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REVIEWS



Associations between extreme temperature exposure and hypertensive disorders in pregnancy: a systematic review and meta-analysis

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ABSTRACT

Background: Hypertensive disorders in pregnancy (HDP) are a major cause of maternal mortality and morbidity. Recent studies indicated that pregnant women are the most vulnerable populations to ambient temperature influences, but it affected HDP with inconsistent conclusions. Our objective is to systematically review whether extreme temperature exposure is associated with a changed risk for HDP. **Method:** We searched PubMed, EMBASE, Web of Science and Cochrane Library databases. We included cohort or case control studies examining the association between extreme temperature exposure before or during pregnancy and HDP. Heat sources such as saunas and hot baths were excluded. We pooled the odds ratio (OR) to assess the association between extreme temperature exposure and preeclampsia or eclampsia. **Results:** Fifteen studies involving 4,481,888 patients were included. Five studies were included in the meta-analysis. The overall result demonstrated that in the first half of pregnancy, heat exposure increases the risk of developing preeclampsia or eclampsia and gestational hypertension, and cold exposure decreases the risk. The meta-analysis revealed that during the first half of pregnancy, heat exposure increased the risk of preeclampsia or eclampsia (OR 1.54, 95% confidence interval (CI): 1.10, 2.15), whereas cold exposure decreased the risk (OR 0.90, 95% CI: 0.84, 0.97). **Conclusion:** The ambient temperature is an important determinant for the development of HDP, especially for preeclampsia or eclampsia. The effects of extreme temperatures may be bidirectional during the different trimesters of pregnancy, which should be evaluated by future studies. This review provided hints of temperature regulation in HDP administration.

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Hypertensive disorders in pregnancy; temperature; cold; heat; meta-analysis


Introduction

Hypertensive disorders in pregnancy (HDP), which are the most common medical complications of pregnancy, occur in 10–15% of all pregnancies worldwide (1–3). HDP include four subtypes, namely, gestational hypertension, preeclampsia or eclampsia, preeclampsia superimposed on chronic hypertension, and chronic hypertension (4). They are a major cause of maternal and offspring morbidity and mortality, especially in low-income and middle-income settings (5,6). The short-term and long-term outcomes of HDP include a preterm delivery for the mother and small for gestational age, stillbirth, and future neurological, cardiovascular, renal and endocrine disorders for the offspring (7–17). The etiology of HDP remain incompletely

clear. Previous studies have reported that seasonal change and extreme temperature are important factors for HDP occurrence.

With the aggravation of global climate change in recent years, it has been documented that pregnant women with developing fetuses and young children are considered the populations that are the most vulnerable to environmental influences (18). Studies that have evaluated the influence of the environment on the perinatal outcomes have used the season as an important variable (19). Because the season itself includes a variety of confounding factors, such as the temperature, humidity, and air quality, recent studies have preferred to explore the impact of a single factor, such as the temperature, on the perinatal outcomes. Two recent systematic reviews showed that global warming

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could increase the incidence of preterm birth, low birth weight, and stillbirth (20,21).^{2,3} However, the effects of the temperature changes on the HDP have not been systematically recognized.

As the most common disease in pregnancy, HDP is considered a special cardiovascular disease that occurs during the perinatal period. It is particularly important to identify the risk factors for HDP and to further improve the perinatal outcomes for mothers and infants. A temperature driver, which is independent of other environmental factors, of HDP may exist (22). Some evidence had indicated that ambient temperature affected HDP (23,24). However, the relationship between HDP and the ambient temperature has been inconsistent in current studies (25–27). The aim of this review is to systematically assess the associations between the temperature exposure and occurrence of HDP.

Materials and methods

Study selection

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines and was registered in the PROSPERO platform (registration number is CRD42021227878). In brief, we searched Medline (PubMed), EMBASE, Web of Science and Cochrane Library in December 2022. ENDNOTE X7 was used as a platform for screening of the titles, abstracts, and full text articles. Screening of the titles, abstracts, and description/MeSH headings was performed independently by two reviewers (YX M and YZ), with any differences reconciled by a third reviewer (TX).

All of the studies regarding temperature or season exposure were screened to identify the association between the temperature exposure and HDP. The reference lists of the included articles were also screened. The authors were contacted in order to obtain additional information.

HDP has been classified into four categories: 1) gestational hypertension, defined as the onset of hypertension (blood pressure $\geq 140/90$ mmHg) after 20 weeks of gestation in previously normotensive women; 2) preeclampsia or eclampsia, diagnosed when hypertension and significant proteinuria develop after the 20th gestational week; 3) preeclampsia superimposed on chronic hypertension, diagnosed as a worsening of hypertension after 20 weeks and with the new development of proteinuria or end organ dysfunction; and 4) chronic hypertension, existing prior to conception or diagnosed before the 20th week of pregnancy (4).

We included studies that met the following criteria: (i) studies examining the incidence of HDP in pregnant women who were exposed to cold/heat temperature before or during pregnancy, as compared to a reference temperature; (ii) cohort study or case control study designs; (iii) studies published in English across all countries; (iv) no restrictions on the published date; and (v) studies that had sufficient information to estimate the outcome. We excluded studies (i) on heat sources such as saunas and hot baths; (ii) systematic reviews, meeting abstracts, letters, editorials, comments, guidelines, and case reports; and (iii) studies that were duplicates or without the adequate outcome measures that we included.

Among all studies that met the inclusion criteria, those that reported effect estimates and could be combined into effect sizes were included in the meta-analysis.

Extracting data, collating, summarizing, and reporting results

Eligible articles were extracted independently in duplicate by two reviewers (YX M and YZ), and all discrepancies were reconciled by the third reviewer (TX). The following data were extracted: authors, year of publication, year(s) of study, study design, countries, sample size, subtypes and definition of HDP. The results were organized into a table that summarized the data, and the table was used to describe the temperature source and measurements, adjusted factors, outcome estimates, and other settings. We did not extract data regarding the impacts of humidity, air pollution or race/ethnicity.

