Original Article

Risk of preterm birth in maternal influenza or SARS-CoV-2 infection: a systematic review and meta-analysis

Xuan Wang[1#], Haiwei Ou[2#], Ying Wu[3], Zengli Xing[3]

[1]Department of Gynaecology and Obstetrics, Haikou Maternal and Child Health Hospital, Haikou, China; [2]Department of Obstetrics, Danzhou People's Hospital, Danzhou, China; [3]Department of Obstetrics, The First Affiliated Hospital of Hainan Medical University, Haikou, China

Contributions: (I) Conception and design: X Wang, H Ou, Z Xing; (II) Administrative support: Y Wu; (III) Provision of study materials or patients: X Wang, H Ou, Z Xing; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: X Wang, H Ou, Z Xing; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Zengli Xing, Bachelor. The First Affiliated Hospital of Hainan Medical University, No. 31, Longhua Road, Longhua District, Haikou 570102, Hainan, China. Email: xingzengli9642@163.com.

Background: Influenza is a major threat to global health and is an important cause of respiratory diseases. However, there was a controversy on the impacts of influenza infection on adverse pregnancy outcomes and the infant's health. This meta-analysis aimed to investigate the impact of maternal influenza infection on preterm birth.

Methods: Five databases, including PubMed, Embase, Cochrane Library, Web of Science, and China National Knowledge Infrastructure (CNKI) were searched for eligible studies on December 29, 2022. The Newcastle-Ottawa Scale (NOS) was used to assess the included quality of the included studies. As for the incidence of preterm birth, odds ratios (OR) and 95% confidence intervals (CIs) were pooled, and the results of the current meta-analysis were displayed in forest plots. Subgroup analyses based on similarity in different aspects were conducted for further analysis. A funnel plot was used to assess the publication bias. All of the above data analyses were performed using STATA SE 16.0 software.

Results: A total of 24 studies involving 24,760,890 patients were included in this meta-analysis. Through the analysis, we found that maternal influenza infection significantly increased the risk of preterm birth (OR =1.52, 95% CI: 1.18 to 1.97, I^2=97.35%, P=0.00). After subgroup analysis based on different types of influenzas, we found that women infected with influenza A and B (OR =2.05, 95% CI: 1.26 to 3.32, I^2=96.14%, P<0.1), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (OR =2.16, 95% CI: 1.75 to 2.66, I^2=0.00%, P<0.1) in pregnancy were at an increased risk of preterm birth, while those infected with influenza A alone or seasonal influenza were not (P>0.1).

Conclusions: Women should take active steps to avoid influenza infection during pregnancy, especially influenza A and B and SARS-CoV-2, to reduce the possibility of preterm birth.

Keywords: Influenza; pregnancy; infant outcome; preterm birth; meta-analysis

Submitted Feb 08, 2023. Accepted for publication Apr 20, 2023. Published online Apr 26, 2023.
doi: 10.21037/tp-23-134
View this article at: https://dx.doi.org/10.21037/tp-23-134

Introduction

Influenza is a major threat to global health and is an important cause of lower respiratory tract infections and other respiratory diseases (1). Although influenza's infection and mortality rates have decreased with the widespread availability of vaccines, it still causes approximately 250,000 to 500,000 deaths globally each year, especially in people over 65 years old (2-4). Approximately 0.6% pregnant women had hospitalization during the influenza season. Influenza-related hospitalizations and deaths are mainly

© Translational Pediatrics. All rights reserved.

caused by associated complications, including pneumonia, cardiovascular events, worsening of chronic underlying disease, and reduced function (5-7). Moreover, influenza infection not only causes adverse pregnancy outcomes but also negatively impacts the infant's health (8,9).

Preterm birth is generally defined as a live birth that occurs before 37 weeks of pregnancy and is a common adverse pregnancy outcome (9). It affects approximately 11% of births worldwide and is a major cause of maternal and fetal morbidity and mortality (10-12). Although many interventions have been evaluated, there is little high-quality evidence to confirm their effectiveness in reducing preterm birth (13,14).

Concerning the effect of influenza infection during pregnancy on preterm birth, most studies have demonstrated that influenza infection did not increase the probability of preterm birth (15-29); however, some other studies found that influenza infection was a risk factor for preterm birth (30-38). Therefore, we conducted this systematic review and meta-analysis to assess the impact of influenza infection on preterm birth and hopefully provide evidence for the need for influenza vaccination of pregnant women and the allocation of medical resources. We present the following article in accordance with the MOOSE reporting checklist (39) (available at https://tp.amegroups.com/article/view/10.21037/tp-23-134/rc).

Highlight box

Key findings

- We searched eligible studies in five databases including PubMed, Embase, Cochrane Library, Web of Science, and CNKI to investigate the impact of maternal influenza infection on preterm birth. This meta-analysis finally included twenty-four studies involving 24,760,890 patients, and we found that maternal influenza infection significantly increased the risk of preterm birth, especially for women infected with influenza A, B, and SARS-CoV-2.

What is known and what is new?

- At present, there is a controversy on the impact of influenza infection on preterm birth.
- This current meta-analysis provides the most reliable results available to resolve this dispute and to provide clinical evidence.

What is the implication, and what should change now?

- Our analysis suggested that doctors and pregnant women should take active steps to avoid influenza infection during pregnancy to reduce the possibility of preterm birth.

Methods

Search strategy

Text words were used to search for eligible studies, and the search strategy included the following terms: pregnancy, influenza, and preterm birth. As for pregnancy, the text words were as follows: pregnancy OR pregnant OR Pregnant women OR mothers OR gestation. As for influenza, the text words were as follows: influenza OR respiratory tract infections OR upper respiratory tract infections OR respiratory infection OR common cold OR acute coryza OR flu OR grippe. The search was restricted to the title, abstract, and keywords. Both English and Chinese language articles were allowed.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (I) influenza infection in pregnant women; and (II) preterm birth was reported. The exclusion criteria were as follows: (I) insufficient data for comparison; (II) insufficient data to assess the pooled effect of influenza on preterm birth; and (III) study types such as conferences abstracts, trials, reviews, meta-analyses, case reports, letters to the editor, or comments.

Study selection

The above search strategy was employed in five databases, including PubMed, Embase, Cochrane Library, Web of Science, and China National Knowledge Infrastructure (CNKI). Next, duplicate records were removed, and then, studies with irrelevant content (according to their titles and abstracts) were excluded. Finally, except for studies without full texts, the remaining studies were independently screened by two authors based on the inclusion and exclusion criteria, while discrepancies between the authors were resolved by group discussion.

