Received: 10 January 2022 | Revised: 16 August 2022 | Accepted: 24 August 2022

DOI: 10.1111/jch.14577

META-ANALYSIS

WILEY

Association between hypertensive disorders during pregnancy and elevated blood pressure in offspring: A systematic review and meta-analysis

Huan Yu MD[1] | Wei Li MD[1] | Zhengxia Mao MD[1] | Lijuan Luo MD[1] | Na He MD[1] | Wenbin Dong MD[1] | Xiaoping Lei MD, PhD[1,2,3]

[1]Division of Neonatology, Department of Pediatrics, Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan, China

[2]Birth Defects Clinical Medical Research Center of Sichuan Province, Sichuan, China

[3]Department of Perinatology, Southwest Medical University, Luzhou, Sichuan, China

Correspondence
Xiaoping Lei, Division of Neonatology, Department of Pediatrics, Affiliated Hospital of Southwest Medical University, 25 Taiping Road, Luzhou, Sichuan 646000, China.
Email: leixiaopingde@126.com

Abstract

Hypertensive disorders during pregnancy (HDP) are associated with cardiovascular disease among mothers and offspring. This meta-analysis was conducted to further explore the associations between maternal HDP and offspring blood pressure (BP). The authors performed a search strategy in PubMed, Embase, Web of Science, and Cochrane library from database inception to January 2022. Twenty-four studies regarding HDP were included, with pregnancy-associated hypertension (PAH), preeclampsia (PE), gestational hypertension (GH), and chronic hypertension included in 12, 16, 6, and 3 studies, respectively. Offspring who were exposed to HDP and PAH in utero had higher systolic BP (2.46 mm Hg, 95% CI: 1.88–3.03 mm Hg; 2.70 mm Hg 95% CI: 1.89–3.51 mm Hg) and diastolic BP (1.38 mm Hg 95% CI: 0.94–1.83 mm Hg; 1.39 mm Hg 95% CI: 0.71–2.06 mm Hg) than those birthed to normotensive mothers. The offspring exposure to PE, GH, and chronic hypertension had higher systolic BP by 1.90 mm Hg (95% CI: 1.39–2.40 mm Hg), 2.47 mm Hg (95% CI: 1.59–3.35 mm Hg), and 7.85 mm Hg (95% CI: 4.10–11.61 mm Hg), respectively, and higher diastolic BP by 0.99 mm Hg (95% CI: 0.50–1.49 mm Hg), 1.04 mm Hg (95% CI: 0.60–1.47 mm Hg), and 2.92 mm Hg (95% CI: 0.98–4.86 mm Hg), respectively. An Egger test and funnel plot confirmed no significant publication bias. In conclusion, offspring exposure to all subtypes of HDP in utero led to higher BP than no exposure. It is necessary to investigate the potential mechanisms to clarify the roles of genetic and environmental factors in these associations, which could provide insight on preventing hypertension and related cardiovascular disease.

KEYWORDS

blood pressure, hypertensive disorders during pregnancy, offspring, the developmental origins of health and disease

1 | INTRODUCTION

Hypertension is a complex multifactor disorder, and its incidence is rapidly increasing worldwide. It is a major cause of cardiovascular deaths, affecting more than one billion people around the world,[1] and it is associated with more than nine million deaths annually.[2] According to "the developmental origins of health and disease (DOHaD)" hypothesis,[3,4] the gestation period is regarded as a critical window for the developmental origin of hypertension.

Hypertensive disorders during pregnancy (HDP), affecting up to 10% of pregnant women worldwide, constitute a risk factor for maternal-fetal morbidity and mortality. HDP are divided into hypertension known before pregnancy or present in the first 20 weeks, including chronic hypertension, white-coat hypertension, and masked hypertension, and hypertension arising de novo at or after 20 weeks, including gestational hypertension (GH), preeclampsia (PE) de novo or superimposed on chronic hypertension, and transient GH.[5] Previous studies have confirmed that women who develop HDP have an increased risk of cardiovascular disease later in life, while there have been studies demonstrating that offspring exposure to HDP in utero is associated with metabolic syndrome,[6] mental and behavioral disorders,[7] asthma,[8] and other conditions. Several reviews have shown that offspring born to mothers with HDP have higher blood pressure (BP).[9] However, a recent systematic review[10] that did not perform a pooled estimate among offspring aged 2–18 years but focused on pregnancies with PE and GH drew conflicting conclusions from the previous systematic reviews.

Previous studies have revealed structural changes in cardiovascular organs among offspring exposed to HDP.[11] In addition, as a genetic-environmental interaction disorder, the role of genetic factors might be considered to explain the true associations between offspring BP and HDP.[12] Evidence has shown that although subtypes of HDP have clear overlap, they also have distinct differences; different pathophysiological pathways are involved in the development and clinical course of the different HDP phenotypes. Thus, different subtypes of HDP may be differently associated with offspring BP. Therefore, we performed a systematic review and meta-analysis for the pooled estimates of the specific effects on the offspring BP in each subtype of HDP.

