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Prevalence and risk factors associated with birth asphyxia among neonates delivered in China: a systematic review and meta-analysis

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Abstract

Background Birth asphyxia is a critical condition caused by an insufficient oxygen supply during delivery, and it poses a major threat to the health of newborns. The present meta-analysis aimed to estimate the prevalence of birth asphyxia among neonates and identify its risk factors in China.

Methods PubMed, EMBASE, Scopus, Web of Science, the China Academic Journals (CNKI), the Chinese Biomedical Literature (CBM), the China Science and Technology Journal Database (VIP), and the WanFang database were searched for related publications. Two researchers independently selected the literature, extracted the relevant data, and assessed its methodological quality. The meta-analysis applied a random-effects model with Stata 17.0 software to calculate the pooled prevalence of birth asphyxia among neonates delivered in China and to merge the odds ratios (ORs) of risk factors. Subgroup analysis was performed on the included studies. Publication bias was assessed by funnel plots and Egger's test.

Results Eighty studies were eligible for inclusion. The overall prevalence of birth asphyxia in newborns was 4.8% (95% CI, 4.5%–5.2%). In the subgroup analyses, the northern area presented the highest prevalence (5.1%; 95% CI, 4.1%–6.3%), followed by the southern area (4.1%; 95% CI, 3.3%–5.1%). The rural setting presented the highest prevalence (6%; 95% CI, 4.6%–7.4%), followed by the urban (4.2%; 95% CI, 4.6%–7.4%) and mixed (5.8%; 95% CI, 5.3%–6.3%) settings. The Apgar score demonstrated the highest prevalence (4.6%; 95% CI, 3.8%–5.4%), followed by the Apgar score with the umbilical artery blood pH (3.7%; 95% CI, 2.2%–5.7%). A significant difference in prevalence was found between studies with sample sizes greater than 5,000 (2.2%; 95% CI, 1.6%–3%) and those with 5,000 or fewer participants (6.2%; 95% CI, 5.5%–7.1%). Furthermore, there was a significant decrease in the incidence of birth asphyxia from 1995–2016 (4.9%; 95% CI, 4.2%–5.9%) to 2017–2023 (3.7%; 95% CI, 2.6%–5%). Placental abruption (OR = 5; 95% CI, 3.08–8.13), placenta previa (OR = 2.57; 95% CI, 1.84–3.58), advanced maternal age (OR = 3.94; 95% CI, 1.46–10.62), primigravida (OR = 5.33; 95% CI, 0.41–68.71), premature birth (OR = 3.36; 95% CI, 2.61–4.32), intrauterine distress (OR = 4.48; 95% CI, 3.47–5.80), stained amniotic fluid (OR = 3.28; 95% CI, 2.25–4.79), macrosomia (OR = 6.30; 95% CI, 0.61–65.22), foetal malformation (OR = 7.44; 95% CI, 1.46–38.02), breech birth (OR = 2.42; 95% CI, 1.24–4.73), caesarean

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section (OR = 1.72; 95% CI, 0.91–3.24), assisted delivery (OR = 13.62; 95% CI, 5.50–33.73), prolonged second stage of labour (OR = 1.43; 95% CI, 0.68–3.01), and malpresentation (OR = 4.20; 95% CI, 2.21–7.99) were major risk factors.

Conclusions The prevalence of birth asphyxia among newborns in China is relatively high. In addition, 14 risk factors are related to neonatal birth asphyxia. Urgent attention needs to be focused on regionalized maternal and child management to address this problem in China.

