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Incidence of neonatal asphyxia and associated risk factors: a systematic review and cumulative meta-analysis

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Abstract

Objectives To analyze the incidence of neonatal asphyxia and its associated related risk factors and provide reference for reducing the incidence and mortality of neonatal asphyxia.

Methods PubMed, Web of Science, CNKI, and Wanfang were searched for cross-sectional/case-control studies (inception-December 31, 2024). After dual-independent screening (PROSPERO: CRD420251118897), 18 studies ($n = 737,839$ neonates) were included. Quality was assessed using AHRQ. Random/fixed-effects models were applied based on I^2 thresholds. Temporal trends were explored via sequential meta-analysis by publication year. Sensitivity and publication bias analyses were conducted.

Results A total of 18 studies was included, involving 737,839 neonates, and the overall quality of the literature was acceptable. The combined incidence of neonatal asphyxia and its 95% CI was 7% (5%, 8%). Factors associated with neonatal asphyxia included instrumental delivery, primiparity, preterm birth, and low birth weight. The pooled ORs and 95% CIs for meta-analyzed risk factors of neonatal asphyxia (instrument-assisted delivery, primiparity, preterm birth, and low birth weight) were 3.10 (1.79, 5.38), 3.51 (2.15, 5.74), 2.18 (1.54, 3.09), and 2.85 (2.33, 3.49), respectively. According to the order of publication, cumulative Meta-analysis showed that the OR values and 95% CI of instrumental delivery, primiparity, preterm birth, and low birth evolved had a trend over time.

Conclusion The incidence of neonatal asphyxia remains an important public health concern. Findings suggest that neonates born following instrumental delivery, or with primiparity, preterm birth, or low birth weight could be considered for more careful monitoring.

Keywords Neonates, Neonatal asphyxia, Risk factors, Cumulative meta-analysis

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Introduction

Neonatal asphyxia, defined as impaired gas exchange during the perinatal period leading to hypoxemia, hypercapnia, and metabolic acidosis [1], remains a critical global health challenge. Globally, the incidence and mortality rates of neonatal asphyxia remain high [2]. According to data released by the World Health Organization (WHO), approximately 800,000 newborns die annually from complications related to neonatal asphyxia, accounting for about 23% of global neonatal deaths [2]. Neonatal asphyxia is also one of the significant causes of death in children under 5 years old, particularly in low- and middle-income countries [3]. The resulting brain damage and sequelae severely impact child survival and development [3]. A surveillance analysis by He et al. on the mortality of children under 5 in Beijing found that neonatal asphyxia accounted for 7.8% of child mortality causes [4]. Neonatal asphyxia can lead to severe systemic and neurological sequelae, primarily due to insufficient blood flow and/or oxygen supply to the fetus or newborn during the perinatal period. When gas exchange in the placenta or lungs is compromised or interrupted, vital organs may experience varying degrees of hypoxia. If the hypoxic state persists and reaches a certain severity, the body will incur an oxygen debt, shifting to anaerobic metabolism [5]. This results in lactate accumulation and acidosis, potentially progressing to hypoxic-ischemic encephalopathy in newborns [6]. In recent years, several studies have explored the determinants of neonatal asphyxia. However, existing studies have reported inconsistent incidence rates and determinants. We conducted a systematic review and cumulative meta-analysis to summarize the existing findings from published observational studies, mainly including neonatal asphyxia incidence, risk estimates (odds ratios OR) and 95% confidence intervals (CI), and associated factors. The aims of this study were to evaluate the incidence and risk factors of neonatal asphyxia and provide evidence for the prevention of its occurrence.

Methods

Search strategy

Relevant studies on the determinants of neonatal asphyxia were retrieved from PubMed, Web of Science, China National Knowledge Infrastructure (CNKI) and Wanfang database. No language restrictions were applied during the initial search. The search was conducted using a combination of subject headings and free words and was limited to studies published from inception to December 31, 2024. The English search formula was ("newborn asphyxia" OR "neonatal asphyxia" OR "birth asphyxia" OR "perinatal asphyxia" OR "hypoxic-ischemic encephalopathy") AND ("prevalence" OR "incidence" OR "rate") AND ("risk factors" OR "determinants" OR "predictors" OR "contributing factors" OR "associations"). The complete search strategies for all databases, including all keywords and subject headings used, are provided in Supplementary Material. After reviewing the titles, abstracts and full texts, relevant articles were further screened based on the inclusion and exclusion criteria. This systematic review adheres to PRISMA guidelines and is PROSPERO-registered (CRD420251118897).

Inclusion and exclusion criteria

Inclusion Criteria (Constructed According to the PECOS Principle): P (Population): Neonates; E (Exposure): Exposure to maternal, perinatal, or neonatal risk factors potentially associated with neonatal asphyxia (e.g., maternal age, pregnancy complications, mode of delivery, low birth weight, prematurity, infections); C (Comparison): Neonates without neonatal asphyxia (i.e., those not exposed to the specified risk factors or serving as the control group in case-control studies); O (Outcomes): Incidence of neonatal asphyxia; risk estimates (odds ratio, OR) and their 95% confidence intervals; associated risk factors; S (Study Design): Cross-sectional studies and case-control studies.

Literature meeting any of the following exclusion criteria was excluded: Conference abstracts; Unavailable full text or incomplete data; Failure to meet inclusion criteria; Lack of adjustment for confounding factors; Duplicate publications; Theses or dissertations.

Data extraction and literature quality assessment

Wang, and Xiao independently and simultaneously performed literature screening, data extraction, and quality assessment of the studies to minimize subjective bias. In case of any discrepancies during the processes of literature screening, data extraction, or quality assessment, the first and second authors resolved them through discussion and re-evaluation of the literature. If any disagreement persisted, consensus was reached through consultation with the corresponding author. The specific process was as follows: Duplicate references were removed using EndNote 20 reference management software, followed by an initial screening of articles based on titles and abstracts, excluding those unrelated to neonatal asphyxia. Subsequently, the following information was extracted from each study: publication year, country, region, study design, sample size, number of outcomes, incidence, risk estimates (odds ratio, OR) with 95% confidence intervals (CI), and relevant factors. Finally, two researchers independently assessed the risk of bias in the included studies using the cross-sectional study quality evaluation tool recommended by the Agency for Healthcare Research and Quality (AHRQ). The tool comprises 11 items, which are as follows: Whether the research objective is clearly stated; Whether the study subjects are

well-defined; Whether the inclusion criteria are explicit; Whether the sample is consecutive or randomized; Whether the study subjects are representative; Whether the exposure and outcome variables are accurately measured; Whether the assessment time and follow-up are clearly described; Whether potential confounding factors are controlled for; Whether missing data are addressed; Whether sample size estimation is provided; Whether appropriate statistical analysis methods are employed. Each item meeting the criteria is scored 1 point, otherwise 0 points. The total score ranges from 0 to 11, with a higher score indicating better study quality.

Statistical indicators

The meta-analysis was performed using Stata 15.0 software. The effect measure was expressed as OR [95% CI]. Heterogeneity among the included studies was assessed, with $P<0.05$ indicating significant heterogeneity. The I^2 statistic was used to evaluate heterogeneity, where $I^2 < 50\%$ suggested no significant heterogeneity, and a fixed-effects model was employed to calculate the pooled effect size. When $I^2 \geq 50\%$, significant heterogeneity was considered present among the studies, and a random-effects model was applied for analysis. Forest plots were generated, and cumulative meta-analysis was conducted based on the publication year of the studies. Sensitivity analysis was performed using the leave-one-out method to examine the stability of the results. Publication bias was assessed using funnel plots and Egger's test. All tests were two-sided, with $P<0.05$ considered statistically significant.

Results

Characteristics and quality assessment of included literature

A total of 2193 articles were retrieved and 1056 were excluded for being duplicates. After reading the titles and abstracts, 910 studies were further excluded, and 227 articles were included for full-text screening. Finally, 18 articles [7–24] were included in the Meta-analysis, as shown in Fig. 1. The present analysis included a total of 18 studies, comprising 737,839 samples. Among these, 10 were cross-sectional studies and 8 were case-control studies. The studies consisted of 9 Asian studies, 4 African studies, 3 American studies, and 2 European studies. The AHRQ evaluation system was used to assess the quality of observational studies, and the quality of bias risk was assessed from 5 domains: selection bias, implementation bias, follow-up bias, measurement bias, and reporting bias. The AHRQ includes 11 quality questions, each of which can be answered with "yes," "no," or "uncertain." Low-quality studies: 0–3 points, medium-quality studies: 4–7 points, high-quality studies: 8–11 points. This study analyzed studies with medium and high quality, as shown in Tables 1 and 2.

