Original Article

# Risk factors for neonatal hyperbilirubinemia: a systematic review and meta-analysis

**Qun Lin[1#], Daomou Zhu[2#], Caihua Chen[3], Yonghong Feng[1], Fenfen Shen[4], Zhenkui Wu[5]**

[1]Neonatal Department, Haikou Maternal and Child Health Hospital, Haikou, China; [2]Department of Emergency, Hainan Women and Children's Medical Center, Haikou, China; [3]Neonatal Department, Hainan Women and Children's Medical Center, Haikou, China; [4]Department of Nursing, Affiliated Haikou Hospital of Xiangya Medical College Central South University, Haikou, China; [5]Department of Pediatrics, Hainan Modern Women and Children's Hospital, Haikou, China

*Contributions:* (I) Conception and design: Q Lin, D Zhu, Z Wu; (II) Administrative support: Z Wu; (III) Provision of study materials or patients: Q Lin, D Zhu, Z Wu; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: Q Lin, D Zhu, Z Wu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

*Correspondence to:* Zhenkui Wu. Department of Pediatrics, Hainan Modern Women and Children's Hospital, No. 18-1, Qiongzhou Avenue, Qiongshan District, Haikou, China. Email: wuzhenkui8084@163.com.

**Background:** Hyperbilirubinemia is the most common cause of neonatal hospitalization and, although it generally has a good prognosis, a significant percentage of neonatal patients maintain a high bilirubin level, which can lead to severe complications, including lifelong disability such as growth retardation, encephalopathy, autism and hearing impairment. The study of risk factors for neonatal hyperbilirubinemia has been controversial. Therefore, we evaluated the risk factors of neonatal hyperbilirubinemia using a meta-analysis.

**Methods:** Relevant English and Chinese studies that discussed risk factors for neonatal hyperbilirubinemia were retrieved from the PubMed, EMBASE, Medline, Central, China National Knowledge Infrastructure (CNKI), Wanfang and China Science Digital Library (CSDL). The literature took newborns as the research object, set up a control group, and observed the relationship between exposure factors and neonatal hyperbilirubinemia. The combined effect size was expressed by odds ratio (OR) and 95% confidence interval (CI). The Chi-square test was used to test heterogeneity of the studies, and if it existed, subgroup analyses were used to explore the source of heterogeneity, and the random-effects model was selected for the combined analysis. The fixed-effects model was chosen for the combined analysis if there was no heterogeneity. Publication bias was assessed using Egger's test and funnel plot.

**Results:** Risk factors for neonatal hyperbilirubinemia were exclusive breastfeeding (BF: OR =1.74, 95% CI: 1.42, 2.12, Z=5.43, P<0.00001); glucose-6-phosphate dehydrogenase deficiency (G6PD: OR =1.62, 95% CI: 1.44, 1.81, Z=8.39, P<0.00001); maternal-fetal ABO blood group incompatibility (OR =1.64, 95% CI: 1.42, 1.89, Z=6.75, P<0.00001); and preterm birth (PTB: OR =1.31, 95% CI: 1.17, 1.47, Z=4.60, P<0.00001); there was no heterogeneity or publication bias among the studies (BF: $\chi^2$=5.34, P=0.25, $I^2$=25%; G6PD: $\chi^2$=4.40, P=0.49, $I^2$=0%; ABO: $\chi^2$=1.91, P=0.75, $I^2$=0%; PTB: $\chi^2$=0.81, P=0.67, $I^2$=0%).

**Conclusions:** Exclusive breastfeeding, G6PD deficiency, ABO incompatibility and premature birth were confirmed as risk factors for neonatal hyperbilirubinemia. Pregnant women with risk factors should be monitored more closely and clinical intervention should be given in a timely manner.

**Keywords:** Neonatal hyperbilirubinemia; risk factors; meta-analysis

Submitted May 05, 2022. Accepted for publication Jun 16, 2022.
doi: 10.21037/tp-22-229
**View this article at:** https://dx.doi.org/10.21037/tp-22-229

## Introduction

Hyperbilirubinemia is the most common cause of neonatal hospitalization (1), and although most newborns with hyperbilirubinemia have a good prognosis (2), approximately 8–11% maintain a high bilirubin level, which may lead to severe complications, including lifelong disability such as growth retardation, encephalopathy, autism and hearing impairment (3-5). The incidence of pathological jaundice is 1% without risk factors of hyperbilirubinemia, whereas it is 59% with risk factors (3).

