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Heart Connections

Integrating Organ, Environmental, and Mental Health Impacts

Meta-analysis & systematic reviews

- Continuing versus withholding renin angiotensin aldosterone system antagonists before noncardiac surgery: A systematic review and meta-analysis
- The effect of Ambient heat exposure early in pregnancy on the frequency of congenital heart defects: A systematic review and meta-analysis
- The Effect of Inotropes in Patients with Advanced Heart Failure: A Meta-Analysis of Randomized Trials
- Effect of Paracetamol on Blood Pressure: A Systematic Review
- Effects of Heated Tobacco Products compared to Conventional Cigarettes on Cardiovascular System: A Systematic Review
- Efficacy and Safety of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) in Cardiac Amyloidosis: A Systematic Review
- Cardiovascular risk and JAK inhibitor for the treatment of spondyloarthritis: A systematic review
- Long working hours and the risk of ischemic cardiac death: A systematic review and meta-analysis
- Cardiovascular and pulmonary response in Internet gaming disorder: A systematic review
- Cardiac Phenotypes and Endophenotypes in Schizophrenia : A systematic Review
- The Effects of TNF-alpha Inhibitors on Subclinical Atherosclerosis and Endothelial Function in Patients with Psoriatic Arthritis: A Systematic Review

The effect of Ambient heat exposure early in pregnancy on the frequency of congenital heart defects: A systematic review and meta-analysis

Impact de l'exposition à la chaleur ambiante intense en début de grossesse sur la fréquence des cardiopathies congénitales: Revue sysématique et meta-analyse

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Abstract

Introduction: Congenital heart defects (CHD) is the most common birth defect worldwide and is associated with several maternal risk factors, such as obesity, diabetes, smoking, and advanced maternal age, as well as environmental exposures, including heat and air pollution.
This systematic review aimed to evaluate the current evidence regarding the impact of maternal exposure to high ambient temperatures during pregnancy on the incidence of CHD in offspring.
Methods: We included comparative studies that directly assessed the relationship between high-temperature exposure during pregnancy and CHD. A comprehensive search of PubMed, Embase, Scopus, and Google Scholar was conducted on 11 December 2024.
All eligible studies were assessed for methodological quality using the MINORS scale, and the risk of bias was evaluated using the Newcastle-Ottawa Scale. Study selection, data extraction, and risk of bias assessment were independently performed by two reviewers.
The odds ratio (OR) was selected as the effect measure. A meta-analysis was conducted using Comprehensive Meta-Analysis Software (version 4), employing random-effects models to calculate pooled ORs with 95% confidence intervals (CIs).
Results: A total of 874 records were identified, and 14 studies were included in the final analysis. These included eight case-control and six cohort studies, predominantly conducted in the United States (n = 5) and China (n = 5). The meta-analysis revealed a statistically significant association between prenatal heat exposure and CHD, with a pooled OR of 1.079 (95% CI: 1.005–1.159). The 95% prediction interval ranged from 0.849 to 1.372. Subgroup analyses revealed a statistically significant association between heat exposure and CHD occurrence in cohort studies (pooled OR: 1.141; 95% CI: 1.005–1.296), whereas no significant association was found in case-control studies (pooled OR: 1.039; 95% CI: 0.934–1.156). Similarly, analysis based on exposure context showed a significant association in the ambient heat exposure subgroup (pooled OR: 1.080; 95% CI: 1.005–1.161), but not in the occasional exposure subgroup (pooled OR: 1.039; 95% CI: 0.634–1.700)
Conclusion: This systematic review and meta-analysis provide evidence that maternal exposure to high ambient temperatures during pregnancy may be associated with an increased risk of CHD in offspring. These findings highlight the importance of integrating counseling on climate-related health risks into both prenatal care and public health policy.
PROSPERO registration number: CRD42024584967

Key words: Hot Temperature, Extreme Heat, Pregnancy, Maternal Exposure, Congenital Abnormalities, Congenital Heart Defects, Meta-analysis, Risk Factors