This review presents the primary findings with a summary (14 of 15 studies on temperature exposure and HDP had a significant association). In addition, tables and figures were constructed in order to show the correlation between HDP and a heat or cold temperature during the pregnancy exposure time window. We attempted to identify the particular critical time window (gestational weeks) that had the largest impacts. These data were tabulated and calculated with an Excel spreadsheet (Microsoft).

Quality of study and publication bias

The quality of the cohort or case – control studies was assessed using the Newcastle – Ottawa Scale (NOS)(28). This scale evaluates the selection of study groups (one star for each term), comparability (up to two stars) and exposure or outcome (one star for each term). A low score indicates a high risk of

bias. The study quality was classified into the following three categories: high quality (scores 7–9), moderate quality (scores 4–6) and low quality (scores 0–3). We planned to use funnel plots to test for the presence of a publication bias, and Egger's linear regression was applied to test for funnel plot asymmetry.

Statistical analysis

The effect estimates were extracted from the tables, figures or published textual descriptions in articles or supplementary materials. For studies that presented effect estimate sizes only in a graph, we extracted the effect estimates and the corresponding 95% CI associated with the reference temperature using the WebPlotDigitizer tool (29). Since studies come from different countries or regions, the standards for extreme and reference temperature are quite diverse. According to the included original studies, when extremely hot corresponds to temperatures above the 90th or 95th percentile, and extremely cold corresponds to temperatures below 10th or 5th percentile, the median temperature is used as the reference temperature (22,30,31). When using specific Celsius temperature as the baseline temperature, extreme temperature is defined as an increase or decrease temperature, with the baseline temperature itself serving as the reference temperature (22,25,26). Therefore, the studies of different outcome groups would be quantitatively pooled by following two types of temperature comparisons: "heat/cold temperature vs. reference temperature" and "1°C increase/decrease vs. reference temperature – using the following formula: $OR = (OR_x)^{1/x}$, where x is the increment/reduction of temperature (for example, $x = 2^\circ\text{C}$) for which OR_x is stated in the original study (32). " This allowed us to quantitatively pool estimates from different studies.

A random effects model was used in the meta-analysis to calculate the pooled estimates for different temperature exposures. The effect estimate was assessed with odds ratio (OR) and 95% confidence intervals (CI), and the P values less than 0.05 were considered statistically significant. The I^2 statistic was used to quantify the heterogeneity of meta-analysis ($I^2 > 50\%$ is considered substantial heterogeneity) (33). Sensitivity analysis was conducted to test the influence of every study by omitting each estimate. Publication bias was assessed by funnel plot and Egger's tests (34), and estimated the number of studies missing by the TRIM and FILL method (35). Data was performed using the Stata software (17.0 version; Stata Corp, College Station, TX).

Results

The literature selection and study characteristics

There were 11,278 records identified (PRISMA flow-chart, Figure 1). We excluded 3,424 studies before the screening. Among the 7,854 records that were screened, 7,746 studies that did not include the influence of the temperature or season exposure on HDP were excluded, and 38 studies were also excluded for missing data. A total of 70 full-text articles were assessed for eligibility, and 55 were excluded due to missing outcomes ($n = 25$) or missing the ambient temperature as an exposure ($n = 30$). In total, 15 of these met our study criteria. Five articles complied with the inclusion criteria for the meta-analysis after additional selection (22,25,26,30,31).

For the study characteristics (Table 1), 13 of 15 were cohort studies (22,25,27,30,31,36–43), and two were case control studies (26,44). All studies were retrospective in design. A total of 4,481,888 patients were analyzed, with a range of 840 to 2,043,182 women who were analyzed per study. The studies were from 13 countries, eight of which (61.5%) were countries with low or middle incomes (22,27,30,31,37–39,41–43). The temperature exposure data, statistical methods and results of the included studies were summarized in Table 2. Eight articles had adjusted for demographic or meteorological variables (maternal age, preexisting diabetes, parity, socioeconomic deprivation, humidity and air pollution) (22,25,26,30,31,39,40,44). Most of the studies (60.0%) found that the temperature (heat or cold exposure was included) was associated with the risk of preeclampsia or eclampsia (9 studies) (25–27,31,38–40,42,43), whereas a few studies showed significant differences between the other subtypes of HDP (22,30).

According to the NOS, the overall methodological quality was good because all of the studies were of high quality, and an additional file shows this in more detail (Supplementary file 1). The NOS quality assessment ranged from 7 to 9 ($\bar{x} = 8.07$). Seven articles (score of 7) had points that were detected because their adjusted factors were unclear (27,36–38,41–43).

Heat exposure and the HDP subgroups in the different trimesters of pregnancy

Fourteen studies analyzed heat exposure and the risk of HDP development (Figure 2) (22,25–27,30,31,36–43). For preeclampsia or eclampsia, there is no significant association during p12 (12 weeks before conception) of pregnancy (22). Heat exposure increased

