PREGNANCY: REVIEW

The Association Between Season and Hypertensive Disorders in Pregnancy: a Systematic Review and Meta-analysis

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Received: 21 March 2022 / Accepted: 10 June 2022 / Published online: 28 June 2022
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Abstract
We assessed the association between season and hypertensive disorders in pregnancy (HDPs). The review protocol was registered in PROSPERO (CRD42021285539). Four databases, the Cochrane Library, PubMed, EMBASE, and Web of Science, were searched until September 29th, 2021. Two authors extracted data independently and used the Newcastle–Ottawa quality assessment scale (NOS) to evaluate study quality. A random effects model and the Mantel–Haenszel method were used to calculate pooled Odds ratios (ORs) and 95% confidence intervals (95% CIs). Subgroup analyses and sensitivity analyses were performed to find the source of heterogeneity and Beggs’s funnel plot and Egger’s test were used to check for the risk of publication bias. Finally, twenty articles were included in the systematic review, and 11 articles were included in the meta-analysis. The qualitative analysis of the association between delivery season and HDPs showed that the odds of HDPs was higher in women who delivered in winter than in those who delivered in summer (OR = 1.18, 95% CI 1.02–1.38, \(P<0.001\)) and all other seasons (OR = 1.17, 95% CI 1.03–1.34, \(P<0.001\)). In the qualitative analysis of the association between conception season and HDPs, four of seven studies suggested that women who conceived in summer had a higher risk of HDPs than those who conceived in other seasons. Based on the evidence to date, we found weakly positive relationships between HDPs and summer conception and winter delivery.

Keywords Season · Hypertensive disorders of pregnancy · Meta-analysis · Odds ratios

Background
Hypertensive disorders in pregnancy (HDPs) are a common obstetric disease, occurring in 5–10% of all pregnancies and accounting for 10–16% of total pregnancy-related deaths [1, 2]. HDPs not only have short-term impacts during pregnancy but also long-term impacts on the health of mothers and their offspring, potentially causing maternal coronary heart disease, stroke, and hypertension in offspring [3–5]. At present, the possible etiology of HDPs is still unclear but some risk factors were demonstrated, such as older age, low maternal educational status, and multiple pregnancies [6, 7]. There are more possible factors that lead to HDPs waiting for us to explore.

Seasonal changes affect the occurrence and development of many diseases, such as cardiovascular diseases, multiple sclerosis, and atopic dermatitis [7–9]. Similarly, seasonal changes also increased the risk of maternal and neonatal mortality and the incidence of delivery complications [10]. Some studies have reported that HDPs were associated with season, but their results were inconsistent. Some researchers reported that the prevalence rates of gestational hypertension and preeclampsia were higher in women who delivered in winter and conceived in summer [7, 11]. However, some studies found no association with season [6] or found an opposite result [12].

Therefore, it is important to synthesize such findings to determine which season or month of delivery or conception is related to HDPs and facilitate HDP management and interventions targeting high-risk groups.

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Methods

The Meta-Analysis of Observational Studies in Epidemiology (MOOSE) [13] and Preferred Reporting Items for Systematic review and Meta-Analyses (PRISMA) [14] guidelines were followed for this systematic review and meta-analysis. This study did not require ethical approval or patient consent. This meta-analysis was registered in PROSPERO (CRD42021285539).

Search Strategy

Four databases, the Cochrane Library, PubMed, EMBASE, and Web of Science, were searched until September 29th, 2021, by two independent authors (LL and XW). Medical Subject Headings (MeSH) terms combined with free text were used to identify studies on associations between seasons and HDPs. The detailed search terms of PubMed can be found in Table 1 and appropriate adjustments were made in other databases. Furthermore, we manually searched the citations of the included articles to prevent omission. After retrieval, we used the Endnote X9 library (Clarivate Analytics, Philadelphia, PA, USA) to check for duplicates and manage references.