Résumé

Introduction : Les cardiopathies congénitales (CC) sont les malformations congénitales les plus fréquentes dans le monde. Elles sont associées à plusieurs facteurs de risque maternels, tels que l'obésité, le diabète, le tabagisme et l'âge maternel avancé, ainsi qu'à des expositions environnementales comme la chaleur et la pollution atmosphérique.
Cette revue systématique visait à évaluer les données disponibles concernant l'impact de l'exposition maternelle à des températures ambiantes élevées pendant la grossesse sur l'incidence des CC chez les enfants.
Méthodes : Nous avons inclus des études comparatives évaluant directement la relation entre l'exposition à des températures élevées pendant la grossesse et les CC. Une recherche exhaustive a été réalisée dans PubMed, Embase, Scopus et Google Scholar le 11 décembre 2024.
Toutes les études éligibles ont été évaluées quant à leur qualité méthodologique à l'aide de l'échelle MINORS, et le risque de biais a été estimé à l'aide de l'échelle Newcastle-Ottawa.
La sélection des études, l'extraction des données et l'évaluation du biais ont été réalisées indépendamment par deux évaluateurs.
L'odds ratio (OR) a été utilisé comme mesure d'effet. Une méta-analyse a été effectuée avec le logiciel Comprehensive Meta-Analysis (version 4) en utilisant des modèles à effets aléatoires pour calculer les OR combinés avec des intervalles de confiance (IC) à 95 %.

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Résultats : Un total de 874 publications ont été identifiées, et 14 études ont été incluses dans l'analyse finale. Celles-ci comprenaient huit études cas-témoins et six études de cohorte, menées principalement aux États-Unis (n = 5) et en Chine (n = 5).
La méta-analyse a révélé une association statistiquement significative entre l'exposition à la chaleur pendant la grossesse et les CC, avec un OR combiné de 1,079 (IC à 95 % : 1,005–1,159). L'intervalle de prédiction à 95 % variait entre 0,849 et 1,372.
Les analyses en sous-groupes ont montré une association significative dans les études de cohorte (OR combiné = 1,141 ; IC à 95 % : 1,005–1,296), et non pas dans les études cas-témoins (OR combiné = 1,039 ; IC à 95 % : 0,934–1,156). L'analyse en sous-groupes basée sur le contexte d'exposition a démontré une association statistiquement significative entre l'exposition à la chaleur et la survenue de cardiopathies congénitales dans le sous-groupe d'exposition à la chaleur ambiante (OR combiné : 1,080 ; IC à 95 % : 1,005–1,161), contrairement au sous groupe d'exposition occasionnelle (OR combiné : 1,039 ; IC à 95 % : 0,634–1,700).
Conclusion : Cette revue systématique et méta-analyse fournit des preuves suggérant que l'exposition maternelle à des températures ambiantes élevées pendant la grossesse pourrait être associée à un risque accru de cardiopathies congénitales chez les nouveau-nés. Ces résultats soulignent l'importance de prodiguer des conseils sur les risques de l'exposition à la chaleur dès le début de la grossesse.
Numéro d'enregistrement PROSPERO : CRD42024584967

Mots clés: Température élevée, chaleur extrême, grossesse, exposition maternelle, anomalies congénitales, malformations cardiaques congénitales, Méta-analyse, Facteurs de risque

Introduction

Congenital heart defects (CHD) is the most common birth defect worldwide, with a global prevalence of 8.22 per 1,000 live births[1].
CHDs are particularly serious due to their unpredictable prognosis. They range from mild forms that may resolve spontaneously without treatment to severe cases that can indicate the termination of a pregnancy or require complex, multidisciplinary postnatal care.
Prevention of CHD requires the identification of risk factors, particularly modifiable ones, to help reduce its prevalence.
A recently published meta-analysis provided strong evidence for an increased risk of CHD associated with maternal obesity, diabetes, smoking, advanced maternal age, increased nuchal translucency, extracardiac anomalies, and a family history of CHD[2,3].
Various original studies have also suggested an association between environmental factors, such as heat exposure, and an increased risk of CHD[4–7]. Experimental research has demonstrated the physiological mechanisms by which elevated temperatures can disrupt foetal organ development and potentially lead to birth defects such as CHD[8,9].
In the context of ongoing climate change driven by global warming, which is increasing the frequency, duration, and severity of extreme heat events, the potential association between prenatal exposure to extreme heat and CHD is becoming increasingly relevant.
The primary question is: How does exposure to high ambient temperatures during pregnancy, particularly during the first trimester, affect the incidence of CHD in offspring, compared to no exposure or exposure to temperatures considered normal for the region?
This systematic review aimed to evaluate the current body of evidence regarding the impact of maternal exposure to high temperatures during pregnancy on the incidence of CHD in offspring.

Methods

Study Protocol

The study protocol was developed according to PRISMA P guidelines [10] and subsequently registered in the PROSPERO database (CRD42024584967). A detailed study protocol was published separately in a previous publication[11].