Meta-analysis of incidence of neonatal asphyxia

Cumulative meta-analysis

A total of 10 studies reported the incidence rate of neonatal asphyxia, including 730,174 newborns. The results of heterogeneity test showed: $P<0.01$, $I^2=99.91\%$, indicating significant heterogeneity, and the random effect model was adopted for analysis. The meta-analysis yielded a pooled incidence rate ratio (IRR) of 1.07 (95% CI: 1.05, 1.09), which corresponds to an absolute incidence of 7% (95% confidence interval (CI): 5% to 8%). This result was statistically significant ($Z=7.533$, $P<0.01$). The cumulative Meta-analysis based on the publication year of the literature showed a clear time trend, as shown in Figs. 2 and 3. To explore the sources of heterogeneity, a subgroup analysis was performed based on different diagnostic criteria. The results indicated statistically significant differences between subgroups ($p=0.01$) (Fig. 4). However, heterogeneity within the subgroups remained high (I^2 >50%), and meta-regression did not support the diagnostic criteria as a significant source of heterogeneity ($p=0.259$).

Subgroup analysis

Subgroup analysis was performed on the 10 studies that reported the incidence of neonatal asphyxia, based on the distribution of research areas, divided into European regions, Asian regions, American regions, and African regions. The subgroup analysis results suggest significant heterogeneity among the groups: $P=0.05$, as shown in Fig. 5.

Neonatal asphyxia risk factor cumulative meta-analysis

Cumulative meta-analysis of instrumental delivery and neonatal asphyxia

Five studies reported the relationship between neonatal asphyxia and instrument-assisted delivery, covering a total of 88,478 newborns. The heterogeneity test results showed: $P<0.01$, $I^2=83.45\%$, indicating significant heterogeneity. The combined OR value was 3.10 (95% CI: 1.79, 5.38), with a statistically significant difference ($P<0.01$). The cumulative Meta-analysis based on the publication year of the literature showed a clear time trend, as shown in Figs. 6 and 7.

Cumulative meta-analysis of primiparity and neonatal asphyxia

A total of 4 studies reported the relationship between newborn asphyxia and primiparity, including 1302 newborns. The results of heterogeneity test showed: $P=0.06$, $I^2=58.90\%$, indicating moderate heterogeneity. A random-effects model was employed for analysis. The

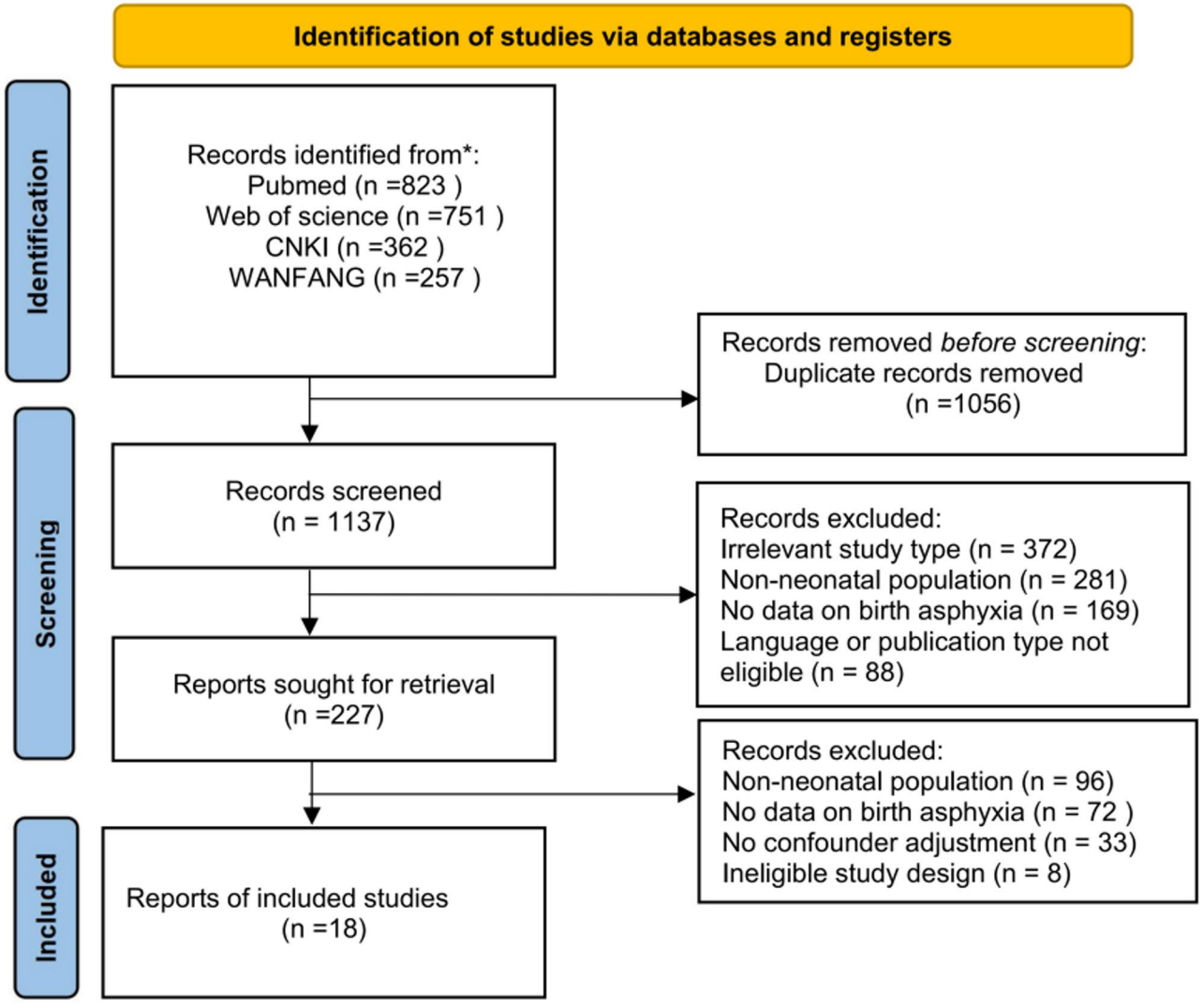

Fig. 1 Flowchart of Literature Screening

pooled OR was 3.51 (95% CI: 2.15, 5.74), showing statistically significant difference ($P<0.01$). The cumulative Meta-analysis based on the publication year of the literature showed a clear time trend, as shown in Figs. 8 and 9.

Cumulative meta-analysis of preterm birth and neonatal asphyxia

Eight studies reported the relationship between newborn asphyxia and preterm birth, including 130,201 newborns. The results of heterogeneity test showed: $P<0.01$, I^2=70.55%, indicating significant heterogeneity, and a random-effects model was used. The pooled OR was 2.18 (95% CI: 1.54, 3.09), showing statistically significant difference ($P<0.01$). The cumulative Meta-analysis based on the year of publication of the literature showed that the results showed a clear time trend, as shown in Figs. 10 and 11.

Meta-analysis of the association between low birth weight and neonatal asphyxia

A total of 7 studies reported the relationship between neonatal asphyxia and low birth weight, including 61,337 neonates. The results of heterogeneity test showed: $P=0.25$, I^2=23.22%, indicating no significant heterogeneity, thus the fixed-effects model was adopted for analysis; the pooled OR was 2.85 (95% CI :2.33, 3.49), showing statistically significant difference ($P<0.01$); the cumulative Meta-analysis based on the year of publication of the literature showed that the results showed a clear time trend, as shown in Figs. 12 and 13.

Sensitivity analysis

In the sensitivity analysis of neonatal asphyxia incidence, the leave-one-out method was employed to sequentially exclude individual studies and recalculate the pooled effect size, evaluating the impact of each study on the

Table 1 Basic characteristics of included literature

Author	Year of Publication	Study Region	Study Type	Sample Size	Incidence	Diagnostic Criteria
Wu [7]	2019	Asia	Cross-sectional Study	22,294	3.29%	Apgar
Sewmehon. A [8]	2023	Africa	Cross-sectional Study	421	20.8%	Apgar
Fitalew. T.A [9]	2022	Africa	Cross-sectional Study	357	27.1%	Apgar
Mandira D [11]	2021	America	Cross-sectional Study	74,002	9%	ICD 10
Avinash K [14]	2021	Asia	Cross-sectional Study	54,492	0.92%	Apgar
Ritbano.A [16]	2019	Africa	Cross-sectional Study	279	5.15%	Apgar
Lilia D [19]	2017	Europe	Cross-sectional Study	8837	3.3%	AAP/ACOG
Ian M [21]	2002	Europe	Cross-sectional Study	22,542	0.9%	Apgar
Mariyo N [23]	2012	Asia	Cross-sectional Study	10,484	4.6%	Apgar
Wu [24]	2004	America	Cross-sectional Study	536,466	4.5%	ICD 9
Melkamu.S [10]	2022	Africa	Case-control study	206	Not Reported	Apgar
Yuli Fitriana [12]	2021	Asia	Case-control study	512	Not Reported	Not Reported
Ghazanfar.N [13]	2021	Asia	Case-control study	426	Not Reported	Apgar
Cui [15]	2021	Asia	Case-control study	5337	Not Reported	Not Reported
Ye [17]	2020	Asia	Case-control study	539	Not Reported	Not Reported
Javier T [18]	2017	America	Case-control study	209	Not Reported	AAP/ACOG
Hafiz M [20]	2014	Asia	Case-control study	240	Not Reported	Apgar
Asad N [22]	2014	Asia	Case-control study	196	Not Reported	Apgar

overall results. The analysis demonstrated that the exclusion of any single study did not significantly alter the pooled effect value, indicating robust stability of the incidence estimates. For the sensitivity analysis of influencing factors for neonatal asphyxia, comparisons were made between fixed-effects and random-effects models. The results showed no significant reversal in the pooled effect values of the factors between the two models, further confirming the robustness and reliability of the study findings as shown in Fig. 14; Table 3.