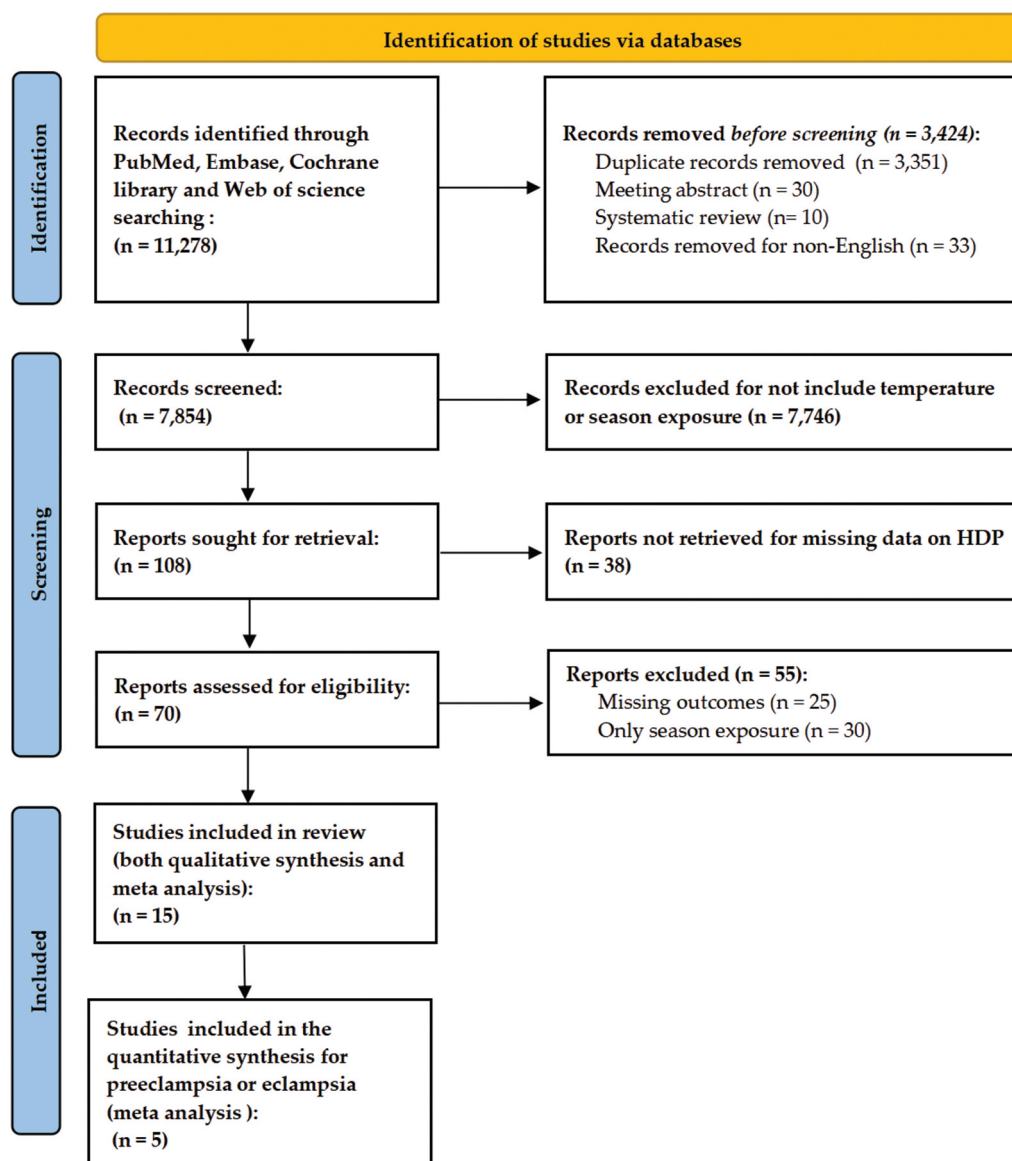


Figure 1. PRISMA flow diagram: preferred reporting items for systematic reviews and meta-analyses.

the risk during w1–20 (the first half of pregnancy) (22,25–27,30,31,39). Four studies had eligible data for conducting meta-analysis (Table 3) (22,25,26,30). The pooled estimate was 1.54 (95% CI 1.10–2.15) (Figure 3(a)). When the studies reported the risk for every 1°C increase, the pooled estimate was 1.07 (95% CI 1.02–1.12) (Figure 3(b)). After 20 weeks of gestation, there was no consistent conclusion: seven studies found that heat exposure decreased the risk (26,30,31,40–43), two studies showed the opposite conclusion (heat exposure increased the risk) (25,38), and one study found no association (27). The pooled estimate from four studies was 1.05 (95% CI 0.67–1.64) (Figure 3(c)) (25,26,30,31). Every 1°C increase, the OR was 1.01 (95% CI 0.96–1.06) (Figure 3(d)).

In addition, heat exposure decreased the risk of gestational hypertension during p12 and increased the risk of gestational hypertension during w1–20 (22). For superimposed preeclampsia or HDP excluding preeclampsia or eclampsia no significant association was observed throughout the pregnancy (22,30).

However, three studies that combined the different subgroups of HDP found inconsistent conclusions between heat exposure and HDP (36,37,41).

Cold exposure and the HDP subgroups in the different trimesters of pregnancy

The association between cold exposure during pregnancy and HDP was reported in all 15 studies

Table 1. Characteristics of the included studies on ambient temperature and HDP.

Author	Country	Study design	Year(s) of study	Subgroup(s) of HDP	HDP (n)	Total women(n)	Definition of HDP	NOS score
2022 Chérie (30)	South Africa	Retrospective cohort	2017–2018	HDP excluding preeclampsia or eclampsia	432	7,986	ACOG	9
2022 Zhao (31)	China	Retrospective cohort	2016–2017	Preeclampsia or eclampsia	412	1,213	The codes of ICD 10	9
2020 Xiong (22)	China	Retrospective cohort	2013–2016	Gestational hypertension	23,704	2,043,182	ACOG, without other recorded obstetric complications or medical complications	9
2020 Shashar (25)	Israel	Retrospective cohort	2004–2013	Preeclampsia	38,166	64,566	The codes of ICD 9	9
2017 Auger (26)	Canada	Case control studies	1989–2012	Preeclampsia	1,940	1,890,711	ISSHP, ICD	9
2014 Nasiri (27)	Iran	Retrospective cohort	2002–2008	Preeclampsia	2,617	20,332	ACOG	7
2014 Morikawa (36)	Japan	Retrospective cohort	2005–2009	HDP	262	301,510	ACOG	7
2014 Melo (37)	Brazil	Retrospective cohort	2000–2006	HDP	13,848	20,125	ACOG	7
2014 Kausar (38)	Pakistan	Retrospective cohort	2008–2012	Eclampsia	5,051	31,331	ACOG	7
2008 Tam (39)	China	Retrospective cohort	1995–2002	Preeclampsia	579	15,402	ISSHP, singleton primiparous pregnancies with preeclampsia	9
2008 Imminki (40)	Netherlands	Retrospective cohort	2002–2003	Preeclampsia	245	11,585	ISSHP, The preeclampsia, eclampsia and HELLP syndrome patients together were called the pre-eclampsia group.	9
1999 Makhseed (41)	Kuwait	Retrospective cohort	1992–1994	HDP and Preeclampsia	1,329	28,262	ACOG	7
1993 Neela (42)	India	Retrospective cohort	1987–1988	Eclampsia	1,457	7,374	Unclear	7
1992 Bergström (43)	Mozambique	Retrospective cohort	1984	Eclampsia	126	37,469	Unclear	7
1988 Alderman (44)	USA	Case control studies	1980–1982	Eclampsia	70	840	Unclear, singleton pregnancies with eclampsia	9

Abbreviations: HDP: Hypertensive Disorders in Pregnancy; NOS: Newcastle-Ottawa Scale; ACOG: American College of Obstetricians and Gynecologists; ISSHP: International Society for the Study of Hypertension in Pregnancy; ICD: International Classification and Disease.