Eligibility Criteria

We included comparative study, that directly evaluated the relationship between high-temperature exposure during pregnancy and CHD, published in English or French. We included any exposure to high external temperatures during the first trimester of pregnancy, regardless of its definition used (intensity, duration) or context (season, regional heat waves, saunas, hot baths, working in high temperature…). We excluded both experimental or modelling studies and those examining the association between maternal fever and CHD in humans.

Information sources and Search strategy

We searched PubMed, Embase, Scopus, and Google Scholar using validated algorithms. A thorough review of the reference lists of all included studies, as well as those of relevant systematic reviews on the same topic, was conducted to ensure comprehensive coverage of the literature. Additionally, we searched for grey literature, such as theses and conference abstracts, to minimise the risk of publication bias. Full search strategies are detailed in the published protocol[11]. Searches were conducted on 11 December 2024.

Study Selection

All records from the combined searches were imported into Zotero for duplicate removal. We then used Covidence to facilitate blinded study selection: two reviewers (MB, EBH) independently screened titles and abstracts of all retrieved publications for inclusion, followed by independent full-text review to determine eligibility. Any discrepancies were resolved through discussion between the two reviewers or, if needed, by consultation with a third reviewer (IA). Full details of the search results and study selection process are documented in a PRISMA flow diagram.

Data Extraction

All articles meeting the eligibility criteria were independently reviewed by two investigators for final data extraction. Any discrepancies between reviewers were resolved through discussion, or by consulting a third author when necessary.
The extracted data included: first author's name, year of publication, article title, journal, country, exposure definition, exposure period, total sample size, outcomes (including all types of CHD), effect size, and corresponding measure of variability (e.g., confidence intervals).
In cases of missing data, the reviewers consulted supplementary materials of the included studies or contacted the corresponding authors via email. If the required data could not be obtained, the team discussed the possibility of excluding the study from the analysis

Classification of Maternal Heat Exposure

We categorized maternal heat exposure into four distinct types, based on the source and temporal characteristics of the temperature data:
1. Ambient Temperature Exposure (Continuous): Defined as daily ambient temperature, typically derived from local meteorological stations. This category includes studies reporting the change in outcome frequency (e.g., CHD incidence) per 1 °C increase in temperature.
2. Extreme Heat Events (EHE) : This category includes studies that defined high-temperature exposure based on a cutoff value during the exposure. Thresholds were based on temperature percentiles within the study region (e.g., >90th or >95th percentile), or set as absolute values (e.g., ≥30 °C), considered extreme by the study authors or regional standards.
If studies reported estimates for multiple EHE thresholds, we prioritized those using the 95th percentile. Exposure was considered present if temperature exceeded the defined threshold on at least one day during the relevant exposure window.
3. Heatwaves (Prolonged Exposure) : Defined as two or more consecutive days where temperatures exceeded a predefined threshold, either: Relative thresholds (e.g., ≥90th or 95th percentile of local daily temperatures), or Absolute thresholds (e.g., >30 °C for ≥3 consecutive days).
4. Artificial or Occupational Heat Exposure : This category includes non-ambient sources of maternal heat exposure, such as Sauna or hot tub use, High-temperature occupational settings (e.g., manufacturing, kitchens)

Risk of Bias Assessment

All studies meeting the selection criteria were appraised for methodological quality using the MINORS scale[12]. The risk of bias was assessed using the Newcastle-Ottawa Scale. Two reviewers (MB, EBH) independently assessed the quality and risk of bias in the included studies. Disagreements were resolved either through discussion between the two reviewers or by consulting a third reviewer (IA). we assessed potential publication bias through visual inspection of funnel plots and by conducting Egger's regression test for funnel plot asymmetry. A p-value less than 0.05 was considered indicative of significant small-study effects suggestive of publication bias. These analyses were performed using Comprehensive Meta-Analysis Software (version 4).

Data Synthesis and Statistical Analysis

The odds ratio (OR) was selected to assess the mean effect size evaluating the association between exposure and outcomes. Each estimate is accompanied by its corresponding 95% confidence interval (CI), which reflects the precision and certainty of the mean effect size. ORs were either extracted directly from the included studies or calculated manually based on the number of events in cases and controls, or from outcomes reported in exposed versus non-exposed populations.
The meta-analysis was conducted using Comprehensive Meta-Analysis Software (version 4), with random-effects models employed to calculate pooled odds ratios with 95% confidence intervals. A forest plot was generated to visually represent the pooled effect. Prediction intervals (PI) were used to account for between-study variability. They enable clinical interpretation of heterogeneity by estimating the range within which the true effect size is expected to lie in future studies[13].
A sensitivity analysis was conducted using a leave-one-out meta-analysis to evaluate the robustness of the pooled estimates. To address the heterogeneity, subgroup analyses were performed based on study design, exposure context, and exposure definition.