Publication bias

This study strictly adhered to the inclusion and exclusion criteria and employed Egger's test to assess publication bias. The results showed that the *P*-value of Egger's test for the incidence of neonatal asphyxia was 0.498 (> 0.05), indicating no significant publication bias. In the bias analysis of various risk factors, only instrumental delivery demonstrated potential publication bias in relation to neonatal asphyxia ($P = 0.019 < 0.05$). In contrast, the Egger's test *P*-values for primiparity, low birth weight, and preterm birth were all greater than 0.05, with no significant bias detected. Overall, the main conclusions of this study exhibit good stability and reliability.

Discussion

Although the primary risk factors examined in this study have been reported in some previous literature, our research encompasses a broader time span, incorporating the latest multi-regional studies published up to 2023. By employing a cumulative meta-analysis approach, we reveal temporal trends in incidence and associated risk factors, which distinguishes our work from the static perspective of traditional meta-analyses. Furthermore, this study includes data from multiple countries across Asia, Africa, the Americas, and Europe, thereby effectively addressing the limitation of the limited geographical coverage in prior research. This study conducted a meta-analysis based on 18 observational studies to assess the incidence and associated risk factors of neonatal asphyxia, providing evidence for targeted prevention and intervention strategies. The pooled incidence of neonatal asphyxia was 1.07% (95% CI: 1.05–1.09), which is largely consistent with previously reported data [25]. The results exhibited substantial heterogeneity. Subgroup analysis and meta-regression based on diagnostic criteria revealed that the criteria were not a significant source of this heterogeneity. Cumulative meta-analysis indicated an increasing trend in the incidence of birth asphyxia over time, which may be associated with the recent inclusion of more studies from high-incidence regions such as Ethiopia, where the incidence can be as high as 19.4%. However, considerable variation in the incidence of birth asphyxia was observed across the included studies (0.92%–27.1%), which may be related to disparities in healthcare standards among different regions [26]. Developed countries may have better postnatal asphyxia screening strategies and management of idiopathic etiologies, contributing to reduced incidence, mortality, and associated complications of neonatal asphyxia. In developing countries, neonatal asphyxia remains a major cause of illness and death among newborns. Perinatal hypoxic events—including maternal/fetal hemorrhage, umbilical cord compression, uterine rupture, or shoulder dystocia—compromise oxygenated blood supply to the fetus. Such hypoxic-ischemic insults can induce multi-organ

Table 2 Quality assessment of included literature

Author	Publication Year	1. Selection Bias	2. Performance Bias	3. Attrition Bias	4. Measurement Bias	5. Reporting Bias	6. Sample Size	7. Description of Intervention	8. Analytical Methods	9. Confounding Factors	10. Interpretation of Results	11. Conflicts of Interest	Total Score	Quality Assessment
Wu	2019	1	1	1	1	1	0	1	0	0	1	0	7	Medium
Sewmehon.A	2023	1	1	1	1	1	1	1	0	0	0	0	7	Medium
Fitalew.T.A	2022	1	1	1	1	1	0	1	0	0	0	0	6	Medium
Melkamu.S	2022	1	1	1	1	1	0	1	0	0	1	0	7	Medium
Mandira D	2021	1	1	1	1	1	1	0	0	1	1	0	8	High
Yuli Fitriana	2021	1	1	1	1	1	0	1	0	0	0	0	6	Medium
Ghazanfar.N	2021	1	1	1	1	1	0	0	1	0	0	1	7	Medium
Avinash K	2021	1	1	1	1	1	1	1	0	0	1	0	8	High
Cui	2021	1	1	1	1	1	0	0	1	0	0	1	7	Medium
Ritbano.A	2019	1	1	1	1	1	1	1	0	0	1	0	8	High
Ye	2018	1	1	1	1	1	0	1	0	1	0	0	7	Medium
Javier T	2017	1	1	1	1	1	1	1	0	1	0	0	8	High
Lilia D	2017	1	1	1	1	1	0	0	1	0	0	1	7	Medium
Hafiz M	2014	1	1	1	1	1	0	0	1	0	0	1	7	Medium
Ian M	2002	1	1	1	1	1	1	1	0	0	1	0	8	High
Asad N	2014	1	1	1	1	1	0	1	0	1	0	1	8	High
Mariyo N	2012	1	1	1	1	1	1	1	0	0	0	0	7	Medium
Wu	2004	1	1	1	1	1	1	1	0	0	1	0	8	High