The risk factors of neonatal hyperbilirubinemia are diverse, complex and interconnected. For example, the age and gestational age of the pregnant woman will affect or change the feeding mode, and perinatal diseases may affect the delivery method, causing a series of chain reactions. The research on the risk factors of neonatal hyperbilirubinemia has always been controversial; for example, Chen *et al.* (6) believed that exclusive breastfeeding was a risk factor. Scrafford *et al.* (7) believed that exclusive breastfeeding may be a protective factor for specific neonatal hyperbilirubinemia. Chen *et al.* (8) concluded that high breastfeeding frequency can reduce the incidence of hyperbilirubinemia. Huang *et al.* (9) considered that preterm birth, exclusive breastfeeding, blood group incompatibility, and glucose-6-phosphate dehydrogenase (G6PD) deficiency are risk factors for the disease. Kaplan *et al.* (10) considered that only G6PD, blood group inappropriate disease risk factors. The reason for these differences in our analysis is the presence of bias in the subjects studied in separate studies. The socioeconomic conditions and cultural background of different regions may have some influence on the results. Therefore, it is of great clinical significance to determine the risk factors of neonatal jaundice to effectively reduce the risk of neonatal hyperbilirubinemia and the incidence of related complications. Most of the studies are retrospective analysis, the sample size is small, and the evidence level is low, which cannot support the conclusion. In the present study we performed a necessary meta-analysis to clarify the risk factors of neonatal hyperbilirubinemia and provide clues for clinical early intervention and prevention. We present the following article in accordance with the MOOSE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-229/rc).

## Methods

### *Literature retrieval*

A literature search was conducted in the PubMed, EMBASE, Medline, Central, China National Knowledge Infrastructure (CNKI), Wanfang and China Science Digital Library (CSDL) databases, using the keywords "neonatal hyperbilirubinemia" or "jaundice" and "risk factors" and selecting English and Chinese studies. The retrieval date was April 1, 2022.

### *Literature screening*

Inclusion criteria: (I) newborns; (II) subjects allocated to experimental and control groups; (III) investigation of exposure factors of newborns or mothers, including at least one of exclusive breastfeeding, G6PD deficiency, maternal and infant ABO incompatibility, and preterm birth; (IV) outcome was neonatal hyperbilirubinemia; (V) observational studies: cohort, case-control or cross-sectional study; (VI) results included the odds ratio (OR) and 95% confidence interval (CI) of exposure factors or could be calculated from the data.

Exclusion criteria: (I) repeat reports; (II) adult subjects; (III) no control group; (IV) incomplete data and unable to be supplemented through contact with the author(s).

### *Data extraction*

Two researchers jointly extracted the data required for the analysis, including the author(s), title, date of publication, research type, number of researchers, number of cases of neonatal jaundice, number of exclusively breastfed newborns, number of ABO-incompatible newborns, of premature babies. An attempt was made to contact the author(s) for missing data. Differences in opinions were resolved by consensus of the two researchers.

### *Literature quality evaluation*

The Newcastle-Ottawa scale (NOS) was used to evaluate literature quality, comprising the selectivity and comparability of research methods, exposure factors,