(Figure 4) (22,25–27,30,31,36–44). For preeclampsia or eclampsia, cold exposure increased the risk during preconception (22), whereas it decreased the risk during w1–20 (22,25–27,39). We conducted a meta-analysis on four studies with eligible data during w1–20 (Table 3) (22,25,26,30). The pooled effect of cold exposure was 0.90 (95% CI 0.84–0.97) (Figure 5(a)). For every 1°C decrease, the pooled estimate was 0.99 (95% CI 0.98–1.00) (Figure 5(b)). After 20 weeks of gestation, there was no consistent conclusion. Seven studies reported that cold exposure increased the risk (26,30,31,40–43), two studies found that cold exposure decreased the incidence of preeclampsia or eclampsia (25,38), and the remaining two articles found that there was no association (27,44). The pooled effect of cold exposure was 1.13 (95% CI 0.84–1.53) (Figure 5(c)). For every 1°C decrease, the pooled estimate was 1.02 (95% CI 0.98–1.05) (Figure 5(d)) (25,26,30,31).

Cold exposure also increased the risk of gestational hypertension during preconception and decreased the risk during w1–20 (22). No significant association was observed between cold exposure and superimposed preeclampsia (22). For HDP excluding preeclampsia or eclampsia, cold exposure increased the risk after 20 weeks of gestation, no significant association was observed during w1–20 (30).

The studies that combined the different subgroups of HDP had inconsistent conclusions for the association between cold exposure and HDP (36,37,41).

Sensitivity analyses and publication bias diagnostics

Sensitivity analyses showed that excluding any study did not change the overall estimates for temperature exposure, indicating that the results were robust (Supplementary file 2). Next, we evaluated the possibility of publication bias. The funnel plot was roughly symmetrical (Supplementary file 3) and Egger test (heat exposure: $p = 0.187$; cold exposure: $p = 0.319$) showed no evidence of publication bias in the association of heat or cold exposure with preeclampsia or eclampsia.

Discussion

In this review, 15 studies involving more than 4 million patients from diverse countries appeared to support the significant association of temperature exposure with HDP (Table 1). Most of the studies found a statistically significant risk of HDP after heat or cold temperature exposure (Table 2).

Table 2. Summary of temperature exposure data, statistical methods and results.

Author	Temperature Source	Measurement	Exposure time window	Method	Adjusted factors	HDP and subgroups	Outcome		
							Category	Extreme temperature	Mean temperature
2022 Chéité (30)*	Johannesburg, South Africa	Weekly mean temperature (cold and heat temperatures were defined as the 5th and 95th percentiles of daily mean temperature.	(1) early pregnancy (2–5 weeks' gestation)	Cox proportional hazards regression analyses	season of birth, maternal age, ethnicity (PHI model only), parity, gravidity, and HIV status.	HDP excluding preeclampsia or eclampsia	early pregnancy HR(95%CI) Heat 1.36 (0.84–2.19) Cold 1.01 (0.60–69)		None
			(2) Late pregnancy(29 weeks after conception)				Late pregnancy Heat 1.00 (0.77–1.29) Cold 1.86 (1.36–2.53)		Early pregnancy: Cold exposure had no association. Late pregnancy: Cold exposure increased risk. Heat exposure had no association at any time during gestation.
2022 Zhao (31)*	Nanjing, China	(1) Daily minimum and maximum temperatures a. very cold(10th percentile) b. cold (25th percentile) c. hot(75th percentile) d. very heat (90th percentile) 2. Daily mean temperatures	after 20 w time of delivery)	The distributed lag nonlinear model (DLNM)	relative humidity, SO ₂ ,NO ₂ , CO, O ₃ , PM10 and PM2.5	Preeclampsia or eclampsia	early pregnancy HR(95%CI) Heat 1.79 (1.19–2.71) Cold 1.18 (0.70–1.95) Late pregnancy Heat 0.86 (0.70–1.04) Cold 1.52 (1.13–2.04) after 20 w RR(95%CI) Very cold 1.65 (1.07–2.54) Cold 1.55 (1.10–2.19) Heat 0.64 (0.48–0.87) Very heat 0.64 (0.44–0.94)	RR(95%CI) 1.73 (1.06–2.83) 1.62 (1.14–2.29) 0.68 (0.50–0.91) 0.64 (0.43–0.97)	Early pregnancy: Heat temperature increased risk, cold exposure had no association Late pregnancy: Heat exposure decreased risk and cold temperature increased risk. after 20 w: Heat exposure decreased the risk, cold exposure increased the risk.
2020 Xiong (22)*	Chinese mainland, at the county level,	1.extreme temperatures a. very cold(<5th percentile) b. moderate cold (5th –10th percentile) c. moderate heat(90th – 95th percentile) d. very heat (>95th percentile) 2. Weekly mean temperature (°C) a. very cold (–17.2°C) b. Very heat (29.5°C)	1p12 (12 weeks before conception) 2.w1–20 (20 weeks after conception)	1.extreme temperatures: a logistic regression; 2.average temperature (weekly); pooled cumulative exposure-response curves	region, hospital level, number of antenatal visits, maternal education, marital status, maternal age, parity, number of fetuses, elevation, humidity, and air pollution exposure.	Gestational hypertension	p12 Very cold Moderate cold Moderate heat Very heat w1–20 Very cold Moderate cold Moderate heat Very heat p12 Very cold Moderate cold Moderate heat Very heat	OR (95%CI) 1.28 (1.14–1.43) 1.06 (0.97–1.16) 0.88 (0.81–0.95) 0.91 (0.83–0.98) 0.87 (0.80–0.94) 0.80 (0.75–0.87) 1.19 (1.12–1.28) 1.10 (1.03–1.17)	aOR (95%CI) 1.86 (1.62–2.14)– 0.79 (0.74–0.85) 0.53 (0.44–0.62)– 1.29 (1.21–1.38) w1–20: Heat exposure increased the risk of preeclampsia or eclampsia and gestational hypertension. w1–20: Heat exposure increased the risk of preeclampsia or eclampsia and gestational hypertension, and it was opposite in cold exposure. No significant association was observed between temperature and superimposed preeclampsia
						Preeclampsia or eclampsia	OR (95%CI) 1.22 (1.12–1.32) 0.98 (0.91–1.05) 0.94 (0.88–1.01) 0.96 (0.89–1.02) 0.89 (0.84–0.94) 0.86 (0.81–0.92) 1.13 (1.07–1.19) 1.16 (1.11–1.22)	aOR (95%CI) 1.44 (1.29–1.61)– 0.91 (0.86–0.96)– 0.61 (0.54–0.69)– 1.23 (1.16–1.30)	
						Superimposed eclampsia	OR (95%CI) 0.86 (0.62–1.20) 0.85 (0.60–1.21) 1.06 (0.83–1.37) 1.01 (0.78–1.32) 1.20 (0.89–1.60) 1.25 (0.95–1.65) 0.98 (0.80–1.25) 1.00 (0.77–1.31)	aOR (95%CI) 1.26 (0.68–2.33)– 1.03 (0.77–1.37) 1.14 (0.56–2.32)– 0.93 (0.68–1.28)	