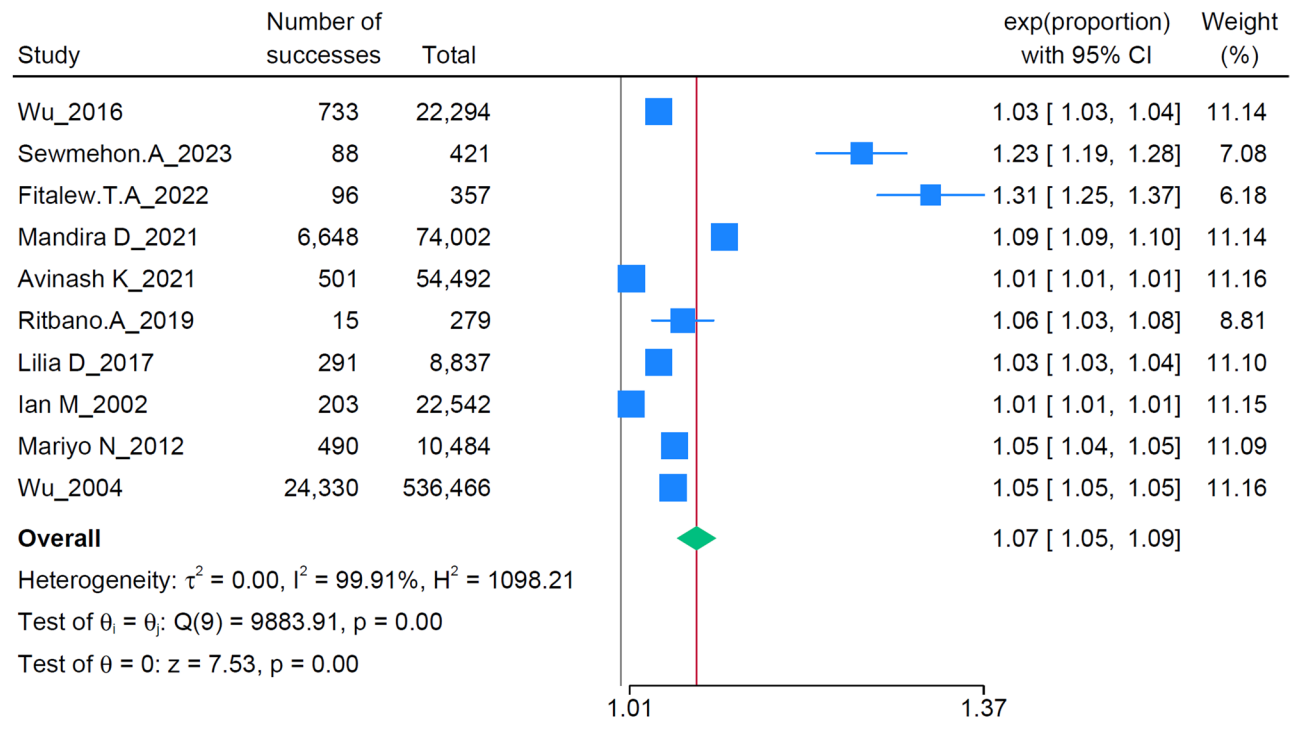

Fig. 2 Forest Plot of Neonatal Asphyxia Incidence Rate

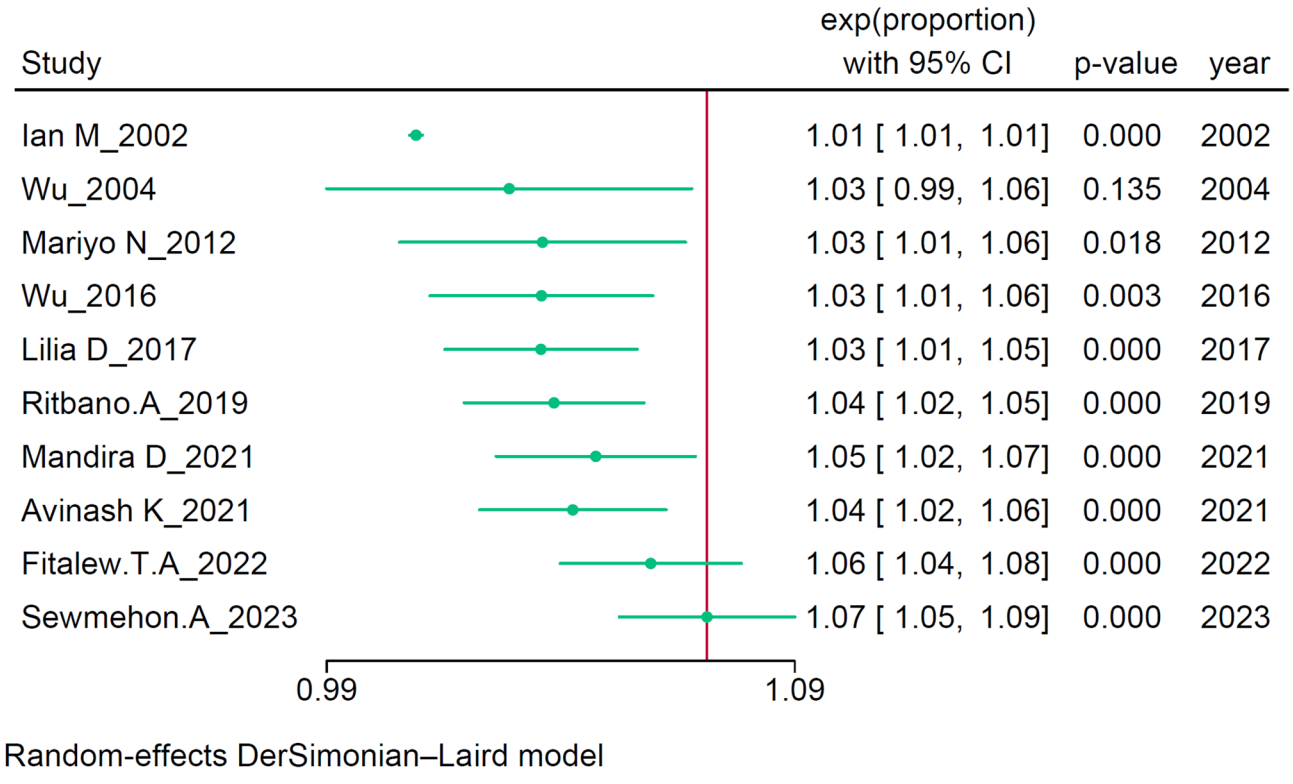

Fig. 3 Cumulative Meta-analysis of Incidence of Neonatal Asphyxia

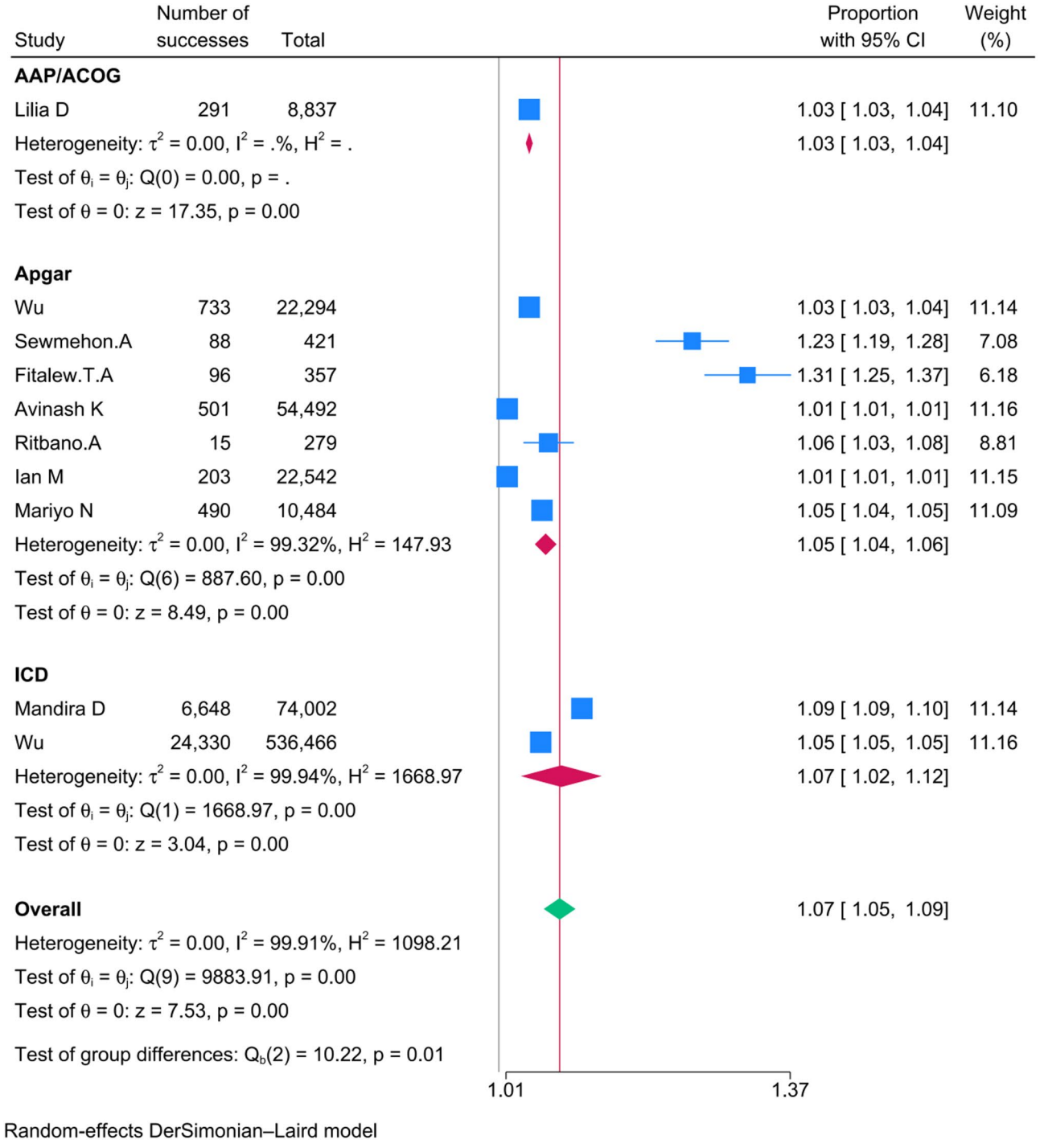

Fig. 4 Subgroup Analysis of Incidence by Diagnostic Criteria

damage and significantly contribute to global neonatal morbidity and mortality [27]. In most cases, the infant successfully recovers from the hypoxic episode, however, some patients may develop ischemic brain damage leading to permanent neurological diseases such as seizures, cerebral palsy, cognitive delays and motor disorders [28]. Therefore, this study conducted subgroup analyses by dividing the participants into four groups based on geographic regions: Europe, Asia, the Americas, and Africa. The results revealed significant heterogeneity among the groups (P = 0.05), indicating notable differences in incidence rates across regions. This may reflect disparities in healthcare resources, obstetric management, socioeconomic conditions, and environmental factors among