Results

Study Selection

A total of 874 records were identified through final searches of published and grey literature sources (Figure 1). After removing 270 duplicates, 604 records remained for title and abstract screening. Of these, 21 articles were selected for full-text review to assess eligibility. Following the exclusion of seven articles (detailed in Table S1), 14 studies were included in the final analysis.

Study Characteristics

The included studies comprised eight case control and six cohort designs, predominantly conducted in the United States (n = 5) and China (n = 5). Twelve studies evaluated the association between ambient heat exposure and CHD[4–7,14–21], while Gong et al. and Tikkanen et al. investigated occupational high temperature exposure and sauna bathing, respectively[22,23]. Main study characteristics are detailed in Table 1.

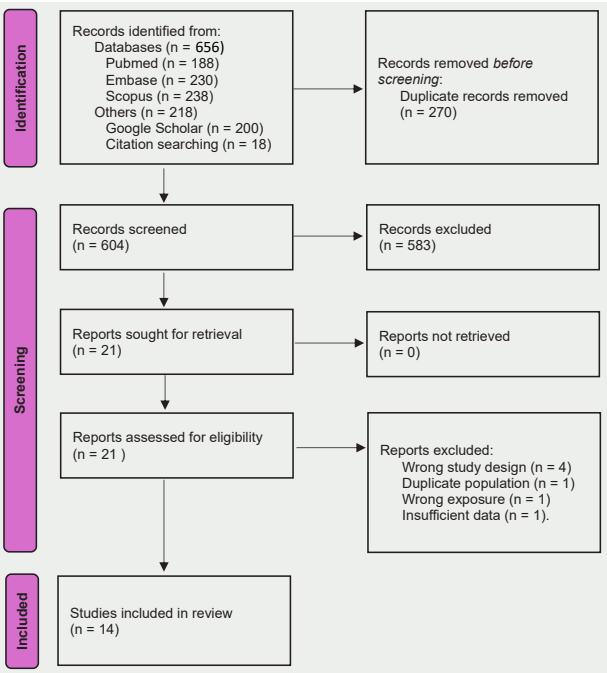

Figure 1. PRISMA Flow Diagram of Study Selection

Risk of Bias

The quality assessment and risk of bias for the included studies are presented in Table 1. The detailed items of the MINORS and NOS scales are presented in Tables S2 and S3. Visual inspection of the funnel plot did not indicate asymmetry (Figure 2), and Egger's test for small-study effects was not statistically significant (p = 0.101), suggesting no evidence of publication bias.

Outcomes

Meta-analysis of the association between CHD and heat exposure during pregnancy across the 14 included studies demonstrated a statistically significant association, with a pooled OR of 1.079 (95% CI: 1.005–1.159), as shown in Figure 3.

Table 1. Main Characteristics of Included Studies

First author, Year	Country	Study period	Study type	Population	Expsoure period	Measure of heat expsoure	NOS	MINORS
Zhang, 2024	China	2013-2018	Case-control	Cases : 643 Controls: 3215	1-12 weeks 13-27 weeks	Daily mean temperature	8	16
Requia, 2024	Brazil	2001-2018	Case-control	11 254 120	1-12 weeks 13-28 weeks	Daily mean temperature	7	16
Xu, 2023	China	2019-2020	Cohort	983 523	All gestational weeks	Daily mean temperature	5	17
Zhang, 2023	United States	2000-2004	Cohort	2 352529	3-12 weeks	Extreme heat (above 95th percentile)	6	18
Jiang, 2021	China	2015-2018	Case-control	Cases :921 Controls:9210	First trimester	Monthly extremely intense heat exposure (maximum temperature above 95th percentile)	8	18
Yu, 2021	China	2015-2019	Cohort	1 918 105	2-8 weeks	Heat waves (≥ 2 consecutives days with maximum temperature above 95th percentile)	6	16
Stingone, 2019	United States	1999-2007	Case-control	Cases :2632 Controls:4033	3-8 weeks	Heat waves (≥ 2 consecutives days with maximum temperature above 95th percentile)	8	16
Lin, 2018	United States	1997-2007	Case-control	Cases :5848 Controls:5742	3-8 weeks	Extreme heat events (maximum temperature above 95th percentile)	8	16
Auger, 2017	Canada	1988-2012	Cohort	704209	2-8 weeks	Extreme heat events: days with maximum temperature ≥30°C	6	18
Gong, 2017	China	NR	Cohort	5381	6monthes before pregnancy—prenatal examination	Working in high temperature	5	13
Agay Shay, 2013	Israel	2000-2006	Cohort	135527	3-8 weeks	Extreme heat events (days with mean temperature above 90th percentile)	7	17
Van Zutphen, 2012	United States	1992-2006	Case-control	Cases :6422 Controls:59328	3-8 weeks	Heat waves (≥ 3 consecutive days with mean temperature above 90th percentile)	8	17
Judge, 2004	United States	1988-1991	Case-control	Cases :502 Controls:1066	2-9 weeks	Extreme heat events: days with maximum temperature > 38°C	8	17
Tikkanen, 1991	Finland	1982-1984	Case-control	Cases :573 Controls:1055	First trimester	Sauna bathing	9	20