Selection Criteria

Inclusion Criteria

1. The exposure of interest was season or month of delivery or conception.
2. The investigation outcome was HDPs including gestational hypertension, preeclampsia or eclampsia, chronic hypertension, and superimposed preeclampsia. The classification refers to the American College of Obstetricians and Gynecologists (ACOG) guidelines [15].
3. The study design was a case-control, cohort, or cross-sectional design.
4. ORs and 95% CIs or relevant data that could be computed were provided.

Exclusion Criteria

1. Studies for which the full text was not available.
2. Studies that were not published in English.

Data Extraction and Quality Assessment

We (Lingyun Liao, Yangxue Yin, and Rong Zhou) designed a data extraction table during the full-text review stage. Two authors (Min Liu and Yijie Gao) extracted the data independently. The information recorded included first author, published year, study region, research type, sample size, study period, exposure definition, and outcome definition. We also recorded adjusted ORs and 95% CIs or crude ORs and 95% CIs from the original data if provided. If necessary, authors were contacted for additional details or figure data.

Based on the UK’s official weather service definition (https://www.metoffice.gov.uk/weather/learn-about/weather/seasons/spring/when-does-spring-start), March is regarded as the beginning of spring, and spring, summer, autumn, and winter are defined in three-month increments. When the study country or region was in the Southern Hemisphere, we adjusted the seasons accordingly. We used Google maps (https://www.maps.google.com) to estimate the average latitudes of countries and regions.

If a disagreement arose, we consulted a third author (Xiaohong Wei) or discussed until consensus was reached. Only studies that had sufficient data for calculation were included in the meta-analysis.

| Table 1 | Search strategy for PubMed |
|-------------------|--------------------------|
| **Outcome:** hypertensive disorders of pregnancy |
| #1 | MeSH terms “hypertension, pregnancy induced”[MeSH Terms] OR “pre eclampsia”[MeSH Terms] OR “Eclampsia”[MeSH Terms] |
| #2 | Title/abstract “hypertension pregnancy induced” OR “pregnancy induced hypertension” OR “gestational hypertension” OR “hypertension gestational” OR “transient hypertension pregnancy” OR “pregnancy transient hypertension” OR “pregnancy hypertension” OR “hypertension in pregnancy” OR “pre eclampsia” OR “Preeclampsia” OR “pregnancy toxemias” OR “pregnancy toxemia” OR “edema proteinuria hypertension gestosis” |
| #3 | #1 OR #2 |
| **Exposure:** season |
| #4 | MeSH terms “seasons”[MeSH Terms] OR “climate”[MeSH Terms] OR “meteorology”[MeSH Terms] OR “weather”[MeSH Terms] OR “temperature”[MeSH Terms] |
| #5 | Title/abstract “season*” OR “summer” OR “spring” OR “autumn” OR “winter” OR “climate*” OR “meteorology*” OR “weather*” OR “temperature*” OR “Cold” OR “frigidity” OR “Hot” OR “Heat” |
| #6 | #4 OR #5 |
| #7 | #3 AND #6 |
Study quality was evaluated by two authors (Lingyun Liao and Xiaohong Wei) with the NOS for case–control and cohort studies, and adapted NOS for cross-sectional studies [16, 17], which includes three categories and eight items, with a total score of nine. A NOS score of seven or higher indicated high quality.

**Statistical Analysis**

Stata/SE 15.1 (StataCorp, College Station, TX, USA) was used for the quantitative analysis. In studying the relationship between season of delivery and preeclampsia, summer was chosen as the reference month because most previous studies suggested that the prevalence associated with summer delivery was low [7, 18–21]. Similarly, winter was chosen as the reference season in the analysis of conception season [22–26].

A random effects model and the Mantel–Haenszel method were used to calculate pooled ORs and 95% CIs. ORs were displayed using a forest plot. Heterogeneity was estimated by the Cochrane $Q$ statistic ($P < 0.1$ indicates the existence of heterogeneity) and inconsistency index ($I^2$) (low: 25–50%; moderate: 50–75%; high: 75–100%). To explore the source of heterogeneity, subgroup analyses and sensitivity analyses were performed. Subgroup analyses were performed according to the year the study was conducted, the latitude of the study area, sample size, and the exclusion of risk factors in different study designs. In addition, we used a stepwise elimination method to perform the sensitivity analysis and verify the robustness of the results. Begg’s funnel plot and Egger’s test were used to check for the risk of publication bias.