Data collection

All clinic information were collected from medical records. The following data were collected from the selected studies: first author, published year, published country, study period, sample size, study type, influenza type, cut-off or definition of preterm birth, findings, and Newcastle-Ottawa Scale (NOS) score. Patients were divided into the influenza-positive group and the influenza-negative group, and the

© Translational Pediatrics. All rights reserved.

number of preterm birth were collected. Two authors independently extracted data and reached a consensus to prevent any extraction errors.

Quality assessment

The NOS score was used to assess the quality of the included studies based on selection, comparability, and outcome (40). Cohort selection included the representativeness of exposure, selection of the non-exposure, ascertainment of exposure, and demonstration that the outcome was not present at the start. Comparability was based on the design and analysis of cohorts. The assessment of outcome included assessment, long follow-up for outcomes to occur, and adequacy of follow-up. Studies that scored >7 were considered high quality; otherwise, the study was considered low quality.

Statistical analysis

As for the risk of preterm birth in women infected with influenza, odds ratios (ORs) and confidence intervals (CIs) were preferred and were estimated using raw data from reconstructed 2*2 tables. The effect values including relative risks (RRs) and hazards ratios (HRs) were crudely used as ORs. Then, the ORs and CIs were pooled using the random-effect model, and P<0.1 was considered statistically significant.

The I^2 value and the chi-squared test were used to evaluate the statistical heterogeneity (41,42); the I^2<30% was considered non-important, 30–60% was considered moderate, and >60% was considered substantial. A forest plot was used to display the results of the meta-analysis. Subgroup analysis based on similarity in different aspects was used for further analysis. A funnel plot was used to assess the publication bias. All data analyses were performed using STATA SE V16.0 software.

Results

Study selection

A total of 951 studies were identified after performing the search strategy in five databases on December 29, 2022 (151 studies in PubMed, 206 studies in Embase, 25 studies in Cochrane Library, 542 studies in Web of Science, and 27 studies in CNKI). Among these, 214 duplicate records were removed before screening. Then, 685 records were excluded after examining their titles and abstracts. Eight studies with unavailable full text were excepted, 20 studies were excluded because no comparisons or critical data were missing, and 24 studies were finally selected based on the inclusion and exclusion criteria (*Figure 1*).

Study characteristics

The current meta-analysis included 24 eligible studies involving 24,760,890 patients. Ten studies were conducted in the USA, four studies were conducted in Canada, two studies were conducted in Norway, and the remaining studies were conducted in Hungary, Thailand, Turkey, Spain, the UK, Brazil, Korea, and Sweden. The year of publication ranged from 2003 to 2022, and all of the included studies were cohort studies. The influenza types included seasonal influenza, influenza A (H1N1, H3N1, H3N2), influenza B (Yamagata, Victoria), and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Other study data including the author, study period, sample size, cut-off or definition of preterm birth, findings, and NOS score were shown in *Table 1*.

Preterm birth of influenza infection

Although more than half of the included studies reported that influenza infection was not associated with preterm birth, the current meta-analysis found there were more preterm births in women infected with influenza during pregnancy (OR =1.52, 95% CI: 1.18 to 1.97, I^2=97.35%, P=0.00). Notably, one study provided separate ORs for two influenza types. See *Figure 2*.

Preterm births according to the different types of influenza

A subgroup analysis was conducted according to the similarity in influenza types and found that there were still more preterm births in women infected with influenza A and B (OR =2.05, 95% CI: 1.26 to 3.32, I^2=96.14%, P<0.1) and SARS-CoV-2 (OR =2.16, 95% CI: 1.75 to 2.66, I^2=0.00%, P<0.1). However, infection with influenza A alone (OR =1.38, 95% CI: 0.96 to 2.00, I^2=85.36%, P>0.1) or seasonal influenza (OR =1.15, 95% CI: 0.91 to 1.44, I^2=91.93%, P>0.1) did not increase the risk of preterm birth. Moreover, statistical heterogeneity remained high within most subgroups; the only subgroup in which heterogeneity was substantially reduced was that containing only studies of SARS-CoV-2. However, there was significant heterogeneity

© Translational Pediatrics. All rights reserved.

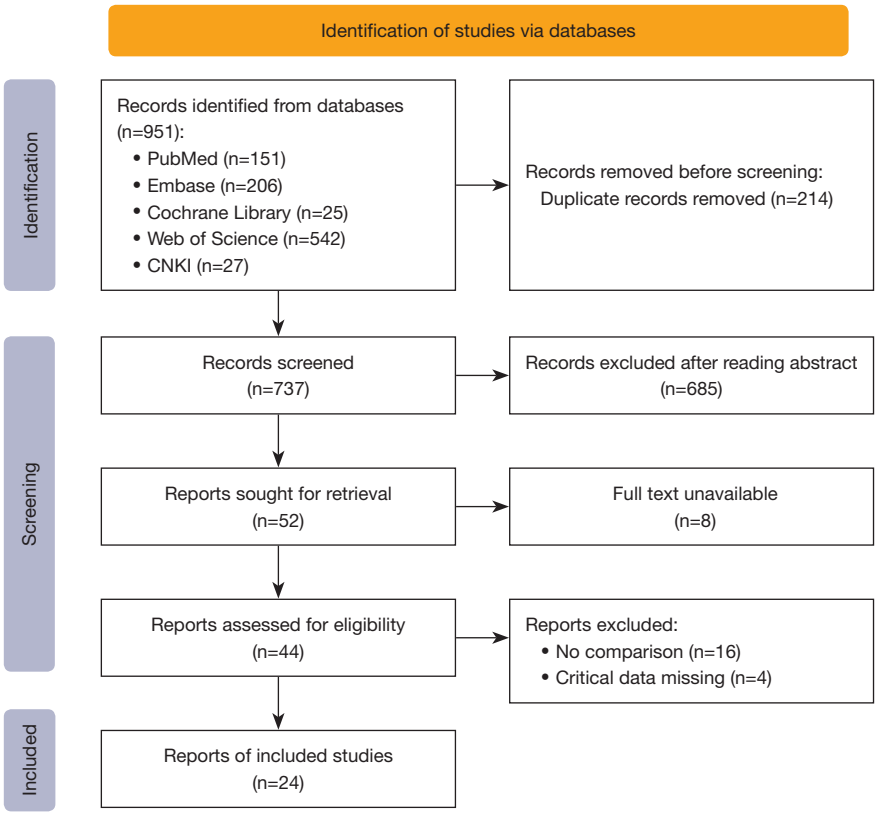

Figure 1 Flowchart of study selection. CNKI, China National Knowledge Infrastructure.

between the subgroups (P=0.00), which signified that the influenza subtypes might be a source of heterogeneity (*Figure 3*).