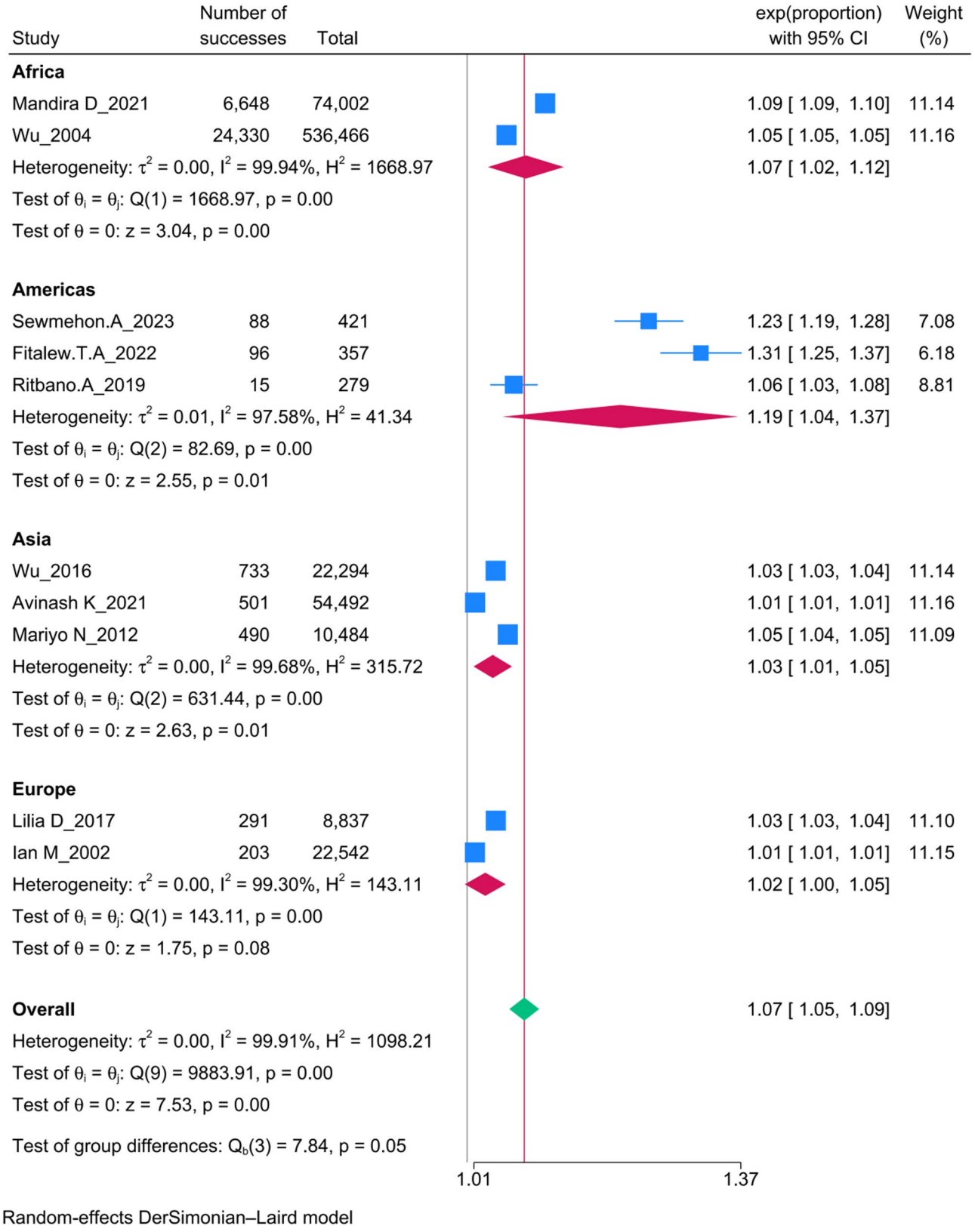

Fig. 5 Subgroup Analysis of the Incidence of Neonatal Asphyxia Based on the Regional Distribution of Studies

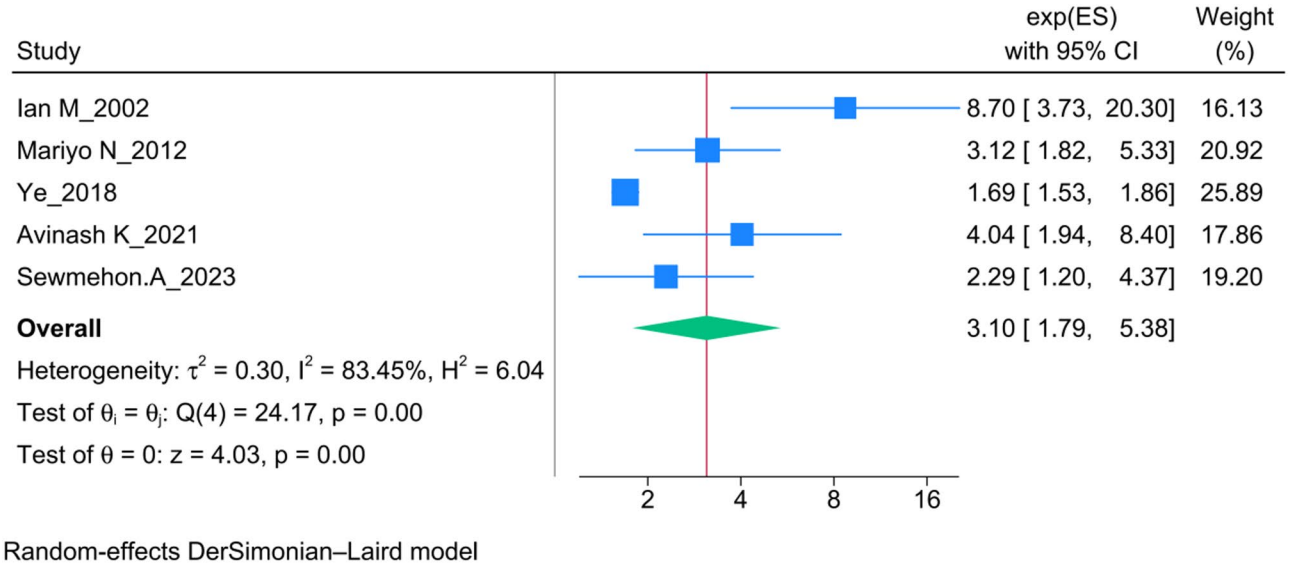

Fig. 6 Forest Plot of the Association between Instrumental Delivery and Neonatal Asphyxia

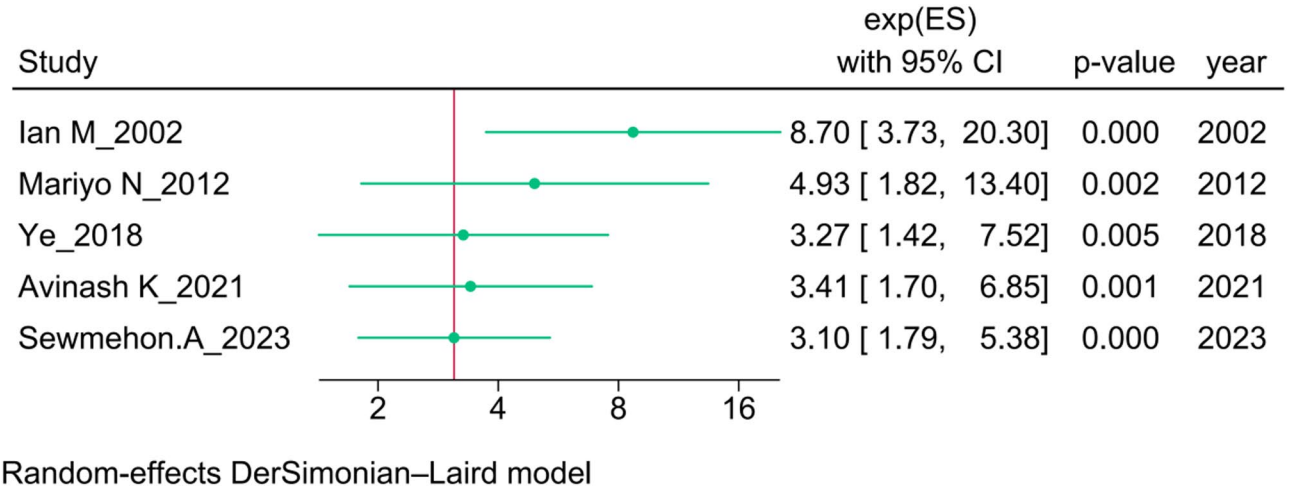

Fig. 7 Cumulative Meta-Analysis of Instrumental Delivery and Neonatal Asphyxia

regions, which significantly influence the incidence of neonatal asphyxia. Thus, the overall pooled incidence rate of this study should be interpreted cautiously in conjunction with regional characteristics. The findings underscore the need for additional region-specific studies to enhance understanding of neonatal asphyxia, which is crucial for accurately identifying risk factors and implementing effective prevention and early intervention strategies.