**Results**

**Study Selection**

Figure 1 shows the literature selection process in detail. A total of 2759 studies were retrieved for further screening based on the established selection criteria. After removing duplicates, the titles and abstracts of 2140 studies were screened, and 2007 unqualified studies were excluded. Finally, we screened the full texts of the remaining and

![Fig. 1 PRISMA flow diagram of study process](image)
excluded 113 unqualified studies. Consequently, twenty studies were included in the systematic review [6, 7, 11, 12, 18–33], and eleven studies with sufficient quantitative data were included in the meta-analysis [6, 7, 18–21, 27–31].

**Study Characteristics and Quality Assessment**

Table 2 and supplementary Tables 1, 2, 3 and 4 show the detailed descriptions and quality assessments of all the studies included in the review. Studies were carried out in 7 countries, all from the Northern Hemisphere, with different latitudes. All disease-related data was extracted from medical records. Fourteen studies reported the relationship between delivery season or month and HDPs [6, 7, 11, 18–21, 26–32], while seven studies reported the relationship between conception season or month and HDPs [12, 22–26, 33]. The outcome definition was not completely uniform. Some studies focused on comprehensive HDPs, while other studies focused on only preeclampsia. Using the quality assessment guidelines [16], seventeen studies were considered to be high quality (score of 7 or more). Three articles scored six points because they lacked ample control of confounding factors, such as singleton pregnancy or maternal-related disease history.

**Season of Delivery and HDPs**

Fourteen articles assessed the relationship between delivery season and HDPs [6, 7, 11, 18–21, 26–32], and 11 articles with sufficient data were included in the meta-analysis [6, 7, 18–21, 27–31]. Because the heterogeneity between studies was high ($I^2 > 25\%$), we used a random effects model to pool the ORs and 95% CIs.

With summer delivery as the reference, a significant association between HDPs and winter delivery (Fig. 2, OR = 1.18, 95% CI = 1.02–1.38) was found, but there was no association with spring delivery (Fig. 2, OR = 1.09, 95% CI = 0.97–1.22) or fall delivery (Fig. 2, OR = 1.01, 95% CI = 0.92–1.11).

Subgroup analyses were carried out according to latitude, sample size, whether multiple pregnancies were excluded, and the year the study was conducted in the studies. The results of the associations of HDPs with winter delivery and summer delivery were as follows. After the subgroup analysis included only studies conducted after 2002 (Fig. 3a), the heterogeneity decreased significantly, and a stronger association was observed (OR = 1.34, 95% CI = 1.06–1.71). In the latitude subgroup analysis (Fig. 3b), the heterogeneity decreased slightly, and a stronger association was observed in high-latitude countries (OR = 1.62, 95% CI = 1.20–2.20) and middle-latitude countries (OR = 1.24, 95% CI = 1.00–1.55). However, at low latitudes, the result was nonsignificant (OR = 0.90, 95% CI = 0.76–1.05). In two studies that excluded risk factors for multiple pregnancies, the studies by Li (OR = 1.56, 95% CI = 0.91–2.69) and Rylander (OR = 1.99, 95% CI = 1.33–2.98) showed the same significant associations between HDPs and winter delivery (Fig. 3c). When stratified by excluding studies with a sample size < 10,000, the heterogeneity did not change considerably, and the correlation between HDPs and winter delivery remained positive (Fig. 3d) [7, 21]. The results of the subgroup analyses for spring and fall delivery versus summer delivery were nonsignificant (Supplementary Fig. 1).

The sensitivity analysis suggested that no single study altered the association (Fig. 4a–c). In the publication bias test, three Begg’s funnel plots were symmetric (Fig. 5a–c), and Egger’s test was nonpositive (Supplementary Fig. 2).