Preterm birth in different areas

As the spread of influenza varies geographically, studies were divided into four continent groups according to the countries in which they were carried out. Following the subgroup analysis, we found that influenza infection was still a risk factor in North America (OR =1.55, 95% CI: 1.09 to 2.21, I^2=96.71%, P<0.1), Europe (OR =1.56, 95% CI: 1.01 to 2.41, I^2=92.38%, P<0.1), and Asia (OR =1.41, 95% CI: 1.34 to 1.49, I^2=0%, P<0.1). However, statistical heterogeneity remained high within most subgroups, and the heterogeneity between the subgroups was not significant (*Figure 4*).

Preterm birth during different periods

We identified a significant number of studies that focused on the 2009–2010 pandemic and grouped them according to the study period. The analysis showed that influenza infection had no significant effect on preterm birth before 2009 (OR =1.52, 95% CI: 0.81 to 2.85, I^2=99.08%, P>0.1) but increased the risk of preterm birth during 2009–2010 (OR =1.35, 95% CI: 1.11 to 1.66, I^2=83.58%, P<0.1) and after 2010 (OR =2.04, 95% CI: 1.51 to 2.75, I^2=36.32%, P<0.1). However, statistical heterogeneity remained high within most subgroups, and the heterogeneity between the subgroups was not significant (*Figure 5*).

Publication bias

A funnel plot was used to assess the publication bias. Although there were some points outside the 95% CIs, the funnel plot remained relatively symmetrical (*Figure 6*).

Sensitivity analysis

Each study was sequentially excluded for sensitivity analysis, and the results were not significantly different, which meant

© Translational Pediatrics. All rights reserved.

Table 1 Baseline characteristics of the included studies

Author	Year	Country	Study period	Sample size	Study type	Influenza type	Cut-off or definition of PTB	Findings	NOS score
Acs N (15)	2006	Hungary	1980–1996	38151	Cohort	Seasonal	37 completed weeks (259 days)	Mothers with influenza in pregnancy had a lower proportion of PTB	8
Cox S (30)	2006	USA	1998–2002	6277508	Cohort	Influenza A(H3N2), A(H3N1), and B	International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code 644	During influenza season, hospitalized pregnant women with respiratory illness had significantly longer lengths of stay and higher odds of delivery complications compared to hospitalized pregnant women without respiratory illness	9
Dawood FS (16)	2021	Thailand	2017–2018	11277	Prospective cohort	87% influenza A (H1N1, H3N2), and 13% influenza B (Yamagata, Victoria)	37 weeks	Antenatal influenza was not associated with PTB	8
Doyle TJ (31)	2013	USA	2009–2010	295934	Retrospective cohort	Influenza A(H1N1)	37 weeks	Children born to women with pH1N1 illness during pregnancy were at an increased risk of PTB	9
Ersoy AO (17)	2017	Turkey	2014–2015	35	Cohort	77.8% influenza A and 22.2% influenza B	37 weeks	Preterm deliveries in pregnant women did not differ significantly between influenza-positive and influenza-negative pregnant women in a non-vaccinated study population	5
Fell DB (18)	2018	Canada	2009–2011	192082	Retrospective cohort	Influenza A (H1N1)	37 completed weeks	In the general obstetrical population, there was no association between pH1N1 influenza illness and PTB	9
Hansen C (19)	2012	USA	2008–2010	107889	Cohort	25% seasonal virus and 75% Influenza A (H1N1)	37 weeks	Among infants delivered by women with a diagnosis of A(H1N1)pdm09 or seasonal influenza virus infection, the prevalence of PTB was similar to those among infants delivered by women without a diagnosis	9
Hartert TV (20)	2003	USA	1985–1993	880	Matched cohort study	Seasonal influenza	37 completed weeks	We detected no significant increase in the adverse perinatal outcomes associated with respiratory hospitalizations during the influenza season	6
Laake I (21)	2018	Norway	2009	1258	Cohort	Influenza A (H1N1)	37 completed weeks	No significant associations between influenza and risk of PTB were observed	7
Martin A (32)	2013	USA	1998–2008	15739700	Cohort	Influenza A (H1N1, H3N2) and B	ICD-9-CM diagnosis code 644.2	Among live births, there were higher odds of preterm delivery	9

Table 1 *(continued)*

© Translational Pediatrics. All rights reserved.

Table 1 *(continued)*

Author	Year	Country	Study period	Sample size	Study type	Influenza type	Cut-off or definition of PTB	Findings	NOS score
McNeil SA (22)	2011	Canada	1990–2002	132588	Retrospective cohort study	Seasonal influenza	37 weeks	Infants who were born to mothers who had been hospitalized for respiratory illness during the influenza season at any time during pregnancy were not associated with PTB	9
Morken NH (23)	2011	Norway	1999–2008	265931	Prospective cohort	Seasonal influenza	between gestational weeks 22 + 0 days and 36 + 6 days	Only ear-nose-throat infection in early pregnancy was associated with an increased risk of spontaneous preterm delivery	9
Naresh A (24)	2013	USA	2009–2010	841	Multicenter observational cohort study	Influenza A (H1N1)	37 completed weeks	Pregnant women with mild clinical illness secondary to 2009 H1N1 influenza were not at a greater risk of adverse pregnancy outcomes	6
Newsome K (33)	2019	USA	2009	1941	Matched retrospective cohort	Influenza A (H1N1)	37 weeks	Severely ill women with 2009 H1N1 influenza during pregnancy were more likely to have adverse birth outcomes than women without influenza	7
Nieto-Pascual L (25)	2013	Spain	2009–2010	168	Cohort	Influenza A (H1N1)	37 weeks	No differences were found between the obstetric and perinatal outcomes of both affected and unaffected or treated and untreated cohorts	6
Pierce M (34)	2011	UK	2009–2010	1476	Cohort	Influenza A (H1N1)	37 weeks	Women infected with 2009/H1N1 influenza in pregnancy were at risk of poor pregnancy outcomes, with an increased risk of preterm and very preterm delivery	7
Prasad N (26)	2019	USA	2012–2015	83	Cohort	Influenza A (H1N1, H3N2) and B	37 weeks	There was no significant difference in premature delivery between influenza-positive and influenza-negative patients	5
Regan AK (35)	2020	Canada	2009	4750	Retrospective cohort	Seasonal influenza	between ≥20 and <37 weeks	Compared to non-hospitalized women, the risk of PTB was greater among women hospitalized with influenza-associated acute respiratory or febrile illness	7
Regan AK (36)	2022	USA	2020–2021	78283	Cohort	SARS-CoV-2	NA	Prenatal SARS-CoV-2 infection was associated with an increased risk of adverse pregnancy outcomes	8
Rogers VL (27)	2010	USA	2003–2004	31064	Prospective observational study	Influenza A (H3N2)	37 weeks	Compared with our general obstetric population, there was no significant difference in obstetric or neonatal complications	8

Table 1 *(continued)*

© Translational Pediatrics. All rights reserved.