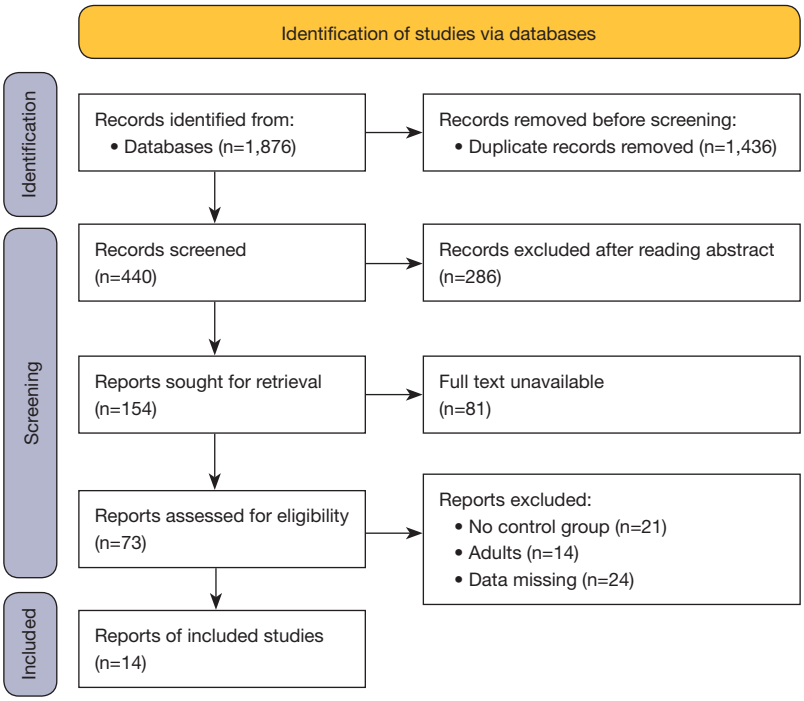


**Figure 1** Flow chart of literature screening.

and outcomes. NOS score ≥6 was classified as low risk of bias, otherwise high risk of bias. The risk of bias in cross-sectional studies was assessed using the Joanna Briggs Institute (JBI) cross-sectional study volume risk of bias assessment criteria, with a total score of 20 points. A JBI score >14 was considered low risk of bias. Differences in opinions were resolved by consensus of the two researchers.

### *Statistical analysis*

We used Cochrane RevMan5.3 software for statistical analysis of the data. Adjusting for confounding factors, OR values were calculated by multivariate analysis, or obtained directly from the literature. The OR value and 95% CI were used to describe the effect quantity. The Chi-square test was used and when the heterogeneity statistic $I^2$ corrected by degrees of freedom was >50% or P<0.1, it was considered there was heterogeneity. Subgroup analyses was used to explore the causes of heterogeneity. When heterogeneity could not be eliminated, only reviews were performed without pooling results. When the $I^2$ corrected by degrees of freedom was ≤50% and P≥0.1, it was considered that there was no heterogeneity, and the fixed-effects model was used. Publication bias was assessed using funnel plots and Egger's test. In this study, OR values were calculated or obtained from cohort studies, case-control studies and cross-sectional studies, and in the absence of heterogeneity, pooled analyses could be performed. Two-way P<0.05 indicated statistically significant.

## Results

### *Characteristics of the included studies*

A total of 1,876 studies were retrieved from the databases and a total of 14 articles were screened according to the inclusion criteria (6-19). The flow chart of literature screening is shown in *Figure 1*. Among the 14 studies, 5 were cohort studies, 4 were case-control studies, and 5 were cross-sectional studies. There were 2 studies from the Chinese literature, and 12 from the English literature. The baseline information of the studies and NOS/JBI scores are shown in *Tables 1*,*2*.

### *Identified risk factors for neonatal hyperbilirubinemia*

#### Exclusive breastfeeding

A total of 5 studies of the association between breastfeeding and neonatal hyperbilirubinemia were included in our meta-analysis. There was no heterogeneity among them

**Table 1** Characteristics of the included studies and NOS/JBI scores

| Author | Year | Language | Study type | n | NOS/JBI |
|---|---|---|---|---|---|
| Chen *et al.* (6) | 2011 | English | Cohort | 313 | 7 |
| Scrafford *et al.* (7) | 2013 | English | Cross-sectional | 18,985 | 14 |
| Chen *et al.* (8) | 2015 | English | Cohort | 98 | 7 |
| Huang *et al.* (9) | 2009 | English | Cohort | 1,034 | 8 |
| Kaplan *et al.* (10) | 1998 | English | Case-control | 98 | 8 |
| Ketsuwan *et al.* (11) | 2017 | English | Case-control | 176 | 6 |
| Mojtahedi *et al.* (12) | 2018 | English | Cross-sectional | 200 | 12 |
| Najib *et al.* (13) | 2013 | English | Cohort | 1,134 | 6 |
| Owa (14) | 1989 | English | Case-control | 234 | 8 |
| Thielemans *et al.* (15) | 2021 | English | Cross-sectional | 1,710 | 12 |
| Thielemans *et al.* (16) | 2018 | English | Cross-sectional | 2,980 | 12 |
| Yu *et al.* (17) | 1992 | English | Cohort | 12,379 | 6 |
| Xiong *et al.* (18) | 2019 | Chinese | Case-control | 200 | 5 |
| Dai & Cheng (19) | 2011 | Chinese | Cross-sectional | 206 | 10 |

NOS, Newcastle-Ottawa scale; JBI, Joanna Briggs Institute.