(Continued)

Table 2. (Continued).

Author	Temperature Source	Measurement	Exposure time window	Method	Adjusted factors	HDP and subgroups	Outcome		
							Category	Extreme temperature	Mean temperature
2020 Shashar (25)	Southern Israel	Daily mean temperature (°C) a. heat ($\geq 25^{\circ}\text{C}$) b. cold ($\leq 25^{\circ}\text{C}$)	1.w1–12 (first trimester)	generalized estimating equation (GEE)	maternal age, gravidity, multiple pregnancies and a history of preeclampsia in past deliveries	Preeclampsia, Bdoun-Arab ethnicity	w1–12 heat	RR (95%CI) 2.91 (1.98–4.28)	None
			2.w13–24 (second trimester) 3.After 24 w (third trimester)	Poisson multivariable regression models			w13–24 heat cold after 24 w heat cold	0.88 (0.49–0.94) 0.83 (0.60–1.15) 0.90 (0.73–1.13) 2.37 (1.75–3.20) 0.62 (0.44–0.87)	w1–12 and after 24 w: Heat exposure increased risk. w1–12 and after 24 w: Cold exposure decrease the risk. w13–24: No significant association was observed.
2017 Auger (26)*	Quebec from Environment Canada.	Monthly mean temperature (°C) a.Heat (20°C) b.Cold (–15°C)	1.w1–4 (4-week exposure window after conception)	log-binomial regression models	maternal age, preexisting diabetes, parity, socio-economic deprivation, place of residence, period and humidity	Preeclampsia, Jewish ethnicity	w1–12 heat cold w13–24 heat cold after 24 w heat cold	RR (95%CI) 2.38 (1.50–3.80) 1.01 (0.69–1.47) 0.90 (0.61–1.33) 1.22 (0.96–1.57) 1.94(1.34–2.81) 0.89 (0.60–1.34)	None
			2.After 27 w (4-week exposure window before delivery)				w1–4 Heat Cold After 27 w Heat Cold	RR (95%CI) 1.08 (1.06–1.11) 0.97 (0.93–1.01) 0.85 (0.82–0.88) 1.01 (0.96–1.03)	w1–4: Heat exposure increased the risk and cold exposure decreased the risk. after 27 weeks: It was opposite.
2014 Nasiri (27)	Iran	Monthly mean temperature (°C)	1. w1–4 (time of conception) 2.After 20 w (time of delivery)	Duncan's test, Multivariable logistic regression	unclear	Preeclampsia	w1–4	None	$p=0.0001$ (regression line inclination: 0.071 ± 0.01) w1–4: Heat exposure increased the risk and cold exposure decreased the risk. after 20 w: No significant relationship.
2014 Morikawa (36)	Tokyo	Monthly mean temperature (°C)	1. w1–4 (time of conception) 2.After 22 w (time of delivery)	Bonferroni's method, t-test	unclear	HDP	w1–4 after 22 w	No significant relationship the incidence of HDP was lowest in hot temperature ($p<0.05$)	None
2014 Melo (37)	Recife, Brazil	Monthly mean temperature (°C)	after 20 w (time of delivery)	Pearson's correlation coefficient	unclear	HDP	after 20 w	None	$p=0.046$ ($r = -0.26$) Heat exposure decreased the risk, cold exposure increased the risk.
2014 Kausar (38)	Pakistan	Monthly maximum temperature (°C)	after 20 w (time of delivery)	Pearson's correlation coefficient	unclear	Eclampsia	after 20 w	$p<0.05$ ($r = 0.516$)s	Heat exposure increased the risk, cold exposure decreased the risk.
2008 Tam (39)	Eastern New Territories, Hong Kong	Mean heat index (°F); the daily maximum temperature; the lowest heat index: the temperature $<57^{\circ}\text{F}$	w1–4 (time of conception)	The cross-correlation function	maternal age and fetal sex	Preeclampsia	w1–4	OR (95%CI): 2.80 (1.50–5.20)	Heat exposure increased the risk, cold exposure was an decreased risk.

(Continued)

Table 2. (Continued).