Based on the above results, we further compared winter delivery with delivery in other seasons. The result yielded a statistically significant result (OR = 1.17, 95% CI = 1.03–1.34, $P^2 = 75.4\%$) (Fig. 6a). In the subgroup analysis included only studies conducted after 2002 (Fig. 7a), the heterogeneity among included studies also decreased significantly, and a stronger association still existed (OR = 1.33, 95% CI = 1.05–1.68). The remaining three subgroup analyses did not significantly reduce the interstudy heterogeneity (Fig. 7b–d). The results of the sensitivity analysis were stable (Fig. 6b). Symmetrical Begg’s funnel plots (Fig. 6c) and Egger’s test showed that there was no publication bias (Supplementary Fig. 2).

Two of the remaining three studies that were not included in the quantitative analysis revealed that the risk of HDPs was highest when women delivered in the winter months [11, 32], which was consistent with our quantitative analysis. Morikawa reported that the relative risks of pregnancy-induced hypertension were 1.12 (95% CI = 1.06–1.19) for delivery in January–February and 1.16 (95% CI = 1.09–1.22) for delivery in March–April compared with delivery in July–August [11]. Magnus reported that delivery in August was associated with the lowest risk of preeclampsia, while the risk was highest in the winter months (for December, adjusted OR = 1.26, 95% CI = 1.20–1.31) [32]. However, Phillips found that there were no significant differences in the rates of preeclampsia in women with winter and spring deliveries, but women with summer deliveries (OR = 0.63, 95% CI = 0.39–0.99 vs. spring) and fall deliveries (OR = 0.60, 95% CI = 0.37–0.98 vs. spring) had reduced odds of developing preeclampsia [26].

**Season of Conception and HDPs**

Seven studies assessed the relationship between conception season or month and HDPs. Unfortunately, we were not able to pool the ORs because the control seasons or months were different for each study and the raw data were not available.
| Author                  | Publication year | Study region            | Study design                  | Period            | Total/case (n) | Exposure definition               | Outcome definition                       | Latitude | Income group | NOS |
|------------------------|------------------|-------------------------|-------------------------------|-------------------|----------------|-----------------------------------|------------------------------------------|----------|--------------|-----|
| Rohr Thomsen et al     | 2020             | Denmark                 | Cohort                        | 1989–2010         | 50,665/4285   | Month of conception               | HDPs                                      | Middle   | High         | 8   |
| Farzaneh et al         | 2019             | Sistan and Baluchestan, Iran | Nested case–control          | 2017              | 540/270        | Season of delivery                | Preeclampsia                              | Low      | Middle       | 7   |
| Shayan et al           | 2019             | Hamadan, Iran           | Case–control                  | 2005–2015         | 1458/729       | Season of conception              | Preeclampsia                              | Middle   | Middle       | 6   |
| Weinberg et al         | 2017             | Norway                  | Cohort                        | 1999–2009         | 356,662/13959 | Month of conception               | Preeclampsia and eclampsia               | High     | High         | 8   |
| Li et al               | 2016             | Hunan, China            | Cohort                        | 2010–2011         | 6223/449       | Season of delivery                | Preeclampsia                              | Middle   | Middle       | 7   |
| Ali et al              | 2015             | Sudan                   | Case–control                  | 2008–2010         | 306/153        | Month of delivery                 | HDPs                                      | Low      | Low          | 7   |
| Tran et al             | 2015             | Paris, France           | Cohort                        | 2008–2011         | 63,633/526     | Season of conception              | Preeclampsia with severe features         | Middle   | High         | 8   |
| Morikawa et al         | 2014             | Japan                   | Cohort                        | 2005–2009         | 301,501/13848 | Season of delivery                | HDPs                                      | Middle   | High         | 8   |
| Luo et al              | 2013             | Sichuan, China          | Case–control                  | 2007–2010         | 1300/60        | Season of delivery                | Preeclampsia                              | Middle   | Middle       | 7   |
| Wellington et al       | 2012             | TX, USA                 | Cohort                        | 2001              | 31,207/12481  | Season of delivery                | Preeclampsia and eclampsia               | Middle   | High         | 7   |
| Rylander et al         | 2011             | Sweden                  | Cohort                        | 1990–1994         | 482,659/182    | Season of delivery                | Eclampsia                                | High     | High         | 8   |
| Bullock et al          | 2011             | OK, USA                 | Cohort                        | 2005–2007         | 3050/176       | Month of delivery                 | Preeclampsia                              | Middle   | High         | 6   |
| Tam et al              | 2008             | Hong Kong, China        | Cohort                        | 1995–2002         | 15,402/245     | Season of conception              | Preeclampsia                              | Low      | Middle       | 8   |
| Sonoori et al          | 2007             | Gilan, Iran             | Cross-sectional               | 1999–2001         | 12,142/397     | Season of delivery                | Preeclampsia                              | Middle   | Middle       | 7   |
| Rudra et al            | 2005             | WA, USA                 | Cross-sectional               | 1987–2001         | 83,228/6680    | Month of conception               | Preeclampsia                              | Middle   | High         | 7   |
| Phillips et al         | 2004             | VT, USA                 | Case–control                  | 1995–2003         | 7904/142       | Season of conception and delivery | Preeclampsia                              | Middle   | High         | 7   |
| Magnus et al           | 2001             | Norway                  | Cohort                        | 1967–1998         | 1,869,388/51801| Month of delivery                 | Preeclampsia                              | High     | High         | 7   |
| Makhseed et al         | 1999             | Kuwait                  | Case–control                  | 1992–1994         | 26,805/692     | Month of delivery                 | Preeclampsia                              | Low      | High         | 6   |
| Ros et al              | 1998             | Sweden                  | Cohort                        | 1987–1993         | 10,193/557     | Season of delivery                | Eclampsia                                 | High     | High         | 8   |
| Jamelle et al          | 1998             | Pakistan                | Case–control                  | 1996              | 18,878/395     | Month of delivery                 | Eclampsia                                 | Low      | Middle       | 6   |

