RESEARCH

Ambient temperature and female infertility prevalence: an ecological study based on the 2019 global burden of disease study

Jiahua Qian^{1,2}, Yuhe Si^{1,2}, Yihao Chen³, Yushu Zhu^{1,2}, Jiayu Zhu³, Chunbao Mo^{4,5,6*} and Jianxiong Ma^{1,2,7*}

Abstract

Background The impact of climate change on human health is well established; however, its effect on the prevalence of female infertility is poorly understood. In this study, we aimed to investigate the association between ambient temperature changes and the prevalence of female infertility.

Methods In this ecological study, 174 countries and regions were included. We utilized 2000–2019 data on the age-standardized prevalence rate (ASPR) of female infertility and temperature data from Global Burden of Disease, ERA5 (fifth generation European Centre for Medium-Range Weather Forecasts atmospheric reanalysis for the global climate), and Coupled Model Intercomparison Project Phase 6 databases. Temperature over 12 months was averaged to express the annual temperature estimates, and the deviance percentage of temperature (DPT) was calculated based on the 20-year average temperature. Three-node restricted cubic spline curves were used to evaluate the association between temperature and the ASPR of female infertility. Linear mixed-effects models, with country code as a random effect, were used to estimate the effect size (β) and 95% confidence interval (CI) for DPT and the ASPR of female infertility. Adjusted linear mixed-effects models were used to predict the impact of future temperature changes (2020–2030) on the ASPR of female infertility.

Results Between 2000 and 2019, a U-shaped relationship was observed between temperature and the ASPR of female infertility, with the lowest ASPR occurring at 15 °C. Increased DPT was associated with an increased ASPR of female infertility, with an adjusted β (95% CI) of 78.952 (10.514, 147.710). Future temperature increases will further elevate the ASPR of female infertility.

Conclusion Globally, temperature changes may be associated with an increase in the ASPR of female infertility. **Keywords** Climate change, Temperature fluctuations, Reproductive health, Heat stress

molipol@163.com Jianxiong Ma daxiong1990@zcmu.edu.cn ¹Department of Nephrology, the First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine), Hangzhou 310006, Zhejiang, China ²The First Clinical Medical College, Zhejiang Chinese Medical University, Hangzhou 310053, Zhejiang, China

³The Second Clinical Medical College, Zhejiang Chinese Medical University, Hangzhou 310053, Zhejiang, China





*Correspondence:

Chunbao Mo

⁴Reproductive Medicine, Guangxi Medical and Health Key Discipline Construction Project, The Affiliated Hospital of Youjiang Medical University for Nationalities, Baise 533000, Guangxi, China ⁵Industrial College of Biomedicine and Health Industry, Youjiang Medical University for Nationalities, Baise 533000, Guangxi, China ⁶Engineering Research Center for Precise Genetic Testing of Ethnic

Groups Residing in the Guangxi Zhuang Autonomous Region, Baise 533000 Guangxi, China ⁷Zhejiang Key Laboratory of Research and Translation for Kidney

Deficiency-Stasis-Turbidity Disease, Hangzhou 310006 Zhejiang, China

© The Author(s) 2025. Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creati vecommons.org/licenses/by-nc-nd/4.0/.

Open Access



Background

Infertility is defined as the failure to establish a pregnancy after 12 months of regular unprotected sexual intercourse [1]. Globally, an estimated 17.5% (approximately one in six) of the adult population is affected by infertility, with female infertility accounting for approximately 30–50% of all cases [2, 3]. Over the past 30 years, the number of female infertility cases worldwide has increased by 56.71 million, with an average annual growth rate of 7.28% [4]. This has led to a continued decline in global fertility rates and a substantial disease burden, becoming a public health issue that cannot be ignored.

Common factors affecting female fertility include lifestyle (such as smoking and excessive drinking) and age [5, 6]. However, increasing evidence suggests that environmental factors are closely associated with female infertility. For example, prolonged exposure to certain chemicals may interfere with hormone secretion, leading to decreased fertility [7]. Continuous exposure to air pollution, heavy metals, and radiation may lead to infertility or increase the risk of pregnancy complications such as miscarriage [8, 9].

Generally, the ambient temperature refers to the actual air temperature of the environment. Temperature fluctuations and extreme weather events are important aspects of climate change [10]. The global average temperature in 2023 was 1.45 °C higher than the pre-industrial levels [11]. Although humans can regulate their body temperature to maintain homeostasis within certain limits, a long-term rise in the global average temperature will lead to increased heat exposure in the human body, posing potential health risks, especially to female reproductive health [12]. Moreover, higher ambient temperature exposure is associated with lower female follicle counts [13] and adverse pregnancy outcomes [14]. However, research on the relationship between ambient temperature and female infertility is limited, and the association between long-term temperature changes and female infertility at a global scale remains unknown.

We designed an ecological study to evaluate the association between ambient temperature changes and the prevalence of female infertility, quantifying the risk across regions, mainly based on data on female infertility prevalence from the Global Burden of Disease (GBD) public database. We hypothesized that long-term temperature changes are associated with an increased risk of female infertility.

Methods

Sources of data

Our study mainly used GBD data, including age-standardized female infertility prevalence (ASPR), Smoking Tobacco Use Prevalence (Smoking prevalence), air pollution exposure estimates (particulate matter [PM], nitrogen dioxide [NO₂], and ozone [O₃]), and the sociodemographic index (SDI). Temperature data were obtained from the Fifth Generation European Center for Medium-Range Weather Forecasts (ECMWF) atmospheric reanalysis of the global climate (ERA5). Future temperature projections for 2020–2030 were obtained from Phase 6 of the Coupled Model Intercomparison Project (CMIP6). Age-standardized female alcohol consumption per capita (APC) was obtained from The Global Health Observatory (GHO).