2 | METHOD

2.1 | Search strategy and selection criteria

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table S1),[13] and the supporting data can be found at the PROSPERO website (https://www.crd.york.ac.uk/prospero/) with registration number CRD 42018110872. The detailed protocol has been previously published,[14] and approval was not required because the data are anonymous in peer-reviewed review papers. We performed a detailed search strategy in PubMed, Embase, Web of Science, and Cochrane library from database inception to January 2022 (sText).

These studies were included based on definitions of HDP. Because BP of newborns is affected by diseases other than HDP, the term "offspring" was used to refer to children greater than 1 month. In this review, HDP were divided into chronic hypertension, GH, and PE.[5] HDP were defined as systolic BP $\geq$ 140 and/or diastolic BP $\geq$ 90 mm Hg during pregnancy. PE was defined as persistent de novo hypertension that develops at or after 20 weeks of gestation, plus proteinuria or other evidence of systemic involvement by $\geq$ 1 maternal organ dysfunction (including renal damage, liver involvement with or without right upper quadrant or epigastric abdominal pain, neurological complications, hematological complications, and uteroplacental dysfunction). GH was defined as persistent de novo hypertension that develops at or after 20 weeks of gestation in the absence of features of PE. Chronic hypertension referred to high BP predating the pregnancy or recognized at < 20 weeks of gestation. Pregnancy-associated hypertension (PAH) mainly included GH and PE. The study search and selection were conducted by independent reviewers (H.Y. and [Z.M. or W.L.]), respectively. Another reviewer (X.L.) was consulted when disagreements occurred regarding the inclusion eligibility of a study. When the same participant cohort was reported in multiple studies, we used the study with the largest sample. A total of 24 cohort studies included after the detailed evaluation (Figure S1).[15–37] Except for three studies being matched by factors such as offspring's age, sex, and birth weight,[20,26,32] all studies were natural cohort studies.

2.2 | Data extraction and evidence evaluation

The data extraction was independently conducted by two authors (H.Y. and [Z.M. or W.L.]). For each study, based on a standardized data collection form, we extracted the relevant information such as title, population description, offspring age, BP measurement, HDP definitions, sample size, adjusted factors, and BP. If the studies provided the outcome of interest without using mean difference (MD) and standard deviation, the RevMan Calculator (https://training.cochrane.org/resource/revman-calculator) was used. In addition, when a key message was not obtained, we contacted the authors at least twice (except when not found). All primary results obtained from the authors were preferentially used in the meta-analysis. In addition, the assessment of the risk of bias conducted using the ROBINS-I (Risk Of Bias In Nonrandomized Studies-of Interventions) tool.[38]

2.3 | Data analyses

The meta-analysis was conducted with Review Manager software (version 5.3) and Stata software, version 16 (Stata Corp, College Station, TX, USA), based on an inverse variance method. As there is greater chance of random error in observational studies, the pooled MDs and 95% confidence intervals (CIs) in BP between the offspring of mothers with HDP and normotensive mothers were calculated using a random-effect model. We also performed the overall pooled MD of BP based on the outcome with and without adjustment for confounders.