Table 1 *(continued)*

Author	Year	Country	Study period	Sample size	Study type	Influenza type	Cut-off or definition of PTB	Findings	NOS score
da Silva AA (28)	2014	Brazil	2009	243	Prospective cohort study	82.7% influenza A (H1N1), and 17.3% seasonal influenza A	37 weeks	There were no differences in the perinatal outcomes	5
Song JY (37)	2020	Korea	2007–2010	1563626	Retrospective cohort study	ICD-10 code J09, J10, and J11	37 weeks	Multivariate analysis revealed that maternal influenza infection significantly increased the risk of PTB	9
Stephansson O (38)	2022	Sweden	2020–2021	14665	Prospective cohort study	SARS-CoV-2	37+0 weeks	Compared with term births, test-positivity was higher in medically-indicated PTB but not significantly increased in spontaneous PTB	8
Tuyishime JD (29)	2003	Canada	2002	517	Cohort	Influenza A	NA	There was no indication of an increased frequency of adverse perinatal outcomes associated with influenza-like illness during pregnancy	6

Note: 37 completed weeks means 37+0 weeks; 37 weeks means for 37+0 weeks to 37+7 weeks. NOS, Newcastle-Ottawa Scales; PTB, preterm birth NA, not assessed; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2.

© Translational Pediatrics. All rights reserved.

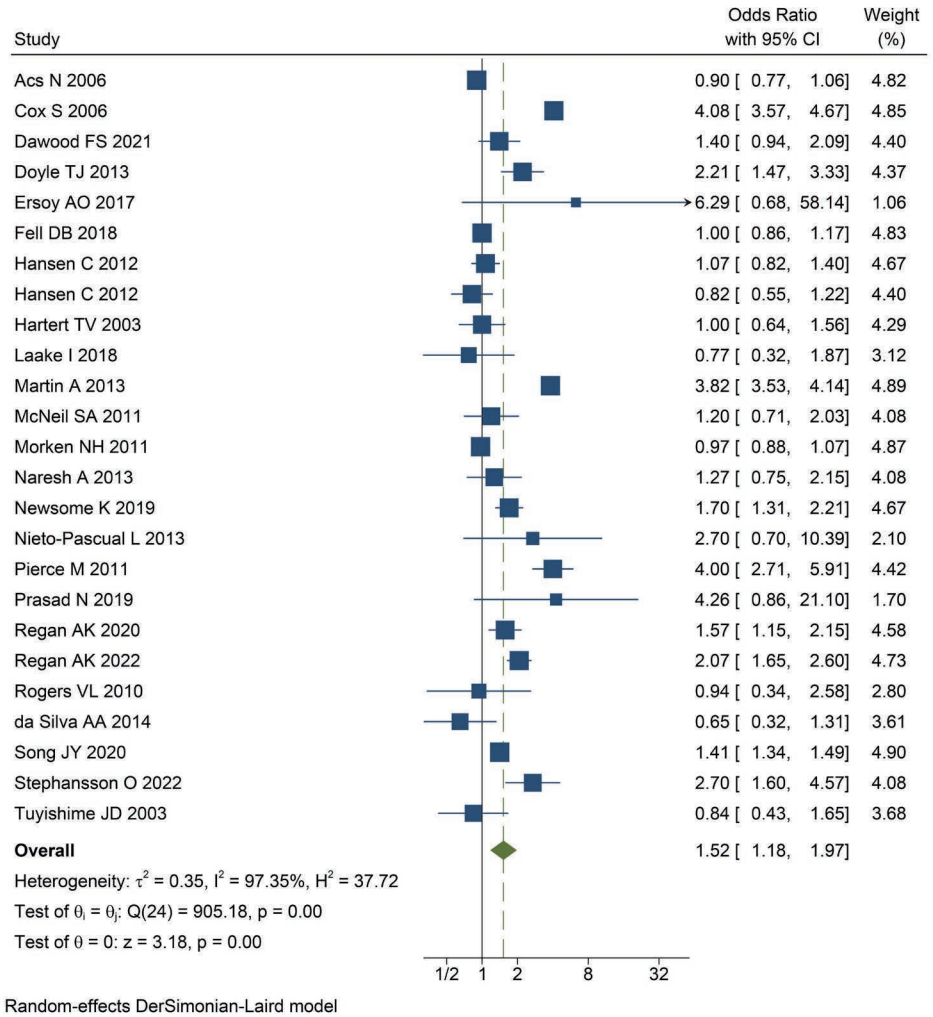

Figure 2 Preterm birth with maternal influenza infection. 95% CI, 95% confidence interval.

the results were relatively robust.

Discussion

This meta-analysis included 24 studies and found that pregnant women infected with influenza during pregnancy had a higher risk of preterm birth, especially for the influenza A and B and SARS-CoV-2 viruses.

Preterm birth is a syndrome of unclear etiologies, with the majority of cases being spontaneous (43). It can be triggered by a variety of factors, such as infection, cervical pathology, uterine overdistension, progesterone deficiency, and maternal-fetal stress (44-46). These different etiologies can activate complex pathological pathways, leading to uterine contraction, cervical ripening, and fetal membrane rupture (47). While some measures can be taken to identify the risk of preterm birth, such as cervical length measurement by transvaginal ultrasound (TVUE), more interventional triggers need to be identified to reduce the incidence of preterm birth (48).

As for influenza infection, most of the studies included in this meta-analysis revealed that antenatal influenza was not associated with preterm birth (15-29), and some even found a lower proportion of preterm births in mothers with influenza in pregnancy (15,19,21,23,27-29). However, Pierce *et al.* demonstrated that women infected with H1N1 influenza were at risk of an increased risk of preterm and very preterm delivery (34). Moreover, Regan *et al.* also showed that prenatal SARS-CoV-2 infection increased the risk of adverse pregnancy outcomes (36). Based on

© Translational Pediatrics. All rights reserved.