Author	Temperature Source	Measurement	Exposure time window	Method	Adjusted factors	Outcome				
						HDP and subgroups	Category	Mean temperature		
2008 Imminiki (40)	South African	Monthly minimum temperature (°C)	after 20 w (time of delivery)	logistic regressions, Wald-test statistic	maternal age, parity and fetal sex	Preeclampsia or eclampsia	after 20 w	OR (95%CI) 1.00 (referent) 0.90 (0.76–1.07) 8.5 to 10.5 0.96 (0.81–1.14) 10.5 to 10.5 0.90 (0.71°C1.12) 0.62 (0.53–0.72) to12.5 12.5to 14.5 14.5 to16.5	None	Heat exposure decreased the risk, cold exposure increased the risk.
1999 Makhseed (41)	Kuwait	Monthly mean Temperature (°C)	after 20 w (time of delivery)	Pearson correlation and linear regression	unclear	HDP	after 20 w	None	Incidence (95%CI) 0.46% (0.43–0.49) 0.36% (0.34–0.39)	For HDP, heat exposure increased the risk, cold exposure decreased the risk. It was reverse for preeclampsia.
						Preeclampsia	Hot Cold after 20 w	None	Incidence (95%CI) 0.32% (0.29–0.36) 0.41% (0.37–0.45)	
1993 Neela (42)	India	Monthly mean temperature (°C)	after 20 w (time of delivery)	linear regression	unclear	Eclampsia	after 20 w	None	p<0.01 (r = –0.77)	Heat exposure decreased the risk, cold exposure increased the risk.
1992 Bergström (43)	Maputo	Monthly mean temperature (°C)	after 20 w (time of delivery)	Linear regression analysis, t-test	unclear	Eclampsia	after 20 w	None	p<0.005(r = –0.78)	Heat exposure decreased the risk, cold exposure increased the risk.
1988 Alderman (44)	Washington	Daily mean temperature (°C, cold temperature)	after 20 w (time of delivery)	Straatification and Mantel-Haenszel adjustment	maternal age, parity, race, and month antenatal care	Eclampsia	after 20 w	None	OR (95%CI) 1.00(referent) 1.20(0.70–2.00) 0.80(0.50–1.50) 1.00 (0.50–1.70) 1.00 (0.50–1.70) ~10	Cold exposure had no association with eclampsia.

Abbreviations: HDP: Hypertensive Disorders in Pregnancy; CI: confidence interval; OR, odds ratio; RR: risk ratio; HR: hazard ratio. *means that the study made the adjustments for multiple comparisons.

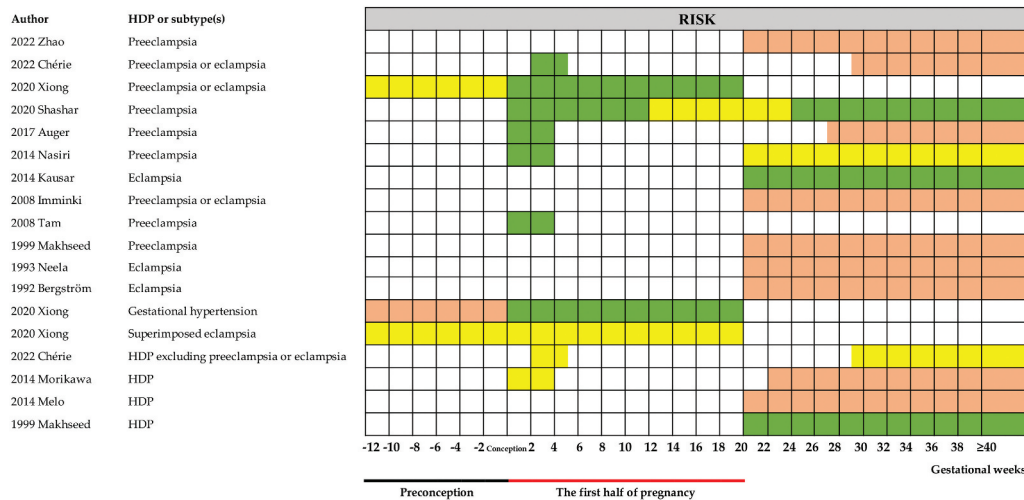


Figure 2. Analysis of the associations between heat exposure and HDP by the gestational weeks of pregnancy. Green shading indicates the period of increased risk during pregnancy after heat exposure. Orange shading indicates the studies that showed a decreased risk. Yellow shading indicates that heat exposure and HDP have no association.

Table 3. Meta-analysis results between extreme temperature exposure and preeclampsia or eclampsia during the gestational weeks.

	No of studies	Average effect size (OR (95% CI))	I ² (%)	T ²	p value
Heat exposure during w1–20 ^a					
Heat exposure vs. reference temperatures	4	1.54 (95% CI 1.10–2.15)	99.33	0.15	0.01
Every 1°C temperature increase	4	1.07 (95% CI 1.02–1.12)	97.20	0.00	0.00
Heat exposure after 20 weeks of gestation					
Heat exposure vs. reference temperatures	4	1.05 (95% CI 0.67–1.64)	96.35	0.29	0.83
Every 1°C temperature increase	4	1.01 (95% CI 0.96–1.06)	94.96	0.00	0.81
Cold exposure during w1–20					
Cold exposure vs. reference temperatures	4	0.90 (95% CI 0.84–0.97)	66.34	0.00	0.01
Every 1°C temperature decrease	4	0.99 (95% CI 0.98–1.00)	86.32	0.00	0.09
Cold exposure after 20 weeks of gestation					
Cold exposure vs. reference temperatures	4	1.13 (95% CI 0.84–1.53)	87.30	0.11	0.43
Every 1°C temperature decrease	4	1.02 (95% CI 0.98–1.05)	87.99	0.00	0.40

^aw-20 means the first half of pregnancy.