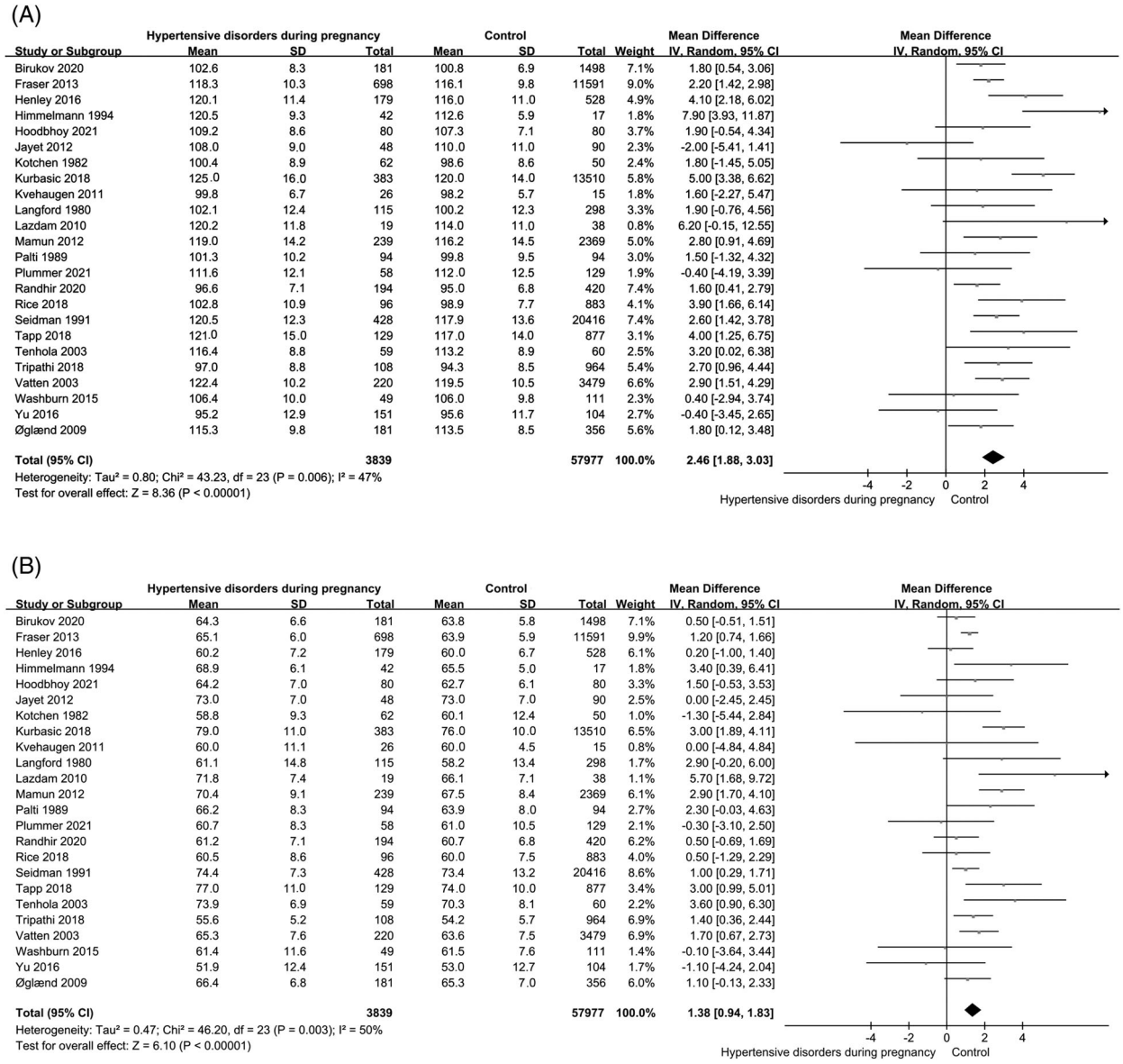

FIGURE 1 Mean difference in BP in mm Hg between offspring exposure to hypertensive disorders during pregnancy in utero and controls. (A) systolic BP; (B) diastolic BP

Heterogeneity was initially assessed by studying the forest plot generated for the outcomes. To explore sources of heterogeneity, the meta-regression analysis was used to investigate the potential effects of several confounders; subgroup analysis was subsequently performed. The Egger test was used to evaluate publication bias in all of the groups, and the funnel plots were reported for publication bias when more than nine studies were analyzed. In addition, sensitivity analysis was used to assess the stability of the results. An overall grading of the evidence was performed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[39]

3 | RESULTS

The characteristics of the included studies are summarized in Table S2. In total, data from 3839 offspring exposed HDP in utero and 57977 offspring from normotensive mothers were analyzed. Compared to the normotensive group, the HDP group had higher systolic BP (MD 2.46 mm Hg, 95% CI: 1.88–3.03 mm Hg) and diastolic BP (MD 1.38 mm Hg, 95% CI: 0.94–1.83 mm Hg) (Figure 1). The pooled MDs in systolic and diastolic BP between the offspring exposed to PAH and those not exposed were 2.70 mm Hg (95% CI: 1.89–3.51 mm Hg) and 1.39 mm Hg (95% CI: 0.71–2.06 mm Hg) (Figure S2). Compared to the normotensive offspring, the offspring of mothers with PE had higher systolic BP (MD 1.90 mm Hg, 95% CI: 1.39–2.40 mm Hg) and diastolic BP (MD 0.99 mm Hg, 95% CI: 0.50–1.49 mm Hg) (Figure 2). Further, offspring exposed to GH also had higher systolic BP (MD 2.47 mm Hg, 95% CI: 1.59–3.35 mm Hg) and diastolic BP (MD 1.04 mm Hg, 95% CI: 0.60–1.47 mm Hg) (Figure 3). The MDs in systolic BP and diastolic BP were 7.85 mm Hg (95% CI: 4.10–11.61 mm Hg) and 2.92 mm Hg (95% CI: 0.98–4.86 mm Hg) between the offspring of mothers with chronic hypertension and normotensive ones (Figure 4).