NOS: Newcastle-Ottawa Scale; MINORS : methodological index for non-randomized studies

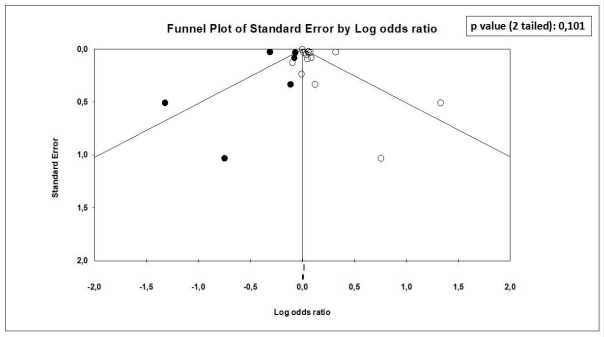

Figure 2. Funnel Plot Assessing Publication Bias

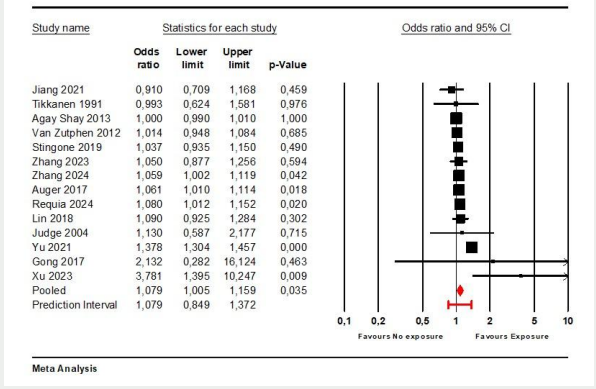

Figure 3. Forest Plot of the association between maternal heat exposure and congenital heart defects

Although heterogeneity was trivial, it should still be acknowledged and explored.

The 95% PI ranged from 0.849 to 1.372, indicating a trivial heterogeneity of the true effect size across different study settings of similar future populations.

To explore the sources of heterogeneity, we performed subgroup analyses based on study design, exposure context, and exposure definition.

Subgroup analysis based on study design (Figure 4) showed a statistically significant association between heat exposure during pregnancy and CHD in the cohort study subgroup (pooled OR = 1.141, 95% CI: 1.005–1.296; PI: 0.842–1.546), but not in the case-control study subgroup (pooled OR = 1.039, 95% CI: 0.934–1.156).

Subgroup analysis based on exposure context demonstrated a statistically significant association between heat exposure and CHD occurrence only in the ambient heat exposure subgroup, with a pooled OR of 1.080 (95% CI: 1.005–1.161) (Figure S1) and a PI ranging from 0.849 to 1.375.

Figures S2 and S3 present forest plots of the subgroup analyses based on exposure definition and country, respectively. These analyses did not show a statistically significant association between heat exposure during pregnancy and the occurrence of CHD.

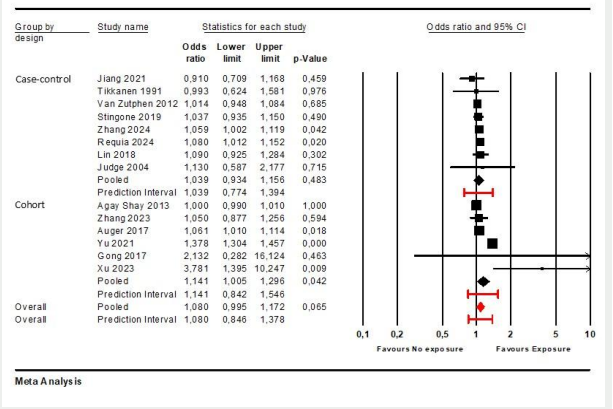

Figure 4. association between heat exposure during pregnancy and congenital heart defects: Subgroup analysis by study design

Discussion

This systematic review and meta-analysis explored the impact of heat exposure during pregnancy on the occurrence of CHD. Our findings indicate that pregnant women exposed to high temperatures had a modest but statistically significant increased risk of CHD in their offspring (pooled OR=1.079; 95% CI: 1.005–1.159). The association was more pronounced in cohort studies and in those focusing on ambient temperature exposure compared to occasional exposure.