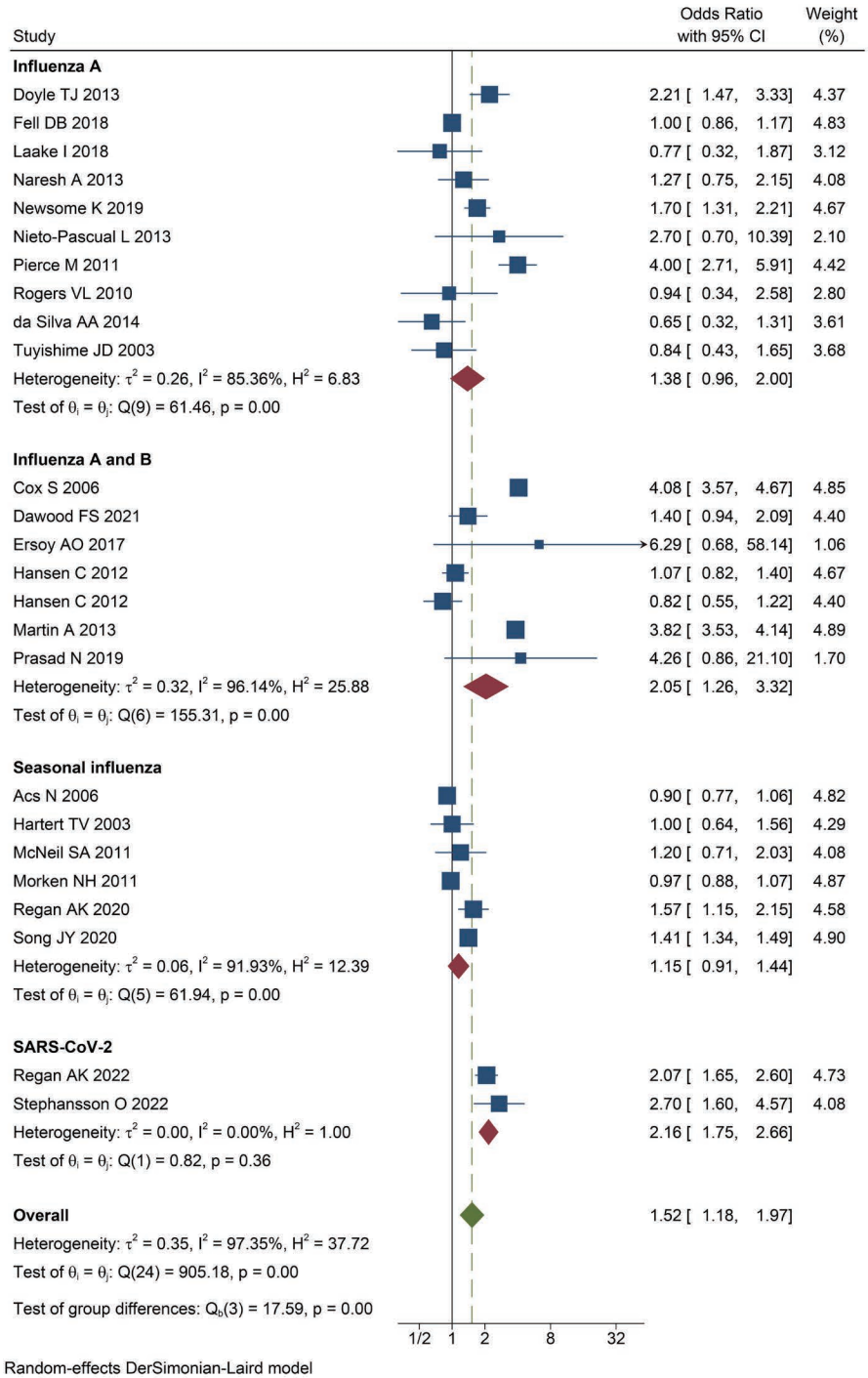

Figure 3 Preterm birth with different influenza types. 95% CI, 95% confidence interval.

the current inconsistencies in the literature, we hoped to provide more accurate results through meta-analysis to guide clinical decisions.

The potential effects of the influenza virus on the mother and fetus are not well understood. Since influenza viruses are rarely passed through the placenta, the infection is more likely to cause preterm birth through other mechanisms, such as maternal fever and inflammatory responses (49-51).

© Translational Pediatrics. All rights reserved.