This study found that compared to newborns with spontaneous deliveries, the likelihood of neonatal asphyxia in newborns assisted with obstetrical instruments was 3.10 times higher (OR = 3.10, 95% CI = 1.79, 5.38). The results are consistent with those of the study by Ana Ferraz et al. [29]. This may be due to the fact that obstetrical instrument deliveries can cause birth injury leading to asphyxia. Obstetrical instrument deliveries may affect different parts of the cranial bleeding; subdural, subarachnoid, parenchymal or intracerebral bleeding may occur due to the pressure exerted by the vacuum and forceps extractors in the dura, arachnoid, brain substance, or ventricles. This can lead to cranial cerebral bleeding, intracranial bleeding, infection, and vascular anomalies, which can progress to neonatal asphyxia [30]. The cumulative meta-analysis results indicate that the association between instrumental delivery and neonatal asphyxia has gradually stabilized and weakened over time, which may be related to the rising cesarean section rates and overall improvements in obstetric care in recent years. Additionally, it is important to note that instrumental-assisted delivery is typically an intervention employed in response to obstetric complications, such as

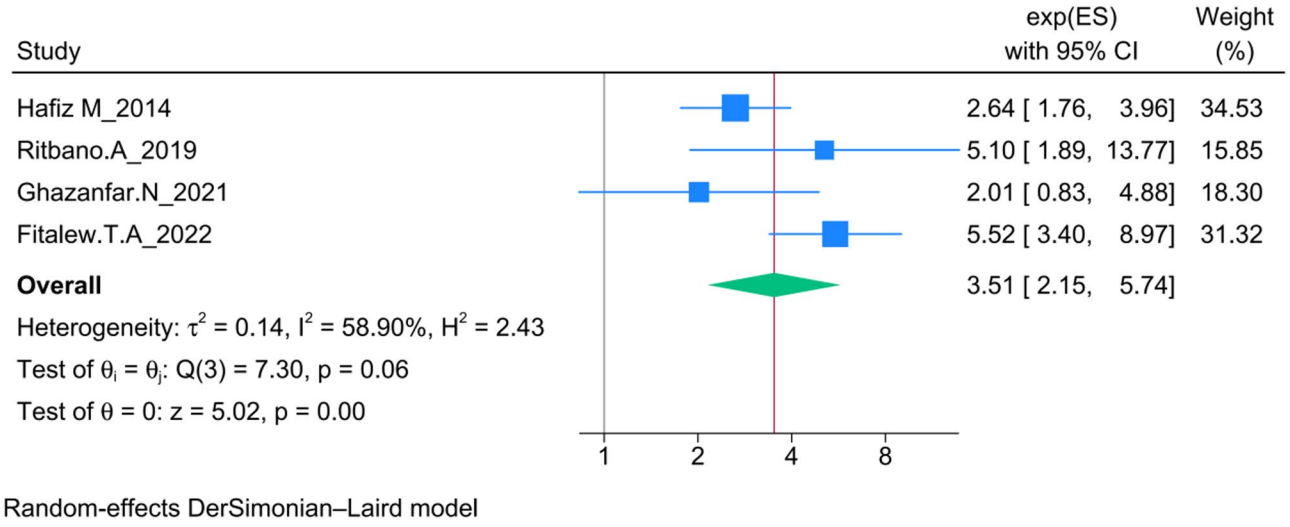

Fig. 8 Forest Plot of the Association between Primiparity and Neonatal Asphyxia

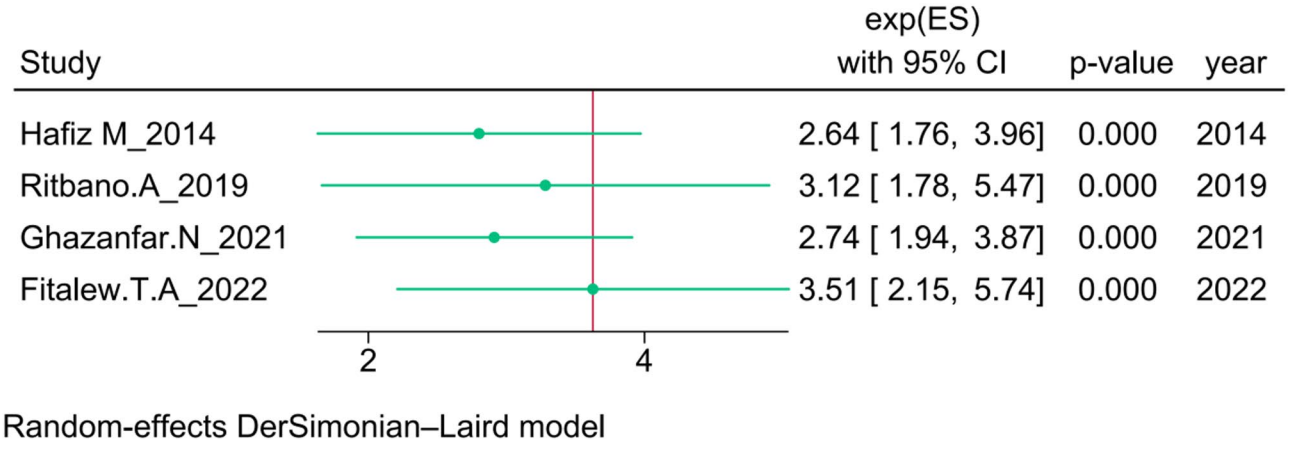

Fig. 9 Cumulative Meta-Analysis of First Birth and Neonatal Asphyxia

prolonged second-stage labor, cephalopelvic disproportion, or fetal distress—all of which are established risk factors for neonatal asphyxia. Therefore, instrumental delivery may not directly cause asphyxia but rather represents a "coping behavior" due to preexisting high-risk conditions, suggesting potential reverse causality. Further research with novel study designs is needed to explore the causal mechanisms between the two.

The findings of this study underscore high-risk factors associated with neonatal asphyxia, particularly among infants with low birth weight, preterm delivery, and those born from primiparous pregnancies. These factors not only increase the likelihood of asphyxia but may also complicate clinical management. Early screening and precise triage measures are especially crucial for these populations. Specifically, enhanced monitoring and timely intervention—such as intensified fetal heart rate surveillance, appropriate oxygen therapy, and assisted ventilation—can effectively reduce the occurrence of neonatal asphyxia in low-birth-weight and preterm infants. Even in resource-limited settings, where technical and equipment shortages may exist, effective perinatal management can still be achieved through optimized resource allocation. For example, training programs for primary healthcare and obstetric staff can improve risk assessment capabilities during pregnancy, thereby strengthening prevention and response strategies for neonatal asphyxia. Particularly in resource-constrained environments, early identification of high-risk cases and prioritized monitoring represent essential approaches to mitigating asphyxia risks. Optimizing the distribution and use of medical resources to ensure timely care for high-risk mothers and newborns is a feasible strategy for enhancing the quality of perinatal care.

This study utilized Egger's test to assess potential publication bias. It is important to note, however, that Egger's test may exhibit low statistical power when the number of included studies is small, which could limit its ability to

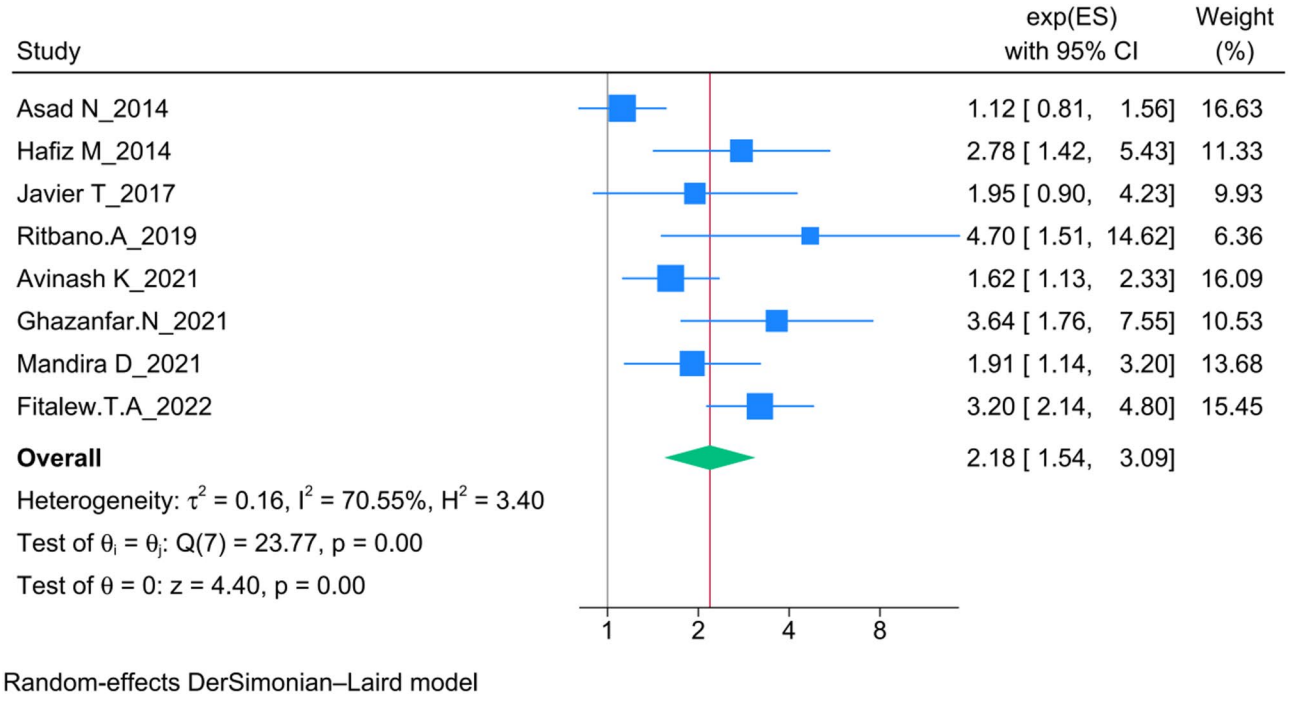

Fig. 10 Forest Plot of the Association between Preterm Birth and Neonatal Asphyxia