HDPs, hypertensive disorders in pregnancy; NOS, Newcastle–Ottawa quality assessment scale
**Fig. 2** a–c The forest plots show the association between HDPs and a certain season delivery compared with summer delivery. **a** Winter delivery; **b** spring delivery; **c** autumn delivery

### Winter vs summer

| Study                          | OR (95% CI) | Weight |
|--------------------------------|-------------|--------|
| Farzaneh et al. (2019)         | 1.00 (0.63, 1.60) | 6.43   |
| Li et al. (2018)                | 1.56 (0.91, 2.69) | 5.28   |
| Ali et al. (2015)               | 1.03 (0.43, 2.49) | 2.50   |
| Luo et al. (2013)               | 1.75 (1.27, 2.40) | 9.63   |
| Wellington et al. (2012)        | 1.04 (0.99, 1.09) | 16.53  |
| Rylander et al. (2011)          | 1.99 (1.33, 2.98) | 7.61   |
| Bullock et al. (2011)           | 1.15 (0.75, 1.77) | 7.07   |
| Soroosi et al. (2007)           | 1.11 (0.83, 1.49) | 10.28  |
| Mahdaseh et al. (1999)          | 0.90 (0.72, 1.12) | 12.23  |
| Ros et al. (1998)               | 1.44 (1.13, 1.85) | 11.62  |
| Jamelle et al. (1998)           | 0.85 (0.65, 1.12) | 10.83  |
| Overall (I-squared = 68.9%, p = 0.000) | 1.18 (1.02, 1.38) | 100.00 |