**Table 2** NOS scores of included literatures

| Study | Selection | | | | Comparability | Exposure | | | NOS |
|---|---|---|---|---|---|---|---|---|---|
| | Adequate definition of case | Representativeness of the case | Selection of controls | Definition of controls | control for important factor | Ascertainment of exposure | Same method of ascertain for cases and controls | Non-response rate | |
| Chen (6) | * | * | * | * | * | * | * | – | 7 |
| Chen (8) | * | * | * | * | * | – | * | * | 7 |
| Huang (9) | * | * | * | – | ** | * | * | * | 8 |
| Kaplan (10) | * | * | – | * | ** | * | * | * | 8 |
| Ketsuwan (11) | * | * | * | – | * | * | – | * | 6 |
| Najib (13) | * | * | * | – | – | * | * | * | 6 |
| Owa (14) | * | * | * | – | ** | * | * | * | 8 |
| Yu (17) | * | * | * | * | * | – | * | – | 6 |
| Xiong (18) | * | * | * | * | – | * | – | – | 5 |

NOS, Newcastle-Ottawa scale.

($\chi^2$=5.34, P=0.25, $I^2$=25%), so the fixed-effects model was used. Exclusive breastfeeding was identified as a risk factor (OR =1.74, 95% CI: 1.42, 2.12, Z=5.43, P<0.00001). The Egger test and funnel diagram in *Figure 2* shows the scatter points distributed within the CI, roughly symmetrically, and there was no publication bias (P>0.05) (*Figure 3*).

### Glucose-6-phosphate dehydrogenase (G6PD) deficiency

A total of 6 studies of the association between G6PD deficiency and neonatal hyperbilirubinemia were included in our meta-analysis. There was no heterogeneity among them ($\chi^2$=4.40, P=0.49, $I^2$=0%), so the fixed-effects model

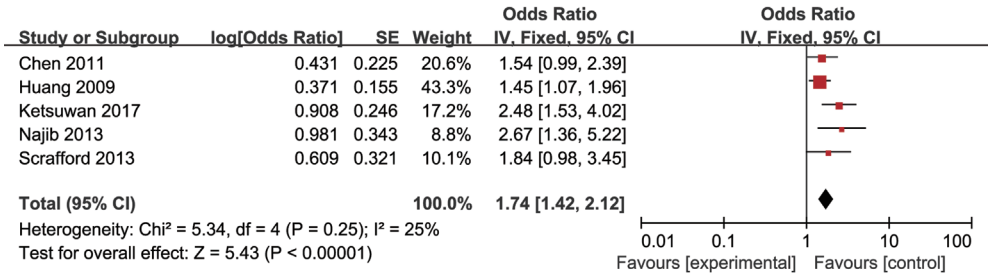


**Figure 2** Forest diagram of the correlation between exclusive breastfeeding and neonatal hyperbilirubinemia. SE, standard error; CI, confidence interval.

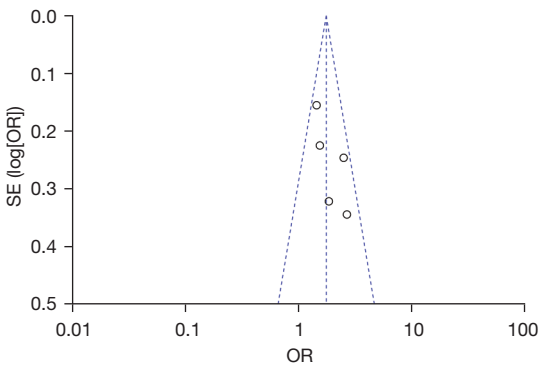


**Figure 3** Funnel plot of the correlation between exclusive breastfeeding and neonatal hyperbilirubinemia. OR, odds ratio; SE, standard error.