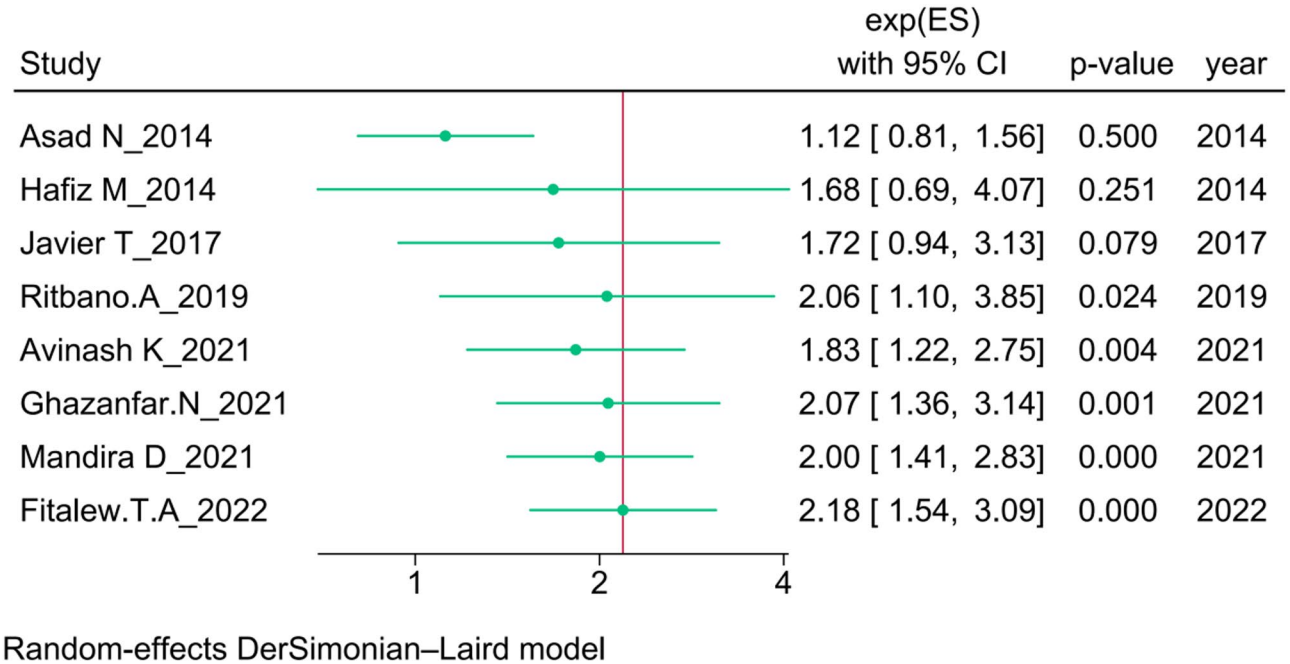

Fig. 11 Cumulative Meta-Analysis of Preterm Birth and Neonatal Asphyxia Incidence

accurately detect bias. Therefore, although a statistically significant association was observed between instrumental delivery and neonatal asphyxia ($P = 0.019$), this result may be influenced by underlying bias or random error. In light of the limitations of Egger's test, the findings should be interpreted with caution, and future studies with larger sample sizes alongside more robust bias detection methods are recommended to verify the reliability of this association.

Additionally, this study reveals a strong association between neonatal asphyxia and low birth weight, with neonates of low birth weight having a 2.85 times higher risk of neonatal asphyxia compared to those of normal birth weight. This finding is consistent with the study by

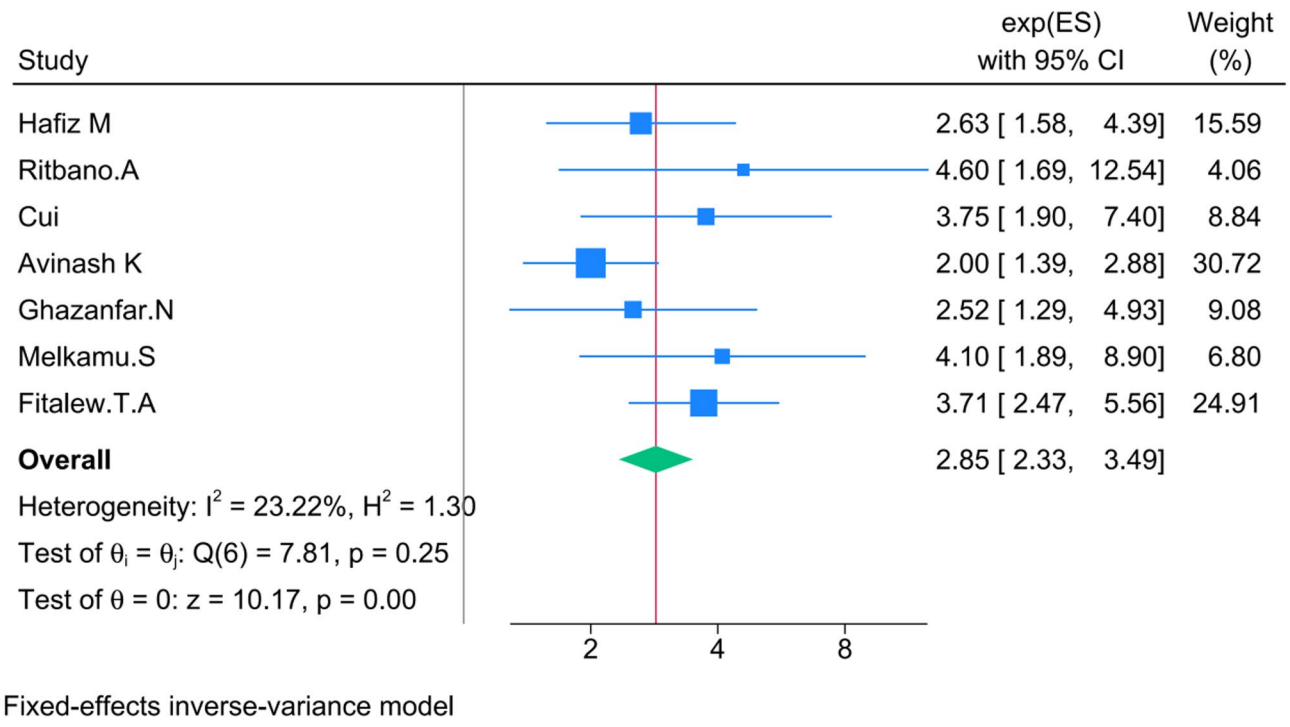

Fig. 12 Forest Plot of the Association between Low Birth Weight and Neonatal Asphyxia

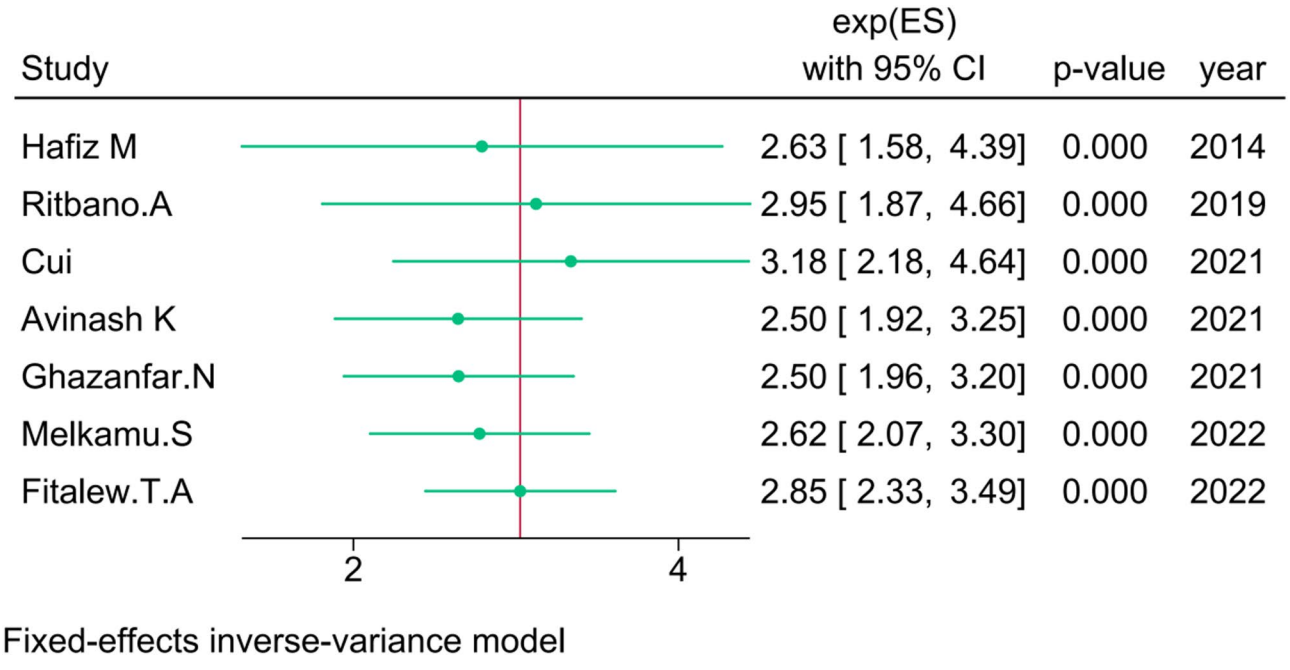

Fig. 13 Cumulative Meta-Analysis of Low Birth Weight and Neonatal Asphyxia

M-A Techane et al. [31]. This may be attributed to poor pulmonary surfactant, lung immaturity, weak respiratory muscles, and rib cage deformities in low birth weight neonates, leading to neonatal asphyxia [32].