**NOTE:** Weights are from random effects analysis

### Spring vs summer

| Study                          | OR (95% CI) | Weight |
|--------------------------------|-------------|--------|
| Farzaneh et al. (2019)         | 1.00 (0.61, 1.65) | 4.30   |
| Li et al. (2018)                | 1.10 (0.61, 2.00) | 3.19   |
| Ali et al. (2015)               | 0.36 (0.14, 0.94) | 1.37   |
| Luo et al. (2013)               | 1.60 (1.16, 2.16) | 8.50   |
| Wellington et al. (2012)        | 1.00 (0.95, 1.06) | 26.36  |
| Rylander et al. (2011)          | 1.10 (0.71, 1.72) | 5.29   |
| Bullock et al. (2011)           | 1.17 (0.75, 1.72) | 5.30   |
| Soroosi et al. (2007)           | 1.21 (0.89, 1.64) | 9.23   |
| Mahdaseh et al. (1999)          | 1.14 (0.92, 1.40) | 14.20  |
| Ros et al. (1998)               | 1.16 (0.91, 1.50) | 11.74  |
| Jamelle et al. (1998)           | 0.87 (0.66, 1.15) | 10.51  |
| Overall (I-squared = 42.5%, p = 0.065) | 1.09 (0.97, 1.22) | 100.00 |

**NOTE:** Weights are from random effects analysis

### Fall vs summer

| Study                          | OR (95% CI) | Weight |
|--------------------------------|-------------|--------|
| Farzaneh et al. (2019)         | 1.00 (0.62, 1.62) | 3.55   |
| Li et al. (2018)                | 1.15 (0.65, 2.04) | 2.61   |
| Ali et al. (2015)               | 0.94 (0.33, 2.64) | 0.83   |
| Luo et al. (2013)               | 0.81 (0.58, 1.12) | 6.96   |
| Wellington et al. (2012)        | 0.98 (0.94, 1.04) | 36.02  |
| Rylander et al. (2011)          | 1.13 (0.71, 1.79) | 3.85   |
| Bullock et al. (2011)           | 1.21 (0.79, 1.85) | 4.45   |
| Soroosi et al. (2007)           | 1.10 (0.83, 1.47) | 8.62   |
| Mahdaseh et al. (1999)          | 1.08 (0.88, 1.34) | 13.64  |
| Ros et al. (1998)               | 1.29 (1.00, 1.66) | 10.45  |
| Jamelle et al. (1998)           | 0.71 (0.54, 0.94) | 9.02   |
| Overall (I-squared = 26.8%, p = 0.189) | 1.01 (0.82, 1.11) | 100.00 |

**NOTE:** Weights are from random effects analysis
Four studies supported that conception in summer increased the risk of developing HDPs [22, 24–26]. Rohr Thomsen showed that women who conceived in August (OR = 1.35, 95% CI = 1.11–1.64) had the highest risk of gestational hypertension, and those who conceived in June (OR = 1.17, 95% CI = 0.94–1.45) had the highest risk of preeclampsia, which occurred in both the summer months [22]. Tran found that conception in summer was associated with the highest risk of severe preeclampsia (OR = 1.53, 95% CI = 1.27–1.85, vs. winter) [24]. Tam (OR = 1.7, 95% CI = 1.2–2.5, vs. autumn) and Phillips (OR = 1.7, 95% CI = 1.1–2.8 vs. spring) revealed that conception in summer was associated with an increased risk of preeclampsia [25, 26].

However, the results of 3 studies were not consistent with the above conclusion. Rudra reported that conception in February (OR = 1.17, 95% CI = 1.03–1.33 vs. January) and April (OR = 1.18, 95% CI = 1.03–1.34 vs. January) through August (OR = 1.14, 95% CI = 1.01–1.30 vs. January) was associated with significantly higher risks of preeclampsia [33]. However, Shayan found that conception in autumn increased the odds of preeclampsia (OR = 1.13, 95% CI = 0.73–1.76, vs. winter) and that conception in summer was associated with the lowest odds of preeclampsia (OR = 0.26, 95% CI = 0.17–0.38, vs. winter) [12]. Weinberg revealed that women who conceived in spring had a higher risk of HDPs, while those that conceived in autumn had a lower risk [23].
Fig. 4  a–c Sensitivity analysis of HDPs and a certain season delivery compared with summer delivery; a winter delivery; b spring delivery; c autumn delivery
Fig. 5  a–c Begg’s funnel plots of HDPs and a certain season delivery compared with summer delivery;  
  a Winter delivery;  
  b Spring delivery;  c Autumn delivery
Fig. 6  a The forest plots show the association between HDPs and winter delivery compared with other seasons; the subgroup analysis of sample size; b Sensitivity analysis of HDPs and winter delivery compared with other seasons; c Begg’s funnel plots of HDPs and winter delivery compared with other seasons
Discussion