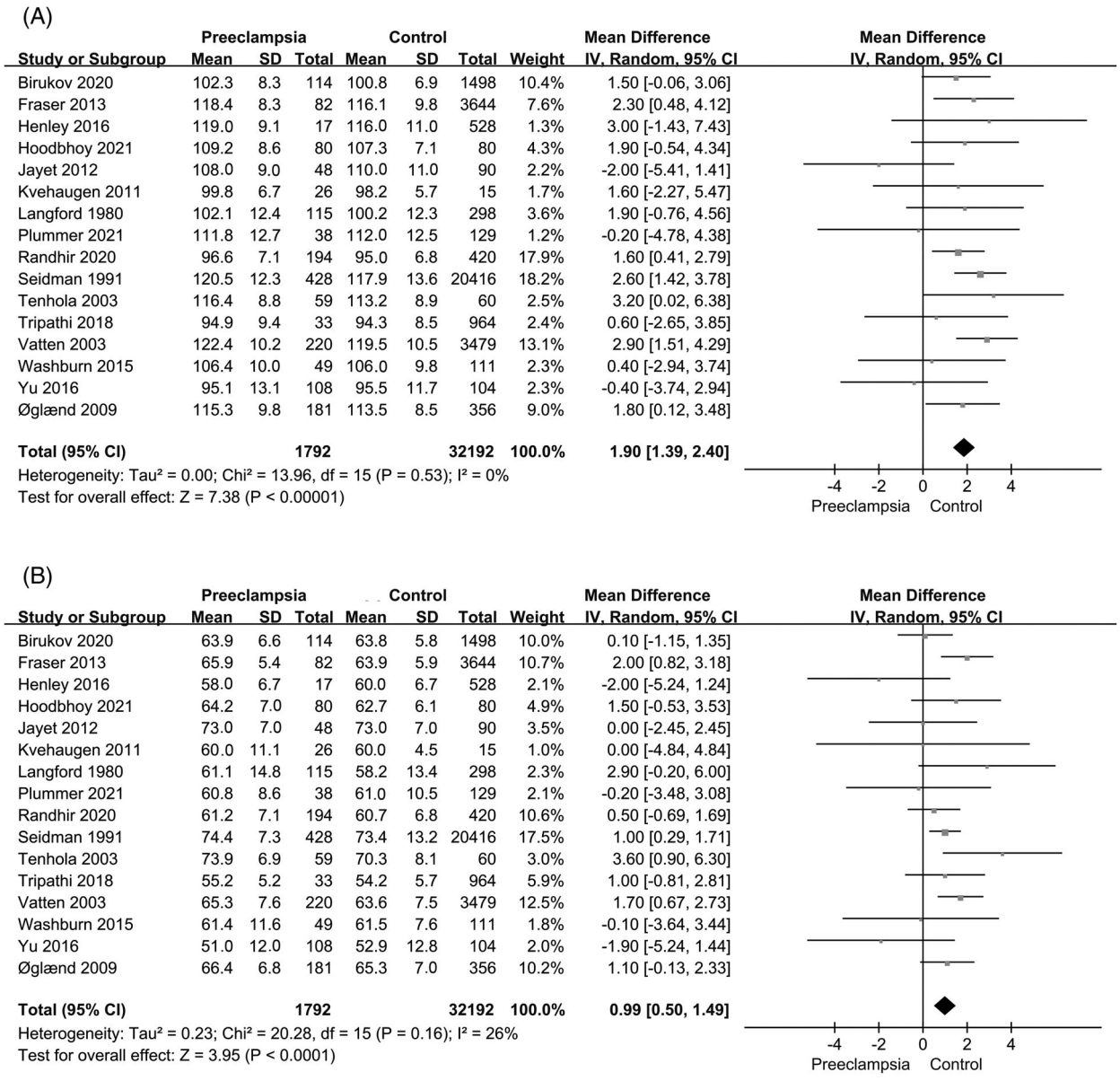

FIGURE 2 Mean difference in BP in mm Hg between offspring exposure to preeclampsia in utero and controls. (A) systolic BP; (B) diastolic BP

In the meta-regression analysis, we found that offspring age accounted for some heterogeneity in the pooled estimates (Table S3). Compared to the offspring < 18 years old, the older offspring of mothers with HDP had higher systolic BP (MD 3.49 mm Hg, 95% CI: 1.74–5.24 mm Hg vs. MD 2.24 mm Hg, 95% CI: 1.69–2.79 mm Hg, $P < 0.0001$) and diastolic BP (MD 2.76 mm Hg, 95% CI: 1.70–3.83 mm Hg vs. MD 1.06 mm Hg, 95% CI: 0.76–1.37 mm Hg, $P < 0.001$), respectively (Figure S3). In the four studies with adjusted results, the pooled MDs between the HDP and the normotensive groups were 2.29 mm Hg (95% CI: 1.20–3.39 mm Hg) in systolic BP and 1.15 mm Hg (95% CI: 0.01–2.30 mm Hg) in diastolic BP, respectively (Figure S5), adjusting for factors such as age, weight/BMI, birth weight, and sex. The adjusted significant MDs in BP between the PE and the normotensive groups were also computed (Figure S6).

Using the ROBINS-I, seven studies were evaluated to have a low risk of bias, with fourteen for moderate and two for serious (Figure S7). Further, the GRADE quality of evidence was moderate for systolic BP in PE/GH groups, very low for BP in the chronic hypertension group, and low for other groups (Table S4). There was no evidence of publication bias among the studies assessed by the Egger test with the funnel plot reported in the HDP/PAH/PE groups (Figure S8). The sensitivity analysis demonstrated the stability of the pooled values.

4 | DISCUSSION

The present systematic review and meta-analysis first reported that the offspring exposed to all subtypes of HDP had higher BP than those with no exposure.