The GBD is a comprehensive study of global health metrics that estimates prevalence and incidence across 371 diseases and injuries, 204 countries and regions, and 25 age groups for women, men, and both sexes from 1990 to 2021 [15]. Thirteen countries/regions with missing temperature data and 17 countries/regions with missing APC data were excluded from the study, leaving a total of 174 countries/regions included in the study. The included countries and regions are listed in Table S1. Because only APC data from 2000 to 2019 were available, we limited the time range of the study to 2000–2019. The selection process is detailed in the supplementary materials Figure S1. We collected data on the ASPR of female infertility in 174 countries and regions from 2000 to 2019.

ERA5 is the fifth-generation ECMWF atmospheric reanalysis of the global climate produced by the Copernicus Climate Change Service of the ECMWF. It provides hourly estimates of many atmospheric, land, and oceanic climate variables, covering the period from January 1940 to the present. ERA5 data cover the Earth on a 31 km grid and resolve the atmosphere using 137 levels from the surface to a height of 80 km [16]. We extracted temperature data from the ERA5 dataset for 174 countries and regions from 2000 to 2019. Detailed information on the CMIP6 and GHO databases has been previously published [17, 18].

Assessment of female infertility prevalence

In the GBD framework, infertility is defined based on fertility-related questions asked of married or cohabiting women in population surveys. Because the structure of the questions does not identify which partner is responsible for the couple's infertility, data from a systematic literature review conducted for GBD 2010 were used to estimate the proportion of infertility attributable to female factors. Female infertility cases were identified using the following International Classification of Diseases (ICD) codes: ICD9:628-628.9, V26-V26.49, V26.51, V26.8-V26.9, and V59.7-V59.74 and ICD10: N97-N98.9 [19]. DisMod-MR 2.1 (Disease Modelling Meta-Regression; version 2.1) was used to estimate the prevalence of infertility in couples [20]. The prevalence of female infertility was calculated by multiplying the prevalence of couple infertility by the proportion of infertility attributable to female factors. Individual-level data extracted from the survey were aggregated into GBD age groups, and the age-standardized female infertility prevalence was calculated based on the GBD standard population structure.

Assessment of ambient temperature

This study defined ambient temperature as the air temperature at 2 m above the surface. This temperature was calculated by interpolating between the lowest model level and the Earth's surface, considering atmospheric conditions. We averaged monthly temperature data over 12 months to express the annual temperature estimate and used the deviance percentage of temperature (DPT) to indicate the degree of deviation of the annual temperature from the long-term trend [21]. The calculation method for the DPT is detailed in the Supplementary Materials.

CMIP6 developed the conceptual framework of Shared Socioeconomic Pathways (SSPs), which describes the evolution of future society in the absence of climate change or climate policy. SSP126 envisions a scenario where humanity transitions to sustainable development and low greenhouse gas emissions. However, SSP585 assumes an energy-intensive fossil-fuel-based economic model and depicts a scenario with high greenhouse gas emissions. SSP245 and SSP370 represent intermediate scenarios between these extremes [22].

Assessment of covariates

To minimize the potential influence of confounding factors, we included several variables that may be related to both exposure and outcomes in our analysis. These included SDI, lifestyle (smoking prevalence and APC), and air pollution (PM, NO₂, and O₃). We also included the continents where the countries or regions are located, which may reflect the geographical environment of each country or region.

In the GBD framework, the SDI is a composite indicator of the background social and economic conditions influencing health outcomes in each location. It is calculated based on the total fertility rate, mean education, and lag-distributed income per capita [23]. Smoking prevalence was defined as the daily or occasional use of any tobacco product. GBD incorporates data from 3,625 nationally representative surveys and uses space-time Gaussian process regression to model the prevalence of current and former smoking tobacco use [24]. APC was defined as the total amount of alcohol consumed in 1 year per adult (15 + years), measured in liters of pure alcohol. This includes the sum of the 3-year averages for recorded and unrecorded APC, adjusted for 3-year average visitor consumption. Recorded alcohol consumption refers to official statistics (production, imports, exports, and tax data), whereas unrecorded alcohol consumption refers to alcohol that is not taxed or regulated by government control systems. Visitor consumption considers tourists and residents visiting other countries, with data sourced from the United Nations Visitor Statistics. Continental estimates were derived from the population-weighted averages of countries [25].

The GBD also provides estimates of air pollution, including PM, NO₂, and O₃ pollution, with previously published calculation methods [26].

Statistical analysis

Continuous variables were described as means with standard deviations (SDs). The SDI was divided into five levels (Low, Low-middle, Middle, High-middle, and High) according to GBD definitions [23].