HDPs are one of the main causes of maternal and offspring morbidity and mortality and have a huge impact on pregnant women and their offspring [34, 35]. At present, some studies have shown the risk factors of HDPs, such as older age, low maternal educational status, and multiple pregnancies [6, 7]. And there were also studies showing that the incidence of HDPs was related to the season. However, the results of these studies are not consistent, possibly due to different latitudes, incomes, study designs, etc. Therefore, the best way to resolve this disagreement is to perform a meta-analysis to combine and discuss these results. After our screening, 20 studies were finally included in the systematic review and 11 studies were included in meta-analysis. First, we performed a meta-analysis between delivery season and HDPs. The results showed increased odds of HDPs in women who delivered in winter compared with those who delivered in summer and other seasons. Furthermore, two of the three studies that were not included in the meta supported this finding [11, 32]. Next, although we were unsuccessful in pooling the ORs between HDPs and seasons or months of conception, we found that there were 4 of 7 studies that consistently found women who conceived in summer had a higher risk of HDPs.

Based on our analysis, it was not possible to explain how season factors could affect the onset of HDPs. According to basic research and epidemiological investigations, several possible mechanisms influenced by factors, such as nutrient consumption, vasospasm may explain the correlation between HDPs and winter delivery. Firstly, among the different seasons, there is wide variation in the nutrients consumed by people, resulting in different risks of pregnancy-related diseases. Previous studies reported that vitamin D levels above 30 ng/mL and calcium supplementation were associated with a lower risk of preeclampsia [36, 37], and

Fig. 7 a-d The subgroup analysis between HDPs and winter delivery compared with other seasons; a whether the study was conducted after 2002; b the latitude subgroup analysis; c the subgroup analysis of sample size; d the subgroup analysis of whether multiple pregnancies were excluded
young adults had a three times higher risk of vitamin D deficiency in the winter than in the summer [38]. Secondly, exposure to cold temperatures could lead to vasospasms and subsequent ischemia [39]. These factors may help to understand the reasons for the increased risk of HDPs during winter delivery.

Next, during conception in summer, it may affect the implantation of embryos, reduced plasma volume, infection rates, and blood pressure (BP) rhythms thus affecting the occurrence of HDPs. Here, we discuss some relevant factors. Firstly, Xiong reported that in the early stages of pregnancy, cold temperatures reduced the risks of preeclampsia, eclampsia, and gestational hypertension, whereas hot temperatures increased those risks [40]. As a possible explanation, Krininger reported that heat shock was found to compromise embryo implantation in an animal model [41]. However, impaired embryo implantation is an important pathogenesis of HDPs [42]. Secondly, the incidence of preeclampsia was significantly higher during the dry season than during the rainy season [43, 44]. Water loss resulting in reduced plasma volume in warm months may increase the risk of elevated blood pressure [45]. Thirdly, seasonal fluctuations in infection rates may result in variability in the seasonal occurrence of preeclampsia. For example, the risk of preeclampsia was increased in pregnant women with urinary tract infection, and warmer weather increases the risk of urinary tract infections among women [46, 47]. Fourthly, compared with winter, the frequencies of riser and non-dipper patterns of BP rhythms in the summer season were higher, which is a common finding in HDPs [48, 49]. BP rhythm might be regulated by the peripheral clocks of circadian rhythms and the molecular circadian clock, and the expression of clock gene was increased in placenta of preeclampsia [50, 51]. The central clock of circadian rhythms receives light input directly from the retina for entrainment of time-of-day, while changes in daylength in different seasons may have an impact on circadian rhythms [50, 52]. The above may help explain the increased risk of HDPs in summer conception.