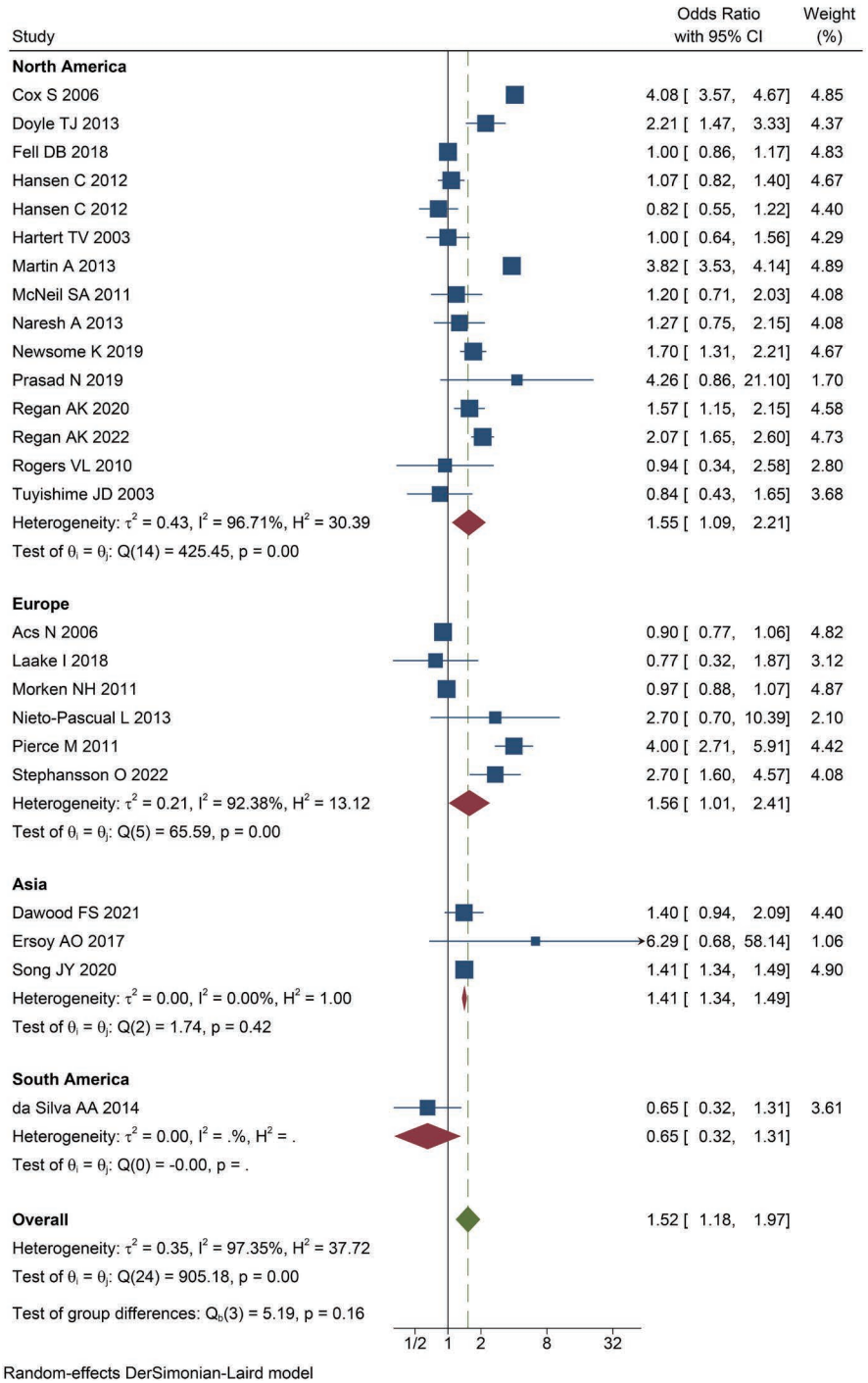

Figure 4 Preterm birth in different areas. 95% CI, 95% confidence interval.

Elevated levels of pro-inflammatory cytokines in the body can cause immune perturbation, leading to the sluggish establishment of immune tolerance and excessive inflammation, which in turn affects placental function (52,53). Notably, feto-maternal immune tolerance is also a key feature in some other pregnancy complications (54,55).

Furthermore, pro-inflammatory cytokines in the vaginal fluid can also play a role in determining the timing

© Translational Pediatrics. All rights reserved.

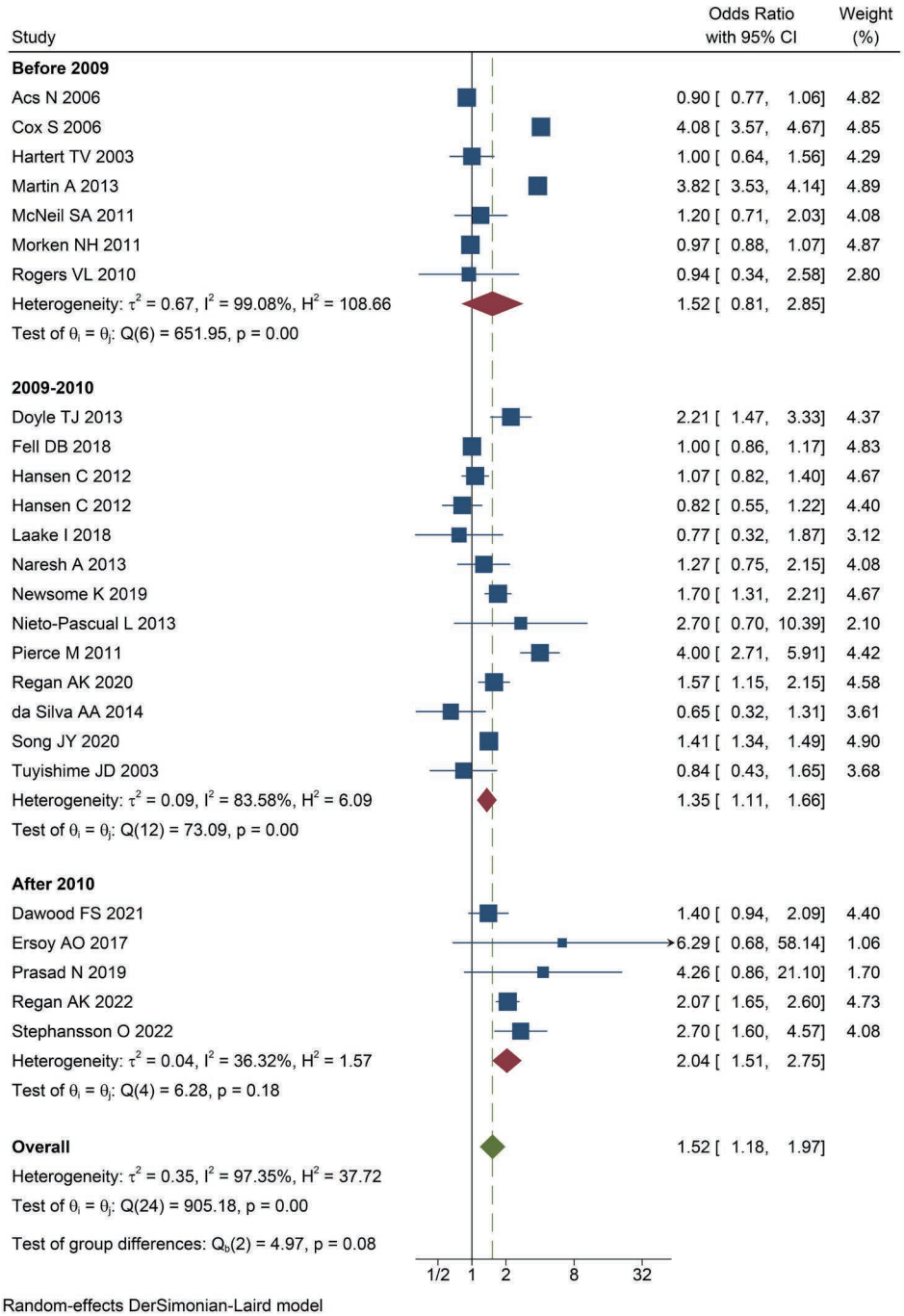

Figure 5 Preterm birth during different periods. 95% CI, 95% confidence interval.

of pregnancy by influencing the microbiome (56). The abundance of taxa associated with preterm birth tends to decrease in the vaginal environment during the entire pregnancy (57,58). Pro-inflammatory cytokines are highly associated with the ecological dysregulation of bacterial taxa (for example, A. vaginae, G. vaginalis, and Megasphaera type 1), which contribute to preterm birth (58,59). However, carriage rates of the vaginal microbiome and specific microbial taxa vary considerably between populations and this mechanism needs to be further validated in a multi-

© Translational Pediatrics. All rights reserved.