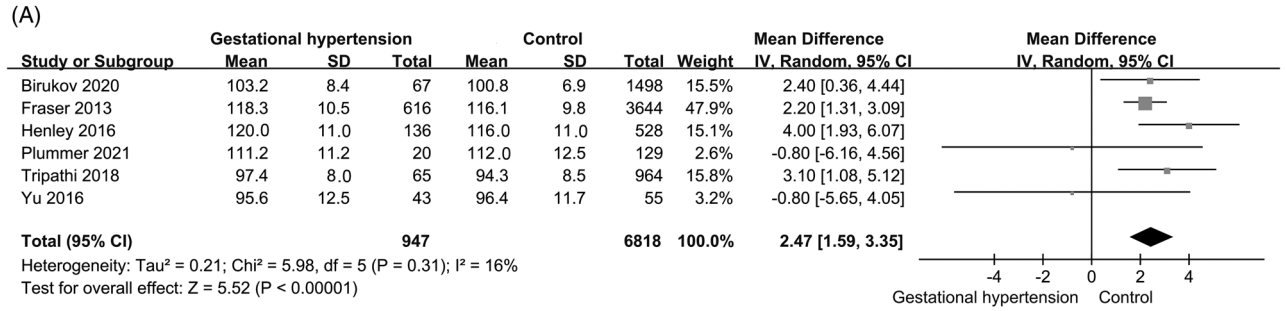

FIGURE 3 Mean difference in BP in mm Hg between offspring exposure to gestational hypertension in utero and controls. (A) systolic BP; (B) diastolic BP

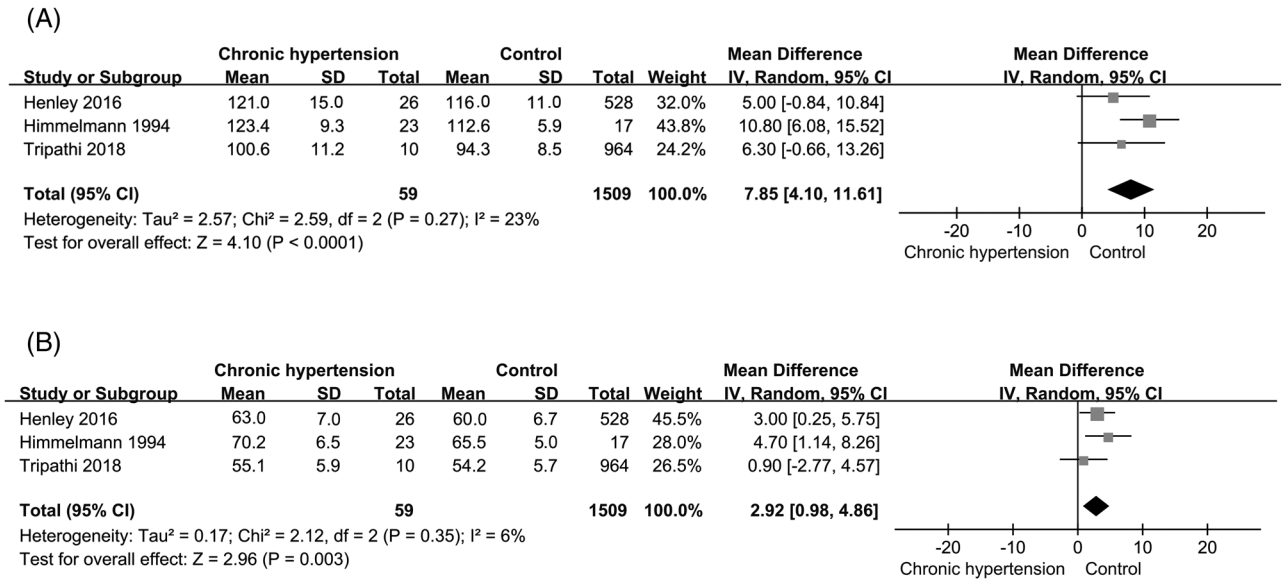

FIGURE 4 Mean difference in BP in mm Hg between offspring exposure to chronic hypertension in utero and controls. (A) systolic BP; (B) diastolic BP

Many studies exploring the health outcomes of offspring exposure to HDP have been conducted and have demonstrated that exposure to PE and GH in utero is associated with higher BP in offspring.[15–17,19,20,27–30] Offspring from PAH pregnancies had higher BP compared to those from normotensive pregnancies.[40] PE offspring also had higher BP than normotensive offspring.[41] However, without the pooled estimate, a recent systematic review drew a conflicting conclusion on the associations between PE and offspring BP.[10] In the present meta-analysis, in line with most of the previous meta-analyses, the findings showed that offspring exposed to any subtype of HDP had higher BP than normotensive offspring. According to the DOHaD hypothesis,[3,4] exposure to any adverse environment in utero during the specific critical windows of fetal development could induce short- and long-term changes in tissues and organs. Furthermore, in

previous studies, some epigenetic changes have been observed in the offspring of mothers with HDP, including DNA methylation in cord blood cells and alterations of the vasculature and cardiac structure.[3,4] These changes could partly explain the associations between exposure to HDP in utero and BP in offspring. Notably, our findings also showed that the offspring in the chronic hypertension group with a longer duration of exposure had a greater elevation in BP than those in the PE/GH groups.