Our analysis is divided into two parts. In the first part, we used geographic detectors and RCS curves to explore the spatial and nonlinear associations between average temperature and average female infertility ASPR between 2000 and 2019. Geographic detectors are a set of statistical methods for detecting spatial heterogeneity and revealing its driving forces [27]. The core idea assumes that if an independent variable has a significant impact on a dependent variable, the spatial distribution of the independent variable and the dependent variable should be similar or spatially correlated. In this study, we used the heterogeneity and factor detection in geographic detectors: spatial heterogeneity detection of Y and the extent to which a factor X explains the spatial heterogeneity of attribute Y, measured by q value. A high q value indicates strong spatial association. For a detailed description of the q value, please see the supplementary materials. We calculated the q value to evaluate the spatial association between temperature, SDI, smoking prevalence, APC, PM, NO_2 , O_3 , and continents and female infertility ASPR. Quintiles were used to distinguish the average temperature, average smoking prevalence, average APC, average PM, average NO₂, and average O₃ between 2000 and 2019 to meet the analysis requirements of the geographic detector. Restricted cubic spline (RCS) curves with three nodes were applied to evaluate the nonlinear association between temperature and female infertility ASPR, and the SDI, smoking prevalence, APC, PM, NO₂, O₃, and continent were adjusted. We also used geographic detectors and RCS curves to analyze the association between temperature and female infertility ASPR at three time points in 2000, 2010, and 2019.

In the second part, we further evaluated the association between DPT and ASPR of female infertility between 2000 and 2019 using linear mixed effects model. In the linear mixed effects model, the country code as a random effect and adjusting for SDI, smoking prevalence, APC, PM, NO₂, O₃, and continent. We also calculated the variance inflation factor (VIF) of the covariates to eliminate the interference of multicollinearity on the model. For subgroup analysis, stratification was performed based on SDI and continents. To assess the association between DPT and ASPR of female infertility in different regions, we stratified the regions following GBD classifications [28].

To predict the potential impact of future temperature changes on the ASPR of female infertility and explore the changing trend of the ASPR of female infertility in the future, we used predicted temperature data (2020–2030) simulated based on the SSP scenarios (including SSP126, 245, 370 and 585) provided by CMIP6 to calculate the DPT of the corresponding years. The DPTs of 2020–2030 were used as inputs in the linear mixed effects model in the second part to generate the predicted values of the ASPR of female infertility under the four SSP scenarios. We then used the non-parametric bootstrap method (model-based (semi-)parametric bootstrap for mixed models, bootMer) to conduct 1000 bootstrap sampling on the predicted values of the mixed effects model, and calculated the 2.5% and 97.5% quantiles of the bootstrap sample results to obtain the 95% confidence interval of the predicted value.

To test the robustness of the results, two sensitivity analyses were performed. (1) We supplemented the data on temperature, female infertility ASPR, SDI, smoking prevalence, PM, NO2, O3 from 1990 to 1999 and repeated the main analysis. Due to the unavailability of APC data for 1990–1999, only SDI, smoking prevalence, PM, NO2, O3, and continent were adjusted in the analysis. (2) We performed square root transformation on the female infertility ASPR between 2000 and 2019 to ensure that the data conforms to a normal distribution and repeated the analysis in the second part above. The analysis was performed using the R software (version 4.3.1) and ArcGIS (version 10.8). Statistical significance was set at P < 0.05.

Results

Study countries or region characteristics

From 2000 to 2019, the mean (SD) of global temperature was 19.11 °C (8.21 °C), and the mean (SD) estimated exposure values for PM, NO₂, and O₃ were 28.19 ug/m³ (17.03 ug/m³), 5.37 ppb (3.60 ppb), and 40.43 ppb (9.81 ppb), respectively. The characteristics of the estimated exposure values for temperature and air pollution, stratified by continent and SDI, are listed in Table 1. The mean (SD) of the global female infertility ASPR was 1764.95 per 100,000 population (1044.47 per 100,000 population), and the mean (SD) of smoking prevalence and APC were 0.11% (0.10%) and 2.31 L/year (1.94 L/year), respectively. Characteristics of smoking prevalence and APC stratified by continent and SDI are presented in Table 2.

The mean temperature and mean female infertility ASPR distributions over the past 20 years is shown in Fig. 1A. The mean temperature in some regions was high, especially in sub-Saharan Africa, the Middle East, South Asia, and Southeast Asia, while the temperature in North America, Europe. and East Asia was relatively low. From the global distribution of female infertility ASPR, the Caribbean, sub-Saharan Africa, Europe, and East Asia were higher than those in other regions. The geographical distribution of ASPR is not necessarily directly related to the average temperature of the region, but high temperature areas seem to be likely to have high ASPR. From 2000 to 2019, we also observed that global temperatures continued to rise, at an accelerating rate (Fig. 1B). Simultaneously, the female infertility ASPR remained stable or even slightly decreased from 2000 to 2005, but from 2005

Table 1 The characteristics of temperature and environmental factors between 2000–2019 by continents and SDI

Variables	Temperature (°C)	PM (ug/m ³)	NO ₂ (ppb)	O ₃ (ppb)
Global	19.11 (8.21)	28.19 (17.03)	5.37 (3.60)	40.43 (9.81)
Continents				
Africa	24.33 (3.30)	36.51 (17.69)	2.74 (1.70)	38.13 (7.69)
Asia	18.60 (8.39)	35.54 (18.37)	7.16 (4.14)	48.71 (9.72)
Europe	8.88 (4.14)	16.74 (6.97)	7.75 (2.23)	42.69 (5.13)
North America	22.69 (7.62)	20.20 (5.42)	4.88 (3.41)	36.12 (6.68)
Oceania	23.14 (5.09)	11.87 (3.15)	1.63 (2.14)	24.01 (6.54)
South America	20.86 (5.12)	23.91 (13.06)	6.34 (2.17)	31.39 (4.58)
SDI				
Low	24.17 (4.17)	38.24 (17.98)	2.56 (1.31)	38.20 (9.54)
Low-middle	21.09 (7.27)	28.96 (14.22)	4.48 (2.55)	39.80 (10.53)
Middle	19.46 (6.81)	24.26 (11.31)	5.67 (3.01)	40.09 (9.94)
High-middle	15.13 (8.14)	23.90 (16.55)	8.11 (3.66)	43.52 (9.38)
High	8.99 (7.04)	14.66 (12.17)	9.05 (3.30)	42.46 (7.57)