Overall, during preconception (p12), cold exposure increases the risk of developing preeclampsia or eclampsia or gestational hypertension, whereas heat exposure decreases the risk of gestational hypertension. In contrast, heat exposure increases the risk of developing preeclampsia or eclampsia or gestational hypertension, and cold exposure decreases the risk of preeclampsia or eclampsia and gestational hypertension during the first half of pregnancy (during w1–20). Meta-analysis of preeclampsia or eclampsia during the first half of pregnancy showed that heat exposure and per 1°C increase caused the higher risk, whereas cold exposure had the lower risk. Interestingly, cold versus heat exposure had opposite effects on preeclampsia or eclampsia and gestational hypertension. Therefore, the effects of extreme temperatures may be bidirectional. Appropriate temperatures may be important to decrease the incidence of preeclampsia or eclampsia and gestational hypertension.

After comparing these risks during preconception with the risks during the first half of pregnancy, the

effect of temperature exposure on preeclampsia or eclampsia and gestational hypertension was opposite in the different time windows (22). Cold exposure increased the risk during preconception, which was consistent with the studies that evaluated blood pressure in the general (non-pregnant) population (45,46). However, during w1–20, heat exposure increased the risk. The explanations are as follows: as the mother gains weight and as the fetus grows, pregnant women decrease their capacity for heat loss and increase their internal heat production (47). Thus, heat exposure, which could disturb thermoregulation, induces the activation of the sympathetic nervous system and increases the risk of preeclampsia or eclampsia and gestational hypertension. Future studies need to further define the exact mechanism and confirm these effects.

We found that there was no consistent conclusion for extreme temperature and HDP after 20 weeks of gestation, this may due to different adjusted factors in

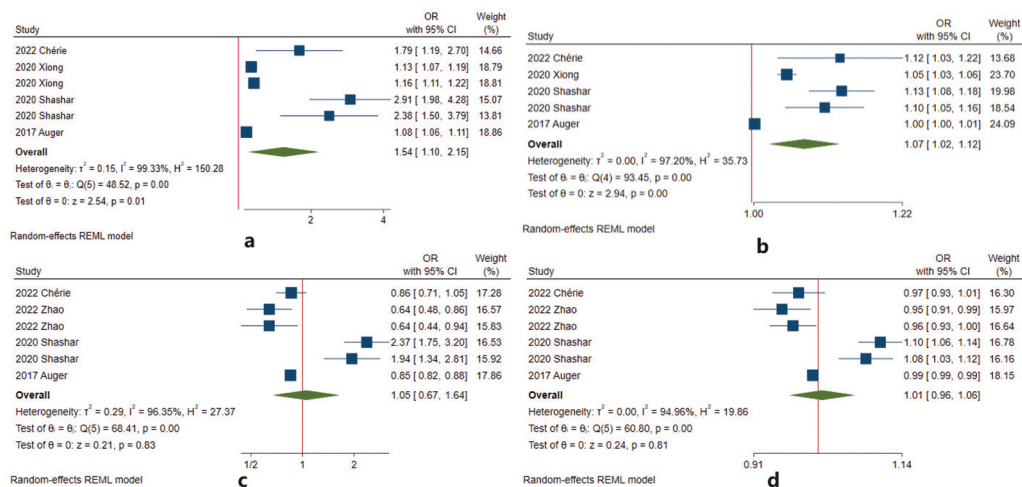


Figure 3. Meta-analysis of the associations between heat exposure and preeclampsia or eclampsia by the gestational weeks of pregnancy. (a) heat temperature during w1–20 vs. reference temperature; (b) 1°C increase during w1–20 vs. reference temperature; (c) heat temperature after 20 weeks of gestation vs. reference temperature; (d) 1°C increase during after 20 weeks of gestation vs. reference temperature.

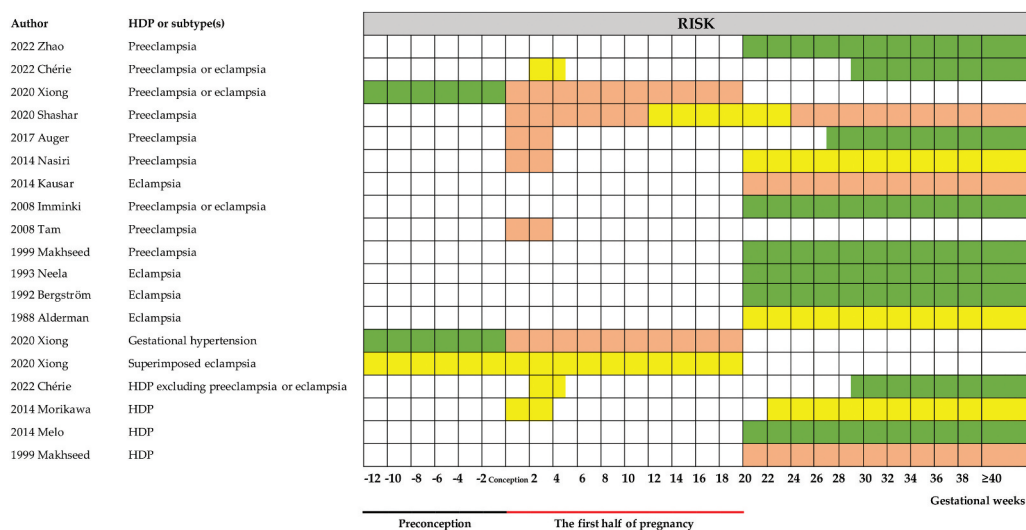


Figure 4. Analysis of the associations between cold exposure and HDP by the gestational weeks of pregnancy. Green shading indicates the period of increased risk during pregnancy after cold exposure. Orange shading indicates the studies that showed a decreased risk. Yellow shading indicates that the temperature and HDP have no association.

individual studies. The interaction among meteorological factors may affect the results of the study. Nine studies that were published between 1988 and 2014 detected the influence of meteorological factors on HDP (27,36–38,40–44). These studies did not adjust for other meteorological factors when exploring the impact of temperature exposure on HDP subgroups. Temperature works in concert with other meteorological variables, including air pollution, latitude and sunlight, and can affect people's health (45,46). This may be one of the important reasons for the

heterogeneity of the results in these studies because of the complexity of the interactions between the temperature and other meteorological variables. Three recent studies (2017–2022) explored the association between ambient temperature exposure and subgroups of HDP and considered the other meteorological variables as confounding factors (26,30,31). They drew a consistent conclusion that heat exposure increased the incidence of preeclampsia or eclampsia and cold exposure decreased the risk after 20 weeks of gestation after adjusting for the other meteorological variables.