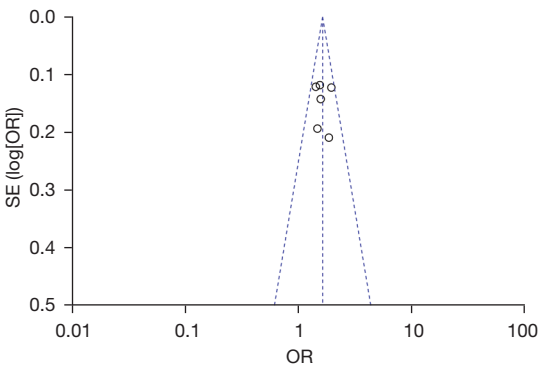


**Figure 5** Funnel plot of the correlation between G6PD deficiency and neonatal hyperbilirubinemia. OR, odds ratio; SE, standard error; G6PD, glucose-6-phosphate dehydrogenase.

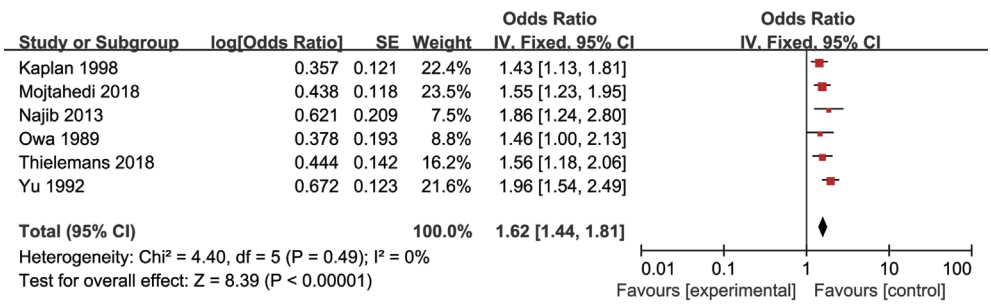


**Figure 4** Forest plot of the correlation between G6PD deficiency and neonatal hyperbilirubinemia. SE, standard error; CI, confidence interval; G6PD, glucose-6-phosphate dehydrogenase.

was used for consolidation. G6PD deficiency was identified as a risk factor (OR =1.62, 95% CI: 1.44, 1.81, Z=8.39, P<0.00001). The Egger test and funnel diagram in *Figure 4* shows the scatter points distributed within the CI, roughly symmetrically, and there was no publication bias (P>0.05) (*Figure 5*).

### Maternal-fetal ABO blood group incompatibility

A total of 5 studies of the correlation between ABO blood group incompatibility and neonatal hyperbilirubinemia were included in our meta-analysis. There was no heterogeneity among them ($\chi^2$=1.91, P=0.75, $I^2$=0%), so the fixed-effects model is used for consolidation. Maternal-fetal ABO blood

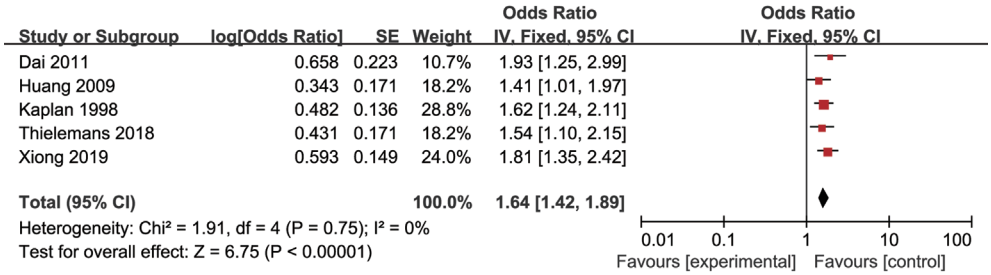


**Figure 6** Forest plot of the correlation between maternal-fetal ABO blood group incompatibility and neonatal hyperbilirubinemia. SE, standard error; CI, confidence interval.