It is believed that the development of hypertension is the combined effect of environmental and genetic factors.[4,42] The main question is whether the major contributor to the elevations regarding offspring exposure to HDP was genetic factors or the adverse intrauterine environment. Although environmental factors contribute to hypertension, genetic pathways are still involved in its pathogenesis. In general, people with a family history have obviously higher risks of hypertension than those with no family history.[43,44] In family-based studies, parental genes could be transmitted to offspring and cause a higher risk of PE in their daughters.[22,45] Thus, mothers with HDP and their offspring might be more likely to have chronic hypertension than normotensive mothers. In addition, some evidence supports that GH, PE and chronic hypertension are caused by similar genes, and pregnant women suffering from PE/GH are prone to chronic hypertension later in life. Sibling studies have also confirmed that, possibly with the same genetic resources, no BP differences were observed between offspring exposed to PE/GH and their nonexposed siblings in utero. Thus, the higher elevation of BP in the offspring of mothers with PE/GH could also be explained by weaker heredity compared to that in the offspring of chronic hypertension mothers. While minor heterogeneity of the pooled estimates was observed in the PE/GH/chronic hypertension group, moderate or significant heterogeneity was observed in the PAH/HDP group, perhaps due to inconsistent exposure.

It was shown that the heterogeneity came from the offspring' age in the meta-regression analysis. This phenomenon may be interpreted by gene-environment interactions; as offspring with susceptibility genes of hypertension age, the effects from lifestyle and other environmental factors become stronger, and the effect of exposure to HDP in utero becomes less obvious.

In the pooled analysis, the study by Hosaka and coworkers[46] was excluded because BP was measured not by medical staff but mother's report at home, which can be affected by various possible factors. Meanwhile, compared to those in other studies, the offspring in this study were from Japanese districts, with unique perinatal exposures to methylmercury and persistent organic pollutants.[47] Long exposures to toxic substances could be confounders for offspring BP, accompanied by other unknown biological variations.

4.1 | Strengths and limitations

In this meta-analysis, we first investigate the associations between different types of HDP and offspring BP, but there are still several limitations that could not be addressed. The major limitation is that BP monitors in the included studies have not been validated for pediatric populations according to the STRIDE BP website (https://stridebp.org/bp-monitors), possibly affecting the results. Although the versions of BP monitors have not been mentioned, the brands of BP monitors (36%) have been validated in adults and most studies used their own standard measurement protocols. In addition, the included observational studies might be more prone to publication bias than randomized clinical trials. Thus, the funnel plot and Egger test were used to assess publication bias, with the sensitivity analysis identifying the stability of the results. Due to the strict criteria used, there was still the possibility of misidentified cases or nonconformity in meeting the current diagnostic criteria. Meanwhile, there were some different confounders adjusted for in different studies, but the pooled estimates with the adjusted data were similar to the whole pooled estimates. BP was higher in offspring exposed to different HDP than in normotensive offspring, but the potential genetic mechanism and the effects of intrauterine exposure remain unclear. Thus, more studies are needed to confirm and investigate these similar associations.

5 | CONCLUSION

In summary, to our knowledge, this meta-analysis is the first to demonstrate that offspring exposed to all subtypes of HDP in utero have higher BP than those with no exposure. Additionally, genetic factors might be a relatively more important pathogenesis than intrauterine environmental factors.

AUTHOR CONTRIBUTIONS

The study sponsor (Huan Yu) designed the study and was involved in the analysis, including search strategy, selection criteria, data extraction, and evidence evaluation, and data analysis, and wrote the first draft of the manuscript. Wei Li participated in the revision and the secondary search, selection studies, data extraction, and evidence evaluation. Zhengxia Mao was involved in search strategy, selection criteria, data extraction, and manuscript revisions. Xiaoping Lei designed the study, critically revised the manuscript, and approved the manuscript for publication. Lijuan Luo, Na He, and Wenbin Dong revised the manuscript.

ACKNOWLEDGEMENTS

We wish to thank Sheryl L. Rifas-Shiman, Emily Oken, and Anna Birukov for providing primary data. We also wish to thank the authors of the studies included for providing relative data. This work was partly supported by the Sichuan Science and Technology Program (http://kjt.sc.gov.cn/), project number 2019YJ0696, to Xiaoping Lei.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ORCID