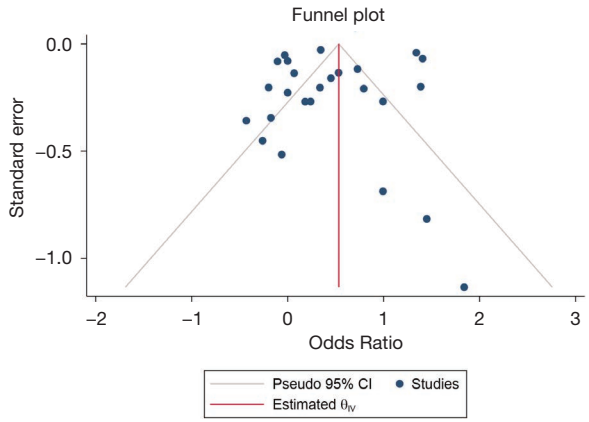

Figure 6 Funnel plot. 95% CI, 95% confidence interval.

ethnic population.

This was the first meta-analysis investigating the impact of maternal influenza infection on preterm birth, but there were some limitations. Firstly, besides influenza-positive patients, this study included pregnant women hospitalized with acute respiratory illness during the influenza season and could not classify them according to the influenza test results. Secondly, further studies on the clinical outcomes of influenza B infection are needed in the future, and more research on the impact of SARS-CoV-2 on pregnancy outcomes is also expected.

Conclusions

Although a majority of studies suggested that influenza infection during pregnancy did not increase the probability of preterm birth, this meta-analysis found that women infected with influenza had a higher risk of preterm birth. We hope that more relevant public health measures such as vaccination can be enacted to increase the awareness of pregnant women and protect them from infection.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-23-134/rc

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-23-134/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-23-134/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Mortality, morbidity, and hospitalisations due to influenza lower respiratory tract infections, 2017: an analysis for the Global Burden of Disease Study 2017. Lancet Respir Med 2019;7:69-89.
2. Iuliano AD, Roguski KM, Chang HH, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet 2018;391:1285-300.
3. Paget J, Spreeuwenberg P, Charu V, et al. Global mortality associated with seasonal influenza epidemics: New burden estimates and predictors from the GLaMOR Project. J Glob Health 2019;9:020421.
4. Demicheli V, Jefferson T, Ferroni E, et al. Vaccines for preventing influenza in healthy adults. Cochrane Database Syst Rev 2018;2:CD001269.
5. Lina B, Georges A, Burtseva E, et al. Complicated hospitalization due to influenza: results from the Global Hospital Influenza Network for the 2017-2018 season. BMC Infect Dis 2020;20:465.
6. MacIntyre CR, Chughtai AA, Barnes M, et al. The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09. BMC Infect Dis 2018;18:637.
7. Malosh RE, Martin ET, Ortiz JR, et al. The risk of lower respiratory tract infection following influenza virus

© Translational Pediatrics. All rights reserved.

infection: A systematic and narrative review. Vaccine 2018;36:141-7.
8. Bhalerao-Gandhi A, Chhabra P, Arya S, et al. Influenza and pregnancy: a review of the literature from India. Infect Dis Obstet Gynecol 2015;2015:867587.
9. Jash S, Sharma S. Pathogenic Infections during Pregnancy and the Consequences for Fetal Brain Development. Pathogens 2022;11:193.
10. Walani SR. Global burden of preterm birth. Int J Gynaecol Obstet 2020;150:31-3.
11. Vogel JP, Chawanpaiboon S, Moller AB, et al. The global epidemiology of preterm birth. Best Pract Res Clin Obstet Gynaecol 2018;52:3-12.
12. Chang E. Preterm birth and the role of neuroprotection. BMJ 2015;350:g6661.
13. Simmons LE, Rubens CE, Darmstadt GL, et al. Preventing preterm birth and neonatal mortality: exploring the epidemiology, causes, and interventions. Semin Perinatol 2010;34:408-15.
14. Menon R. Spontaneous preterm birth, a clinical dilemma: etiologic, pathophysiologic and genetic heterogeneities and racial disparity. Acta Obstet Gynecol Scand 2008;87:590-600.
15. Acs N, Bánhidy F, Puhó E, et al. Pregnancy complications and delivery outcomes of pregnant women with influenza. J Matern Fetal Neonatal Med 2006;19:135-40.
16. Dawood FS, Kittikraisak W, Patel A, et al. Incidence of influenza during pregnancy and association with pregnancy and perinatal outcomes in three middle-income countries: a multisite prospective longitudinal cohort study. Lancet Infect Dis 2021;21:97-106.
17. Ersoy AO, Unlu S, Oztas E, et al. Influenza infections in the 2014-2015 season and pregnancy outcomes. J Infect Dev Ctries 2017;11:766-71.
18. Fell DB, Platt RW, Basso O, et al. The Relationship Between 2009 Pandemic H1N1 Influenza During Pregnancy and Preterm Birth: A Population-based Cohort Study. Epidemiology 2018;29:107-16.
19. Hansen C, Desai S, Bredfeldt C, et al. A large, population-based study of 2009 pandemic Influenza A virus subtype H1N1 infection diagnosis during pregnancy and outcomes for mothers and neonates. J Infect Dis 2012;206:1260-8.
20. Hartert TV, Neuzil KM, Shintani AK, et al. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. Am J Obstet Gynecol 2003;189:1705-12.
21. Laake I, Tunheim G, Robertson AH, et al. Risk of pregnancy complications and adverse birth outcomes after maternal A(H1N1)pdm09 influenza: a Norwegian population-based cohort study. BMC Infect Dis 2018;18:525.
22. McNeil SA, Dodds LA, Fell DB, et al. Effect of respiratory hospitalization during pregnancy on infant outcomes. Am J Obstet Gynecol 2011;204:S54-7.
23. Morken NH, Gunnes N, Magnus P, et al. Risk of spontaneous preterm delivery in a low-risk population: the impact of maternal febrile episodes, urinary tract infection, pneumonia and ear-nose-throat infections. Eur J Obstet Gynecol Reprod Biol 2011;159:310-4.
24. Naresh A, Fisher BM, Hoppe KK, et al. A multicenter cohort study of pregnancy outcomes among women with laboratory-confirmed H1N1 influenza. J Perinatol 2013;33:939-43.
25. Nieto-Pascual L, Arjona-Berral JE, Marín-Martín EM, et al. Early prophylactic treatment in pregnant women during the 2009-2010 H1N1 pandemic: obstetric and neonatal outcomes. J Obstet Gynaecol 2013;33:128-34.
26. Prasad N, Huang QS, Wood T, et al. Influenza-Associated Outcomes Among Pregnant, Postpartum, and Nonpregnant Women of Reproductive Age. J Infect Dis 2019;219:1893-903.
27. Rogers VL, Sheffield JS, Roberts SW, et al. Presentation of seasonal influenza A in pregnancy: 2003-2004 influenza season. Obstet Gynecol 2010;115:924-9.
28. da Silva AA, Ranieri TM, Torres FD, et al. Impact on pregnancies in south Brazil from the influenza A (H1N1) pandemic: cohort study. PLoS One 2014;9:e88624.
29. Tuyishime JD, De Wals P, Moutquin JM, et al. Influenza-like illness during pregnancy: results from a study in the eastern townships, Province of Quebec. J Obstet Gynaecol Can 2003;25:1020-5.
30. Cox S, Posner SF, McPheeters M, et al. Hospitalizations with respiratory illness among pregnant women during influenza season. Obstet Gynecol 2006;107:1315-22.
31. Doyle TJ, Goodin K, Hamilton JJ. Maternal and neonatal outcomes among pregnant women with 2009 pandemic influenza A(H1N1) illness in Florida, 2009-2010: a population-based cohort study. PLoS One 2013;8:e79040.
32. Martin A, Cox S, Jamieson DJ, et al. Respiratory illness hospitalizations among pregnant women during influenza season, 1998-2008. Matern Child Health J 2013;17:1325-31.
33. Newsome K, Alverson CJ, Williams J, et al. Outcomes of infants born to women with influenza A(H1N1)pdm09. Birth Defects Res 2019;111:88-95.
34. Pierce M, Kurinczuk JJ, Spark P, et al. Perinatal outcomes