Keywords Birth asphyxia, Newborns, Prevalence, Risk factors, Systematic review, Meta-analysis

Background

Perinatal asphyxia is an important cause of perinatal morbidity and mortality worldwide. Asphyxiation can lead to many neonatal deaths and child disability incidents, causing damage to multiple organs and long-term prognosis risks [1]. Currently, China uses the Expert Consensus on the Diagnosis of Neonatal Asphyxia (2016) as its standard for diagnosing neonatal asphyxia as follows: 1) mild asphyxia can be diagnosed if the Apgar score at 1 min is ≤ 7 or if the Apgar score at 5 min is ≤ 7, along with a an umbilical artery blood gas analysis (UABGA) pH value < 7.2. 2) severe asphyxia can be diagnosed if the Apgar score at 1 min is ≤ 3 or if the Apgar score at 5 min is ≤ 5, along with an UABGA pH value < 7.0. If the UABGA pH is normal but the Apgar score is ≤ 7, the patient can be diagnosed with a low Apgar score. In health care facilities where UABGA testing is unavailable, a low Apgar score can still be used for diagnosis [2]. Reports have indicated that approximately 25% of neonatal deaths worldwide, among nearly 4 million births, are attributed to neonatal asphyxia, establishing it as the leading cause of neonatal mortality [3–5]. In addition, a survey on the disease burden of neonatal asphyxia by the Maternal and Child Health Centre of the Chinese Centre for Disease Control and Prevention revealed that the incidence rate of neonatal asphyxia in different regions ranges from 1.14% to 11.7%; the national mortality rate for birth asphyxia among children under 5 stands at 221.3 per 105, making neonatal asphyxia the third major cause of disability nationwide, accounting for 8.6% [6]. Neonatal asphyxia is one of the main causes of death and disability among Chinese children, and the disease burden caused by birth asphyxia is considerable [7].

Neonatal birth asphyxia is a prevalent clinical hypoxic condition in newborns, exerting ischaemic and hypoxic effects with widespread organ damage, presenting a significant challenge to child health and societal well-being [8]. Despite a decreasing trend in the incidence of long-term complications and severe adverse outcomes related to neonatal asphyxia, a 1.67% occurrence rate persists, with 1.39% resulting in fatal outcomes even after active resuscitation [9]. Therefore, the identification of risk factors for neonatal birth asphyxia has become increasingly important. Research highlights various risk factors for birth asphyxia, including advanced maternal age (defined as maternal age ≥ 35 years), low maternal educational attainment, perinatal maternal conditions (such as diabetes, hypertension, anaemia, and intrahepatic cholestasis), delivery-related factors (such as mode of delivery), multiple gestations, labour anaesthesia, abnormal foetal presentation, preterm birth (defined as birth before 37 weeks of gestation), low birth weight (defined as birth weight less than 2.5 kg), and abnormalities in the umbilical cord, placenta, or amniotic fluid [10–12]. Moreover, there is a positive correlation between the number of related influencing factors and the likelihood of neonatal birth asphyxia [13].

Surviving neonates with birth asphyxia often have many complications, including impairments to the brain, lungs, kidneys, gastrointestinal system, and cardiovascular functions [14]. Neonatal brain injury caused by asphyxia is one of the major causes of postnatal neurological dysfunction in children. Hypoxic-ischaemic encephalopathy (HIE) refers to brain injury caused by hypoxia and ischaemia resulting from perinatal asphyxia, which clinically manifests as a series of central nervous system abnormalities [15]. According to China's diagnostic criteria [16], HIE can be confirmed if all of the following four criteria are met (if criterion 4 cannot be immediately determined, the case can be considered a provisional diagnosis): 1) a clear obstetric history indicating foetal distress, such as severe foetal distress signs (foetal heart rate < 100 beats/min for more than 5 min and/or grade III meconium staining of amniotic fluid), or a history of significant asphyxia during labour; 2) severe asphyxia at birth, as defined as an Apgar score ≤ 3 at 1 min, persisting at ≤ 5 at 5 min, or an umbilical artery blood pH ≤ 7.00 at birth; 3) neurological symptoms appearing shortly after birth and persisting for more than 24 h; and 4) seizures or brain injury caused by electrolyte disturbances, intracranial haemorrhage, birth trauma, intrauterine infections, hereditary metabolic diseases, or other congenital disorders. A study in Spain revealed that the probability of developing HIE in children with severe asphyxia is 25.6%, and among those with HIE, the incidence of neurological sequelae is 16.5% [17]. These neurological

sequelae include cerebral palsy, intellectual disability, and epilepsy, which can place a significant burden on both the child's family and society.