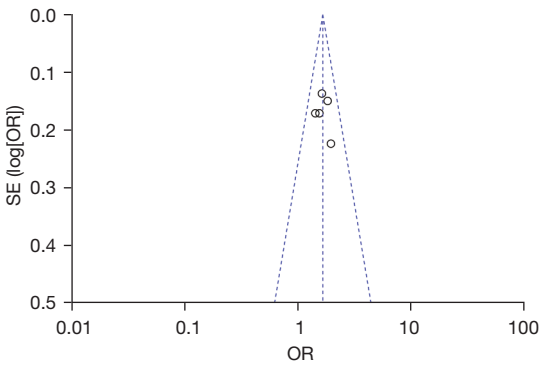


**Figure 7** Funnel plot of the correlation between maternal-fetal ABO blood group incompatibility and neonatal hyperbilirubinemia. OR, odds ratio; SE, standard error.

group incompatibility was identified as a risk factor (OR =1.64, 95% CI: 1.42, 1.89, Z=6.75, P<0.00001). The Egger test and funnel diagram in *Figure 6* shows the scatter points distributed within the CI, roughly symmetrically, and there was no publication bias (P>0.05) (*Figure 7*).

### Premature delivery

A total of 3 studies of the association between preterm birth and neonatal hyperbilirubinemia were included in our meta-analysis. There was no heterogeneity among them ($\chi^2$=0.81, P=0.67, $I^2$=0%), so the fixed-effects model was used for consolidation. Preterm birth was identified as a risk factor (OR =1.31, 95% CI: 1.17, 1.47, Z=4.60, P<0.00001). The Egger test and funnel diagram in *Figure 8* shows the scatter points distributed within the CI, roughly symmetrically, and there was no publication bias (P>0.05) (*Figure 9*).

## Discussion

The results of our meta-analysis revealed exclusive breastfeeding as a risk factor for neonatal hyperbilirubinemia. Infants with breast milk hyperbilirubinemia have a good prognosis (20), but 58–81.4% of infants with severe hyperbilirubinemia are exclusively or mainly breastfed (21). With the popularity of breastfeeding education, the breastfeeding rate has increased, and the incidence rate of breast milk jaundice has increased year by year (22,23). Breast milk jaundice may be related to the presence of glucuronosyltransferase inhibitors in the mother's colostrum and the lack of bilirubin reuptake inhibitors in the infant's small intestine. A partial reason for increased unconjugated bilirubin in breast milk jaundice is that breast milk contains more highly active glucuronic acid, which increases intestinal and liver circulation. The amount of breastfeeding after birth may be related to the severity of jaundice. It should be emphasized that the relationship between breastfeeding and neonatal hyperbilirubinemia is complex. First of all, whether to choose breastfeeding and the method of breastfeeding (including exclusive breastfeeding and mixed feeding) are related to maternal age and mode of delivery. These factors combined influence the occurrence of neonatal hyperbilirubinemia. Secondly, a study showed that exclusive breastfeeding is a risk factor for neonatal hyperbilirubinemia in infants with nutritional problems (7). On the other hand, for infants without nutritional problems, exclusive breastfeeding is protective for neonatal hyperbilirubinemia (7). Another study emphasized that insufficient breastfeeding, rather than breastfeeding per se, is the risk factor for neonatal hyperbilirubinemia (24). Finally, others have reported that increasing breastfeeding frequency can reduce the risk of hyperbilirubinemia (25). The incidence of hyperbilirubinemia was significantly lower in infants who breastfed ≥8 times/day than in infants who breastfed less than that frequency (8). The American Academy of Pediatrics recommends breastfeeding between 8 and 12 times/day in the first few weeks of life (3). The

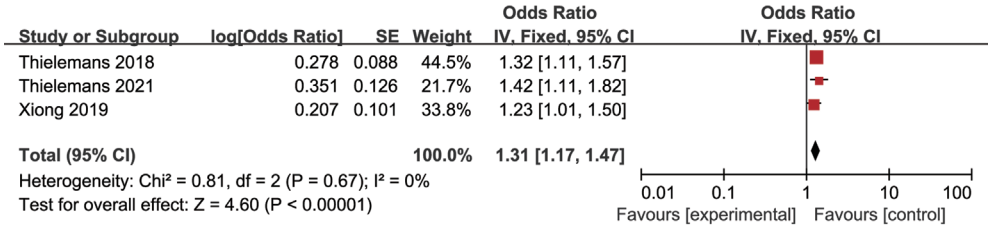


**Figure 8** Forest plot of the correlation between preterm birth and neonatal hyperbilirubinemia. SE, standard error; CI, confidence interval.