Although we studied the conception season and delivery season respectively, we could relate through the gestation period. For example, in the studies on delivery and conception months, women who conceived in hot months generally delivered in cold months in the following year [11, 18, 22, 27, 32]. Women who conceived in June and delivered in March had the highest risk of preeclampsia [22]. The differences in these studies were possibly associated with preterm birth in women with HDPs. For example, many studies have reported that common reasons for indicated preterm births include pre-eclampsia or eclampsia [53–55]. Superimposed preeclampsia increased the risk for preterm birth, especially preterm birth < 32 weeks [56]. Therefore, this could help explain the high incidence of HDPs in women who conceived in summer and delivered in winter.

In this meta-analysis of studies on delivery season, the heterogeneity was high, possibly due to confounding factors such as the year the study was conducted, the latitude of the study area, sample size, and the exclusion of risk factors in different study designs. To solve this problem, we performed subgroup analyses to find the source of the heterogeneity. Heterogeneity decreased considerably when only studies conducted after 2002 were included, and slightly decreased when analyzed by latitude subgroups analysis, which suggested that heterogeneity may stem from the year and latitude in which the study was conducted. In the studies we included in the meta-analysis, the study was conducted from 1987 to 2017. And global average temperature has risen by 0.32 °F (0.18 °C) per decade since 1981, which may have an impact on winter or summer temperatures [57]. The above may help explain why heterogeneity declined after only studies from the last two decades were included.

Most of our studies showed that seasons were related to HDPs, but four studies found the opposite [6, 27, 29, 31]. Three of the four studies were conducted in low latitudes, and one study was in mid-latitudes nearer to low latitudes, where seasonal changes are not obvious. In our subgroup analyses of latitude, heterogeneity slightly decreased and HDPs was not related to delivery season in low latitude. However, two other studies at lower latitudes showed that conceptions during summer had a higher risk of preeclampsia by Phillips and a significant association between HDPs and delivery in winter by Ali. Therefore, latitude may be one of the reasons for this difference. In the future, we need to include more well-designed and high-quality studies. In addition, our sensitivity analysis indicated that our results were valid. Begg’s funnel plots were symmetric, and Egger’s test was nonpositive, which increased the stability of our results.

In our systematic review and meta-analysis, we reported the weakly positive relationships between HDPs and season of delivery and conception. In addition, this is the first quantitative analysis of this topic. However, this study has some limitations. We found heterogeneity in our meta-analysis, and many factors beyond our control, such as the year the study was conducted, the latitude of the study area, sample size, and the exclusion of risk factors in different study designs. Although our sensitivity analysis indicated that our results were valid, additional high-quality studies are needed to reduce heterogeneity in the future. Besides, in the study of the relationship between conception season and HDPs, the reference season or month differed, and original data were not reported, which caused difficulty in performing a meta-analysis.
Conclusion

Based on the evidence to date, we found weakly positive relationships between HDPs and summer conception and winter delivery, which may help us better understand the risk factors of HDPs. Furthermore, the identification of risk factors for the onset of HDPs is important because it could greatly improve pregnancy and fetal outcomes. Therefore, more large-scale multicenter studies and mechanism studies at the molecular biology level are needed in the future to explore the pathogenesis and prevention methods of HDPs.

Abbreviations

HDP: Hypertensive disorders of pregnancy; MOOSE: The Meta-Analysis of Observational Studies in Epidemiology; PRISMA: Preferred Reporting Items for Systematic review and Meta-Analyses; MeSH: Medical Subject Headings; ORs: Odds ratios; 95% CIs: 95% Confidence intervals; NOS: The Newcastle–Ottawa quality assessment scale; BP: Blood pressure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s43032-022-01010-0.

Author Contribution

Lingyun Liao, Yangxue Yin, and Rong Zhou designed the study. Min Liu and Yijie Gao contributed to literature search, data extraction, and statistics. Lingyun Liao and Xiaohong Wei prepared the manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (No. 81571465 and 81871175) and the Key Projects of Sichuan Science and Technology Department (No. 2021YFS0208).

Data Availability

Data will be available from the corresponding author upon reasonable request.

Declarations

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Competing Interests

The authors declare no competing interests.

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