In recent years, research on treatments for HIE has advanced rapidly, with numerous promising new methods emerging. Hypothermia therapy is currently one of the primary clinical treatments for HIE, which involves physical cooling to maintain core body temperature between 30 and 35 °C (86 and 95 °F) to achieve therapeutic effects. According to the latest Expert Consensus on Hypothermia Therapy for Neonatal HIE in China (2022), hypothermia therapy should be initiated within 6 h after birth for infants with HIE. The target temperature is set at 34 °C (93.2 °F), with a range of 3335 °C (91.4 to 95 °F), and the therapy should be maintained for 72 h. Rewarming should be performed gradually at a rate of ≤ 0.5 °C (32.9 °F) per hour, with a total rewarming time of at least 5 h. Mohamed A. Tagin et al. [18] conducted a meta-analysis of seven clinical trials involving 1,214 children and reported that hypothermia therapy improves survival and neurodevelopment in neonates with moderate to severe hypoxic-ischaemic encephalopathy. Both whole-body and selective head cooling are effective treatments. Thus, hypothermia therapy is considered an effective treatment for hypoxic-ischaemic encephalopathy and is widely applied in clinical practice.

Despite the existence of standardized diagnostic criteria for neonatal asphyxia in China, certain clinical studies diverge in that they do not employ umbilical artery blood gas analysis, leading to disparate reported incidence rates. Moreover, owing to China's vast territory and the uneven development of the economy, education, and medical standards across different cities and regions, the causes of neonatal death differ across regions [19]. There are differences in the allocation of medical resources among hospitals of different levels, especially in first-level hospitals (community, township hospitals, and rural health centres) and second-level hospitals. For example, in underdeveloped areas, neonatal deaths are caused mainly by neonatal asphyxia and infection [20]. However, the current specific incidence of neonatal asphyxia in different regions of China is unclear, and a corresponding evidence-based summary of the risk factors that affect its occurrence is lacking. Thus, the present study conducted a systematic review and meta-analysis of the incidence of birth asphyxia and its associated risk factors in China. Such evidence-based synthesis will serve as a robust theoretical foundation for addressing future public health challenges within the field of perinatal medicine, facilitating the development of effective prevention and treatment policies.

Methods

This study was registered with PROSPERO (CRD42023458261) and conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [21].

Search strategy

The following 8 electronic bibliographic databases were searched (from inception until August 3, 2023): PubMed, EMBASE, Scopus, Web of Science, the China Academic Journals (CNKI), the Chinese Biomedical Literature (CBM), the China Science and Technology Journal Database (VIP), and the WanFang database for Chinese Periodicals.

The search strategies were performed through a combination of MeSH terms and free words. The specific search strategies for English databases are shown in the appendix. Additionally, reference lists included in the identified articles were manually searched to identify additional relevant publications, and grey literature was also searched. Some authors were contacted via e-mail to obtain further details or help resolve any uncertainties (Supplementary 1).

Study selection

After the removal of duplicate studies, two investigators independently assessed the eligible publications by screening titles and abstracts according to the inclusion and exclusion criteria. Full-text articles were retrieved when at least one reviewer determined that an abstract was eligible for inclusion. Each publication was assessed independently by both investigators for final study inclusion. Disagreements were resolved by discussion.

The inclusion criteria for the systematic review were as follows: 1) the study area was conducted in China; 2) the study was an observational study (including cohort studies, cross-sectional studies, and case–control studies); 3) the prevalence or risk factors for birth asphyxia among neonates were reported; 4) the exact diagnostic criteria for the identification of birth asphyxia were available; and 5) the study was published in English or Chinese.

The exclusion criteria were as follows: 1) commentaries, letters, duplicate studies, reviews, and duplicate publications; and 2) the full-text article was unavailable.

Data extraction and quality assessment

Data were extracted from the included studies by two independent investigators. The following information was recorded: first author name, publication year, geographical location (province and area), study setting (urban or rural), diagnostic criteria, prevalence of birth asphyxia, and stated risk factors. All extracted data were stored in Microsoft Excel.