While only five individual studies demonstrated a statistically significant association between heat exposure and the occurrence of CHD [4,16,18–20], the pooled effect size in our meta-analysis was statistically significant. Similarly, Krishnakumar et al., in their systematic review and meta-analysis, which had the same objectives but included fewer studies (eight in total) also reported a significant overall estimated effect of extreme heat events on CHD risk, with an OR of 1.12 (95% CI: 1.04–1.34)[24].

The results of this study suggest that external heat exposure can lead to a mild but potentially harmful increase in maternal core temperature. This risk is particularly concerning for pregnant women, who have a reduced thermoregulatory capacity and are therefore more vulnerable to heat stress. Notably, previous studies have established a significant association between maternal hyperthermia and the risk of birth defects[25,26].

Experimental studies suggest that maternal heat exposure, particularly during critical periods of organogenesis, can disrupt embryonic development through multiple biological mechanisms. These include impaired cell proliferation, disruption of gene expression, reduced placental blood flow, oxidative stress, and activation of inflammatory pathways. Consequently, hyperthermia can result in a broad spectrum of structural and functional abnormalities, including CHD and neural tube defects. The risk and severity of these outcomes are closely related to the degree and duration of the temperature elevation[8,9].

Heterogeneity and Subgroup Analyses

The PI ranged from 0.849 to 1.372, suggesting substantial heterogeneity among the included studies. Subgroup analyses were performed to explore and reduce heterogeneity in our study, revealing that between-study variability could be explained by the type of study design and the context of exposure, but not by the definition of exposure or the country in which the study was conducted.

Subgroup analysis revealed a statistically significant association between heat exposure during pregnancy and CHD in cohort studies, but not in case-control studies. This difference may be attributed to the larger population sizes and stronger methodological design of cohort studies, which are less prone to selection and recall bias compared to case-control designs.

Subgroup analysis based on exposure context demonstrated a statistically significant association between heat exposure and CHD occurrence only in the ambient heat exposure subgroup. This finding suggests that ambient temperature exposure, typically estimated using data from meteorological stations, provides a more accurate and objective measure of heat exposure compared to occasional or occupational exposures, which rely on self-reporting and are more prone to recall and measurement bias. Furthermore, these results suggest that prolonged exposure to elevated ambient temperatures may have a greater impact on fetal development than occasional or infrequent exposures.

In the meta-analysis by Krishnakumar et al., stratification by climate zones reduced overall heterogeneity from 91% to 36%, suggesting that climate classification explains a substantial portion of the between-study variability. In contrast, residual heterogeneity remained higher when stratified by exposure type (88%), effect definition (61%), and geographic region (38%). These findings indicate that climate zone may be a more influential source of heterogeneity than other examined factors [24].

Implications for Public Health and Practice

Considering the increasingly prevalent issue of heat exposure, due to global warming, the implementation of effective prevention strategies is both urgent and essential. Such strategies must be implemented at three levels to minimise the frequency and duration of heat exposure experienced by pregnant women.

Firstly, pregnant women should, from the earliest weeks of pregnancy, adopt daily routines that minimize heat exposure on hot days, especially during the spring and summer months.. it is advisable to avoid outdoor exercise during peak heat hours, stay hydrated, use air conditioning when available and avoid hot environments such as crowded public transport or poorly ventilated spaces.

Secondly, sauna bathing or hot tub use should be avoided during the early stages of pregnancy, particularly between weeks 2 and 8 of gestation, even if the evidence is not yet conclusive. This is a simple and precautionary measure.

Thirdly, it is imperative to implement measures that ensure the safety of expectant mothers working in high-temperature environments. Temporary job adjustments or leave during early pregnancy may be appropriate to reduce harmful heat exposure during critical developmental periods. These measures aim not only to reduce the risk of CHD but also to prevent various maternal morbidities and other birth defects (neural tube defects, craniofacial defects…)[28–31].

