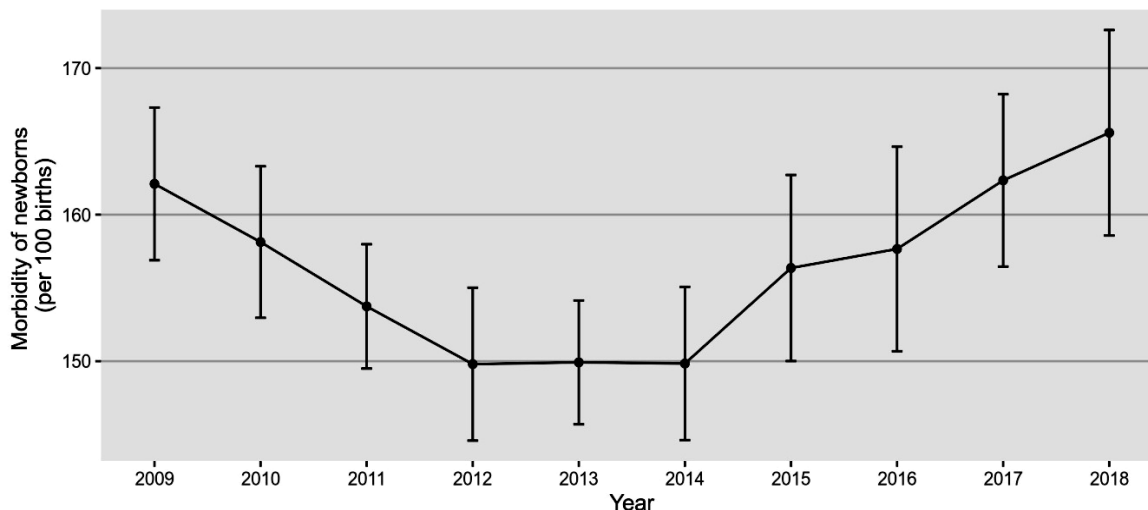


Fig. 5. Morbidity of newborns (per 100 births) in Ukraine from 2009 to 2018 (form 21)

It is important in the field of human health to study the effects of global warming on the health of vulnerable groups, such as expectant mothers, and to predict changes in the health of future generations.

Reducing the frequency of premature births is a national priority of the health care organization of Ukraine [3]. This can only be achieved by monitoring a strategy that focuses on the study of risk factors.

Multifactor analysis allows to determine the numerical risk factors for premature birth. Among the established prognostic markers of spontaneous development of premature birth, the most informative is a comprehensive assessment of age, body mass index and hormonal profile [23].

The negative consequences of pregnancy associated with the indirect effects of global warming are now extremely difficult to predict. They will depend, on the one hand, on the nature of climate change, on the other hand - on the response of pregnant women and fetuses, due to their adaptive mechanisms.

The need to develop and apply a set of preventive measures based on research on the impact of global warming as an etio-pathogenetic factor in premature termination of pregnancy and will reduce the incidence of preterm birth and increase the number of pregnancies with full-term healthy children.

CONCLUSIONS

1. During the 10 years strong correlations have been established between the annual number of premature births and the average annual air temperature.

2. Regression models of preterm birth showed a significant increase in 1, 2, 5, 6, 7, 8, and 10 climatically homogeneous regions and a tendency to increase in 3, 4, 9, 11 and 12 ones.

3. It is projected to increase the annual number of premature births in Ukraine by 2023 by 0.4 cases per 100 births compared to 2018 in conditions of increasing temperature by 0.3°C.

4. Preterm births over the period in which the study was performed were accompanied by high mortality and morbidity of newborns.

5. Perspective way of the scientific research is the study of negative impact of the global warming on the cardiovascular, respiratory, nervous, immune, endocrine systems of the vulnerable groups of humans includes pregnant women, parturients, fetuses and newborns.

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

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