The quality of the included studies was independently evaluated by two investigators, who used a tool for evaluating different studies. The methodological quality of the case–control studies and cohort studies was assessed via the Newcastle–Ottawa Scale (NOS) [22]. The total scores ranged from 0 to 9 points, with scores of 0 to 3, 4 to 6, and 7 to 9 indicating low-, medium-, and high-quality studies, respectively. In addition, the risk of bias in a cross-sectional study was assessed via the instrument Agency for Health care Research and Quality (AHRQ) [23]. This tool has a total of 11 items; if the answer to an object is "no" or "unclear," the item score is "0", and if the answer is "yes," the item score is "1". The total score ranges from 0–11 points, with scores of 0–3, 4–7, and 8–11 points indicating low quality, medium quality, and high quality, respectively [24].

Statistical analyses

For analysis, the data extracted from the included publications were input into the Stata 17.0 software package (Stata Corp LP, College Station, TX). Heterogeneity among studies was tested via Cochrane's Q statistic. The degree of heterogeneity was assessed via the I^2 statistic, with I^2 values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. The pooled prevalence and 95% confidence intervals (CIs) for cancer-related fatigue were calculated via a random effects model when the Cochrane's Q statistic detected significant heterogeneity; otherwise, a fixed effects model was used. $P<0.05$ was the threshold for statistical significance. The findings are illustrated in the form of forest plots. The proportions of participants diagnosed with birth asphyxia were extracted from all included studies to calculate the pooled prevalence of this condition. To assess the risk factors for birth asphyxia, the odds ratios (ORs) and associated 95% CIs were extracted from the included studies, and all eligible available data were summarized. Publication bias was identified via a funnel plot, and asymmetry was tested via Egger's linear regression method ($P<0.1$ was considered significant). To explore the sources of heterogeneity, subgroup analyses were performed on the basis of geographical setting (area), study setting (urban or rural), and method of diagnosis.

Results

Study selection

In the present study, 4,623 records from 8 databases were systematically searched, of which 688 were duplicates. After analysis of the titles and abstracts from 3,935 articles, 209 publications were selected for full-text assessment. Ultimately, 80 full-text studies were considered relevant and included in the meta-analysis. A total of 80 studies from 25 regions in China were included in the meta-analysis, and the pooled sample size was 17,140 neonates with birth asphyxia. The process of study selection is summarized in Fig. 1 according to the PRISMA guidelines (Fig. 2).

Study characteristics and methodologic quality

The included 80 full-text studies covered 20 provinces, 3 municipalities, and 2 autonomous prefectures. Among the studies, 32 studies were conducted in northern China, and 48 studies were conducted in southern China, with the largest number of studies from Guangdong Province ($n=8$) and Zhejiang Province ($n=8$), followed by Sichuan Province ($n=7$), Jiangsu Province ($n=6$), and Henan Province ($n=6$). Moreover, 64, 14, and 2 studies were sourced from urban populations, rural populations, and both populations, respectively. For most of the studies, the source of the study population was a single centre ($n=70$, 87.5%) rather than a multicentre ($n=10$, 12.5%). The sample sizes ranged from 587 to 55,281. In addition, 24 studies reported the risk factors for birth asphyxia. For the diagnostic criteria, almost all the included studies used the Apgar score to determine birth asphyxia. Specifically, 5 studies used a combination of the Apgar score and pH value to diagnose asphyxia, and 40 studies identified the sources of the diagnostic criteria for asphyxia. Regarding the quality of the included studies, 1 was a high-quality study, 55 were medium-quality studies, and 24 were low-quality studies (Table 1).