All values were calculated as the average (SD) of 2000–2019

SDI: sociodemographic index. PM, particulate matter. NO₂, nitrogen dioxide. O₃, ozone

Variables	Female infertility prevalence (per 100,000 population)	Smoking prevalence (%)	APC (L/year)
Global	1764.95 (1044.47)	0.11 (0.10)	2.31 (1.94)
Continents			
Africa	1959.37 (1216.18)	0.04 (0.03)	1.50 (1.44)
Asia	1681.88 (908.77)	0.07 (0.05)	1.15 (1.43)
Europe	1713.45 (834.60)	0.24 (0.06)	4.84 (1.30)
North America	1893.39 (1063.50)	0.08 (0.05)	2.35 (1.03)
Oceania	1629.93 (1015.87)	0.21 (0.10)	1.67 (1.86)
South America	1245.67 (1023.82)	0.13 (0.09)	2.66 (0.70)
SDI			
Low	1794.25 (1160.16)	0.05 (0.05)	1.18 (1.36)
Low-middle	1787.86 (1103.95)	0.07 (0.08)	1.67 (1.18)
Middle	1968.71 (937.90)	0.10 (0.08)	2.18 (1.60)
High-middle	1853.74 (914.96)	0.19 (0.11)	3.54 (2.18)
High	1251.10 (769.03)	0.20 (0.07)	4.49 (1.39)

Fable 2 The characteristics of female infertili	ty prevalence and lifestyle factors b	between 2000–2019 by continents and SDI
--	---------------------------------------	---

All values were calculated as the average (SD) of 2000–2019

SDI, Sociodemographic Index. APC, alcohol consumption per capita



Fig. 1 Distribution and trends for temperature and female infertility prevalence between 2000–2019. (**A**) Global map of local mean temperature over 2000–2019 with five intervals ranging from -5.56 to 28.85 °C and color-scaled dots showing the severity of the local mean prevalence rate (ranging from 76.3 to 5849.7 cases per 100,000 population) of each country over 2000–2019. (**B**) The global temperature change between 2000–2019. (**C**) The global female infertility prevalence change between 2000–2019



Fig. 2 Association between mean temperature and mean female infertility prevalence, 2000-2019. (A) Spatial association between mean temperature and mean prevalence of female infertility. APC, alcohol consumption per capita. *P < 0.05. (B) Nonlinear association between mean temperature and mean prevalence of female infertility

 Table 3
 Association between DPT and prevalence of female infertility between 2000–2019

Group	β (95% CI) [#]	Р
Global	78.952 (10.514, 147.710)	0.024
SDI		
Low SDI	-61.360 (-256.052, 132.223)	0.538
Low-middle SDI	279.162 (94.200, 465.926)	0.004
Middle SDI	6.271 (-105.024, 117.952)	0.913
High-middle SDI	-24.030 (-86.057, 38.877)	0.455
High SDI	37.539 (7.252, 68.012)	0.017
Continents		
Asia	163.425 (-6.449, 334.726)	0.063
Europe	-31.388 (-95.261, 32.948)	0.340
Africa	-85.099 (-263.549, 93.485)	0.353
North America	220.369 (38.062, 402.087)	0.020
South America	51.935 (-295.058, 395.987)	0.773
Oceania	-70.896 (-181.433, 38.354)	0.221

Adjustments were made for SDI, Continent, Smoking prevalence, APC, PM, NO_{2} , and O_3

DPT, deviance percentage of temperature

[#]Unit: per 100,000 population

to 2019, the female infertility ASPR continued to increase at an accelerating rate (Fig. 1C).

Ambient temperature and female infertility prevalence

The geographical detector showed that temperature and female infertility ASPR were associated in the spatial dimension, with a q-value of 0.124 (P < 0.05). No significant spatial association was found between female infertility ASPR and the SDI, smoking prevalence, APC, PM, NO₂, O₃, and continents (P > 0.05) (Fig. 2A). The adjusted RCS curves revealed a U-shaped nonlinear relationship between temperature and female infertility ASPR (for nonlinear, P = 0.001; overall, P = 0.002), with the lowest ASPR observed at a temperature of 15 °C (Fig. 2B). The analysis results using geographic detectors and RCS curves at three time points in 2000, 2010, and 2019 are

were consistent with the above results (Table S2, Figure S2).

DPT and female infertility prevalence

The VIF values of the covariates are shown in Table S3, which show that there is no multicollinearity among the covariates. Globally, DPT was associated with increased female infertility ASPR, with an adjusted β (95% CI) of 78.952 (10.514, 147.710) (Table 3). This indicates that for each 1 point increase in DPT, there is an associated increase of 78.952 per 100,000 population in the female infertility ASPR. Subgroup analyses according to SDI, continent, and region are presented in Table 3; Fig. 3. When stratified by SDI, an association between increased DPT and increased female infertility ASPR was observed only at Low-middle and High SDI levels. By continent, this association was observed only in North America. When stratified by region, an association was observed between increased DPT and increased female infertility ASPR in Andean Latin America, High-income North America, North Africa, and the Middle East. Notably, in Australasia, DPT was negatively correlated with female infertility ASPR.