© Translational Pediatrics. All rights reserved.

after maternal 2009/H1N1 infection: national cohort study. BMJ 2011;342:d3214.
35. Regan AK, Feldman BS, Azziz-Baumgartner E, et al. An international cohort study of birth outcomes associated with hospitalized acute respiratory infection during pregnancy. J Infect 2020;81:48-56.
36. Regan AK, Arah OA, Fell DB, et al. SARS-CoV-2 Infection During Pregnancy and Associated Perinatal Health Outcomes: A National US Cohort Study. J Infect Dis 2022;225:759-67.
37. Song JY, Park KV, Han SW, et al. Paradoxical long-term impact of maternal influenza infection on neonates and infants. BMC Infect Dis 2020;20:502.
38. Stephansson O, Pasternak B, Ahlberg M, et al. SARS-CoV-2 and pregnancy outcomes under universal and non-universal testing in Sweden: register-based nationwide cohort study. BJOG 2022;129:282-90.
39. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. JAMA 2000;283:2008-12.
40. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:603-5.
41. Ioannidis JP. Interpretation of tests of heterogeneity and bias in meta-analysis. J Eval Clin Pract 2008;14:951-7.
42. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60.
43. Couceiro J, Matos I, Mendes JJ, et al. Inflammatory factors, genetic variants, and predisposition for preterm birth. Clin Genet 2021;100:357-67.
44. Jiang M, Mishu MM, Lu D, et al. A case control study of risk factors and neonatal outcomes of preterm birth. Taiwan J Obstet Gynecol 2018;57:814-8.
45. Cobo T, Kacerovsky M, Jacobsson B. Risk factors for spontaneous preterm delivery. Int J Gynaecol Obstet 2020;150:17-23.
46. Kvaratskhelia N, Tkeshelashvili V. Impact of biomedical and behavioral factors on preterm birth. Georgian Med News 2020;(308):19-25.
47. Di Renzo GC, Tosto V, Giardina I. The biological basis and prevention of preterm birth. Best Pract Res Clin Obstet Gynaecol 2018;52:13-22.
48. Ville Y, Rozenberg P. Predictors of preterm birth. Best Pract Res Clin Obstet Gynaecol 2018;52:23-32.
49. Xiao YN, Yu FY, Xu Q, et al. Tropism and Infectivity of Pandemic Influenza A H1N1/09 Virus in the Human Placenta. Viruses 2022;14:2807.
50. Cornish EF, Filipovic I, Åsenius F, et al. Innate Immune Responses to Acute Viral Infection During Pregnancy. Front Immunol 2020;11:572567.
51. Cappelletti M, Della Bella S, Ferrazzi E, et al. Inflammation and preterm birth. J Leukoc Biol 2016;99:67-78.
52. Kim CJ, Romero R, Chaemsaithong P, et al. Chronic inflammation of the placenta: definition, classification, pathogenesis, and clinical significance. Am J Obstet Gynecol 2015;213:S53-69.
53. Green ES, Arck PC. Pathogenesis of preterm birth: bidirectional inflammation in mother and fetus. Semin Immunopathol 2020;42:413-29.
54. Deshmukh H, Way SS. Immunological Basis for Recurrent Fetal Loss and Pregnancy Complications. Annu Rev Pathol 2019;14:185-210.
55. Robertson SA, Care AS, Moldenhauer LM. Regulatory T cells in embryo implantation and the immune response to pregnancy. J Clin Invest 2018;128:4224-35.
56. Fettweis JM, Serrano MG, Brooks JP, et al. The vaginal microbiome and preterm birth. Nat Med 2019;25:1012-21.
57. Freitas AC, Bocking A, Hill JE, et al. Increased richness and diversity of the vaginal microbiota and spontaneous preterm birth. Microbiome 2018;6:117.
58. MacIntyre DA, Chandiramani M, Lee YS, et al. The vaginal microbiome during pregnancy and the postpartum period in a European population. Sci Rep 2015;5:8988.
59. Bayar E, Bennett PR, Chan D, et al. The pregnancy microbiome and preterm birth. Semin Immunopathol 2020;42:487-99.

(English Language Editor: A. Kassem)

Cite this article as: Wang X, Ou H, Wu Y, Xing Z. Risk of preterm birth in maternal influenza or SARS-CoV-2 infection: a systematic review and meta-analysis. Transl Pediatr 2023;12(4):631-644. doi: 10.21037/tp-23-134

© Translational Pediatrics. All rights reserved.