This study has its limitations. Firstly, there is significant heterogeneity which may lead to publication bias. This can be due to the sample size, the nature of the study design, the study environment or region of each study. Despite the apparent heterogeneity in this review, the use of subgroup analysis by study region showed a moderate improvement in the heterogeneity, thus reducing the chance of publication bias. Additionally, most of

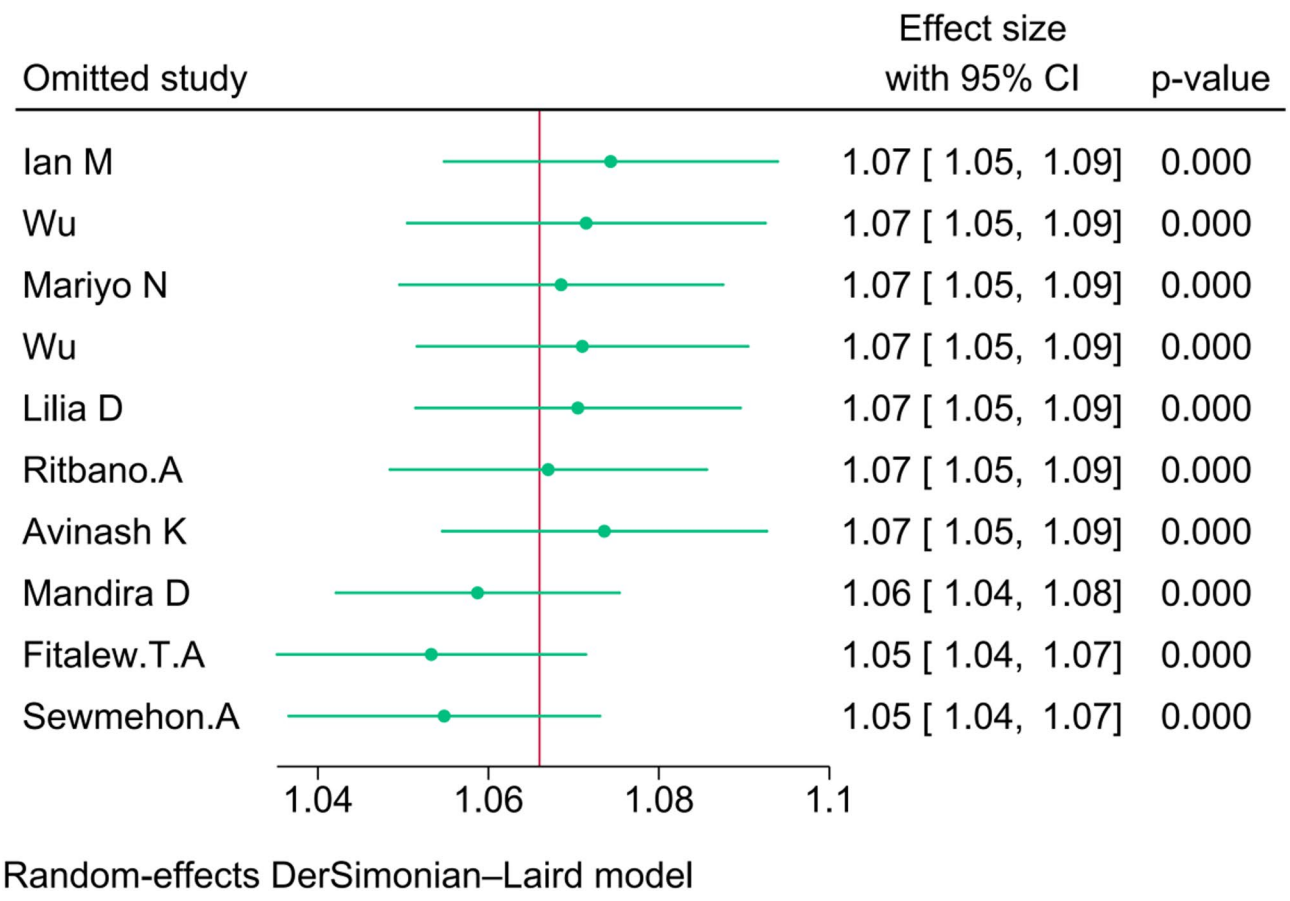

Fig. 14 Sensitivity Analysis of the Incidence of Neonatal Asphyxia

Table 3 Results of Two-Effect models for risk factors associated with newborn asphyxia

Factors	Quantity	Orf (95% CI)	Pf Value	ORr Value (95% CI)	Pr Value
Instrumental delivery	5	1.79(1.63, 1.96)	<0. 01	3.10(1.79, 5.38)	<0. 01
Primipara	4	3.47(2.62, 4.60)	<0. 01	3.51(2.15, 5.74)	<0. 01
Premature Delivery	8	1.90(1.59, 2.26)	< 0. 01	2.18(1.54, 3.09)	< 0. 01
Low Birth Weight	7	2.85(2.33, 3.49)	< 0. 01	2.93(2.30, 3.73)	< 0. 01

OR_f ratio of fixed effect model, OR_r ratio calculated by random effect model P_f fixed effect model test *P* value, *Pr* random effect model test P value

the studies included in this review are cross-sectional, which limits our ability to evaluate causality and may result in the outcome variable being influenced by other confounding variables. Furthermore, due to data and reporting constraints, this study could not perform subgroup analyses or explore moderating effects for potentially critical variables such as socioeconomic status, maternal obesity, and hospital-level factors. These variables have received limited attention in existing literature but could have contributed to a more comprehensive understanding of risk factor mechanisms, enhancing the clinical and theoretical value of this study. Moreover, the included studies generally lacked detailed information on delivery methods (e.g., vaginal or cesarean section), timing of delivery (e.g., emergency or elective), and gestational age, limiting our ability to further assess the impact of different delivery modes on the risk of neonatal asphyxia. Therefore, future systematic reviews or original studies could further investigate the role of such variables to address this gap.

Lastly, since this study primarily relied on pooled analyses of observational studies, although we attempted to minimize bias through stringent inclusion criteria and subgroup analyses, the lack of original individual-level data made it difficult to systematically control for confounding biases (e.g., whether neonates with congenital anomalies were excluded). This may somewhat limit the interpretability of the findings. Future research could incorporate multivariate analyses or propensity score matching methods to enhance the reliability of causal inferences.

Conclusion

This study, through a meta-analysis and cumulative meta-analysis of 18 observational studies, found that the pooled incidence of neonatal asphyxia was 107 (95% CI: 1.05–1.09), with significant variations across different countries and regions. This suggests that the issue remains of high public health importance globally, and the regional disparities may reflect the potential influence of varying healthcare resources and management levels on neonatal asphyxia. The analysis indicated that instrumental delivery, primiparity, preterm birth, and low birth weight were associated with neonatal asphyxia, and these associations exhibited temporal trends, demonstrating sustained clinical relevance. Given that all included studies were observational in design, the results should be interpreted with caution, and causal inferences are limited. Therefore, it may be beneficial to enhance the identification and intervention of these high-risk factors in perinatal management, particularly in primary healthcare settings, by strengthening prenatal screening, risk assessment, and neonatal resuscitation capacity. Additionally, multicenter prospective studies should be encouraged, particularly those validating temporal incidence trends and elucidating the pathways underlying these associations, to further clarify potential causal relationships and provide more robust evidence for reducing neonatal asphyxia rates and improving neonatal outcomes.

Abbreviations

CNKI	China National Knowledge Infrastructure
WHO	World Health Organization
OR	odds ratio
CI	confidence intervals
AHRQ	Healthcare Research and Quality
IRR	incidence rate ratio

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

Conception and design: YPW, SSX and SQZ. Administrative support: All authors. Provision of study materials or patients: All authors. Collection and assembly of data: All authors. Data analysis and interpretation: CBQ. Manuscript writing: All authors. Final approval of manuscript: All authors.

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Data availability

All data generated or analysed during this systematic review are included in this published article and its supplementary information files. The original datasets from the included studies are available from the corresponding publications, as referenced.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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