Future female infertility prevalence

Under all SSP scenarios, the future female infertility ASPR generally exhibited an upward trend (Fig. 4). However, no significant differences were observed in the female infertility ASPR across the different SSP scenarios. Compared to the global level, Australasia and High-income North America are expected to experience higher levels of female infertility ASPR, while Andean Latin America is expected to show a lower level. North Africa and the Middle East is projected to have similar level of infertility ASPR to the global average (Fig. 4). Prediction of female infertility prevalence changes with 95% confidence interval are shown in Figure S3.

Region	β (95% CI) [#]		Р
Asia			
East Asia	-9.2 (-31.1, 12.6)	+	0.453
Central Asia	-51.8 (-240.7, 153.8)		0.615
South Asia	486.6 (-353.9, 1375.6)		0.288
Southeast Asia	351.5 (-343.1, 1038.9)		0.331
High-income Asia Pacific	-41.7 (-90.6, 7.2)	-	0.124
America			
Andean Latin America	373.4 (181.6, 565.2)		0.001
Tropical Latin America	226.0 (-295.4, 726.3)		0.395
Central Latin America	82.6 (-305.4, 463.9)		0.683
Southern Latin America	-21.6 (-71.3, 24.1)	-	0.397
Caribbean	190.8 (-228.0, 599.2)		0.377
High-income North America	212.9 (65.4, 411.0)		0.029
Europe			
Central Europe	8.3 (-86.0, 103.9)	-	0.868
Western Europe	-1.2 (-36.1, 33.7)	+	0.947
Eastern Europe	-51.7 (-261.1, 160.7)		0.640
Africa			
North Africa and Middle East	247.3 (97.8, 398.7)		0.002
Western Sub-Saharan Africa	-329.4 (-722.8, 70.8)		0.109
Eastern Sub-Saharan Africa	-67.6 (-578.2, 441.0)		0.798
Southern Sub-Saharan Africa	-293.7 (-576.2, -0.8)		0.056
Central Sub-Saharan Africa	132.2 (-304.8, 567.9)		0.563
Other regions			
Oceania	1.0 (-128.6, 130.0)	+	0.988
Australasia	-95.1 (-150.8, -42.9)	-=-	0.004
		-800 0 1000	0

Fig. 3 Subgroup analysis of the association between DPT and prevalence of female infertility, 2000–2019. Adjustments were made for the sociodemographic index, smoking prevalence, alcohol consumption per capita, particulate matter, NO2, and O3 levels. DPT, deviance percentage of temperature. #Unit: per 100,000 population

Sensitivity analysis

The characteristics of temperature, female infertility prevalence and other factors between 1990 and 2019 are shown in Table S4 and Table S5. The distribution and trends for temperature and female infertility prevalence between 1990 and 2019 are shown in Figure S4. After including the data from 1990 to 1999, the geographical detector showed that temperature and female infertility ASPR were associated in the spatial dimension and

the adjusted RCS curves revealed a U-shaped nonlinear relationship between temperature and female infertility ASPR (Figure S5). The adjusted linear mixed effects model indicated that DPT was associated with increased female infertility ASPR globally (Table S6).

After square root transformation of the female infertility ASPR from 2000 to 2019, the data all conformed to normal distribution (Table S7). The association between DPT and female infertility ASPR after square root



Fig. 4 Prediction of female infertility prevalence changes under SSP126, SSP245, SSP370, and SSP585. (A) Global prediction. (B) Prediction for North Africa and Middle East. (C) Prediction for Australasia. (D) Prediction for Andean Latin America. (E) Prediction for High-income North America The dotted box shows the enlarged image

transformation was consistent with the original results (Table S8). Overall, the two sensitivity analyses indicated that our results were robust.

Discussion

In this study, we investigated the relationship between temperature changes and the prevalence of female infertility over the past 20 years. Our findings revealed a U-shaped relationship between temperature and female infertility ASPR; the greater the deviation of annual temperature from the long-term trend, the higher the female infertility ASPR. Affected by future temperature changes, the female infertility ASPR is projected to increase.

Studies on the effects of temperature on female fertility are limited, making direct comparisons with previous studies challenging. However, increasing evidence from cohort studies suggests that unsuitable ambient temperatures may be associated with reduced female fertility. Geng et al. conducted a retrospective cohort study using data from 3,452 infertile women in Shanghai, China, and found that both extreme low and high ambient temperatures were significantly associated with adverse pregnancy outcomes of in vitro fertilization cycles [14]. Similarly, Gaskins et al. conducted a prospective cohort study of 631 women in the United States and found that exposure to higher ambient temperatures 90 days before ovarian reserve testing was associated with lower antral follicle counts [13]. Compared with the above studies, we analyzed the relationship between long-term temperature changes and female reproductive health on a global scale from the perspective of female infertility ASPR.

In addition to human studies, similar results have been found in mammalian studies. For example, in an observational study of Spanish herds, Ryosuke Iida et al. found that more than 80% of the herds had decreased fertility when sows were exposed to temperatures ≥ 27 °C, with the farrowing rate also declining in winter [29]. Similarly, Satori et al. found that fertilization rates in dairy cows significantly decreased during summer and attributed this to the effects of heat stress on oocytes [30]. While these studies involve different species, the results emphasize the relationship between temperature and female fertility.