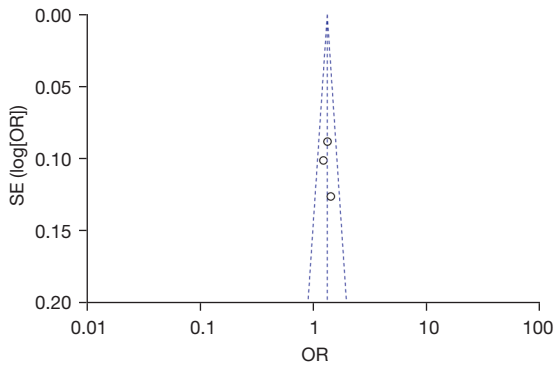


**Figure 9** Funnel plot of the correlation between preterm birth and neonatal hyperbilirubinemia. OR, odds ratio; SE, standard error.

time of first feeding is also associated with neonatal hyperbilirubinemia (11).

The results of our meta-analysis showed that premature delivery was a risk factor for neonatal hyperbilirubinemia, which was consistent with the results of a previous meta-analysis suggesting that premature delivery is a maternal factor (3) affecting the incidence rate of neonatal jaundice. Neonatal hyperbilirubinemia caused by premature birth accounts for 30% of children (3) and may be related to the maturity of uridine diphosphate glucuronosyltransferase. Gestational age is positively correlated with the activity of glucuronosyltransferase diphosphate. Premature delivery may lead to delayed first feeding, insufficient breast milk, infant nutritional disorders, reduced feeding frequency and other problems, which will lead to increased concentration of bilirubin in the newborn's blood.

Maternal-fetal ABO blood group incompatibility and G6PD deficiency were also risk factors for neonatal hyperbilirubinemia, because they both cause hemolysis, a conclusion supported by a previous study (16). ABO blood group incompatibility, G6PD enzyme deficiency, premature delivery, scalp hematoma and Rh blood group incompatibility are the most common risk factors for early neonatal jaundice (16). A previous study showed that the cases of neonatal hyperbilirubinemia caused by ABO blood group incompatibility accounted for 13.3 (3). In two Chinese studies, maternal–fetal blood group incompatibility was considered an independent risk factor for neonatal jaundice (18,19).

There are some limitations to our research. Few of the studies included in the analysis originated in less developed countries, which may affect the results. Secondly, there were relatively few risk factors included in the analysis, which therefore cannot be considered as comprehensively showing neonatal hyperbilirubinemia's risk factors.

There are some limitations to this study. The first is that the included literature is small, the sample size is small, and the coverage is narrow. Second, we analyzed cross-sectional studies, cohort studies, and case-control studies together due to the lack of literature. Low-quality evidence from cross-sectional studies. Finally, exposure variables are few and cannot fully describe risk factors for disease. Multicenter high-quality studies are still needed to confirm our conclusions.

Exclusive breastfeeding, G6PD deficiency, maternal-fetal ABO blood group incompatibility and premature delivery were confirmed as risk factors for neonatal hyperbilirubinemia. Pregnant women with risk factors should be monitored more closely and clinical intervention should be given in a timely manner.

## Acknowledgments

*Funding:* The project was supported by Hainan Province Clinical Medical Center.

## Footnote

*Reporting Checklist:* The authors have completed the MOOSE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-229/rc

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-229/coif). The authors have no conflicts of interest to declare.

*Ethics 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.