Pooled prevalence of birth asphyxia in China

In the 80 studies included in the meta-analysis, the prevalence of birth asphyxia in China ranged from 0.46% to 16.5%. On the basis of a random effects model-based meta-analysis conducted on all data points, the overall incidence of birth asphyxia in neonates in China was estimated to be 4.8% (*95% CI*: 4.5% to 5.2%, $I^2=99.5\%$, $P<0.0001$). Table 2 summarizes the subgroup summary prevalence of birth asphyxia in Chinese neonates. Asphyxia was classified on the basis of geographical setting, study setting, diagnostic criteria for asphyxia, sample size, and study period. The heterogeneity test results were significant ($p<0.001$) in all the subgroups (Table 1). There was clear asymmetry in the funnel plot (Fig. 3) and Egger's test ($p<0.1$), indicating significant publication bias.

According to the subgroup analyses, the prevalence of birth asphyxia in China was the highest among patients in the northern area (5.1%; 95% CI, 4.1%–6.3%), followed by those in the southern area (4.1%; 95% CI, 3.3%–5.1%), and the difference was significant ($P<0.01$). Studies conducted in different settings also revealed a significant difference ($P<0.01$);

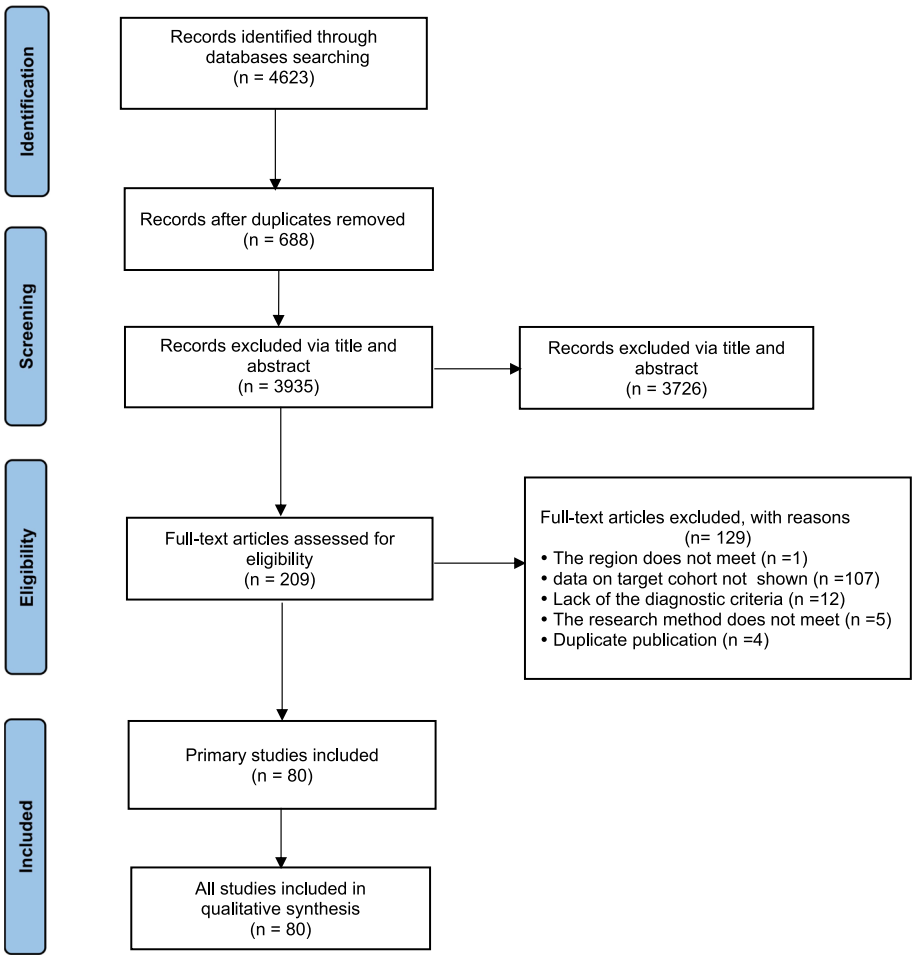

Fig. 1 Flow chart of study selection process for the review

rural settings reported the highest prevalence of birth asphyxia (6%; 95% CI, 4.6%–7.4%), followed by urban settings (4.2%; 95% CI, 4.6%–7.4%) and mixed settings (5.8%; 95% CI, 5.3%–6.3%). Studies using the Apgar score for birth asphyxia diagnosis revealed the highest prevalence of birth asphyxia (4.6%; 95% CI, 3.8%–5.4%), followed by the Apgar score with umbilical artery blood pH (3.7%; 95% CI, 2.2%–5.7%), and this difference was significant ($P < 0.01$). The prevalence of birth asphyxia among neonates was 2.2% (95% CI, 1.6%–3%) for studies that included a sample size greater than 5,000, and it was 6.2% (95% CI, 5.5%–7.1%) for studies that included a sample size of 5,000 or less than 5,000 ($P < 0.01$). For the different study periods, there was a significant difference in studies conducted before and after 2017 ($P < 0.01$). The prevalence of birth asphyxia from 1995–2016 was 4.9% (95% CI, 4.2%–5.9%), which was higher than the prevalence of birth asphyxia from 2017–2023 (3.7%; 95% CI, 2.6%–5%).

Risk factors associated with birth asphyxia among neonates in China

The risk factors for birth asphyxia in China were explored via qualitative analysis of three aspects and 31 items, with 14 significantly different factors (Table 3). The factors were grouped into maternal factors, foetal factors, and labour factors.

Maternal factors

A total of 9 relevant maternal risk factors were identified from the articles, and the meta-analysis identified 4 risk factors that were significantly different, namely, placental abruption, placenta previa, advanced maternal age, and primigravida.