Huan Yu MD https://orcid.org/0000-0001-9078-4563

REFERENCES

1. Hypertension indicators for improving quality and coverage of services, virtual meeting, 1–2 March 2021: report. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
2. Lamirault G, Artifoni M, Daniel M, Barber-Chamoux N, Nantes University Hospital Working Group On Hypertension. Resistant hypertension: novel insights. *Curr Hypertens Rev*. 2020;16(1):61-72.
3. Goyal D, Limesand S, Goyal R. Epigenetic responses and the developmental origins of health and disease. *J Endocrinol*. 2019;242(1):T105-T119.
4. Guarner-Lans V, Ramírez-Higuera A, Rubio-Ruiz M, Castrejón-Téllez V, Soto M, Pérez-Torres I. Early programming of adult systemic essential hypertension. *Int J Mol Sci*. 2020;21(4):1203.
5. Brown M, Magee L, Kenny L, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. *Hypertension*. 2018;72(1):24-43.
6. Kanata M, Liazou E, Chainoglou A, Kotsis V, Stabouli S. Clinical outcomes of hypertensive disorders in pregnancy in the offspring during perinatal period, childhood, and adolescence. *J Hum Hypertens*. 2021;35(12):1063-1073.
7. Robinson R, Lähdepuro A, Tuovinen S, et al. Maternal hypertensive pregnancy disorders and mental and behavioral disorders in the offspring: a review. *Curr Hypertens Rep*. 2021;23(5):30.
8. Conlan N, Maher G, Al Khalaf S, McCarthy F, Khashan A. Association between hypertensive disorders of pregnancy and the risk of asthma, eczema and allergies in offspring: a systematic review and meta-analysis. *Clin Exp Allergy*. 2021;51(1):29-38.
9. Wojczakowski W, Kimber-Trojnar Ż, Dziwisz F, Słodzińska M, Słodziński H, Leszczyńska-Gorzelak B. Preeclampsia and cardiovascular risk for offspring. *J Clin Med*. 2021;10(14):3154.
10. Jansen M, Pluymen L, Dalmeijer G, et al. Hypertensive disorders of pregnancy and cardiometabolic outcomes in childhood: a systematic review. *Eur J Prev Cardiol*. 2019;26(16):1718-1747.
11. Frost A, Suriano K, Aye C, Leeson P, Lewandowski A. The immediate and long-term impact of preeclampsia on offspring vascular and cardiac physiology in the preterm infant. *Front Pediatr*. 2021;9:625726.
12. Odukoya S, Moodley J, Naicker T. Current updates on pre-eclampsia: maternal and foetal cardiovascular diseases predilection, science or myth? : future cardiovascular disease risks in mother and child following pre-eclampsia. *Curr Hypertens Rep*. 2021;23(3):16.
13. Page M, McKenzie J, Bossuyt P, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
14. Yu H, He Y, Mao Z, Dong W, Fu X, Lei X. Hypertensive disorders during pregnancy and elevated blood pressure in the offspring: a systematical review and meta-analysis protocol. *Medicine*. 2019;98(20):e15677.
15. Birukov A, Herse F, Nielsen J, et al. Blood pressure and angiogenic markers in pregnancy: contributors to pregnancy-induced hypertension and offspring cardiovascular risk. *Hypertension*. 2020;76(3):901-909.
16. Fraser A, Nelson S, Macdonald-Wallis C, Sattar N, Lawlor D. Hypertensive disorders of pregnancy and cardiometabolic health in adolescent offspring. *Hypertension*. 2013;62(3):614-620.
17. Henley D, Brown S, Pennell C, Lye S, Torpy D. Evidence for central hypercortisolism and elevated blood pressure in adolescent offspring of mothers with pre-eclampsia. *Clin Endocrinol*. 2016;85(4):583-589.
18. Himmelmann A, Svensson A, Hansson L. Blood pressure and left ventricular mass in children with different maternal histories of hypertension: the hypertension in pregnancy offspring study. *J Hypertens*. 1993;11(3):263-268.
19. Hoodbhoy Z, Mohammed N, Rozi S, et al. Cardiovascular dysfunction in children exposed to preeclampsia during fetal life. *J Am Soc Echocardiogr*. 2021;34(6):653-661.
20. Jayet P, Rimoldi S, Stuber T, et al. Pulmonary and systemic vascular dysfunction in young offspring of mothers with preeclampsia. *Circulation*. 2010;122(5):488-494.
21. Kotchen J, McKean H, Kotchen T. Blood pressure of young mothers and their children after hypertension in adolescent pregnancy: six- to nine-year follow-up. *Am J Epidemiol*. 1982;115(6):861-867.
22. Kurbasic A, Fraser A, Mogren I, et al. Maternal hypertensive disorders of pregnancy and offspring risk of hypertension: a population-based cohort and sibling study. *Am J Hypertens*. 2019;32(4):331-334.
23. Kvehaugen A, Dechend R, Ramstad H, Troisi R, Fugelseth D, Staff A. Endothelial function and circulating biomarkers are disturbed in women and children after preeclampsia. *Hypertension*. 2011;58(1):63-69.
24. Langford H, Watson R. Prepregnant blood pressure, hypertension during pregnancy, and later blood pressure of mothers and offspring. *Hypertension*. 1980;2: 130-133.
25. Mamun A, Kinarivala M, O'Callaghan M, Williams G, Najman J, Callaway L. Does hypertensive disorder of pregnancy predict offspring blood pressure at 21 years? Evidence from a birth cohort study. *J Hum Hypertens*. 2012;26(5):288-294.
26. Palti H, Rothschild E. Blood pressure and growth at 6 years of age among offsprings of mothers with hypertension of pregnancy. *Early Hum Dev*. 1989;19(4):263-269.
27. Plummer M, Andraweera P, Garrett A, et al. Hypertensive disorders of pregnancy and later cardiovascular disease risk in mothers and children. *J Dev Orig Health Dis*. 2021;12(4):555-560.
28. Randhir K, Pisal H, Kadam V, et al. Association of preeclampsia with anthropometric measures and blood pressure in Indian children. *PloS One*. 2020;15(5):e0231989.
29. Rice M, Landon M, Varner M, et al. Pregnancy-associated hypertension and offspring cardiometabolic health. *Obstet Gynecol*. 2018;131(2):313-321.
30. Seidman D, Laor A, Gale R, Stevenson D, Mashiach S, Danon Y. Pre-eclampsia and offspring's blood pressure, cognitive ability and physical development at 17-years-of-age. *Br J Obstet Gynaecol*. 1991;98(10):1009-1014.
31. Tapp R, Hughes A, Kähönen M, et al. Cardiometabolic health among adult offspring of hypertensive pregnancies: the cardiovascular risk in Young Finns Study. *J Am Heart Assoc*. 2018;7(1):e006284.
32. Tenhola S, Rahiala E, Martikainen A, Halonen P, Voutilainen R. Blood pressure, serum lipids, fasting insulin, and adrenal hormones in 12-year-old children born with maternal preeclampsia. *J Clin Endocrinol Metab*. 2003;88(3):1217-1222.
33. Tripathi R, Rifas-Shiman S, Hawley N, Hivert M, Oken E. Hypertensive disorders of pregnancy and offspring cardiometabolic health at mid-childhood: project viva findings. *J Am Heart Assoc*. 2018;7(3):e007426.
34. Washburn L, Brosnihan K, Chappell M, et al. The renin-angiotensin-aldosterone system in adolescent offspring born prematurely to mothers with preeclampsia. *J Renin Angiotensin Aldosterone Syst*. 2015;16(3):529-538.
35. Vatten L, Romundstad P, Holmen T, Hsieh C, Trichopoulos D, Stuver S. Intrauterine exposure to preeclampsia and adolescent blood pressure, body size, and age at menarche in female offspring. *Obstet Gynecol*. 2003;101(3):529-533.
36. Yu G, Aye C, Lewandowski A, et al. Association of maternal antiangiogenic profile at birth with early postnatal loss of microvascular density in offspring of hypertensive pregnancies. *Hypertension*. 2016;68(3):749-759.
37. Øglaend B, Forman M, Romundstad P, Nilsen S, Vatten L. Blood pressure in early adolescence in the offspring of preeclamptic and normotensive pregnancies. *J Hypertens*. 2009;27(10):2051-2054.
38. Sterne J, Hernán M, Reeves B, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.