The association between temperature change and ASPR of female infertility was pronounced in lowmiddle SDI regions, including Andean Latin America, North Africa and the Middle East. A possible explanation is that low-middle SDI regions are usually located in areas where the impact of climate change is severe, such as tropical or subtropical regions, and residents in these regions are vulnerable to extreme heat or temperature fluctuations. In addition, the proportions of outdoor labor populations, which typically rack effective temperature regulation facilities (such as air conditioning or heating equipment), in these regions is high, resulting in a high risk of long-term exposure to unsuitable ambient temperatures [31]. Living environment factors (such as malnutrition and high levels of air pollution) may also interact with the impact of temperature change, further amplifying its negative effects on the reproductive health of women.

We also observed this significant association in high SDI regions, especially in high-income North America. The underlying mechanism remains unclear; however, it may be that these countries have a well-developed public health surveillance system and high-quality data collection capabilities, which makes the data accurate, making the association between temperature deviation and health problems easy to detect. The negative correlation between DPT and female infertility ASPR observed in Australasia may reflect the following factors: countries such as Australia and New Zealand have high socioeconomic levels and good infrastructure, which may alleviate the negative impact of temperature fluctuations; the region focuses on reproductive health education and intervention, which is conducive to the preservation of fertility. Australasia has a relatively stable climate and a small temperature deviation, so its negative effect may be offset by other protective factors [32].

Our research predicts that future temperature rises will increase the ASPR of female infertility, which is consistent with the prediction of Yu et al. (2023) that the global ASPR of female infertility will continue to rise by 2030 [4]. However, compared with the predicted value of 3725.51/100,000 global female infertility ASPR in 2030 by Yu et al., our predicted value is significantly lower. This difference may be attributed to the difference in research methods: Yu et al. used time series modeling to focus on the trend and periodicity of historical data for prediction, and did not evaluate the impact of external factors, which may overestimate the growth of ASPR. We particularly emphasize the contribution of temperature change and consider the synergistic regulatory effects of multiple variables (such as SDI and air pollution). Although this method is helpful in clarifying the impact of temperature change on female infertility, it may lead to a conservative estimate of the growth of ASPR. In addition, compared with Yu et al.'s prediction of the change trend of ASPR in 204 countries, our study predicts the change trend of ASPR in 174 countries. Differences in regional coverage may also lead to different predictions.

In the prediction step, we did not observe significant differences in the female infertility ASPR under different SSP scenarios. This may be attributed to the small differences in the rate of temperature change among the SSP scenarios over a shorter time scale, which may not have a substantial impact on the prevalence of female infertility. However, from a long-term perspective, as climate change intensifies, the effects of different SSP scenarios on the prevalence of female infertility may become more pronounced. Since the current prediction model does not account for these long-term effects, further longterm studies are recommended. In summary, this study and previous studies have revealed the continued upward trend of the ASPR of female infertility in the future. This finding suggests that public health departments should pay careful attention to issues related to female infertility. Simultaneously, climate change, as a potential risk factor affecting reproductive health, deserves additional attention. However, our predictions are based on an idealized model state, that is, the currently observed relationship between DPT and female infertility ASPR will remain

unchanged in the future. The actual situation is complicated, and other variables that have not been considered will affect the prediction. Therefore, these results are suitable as a reference for understanding the future trend of female infertility ASPR changes, rather than specific prevalence predictions.

The mechanism by which environmental temperature affects female reproductive health remains unclear. The temperature gradient in the oviduct plays a role in guiding sperm during fertilization [33], and the lower temperature of the follicular fluid may be crucial for normal oocyte development [34, 35]. Environmental temperature may impair female fertility by affecting the regulation of local temperatures. Additionally, cold exposure can cause estrous cycle disorders and follicular dysplasia in female mice, accompanied by abnormal ovarian progesterone and progesterone levels [36]. Chronic heat stress in mice decreases serum estradiol and aromatase levels in antral follicles but increases the number of atretic follicles and granulosa cells undergoing apoptosis [37]. These findings suggest that environmental temperature may also reduce female fertility by affecting hormone secretion. However, further studies are required to elucidate the underlying mechanisms.

Strength and limitations

To our knowledge, this is the first study to report the adverse effects of temperature changes on women's reproductive health on a global scale. The strength of this study lies in the inclusion of a large number of regions in the analysis and the use of highly reliable data, which ensured the accuracy of the results.

Our study has the following limitations: (1) This is an ecological study. Although we observed an association between ambient temperature and the ASPR of female infertility, our findings cannot be interpreted as causal evidence; therefore, further research remains necessary; (2) this study is based on data at a large spatial scale, which complicates accurately assessing and reflecting individual exposure levels. Therefore, caution is advised when generalizing this conclusion to individual subjects; (3) the prevalence of female infertility is largely related to the medical and health conditions of a country or region. Without fully considering the regional differences in medical conditions, the association between ambient temperature and the ASPR of female infertility may be misestimated. Other environmental pollutants are also important factors affecting the risk of female infertility, which were not considered in this study. (4) Our predictions are based on an idealized model state. However, the actual situation is more complex, and other variables not considered in the model may influence the predictions. Therefore, the results should be interpreted with caution.

In conclusion, an unsuitable ambient temperature may be associated with an increased ASPR of female infertility. The international community should strengthen its attention to the adverse effects of global temperature changes on reproductive health to mitigate the growing trend of infertility in recent years. Further research should be conducted in the future to better evaluate the causal relationship between ambient temperature deviation and female infertility.