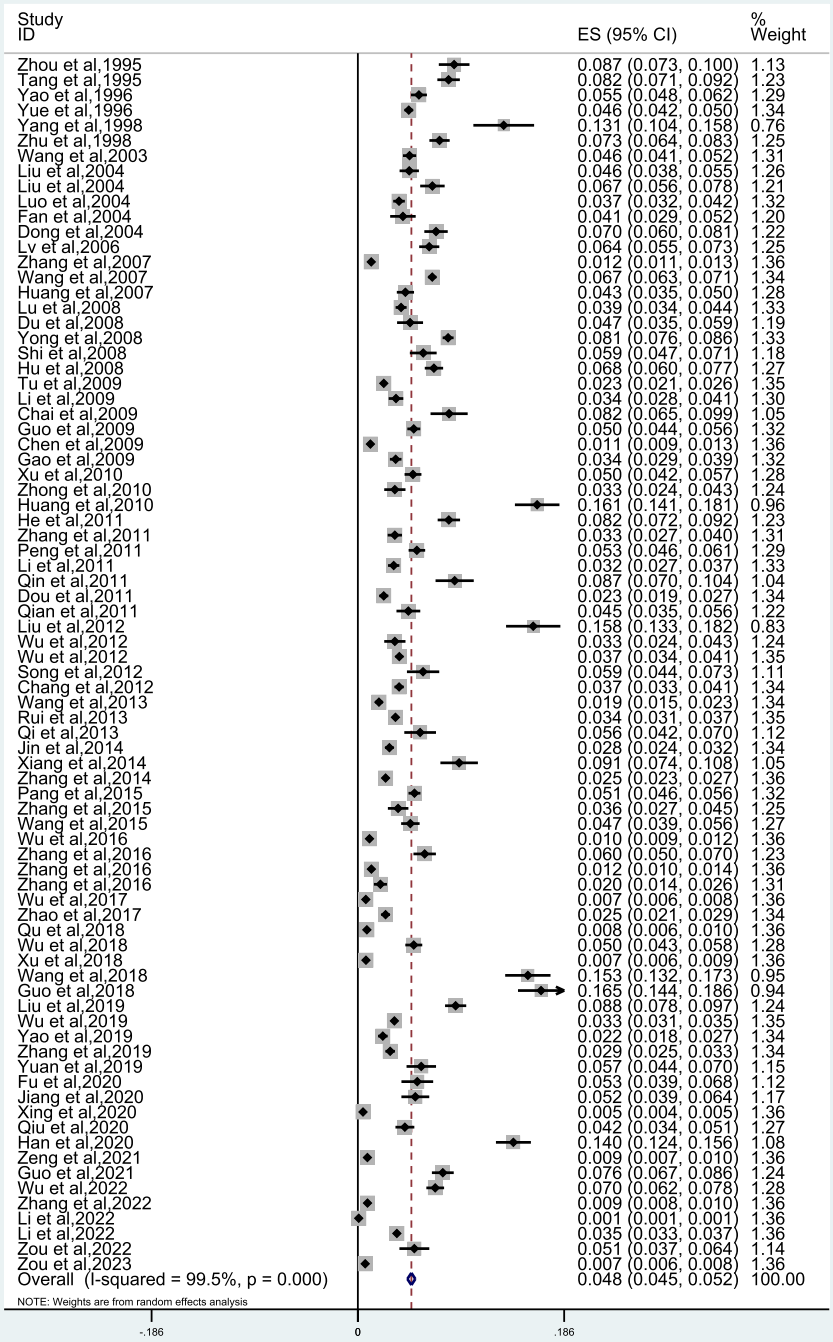

Fig. 2 Forest plot of the prevalence of birth asphyxia among neonates

Foetal factors

A total of 13 related risk factors were extracted, and the meta-analysis identified 5 statistically significant risk factors, including premature birth, intrauterine distress, stained amniotic fluid, macrosomia, and foetal abnormalities.