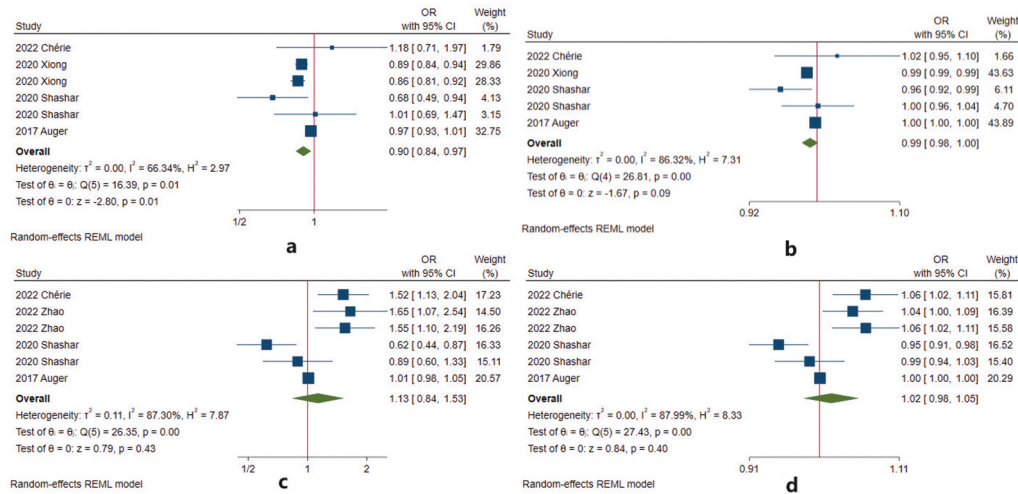


Figure 5. Meta-analysis of the associations between cold exposure and preeclampsia or eclampsia by the gestational weeks of pregnancy. (a) cold temperature during w1–20 vs. reference temperature; (b) 1°C decrease during w1–20 vs. reference temperature; (c) cold temperature after 20 weeks of gestation vs. reference temperature; (d) 1° decrease during after 20 weeks of gestation vs. reference temperature.

Therefore, the associations between ambient temperature exposure (after 20 weeks of gestation) and preeclampsia or eclampsia need to be proven by more studies with appropriate design.

In this review, we found that temperature exposure has unequal effects in different periods of pregnancy. However, all included studies only explored a certain timeframe within the pregnancy rather than the whole pregnancy. Only one study detected the impact of temperature during preconception and found a significant effect (22). In addition, the effects of temperature exposure may be a long-term process rather than a specific short period of time. The critical time window for extreme temperature exposure remains unknown. Therefore, future studies that use multiple temperature exposures (short- and long-term exposure) during the whole pregnancy period may be necessary.

One question should also be raised regarding whether the temperature plays the same role in the different subtypes of HDP. Our previous study detected multiple subtypes of HDP (preeclampsia or eclampsia, gestational hypertension and superimposed preeclampsia) at the same time. The risk of preeclampsia or eclampsia and gestational hypertension was influenced by the ambient temperature, rather than superimposed preeclampsia (22). Two study found that preeclampsia or eclampsia and other subtypes HDP showed different reactions to extreme temperature exposure (30,41). This may be the reason why the studies combining the different subgroups of HDP had inconsistent conclusions (36,37,41). Future studies should address these differences by separately evaluating the influence of temperature with regard to the individual subtype of HDP.

This review has several limitations, which are as follows. First, the conclusion regarding the impact of cold or heat exposure during the preconception period is based on the data from a single study, highlighting the need for more evidence to support this conclusion. Future studies should explore the relationship between temperature and HDP during the preconception period. Similarly, in the first half of the pregnancy, further investigations are necessary as many of the studies included in our analysis had limited coverage, often spanning only a couple of weeks of exposure. A more comprehensive examination of temperature effects in the first half of pregnancy is warranted. Second, we only included English studies, this may cause biased because of the limited number of trials in the existing literature. The exposure measurement standards were not completely uniform in the individual studies, such as the definition of extreme temperature and the time window of the exposure, which may contribute to the heterogeneity. Third, the sensitivity to temperature may be difference in the different subgroups of people. Our previous study found vulnerable subpopulations among mothers who were aged 20–34 years, were highly educated, had singleton births, had low parity, did not have preterm infants, did not have SGA infants, and lived in urban areas (22). Further studies could clarify the susceptibility for extreme temperature in different populations, in order to prevent vulnerable populations from extreme temperature events. Fourth, another temperature variable, indoor temperature, was not evaluated in these studies. The indoor temperatures are affected by the indoor heating system or air conditioning. The effect of indoor temperatures on the risk of HDP should not be ignored, especially under extreme weather

conditions. Evaluating the effect of the indoor temperature should be considered in future studies. Furthermore, the influence of the individual's behavior (the duration outdoors) should be taken into account in future studies to improve the reliability and comparability of the research evidence.

Conclusion

Ambient temperature is an important determinant of HDP, especially for preeclampsia or eclampsia. The effects of extreme temperatures may be bidirectional during the different trimesters of pregnancy. Appropriate ambient temperatures may be important for pregnant women to avoid potential risk of HDP. The study provided hints of temperature regulation in HDP administration, which should be evaluated by future study. Considering the increased incidence of climate extremes and the significant burden of HDP on human health, research and policy in this area is a high priority.

Abbreviations

HDP	Hypertensive Disorders in Pregnancy
NOS	Newcastle-Ottawa Scale
ACOG	American College of Obstetricians and Gynecologists
ISSHP	International Society for the Study of Hypertension in Pregnancy
ICD	International Classification and Disease
CI	confidence interval
OR	odds ratio
RR	risk ratio

Disclosure statement

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Data availability statement

Data sharing is not applicable to this article because there is no new data was created or analyzed.

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