Abbreviations

- APC Alcohol Consumption Per Capita
- ASPR Age-Standardized Prevalence Rate
- CMIP6 Coupled Model Intercomparison Project Phase 6
- DPT Deviance Percentage of Temperature
- ERA5 Fifth Generation European Centre for Medium-Range Weather Forecasts GBD Global Burden of Disease
- GHO Global Health Observatory
- ICD International Classification of Diseases
- NO₂ Nitrogen Dioxide
- O₃ Ozone
- PM Particulate Matter
- RCS Restricted Cubic Spline
- SDI Sociodemographic Index
- SSP Shared Socioeconomic Pathways

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12958-025-01365-4.

Supplementary Material 1

Acknowledgements

We would like to thank Editage (www.editage.cn) for the English language editing.

Author contributions

JHQ, YHS, and YSZ drafted the manuscript. JHQ and YHC performed statistical analyses and created the figures. JXM, CBM, and JYZ contributed to the manuscript review. JXM and CBM conceived the study and contributed to manuscript review. All the authors have read and approved the final manuscript.

Funding sources

This work was supported by the Zhejiang Provincial Natural Science Foundation of China [grant number MS25H270044], Young Elite Scientists Sponsorship Program by CACM [grant number CACM-2022-QNRC2-A01], China Postdoctoral Science Foundation [grant number 2023M743146], Postdoctoral Fellowship Program of CPSF [grant number GZC20232373], and the Zhejiang Chinese Medical University Scientific Research Project for Talent [grant number 2023RCZXZK47].

Data availability

Data supporting the findings of this study are available from the corresponding author upon request (daxiong1990@zcmu.edu.cn).

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 23 November 2024 / Accepted: 13 February 2025 Published online: 22 February 2025

References

- Vander Borght M, Wyns C. Fertility and infertility: definition and epidemiology. Clin Biochem. 2018;62:2–10. https://doi.org/10.1016/j.clinbiochem.2018. 03.012, PMID 29555319.
- Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reprod Biol Endocrinol. 2015;13:37. https://doi.or g/10.1186/s12958-015-0032-1. PMID 25928197.
- Cox CM, Thoma ME, Tchangalova N, Mburu G, Bornstein MJ, Johnson CL et al. Infertility prevalence and the methods of estimation from 1990 to 2021: a systematic review and meta-analysis. Hum Reprod Open. 2022;2022(4):hoac051. https://doi.org/10.1093/hropen/hoac051, PMID 36483694.
- Yu J, Fu Y, Zeng L, Xie P, Li L, Zheng Y. Burden of female infertility in China from 1990 to 2019: a temporal trend analysis and forecasting, and comparison with the global level. Sex Health. 2023;20(6):577–84. doi: 10.1071/SH23029, PMID 37967574.
- García D, Brazal S, Rodríguez A, Prat A, Vassena R. Knowledge of age-related fertility decline in women: A systematic review. Eur J Obstet Gynecol Reprod Biol. 2018;230:109–18. https://doi.org/10.1016/j.ejogrb.2018.09.030, PMID 30248536.
- Farquhar CM, Bhattacharya S, Repping S, Mastenbroek S, Kamath MS, Marjoribanks J et al. Female subfertility. Nat Rev Dis Primers. 2019;5(1):7. https://d oi.org/10.1038/s41572-018-0058-8, PMID 30679436.
- Green MP, Harvey AJ, Finger BJ, Tarulli GA. Endocrine disrupting chemicals: impacts on human fertility and fecundity during the peri-conception period. Environ Res. 2021;194:110694. https://doi.org/10.1016/j.envres.2020.110694, PMID 33385395.
- Ashry M, Rajput SK, Folger JK, Knott JG, Hemeida NA, Kandil OM, et al. Functional role of AKT signaling in bovine early embryonic development: potential link to embryotrophic actions of follistatin. Reprod Biol Endocrinol. 2018;16(1):1. https://doi.org/10.1186/s12958-017-0318-6. PMID 29310676.
- Bala R, Singh V, Rajender S, Singh K. Environment, lifestyle, and female infertility. Reprod Sci. 2021;28(3):617–38. https://doi.org/10.1007/s43032-020-0027 9-3, PMID 32748224.
- Ummenhofer CC, Meehl GA. Extreme weather and climate events with ecological relevance: a review. Philos Trans R Soc Lond B Biol Sci. 2017;372(1723):20160135. https://doi.org/10.1098/rstb.2016.0135, PMID 28483866.
- 11. Clima T, Te W. State of global water resources. Vol. 2024; 2023.
- Tokat MA, Bilgiç D, Yağcan H, Demirdağ C. A factor whose effects on fertility are overlooked: climate change and its consequences. Reprod Biomed Online. 2023;47:103551. https://doi.org/10.1016/j.rbmo.2023.103551.
- Gaskins AJ, Mínguez-Alarcón L, VoPham T, Hart JE, Chavarro JE, Schwartz J et al. Impact of ambient temperature on ovarian reserve. Fertil Steril. 2021;116(4):1052-60. https://doi.org/10.1016/j.fertnstert.2021.05.091, PMID 34116830.
- Geng L, Yang Y, Chen Y, Ye T, Qiu A, Bukulmez O et al. Association between ambient temperature exposure and pregnancy outcomes in patients undergoing in vitro fertilization in Shanghai, China: a retrospective cohort study. Hum Reprod. 2023;38(12):2489-98. https://doi.org/10.1093/humrep/dead192, PMID 37759343.
- GBD. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the global burden of Disease Study 2021. Lancet. 2024;403(10440):2133–61. https://doi.org/10.1016/S014 0-6736(24)00757-8. PMID 38642570.
- Hersbach H, Bell B, Berrisford P, Hirahara S, Horányi A, Muñoz-Sabater J, et al. The ERA5 global reanalysis. Quart J Royal Meteoro Soc. 2020;146(730):1999– 2049. https://doi.org/10.1002/qj.3803.
- Eyring V, Bony S, Meehl GA, Senior CA, Stevens B, Stouffer RJ, et al. Overview of the coupled model Intercomparison Project Phase 6 (CMIP6) experimental design and organization. Geosci Model Dev. 2016;9(5):1937–58. https://doi.or g/10.5194/qmd-9-1937-2016.