Table 1 Characteristics of the included studies

No	Author	Publication Years	Province, City; Area	Study Setting	Sample Size	Number of birth asphyxia	Prevalence	Definition of asphyxia	Quality
1	Zhou, et al. [25]	1995	Qinghai, Xining(N)	U	1594	138	8.66	Apgar score	3
2	Tang, et al. [26]	1995	Shannxi, Xian(N)	U	2819	230	8.15	Apgar score	3
3	Yao, et al. [27]	1996	Inner Mongolia, Hohhot(N)	U	3860	212	5.49	Apgar score	2
4	Yue, et al. [28]	1996	Beijing(N)	U	11,044	506	4.56	Apgar score	4
5	Yang, et al. [29]	1998	Qinghai, Xining(N)	U	587	77	13.12	Apgar score	4
6	Zhu [30]	1998	Beijing(N)	U	3145	231	7.34	Apgar score	4
7	Wang, et al. [31]	2003	Jilin, Panshi(N)	U	4862	226	4.56	Apgar score	4
8	Liu [32]	2004	Beijing(N)	U	2251	104	4.62	Apgar score	4
9	Liu, et al. [33]	2004	Sichuan, Neijiang(S)	U	1984	133	6.7	Apgar score	3
10	Luo [34]	2004	Hubei, Wuhan(S)	U	5000	185	3.7	Apgar score	5
11	Fan, et al. [35]	2004	Shanxi, Taiyuan(N)	U	1135	46	4.05	Apgar score	4
12	Dong, et al. [36]	2004	Guangxi, Guilin(S)	U	2262	159	7	Apgar score	4
13	Lv, et al. [37]	2006	Guangdong, guangzhou(S)	U	2820	181	6.42	Apgar score	3
14	Zhang, et al. [38]	2007	Beijing(N)	U	45,337	545	1.2	Apgar score	4
15	Wang, et al. [39]	2007	Urumqi, Xinjiang(N)	U	17,709	1185	6.69	Apgar score	4
16	Huang [40]	2007	Jiangsu, Changzhou(S)	U	2620	112	4.27	Apgar score	3
17	Lu [41]	2008	Shandong, Jinan(N)	U	5863	228	3.89	Apgar score	3
18	Du, et al. [42]	2008	Inner Mongolia, Tongliao(N)	U	1257	59	2.44	Apgar score	4
19	Yong [43]	2008	Urumqi, Xinjiang(N)	U	11,806	958	8.11	Apgar score	3
20	Shi [44]	2008	Gansu, Gaotai(N)	R	1463	86	5.88	Apgar score	3
21	Hu, et al. [45]	2008	Chongqing(S)	U	3595	246	6.84	Apgar score	4
22	Tu [46]	2009	Beijing(N)	U	12,314	287	2.3	Apgar score	5
23	Li [47]	2009	Jiangsu, Changzhou(S)	U	2975	102	3.42	Apgar score	3
24	Chai [48]	2009	Guangdong,Dongguan(S)	U	1036	85	8.2	Apgar score	3
25	Guo, et al. [49]	2009	Sichuan, Chengdu(S)	M	5470	275	5.03	Apgar score	3
26	Chen, et al. [13]	2009	Guangdong, Dongguan(S)	U	10,376	117	1.13	[a]Apgar score + PH	6