Strengths of the Review

The present review constitutes the second most recent and largest systematic review to date focusing on the association between CHDs and heat exposure. A significant strength and originality of our work lies in the inclusion of both occasional and occupational heat exposures, which are frequently overlooked in the literature and underestimated in people's daily habits during early pregnancy. Furthermore, subgroup analyses and leave-one-out sensitivity analyses have been employed to enhance the robustness and reliability of the findings.

Limitations

A key limitation of the included studies is that those examining the effects of ambient heat exposure, whether based on daily mean temperature or extreme heat events, did not account for occasional or individual-level heat exposures in their analyses. As a result, factors such as sauna use, occupational heat exposure, or access to air conditioning were not considered, potentially introducing residual confounding. Besides, Large differences in exposure definitions across studies represent a significant source of heterogeneity, which can influence effect estimates and limit the comparability and consistency of findings.

Another important limitation concerns the classification of participants without CHD. In many studies, normal birth examination or routine fetal ultrasound was used to define non-CHD cases, without systematic confirmation by postnatal echocardiography. This represents a risk of misclassification bias, as some CHD, particularly mild or late-presenting lesions, may go undetected in utero, such as small atrial or ventricular septal defects, minor valvular abnormalities, partial anomalous pulmonary venous return, coronary artery anomalies, and aortic coarctation[27].

Eleven of the fourteen included studies were conducted in North American or Chinese populations, which limits the generalisability of the findings to other regions and ethnic groups.

Conclusion

This review provides evidence that exposure of pregnant women to high ambient temperatures may increase the risk of CHD in their offspring. While the effect size is modest, the findings have important implications in the context of ongoing climate change. General and

individual preventive strategies should be implemented to limit the frequency and duration of heat exposure for pregnant women, particularly in the early stages of pregnancy.