- Vardell E. Global health observatory data repository. Med Ref Serv Q. 2020;39(1):67–74. doi: 10.1080/02763869.2019.1693231, PMID 32069199.
- Global Burden of Disease Collaborative Network. Global burden of disease Study 2021 (GBD 2021) causes of death and nonfatal causes mapped to ICD codes. Seattle: Institute for Health Metrics and Evaluation (IHME); 2024.
- Institute for Health Metrics and Evaluation (IHME). Epi Visualization. Seattle, WA: IHME, University of Washington, 2024. Available http://vizhub.healthdata. org/epi(link is external).
- Closet M, Feindouno S, Guillaumont P, Simonet C. A physical vulnerability to climate change index: which are the most vulnerable developing countries? 2017.
- O'Neill BC, Tebaldi C, van Vuuren DP, Eyring V, Friedlingstein P, Hurtt G, et al. The scenario model intercomparison project (ScenarioMIP) for CMIP6. Geosci Model Dev. 2016;9(9):3461–82. https://doi.org/10.5194/gmd-9-3461-2016.
- Global Burden of Disease Collaborative Network. Global Burden of Disease Study. (GBD 2019) Socio-demographic Index (SDI) 1950–2019. Seattle: Institute for Health Metrics and Evaluation (IHME), 2020. Available from: https://d oi.org/10.6069/D8QB-JK35
- Global Burden of Disease Collaborative Network. Global Burden of Disease Study. (GBD 2019) Smoking prevalence, pp. 1990–2019. Institute for Health Metrics and Evaluation (IHME), Seattle, 2021. Available from: https://doi.org/1 0.6069/FVQE-GR75
- World Health Organization. Global Information System on Alcohol and Health (GISAH). World Health Organization; 2016.
- Global Burden of Disease Collaborative Network. Global Burden of Disease Study. (GBD 2019) Air Pollution Exposure Estimates 1990–2019. Seattle: Institute for Health Metrics and Evaluation (IHME), 2021. https://doi.org/10.60 69/70JS-NC54
- Jinfeng W, Chengdong X. Geodetector: principles and prospects. Acta Geogr Sin. 2017;72.
- Global Burden of Disease Collaborative Network. *Global burden of distudy* Study 2016 (GBD 2016) location hierarchies. Seattle: Institute for Health Metrics and Evaluation (IHME); 2017.
- Iida R, Piñeiro C, Koketsu Y. Timing and temperature thresholds of heat stress effects on fertility performance of different parity sows in Spanish herds. J Anim Sci. 2021;99(7):skab173. https://doi.org/10.1093/jas/skab173, PMID 34036340.

- Sartori R, Sartor-Bergfelt R, Mertens SA, Guenther JN, Parrish JJ, Wiltbank MC. Fertilization and early embryonic development in heifers and lactating cows in summer and lactating and dry cows in winter. J Dairy Sci. 2002;85(11):2803–12. https://doi.org/10.3168/jds.S0022-0302(02)74367-1. PMID 12487447.
- Ioannou LG, Foster J, Morris NB, et al. Occupational heat strain in outdoor workers: a comprehensive review and meta-analysis[J]. Temperature. 2022;9(1):67–102.
- Salinger MJ, Diamond HJ, Renwick JA. Surface temperature trends and variability in New Zealand and surrounding oceans[J]. Weather Clim. 2020;40(1):32–51.
- Grinsted J, Kjer JJ, Blendstrup K, Pedersen JF. Is low temperature of the follicular fluid prior to ovulation necessary for normal oocyte development? Fertil Steril. 1985;43(1):34–9. https://doi.org/10.1016/s0015-0282. (16)48314-7, PMID 3155508.
- Aroyo A, Yavin S, Arav A, Roth Z. Maternal hyperthermia disrupts developmental competence of follicle-enclosed oocytes: in vivo and ex vivo studies in mice. Theriogenology. 2007;67(5):1013-21. https://doi.org/10.1016/j.therio genology.2006.12.001, PMID 17212968.
- Wang JZ, Sui HS, Miao DQ, Liu N, Zhou P, Ge L, et al. Effects of heat stress during in vitro maturation on cytoplasmic versus nuclear components of mouse oocytes. Reproduction. 2009;137(2):181–9. https://doi.org/10.1530/REP-08-03 39. PMID 19029342.
- Ding M, Lu Y, Wen Q, Xing C, Huang X, Zhang Y, et al. Ovarian PERK/NRF2/ CX43/StAR/progesterone pathway activation mediates female reproductive dysfunction induced by cold exposure. Sci Rep. 2024;14(1):10248. https://doi. org/10.1038/s41598-024-60907-9. PMID 38702372.
- Li J, Gao H, Tian Z, Wu Y, Wang Y, Fang Y, et al. Effects of chronic heat stress on granulosa cell apoptosis and follicular atresia in mouse ovary. J Anim Sci Biotechnol. 2016;7:57. https://doi.org/10.1186/s40104-016-0116-6. PMID 27708774.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.