39. Guyatt G, Oxman A, Vist G, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924-926.
40. Thoulass J, Robertson L, Denadai L, et al. Hypertensive disorders of pregnancy and adult offspring cardiometabolic outcomes: a systematic review of the literature and meta-analysis. *J Epidemiol Community Health*. 2016;70(4):414-422.
41. Davis E, Lazdam M, Lewandowski A, et al. Cardiovascular risk factors in children and young adults born to preeclamptic pregnancies: a systematic review. *Pediatrics*. 2012;129(6):e1552-e1561.
42. Kokubo Y, Padmanabhan S, Iwashima Y, Yamagishi K, Goto A. Gene and environmental interactions according to the components of lifestyle modifications in hypertension guidelines. *Environ Health Prev Med*. 2019;24(1):19.
43. Zhang C, Zeng Q, Liu Y, et al. Family history of hypertension and cobalt exposure synergistically promote the prevalence of hypertension. *Biol Trace Elem Res*. 2022;200(3):943-952.
44. Geelhoed J, Fraser A, Tilling K, et al. Preeclampsia and gestational hypertension are associated with childhood blood pressure independently of family adiposity measures: the Avon longitudinal study of parents and children. *Circulation*. 2010;122(12):1192-1199.
45. Alsnes I, Vatten L, Fraser A, et al. Hypertension in pregnancy and offspring cardiovascular risk in young adulthood: prospective and sibling studies in the HUNT Study (Nord-Trøndelag Health Study) in Norway. *Hypertension*. 2017;69(4):591-598.
46. Hosaka M, Asayama K, Staessen J, et al. Relationship between maternal gestational hypertension and home blood pressure in 7-year-old children and their mothers: Tohoku study of child development. *Hypertens Res*. 2015;38(11):776-782.
47. Tatsuta N, Murata K, Iwai-Shimada M, Yaginuma-Sakurai K, Satoh H, Nakai K. Psychomotor ability in children prenatally exposed to methylmercury: the 18-month follow-up of Tohoku study of child development. *Tohoku J Exp Med*. 2017;242(1):1-8.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Yu H, Li W, Mao Z, et al. Association between hypertensive disorders during pregnancy and elevated blood pressure in offspring: A systematic review and meta-analysis. *J Clin Hypertens*. 2022;24:1397–1404. https://doi.org/10.1111/jch.14577