## References

1. Yu B, Hu F. Exploration of the pathogenic factors of neonatal jaundice and the clinical effect of blue phototherapy. Am J Transl Res 2021;13:6802-6.
2. Kuniyoshi Y, Tsujimoto Y, Banno M, et al. Neonatal jaundice, phototherapy and childhood allergic diseases: An updated systematic review and meta-analysis. Pediatr Allergy Immunol 2021;32:690-701.
3. Boskabadi H, Rakhshanizadeh F, Zakerihamidi M. Evaluation of Maternal Risk Factors in Neonatal Hyperbilirubinemia. Arch Iran Med 2020;23:128-40.
4. Okumura A, Ichimura S, Hayakawa M, et al. Neonatal Jaundice in Preterm Infants with Bilirubin Encephalopathy. Neonatology 2021;118:301-9.
5. Kujabi ML, Petersen JP, Pedersen MV, et al. Neonatal jaundice and autism spectrum disorder: a systematic review and meta-analysis. Pediatr Res 2021;90:934-49.
6. Chen CF, Hsu MC, Shen CH, et al. Influence of breast-feeding on weight loss, jaundice, and waste elimination in neonates. Pediatr Neonatol 2011;52:85-92.
7. Scrafford CG, Mullany LC, Katz J, et al. Incidence of and risk factors for neonatal jaundice among newborns in southern Nepal. Trop Med Int Health 2013;18:1317-28.
8. Chen YJ, Yeh TF, Chen CM. Effect of breast-feeding frequency on hyperbilirubinemia in breast-fed term neonate. Pediatr Int 2015;57:1121-5.
9. Huang A, Tai BC, Wong LY, et al. Differential risk for early breastfeeding jaundice in a multi-ethnic Asian cohort. Ann Acad Med Singap 2009;38:217-24.
10. Kaplan M, Vreman HJ, Hammerman C, et al. Combination of ABO blood group incompatibility and glucose-6-phosphate dehydrogenase deficiency: effect on hemolysis and neonatal hyperbilirubinemia. Acta Paediatr 1998;87:455-7.
11. Ketsuwan S, Baiya N, Maelhacharoenporn K, et al. The Association of Breastfeeding Practices with Neonatal Jaundice. J Med Assoc Thai 2017;100:255-61.
12. Mojtahedi SY, Izadi A, Seirafi G, et al. Risk Factors Associated with Neonatal Jaundice: A Cross-Sectional Study from Iran. Open Access Maced J Med Sci 2018;6:1387-93.
13. Najib KS, Saki F, Hemmati F, et al. Incidence, risk factors and causes of severe neonatal hyperbilirubinemia in the South of iran (fars province). Iran Red Crescent Med J 2013;15:260-3.
14. Owa JA. Relationship between exposure to icterogenic agents, glucose-6-phosphate dehydrogenase deficiency and neonatal jaundice in Nigeria. Acta Paediatr Scand 1989;78:848-52.
15. Thielemans L, Peerawaranun P, Mukaka M, et al. High levels of pathological jaundice in the first 24 hours and neonatal hyperbilirubinaemia in an epidemiological cohort study on the Thailand-Myanmar border. PLoS One 2021;16:e0258127.
16. Thielemans L, Trip-Hoving M, Landier J, et al. Indirect neonatal hyperbilirubinemia in hospitalized neonates on the Thai-Myanmar border: a review of neonatal medical records from 2009 to 2014. BMC Pediatr 2018;18:190.
17. Yu MW, Hsiao KJ, Wuu KD, et al. Association between glucose-6-phosphate dehydrogenase deficiency and neonatal jaundice: interaction with multiple risk factors. Int J Epidemiol 1992;21:947-52.
18. Xiong F L, Cheng B, Shi N L, et al. Risk factors for neonatal hyperbilirubinemia and related preventive measures. Journal of Southwest Medical University 2019;42:454-7.
19. Dai X, Cheng GP. Analysis on pathogenesis and risk factors of hyperbilirubinemia in neonates. Clin J Med Offic 2011;39:957-9.
20. Li Y, Shen N, Li J, et al. Changes in Intestinal Flora and Metabolites in Neonates With Breast Milk Jaundice. Front Pediatr 2020;8:177.
21. Sgro M, Campbell D, Shah V. Incidence and causes of severe neonatal hyperbilirubinemia in Canada. CMAJ 2006;175:587-90.

22. Prameela KK. Breastfeeding during breast milk jaundice - a pathophysiological perspective. Med J Malaysia 2019;74:527-33.
23. Yang L F, Li J, Hu R, et al. Association of fatty acid composition in human milk with breast milk jaundice in neonates. Zhongguo Dang Dai Er Ke Za Zhi 2020;22:1256-60.
24. Gourley GR. Breast-feeding, neonatal jaundice and kernicterus. Semin Neonatol 2002;7:135-41.
25. Salas AA, Salazar J, Burgoa CV, et al. Significant weight loss in breastfed term infants readmitted for hyperbilirubinemia. BMC Pediatr 2009;9:82.

(English Language Editor: K. Brown)

**Cite this article as:** Lin Q, Zhu D, Chen C, Feng Y, Shen F, Wu Z. Risk factors for neonatal hyperbilirubinemia: a systematic review and meta-analysis. Transl Pediatr 2022;11(6):1001-1009. doi: 10.21037/tp-22-229