References

1. Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019 Apr 1;48(2):455–63.
2. Khalilipalandi S, Lemieux A, Lauzon-Schnittka J, Perreault L, Dubois M, Tousignant A, et al. Systematic Review and Meta-analysis of Prenatal Risk Factors for Congenital Heart Disease: Part 1, Maternal Chronic Diseases and Parental Exposures. Can J Cardiol. 2024 Dec;40(12):2476–95.
3. Lemieux A, Khalilipalandi S, Lauzon-Schnittka J, Taillefer V, Tousignant A, Perreault L, et al. Meta-Analysis of Risk Factors for Congenital Heart Disease: Part 2, Maternal Medication, Reproductive Technologies, and Familial and Fetal Factors. Can J Cardiol. 2024 Dec;40(12):2496–511.
4. Auger N, Fraser WD, Sauve R, Bilodeau-Bertrand M, Kosatsky T. Risk of Congenital Heart Defects after Ambient Heat Exposure Early in Pregnancy. Environ Health Perspect. 2017 Jan;125(1):8–14.
5. Stingone JA, Luben TJ, Sheridan SC, Langlois PH, Shaw GM, Reefhuis J, et al. Associations between fine particulate matter, extreme heat events, and congenital heart defects. Environmental Epidemiology. 2019 Dec;3(6):e071.
6. Judge CM, Chasan-Taber L, Gensburg L, Nasca PC, Marshall EG. Physical exposures during pregnancy and congenital cardiovascular malformations. Paediatric Perinatal Epid. 2004 Sep;18(5):352–60.
7. Jiang W, Liu Z, Ni B, Xie W, Zhou H, Li X. Independent and interactive effects of air pollutants and ambient heat exposure on congenital heart defects. Reproductive Toxicology. 2021 Sep;104:106–13.
8. Edwards MJ. Review: Hyperthermia and fever during pregnancy. Birth Defects Res A Clin Mol Teratol. 2006 Jul;76(7):507–16.
9. Samuels L, Nakstad B, Roos N, Bonell A, Chersich M, Havenith G, et al. Physiological mechanisms of the impact of heat during pregnancy and the clinical implications: review of the evidence from an expert group meeting. Int J Biometeorol. 2022 Aug;66(8):1505–13.
10. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021 Mar 29;372:n160.
11. Benali M, Ayadi I, Jaouhari S, Bouslama M, Hannachi MW, Ben Hamida E. The effect of ambient heat exposure early in pregnancy on the frequency of congenital heart defects: systematic review protocol. Tunis Med. 2025;103(5):553-556.
12. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ J Surg. 2003 Sep;73(9):712–6.
13. Dziri C, Fingerhut A. Up-to-date composition and critical appraisal of meta-analyses of comparative studies. Ann Laparosc Endosc Surg. 2025 Jan;10:4–4.
14. Agay-Shay K, Friger M, Linn S, Peled A, Amitai Y, Peretz C. Ambient temperature and congenital heart defects. Human Reproduction. 2013 Aug 1;28(8):2289–97.
15. Lin S, Lin Z, Ou Y, Soim A, Shrestha S, Lu Y, et al. Maternal ambient heat exposure during early pregnancy in summer and spring and congenital heart defects - A large US population-based, case-control study. Environ Int. 2018 Sep;118:211–21.
16. Requia WJ, Papatheodorou S. Maternal exposure to ambient temperature and birth defects in Brazil: a nationwide case–control study of over 11 million newborns. Int J Biometeorol. 2024 Nov;68(11):2297–305.
17. Van Zutphen AR, Lin S, Fletcher BA, Hwang SA. A Population-Based Case–Control Study of Extreme Summer Temperature and Birth Defects. Environ Health Perspect. 2012 Oct;120(10):1443–9.
18. Xu W, Li D, Shao Z, You Y, Pan F, Lou H, et al. The prenatal weekly temperature exposure and neonatal congenital heart disease: a large population-based observational study in China. Environ Sci Pollut Res. 2022 Dec 29;30(13):38282–91.
19. Yu X, Miao H, Zeng Q, Wu H, Chen Y, Guo P, et al. Associations between ambient heat exposure early in pregnancy and risk of congenital heart defects: a large population-based study. Environ Sci Pollut Res Int. 2022 Jan;29(5):7627–38.
20. Zhang H, Feng Y, Huang J, Zhang F, Zhuo S, Liu H. Identifying the critical windows of temperature extremes exposure and congenital heart diseases. Int J Biometeorol. 2024 Nov;68(11):2399–411.
21. Zhang Y, Sun F, Yuan K, Du Y, Wu L, Ge Y, et al. Ambient temperature and major structural anomalies: A retrospective study of over 2 million newborns. Science of The Total Environment. 2023 Jul;882:163613.
22. Tikkanen J, Heinonen OP. Maternal hyperthermia during pregnancy and cardiovascular malformations in the offspring. Eur J Epidemiol [Internet]. 1991 Nov [cited 2025 Jul 10];7(6). Available from: http://link.springer.com/10.1007/BF00218673
23. Gong W, Liang Q, Zheng D, Zhong R, Wen Y, Wang X. Congenital heart defects of fetus after maternal exposure to organic and inorganic environmental factors: A cohort study. Oncotarget. 2017;8(59):100717–23.
24. Krishnakumar M, Hari A, Gutjahr G, Bendapudi P, Ahamed H, Prabhakaran P, et al. Impact of exposure to extreme heat events during pregnancy on the incidence of congenital heart disease in offspring: a meta-analysis. BMJ Paediatr Open. 2024 Dec 9;8(1):e002848.
25. Shi QY, Zhang JB, Mi YQ, Song Y, Ma J, Zhang YL. Congenital heart defects and maternal fever: systematic review and meta-analysis. J Perinatol. 2014 Sep;34(9):677–82.
26. Yang G, Deng X, Xiao J, Huang P, Zhang K, Li Y. Maternal fever during preconception and conception is associated with congenital heart diseases in offspring: An updated meta-analysis of observational studies. Medicine (Baltimore). 2021 Mar 5;100(9):e24899.
27. Sun HY. Prenatal diagnosis of congenital heart defects: echocardiography. Transl Pediatr. 2021 Aug;10(8):2210–24.
28. Lakhoo DP, Brink N, Radebe L, Craig MH, Pham MD, Haghighi MM, et al. A systematic review and meta-analysis of heat exposure impacts on maternal, fetal and neonatal health. Nat Med. 2025 Feb;31(2):684–94.
29. Jiao A, Sun Y, Avila C, Chiu V, Slezak J, Sacks DA, et al. Analysis of Heat Exposure During Pregnancy and Severe Maternal Morbidity. JAMA Netw Open. 2023 Sep 7;6(9):e2332780.
30. Haghighi M, Wright C, Ayer J, Urban M, Pham M, Boeckmann M, et al. Impacts of High Environmental Temperatures on Congenital Anomalies: A Systematic Review. IJERPH. 2021 May 5;18(9):4910.
31. Bruckner TA, Trinh NTH, Lelong N, Madani K, Slama R, Given J, et al. Climate Change and Congenital Anomalies: A Population-Based Study of the Effect of Prolonged Extreme Heat Exposure on the Risk of Neural Tube Defects in France. Birth Defects Research. 2024 Sep;116(9):e2397.