27	Gao, et al. [50]	2009	Sichuan, Chengdu(S)	R	4676	159	3.4	Apgar score	3
28	Xu, et al. [51]	2010	Sichuan, Chengdu(S)	U	3147	156	4.96	Apgar score	3
29	Zhong [52]	2010	Guizhou, Guiyang(S)	R	1353	45	3.3	Apgar score	3
30	Huang, et al. [53]	2010	Jiangxi, Jinggangshan(S)	U	1296	209	16.1	Apgar score	6
31	He [54]	2011	Henan, Huojia(N)	R	2835	232	8.18	Apgar score	3
32	Zhang [55]	2011	Henan, Shangqiu(N)	U	3008	100	3.32	Apgar score	4
33	Peng, et al. [56]	2011	Guangxi, Guilin(S)	U	3486	185	5.31	Apgar score	3
34	Li [57]	2011	Beijing(N)	U	4594	148	3.22	Apgar score	3
35	Qin, et al. [58]	2011	Shanghai(S)	U	1034	90	6.8	Apgar score	3
36	Dou, et al. [59]	2011	Hebei, baoding(N)	U	5284	123	2.33	Apgar score	3
37	Qian [60]	2011	Anhui, Hefei(S)	U	1453	66	4.54	Apgar score	4
38	Liu, et al. [61]	2012	Sichuan, Xichang(S)	R	856	135	15.77	Apgar score	4
39	Wu, et al. [62]	2012	Jiangxi, Shanggao(S)	R	1353	45	3.3	Apgar score	4
40	Wu, et al. [63]	2012	Hubei, Suizhou(S)	U	11,256	420	3.73	[a]Apgar score + PH	6
41	Song, et al. [64]	2012	Gansu, Dingxi(N)	U	1006	59	5.9	Apgar score	3
42	Chang [65]	2012	Henan, Zhengzhou(N)	U	7842	291	3.71	Apgar score	5
43	Wang [66]	2013	Anhui, Hefei(S)	U	5489	104	1.89	Apgar score	5
44	Rui, et al. [67]	2013	Jiangsu, Gaochun(S)	R	16,749	566	3.38	Apgar score	5
45	Qi [68]	2013	Henan, Fengqiu(N)	R	1000	56	5.6	Apgar score	5
46	Jin, et al. [69]	2014	Zhejiang, Yiwu(S)	U	6592	187	2.84	Apgar score	6
47	Xiang, et al. [70]	2014	Jiangsu, Guanyun(S)	R	1120	102	9.11	Apgar score	3
48	Zhang, et al. [71]	2014	Shanghai(S)	U	21,047	525	2.38	Apgar score	2
49	Pang, et al. [72]	2015	Guangdong, Zhanjiang(S)	U	6463	329	5.09	Apgar score	5
50	Zhang [73]	2015	Zhejiang, Shengsi(S)	R	1575	57	3.6	Apgar score	5
51	Wang [74]	2015	Heibei, Baoding(N)	R	2500	118	4.72	Apgar score	5

Table 1 (continued)

No	Author	Publication Years	Province, City; Area	Study Setting	Sample Size	Number of birth asphyxia	Prevalence	Definition of asphyxia	Quality
52	Wu, et al. [75]	2016	Jiangsu, Suzhou(S)	U	17,666	185	1.05	Apgar score	5
53	Zhang [76]	2016	Henan, Fangcheng(N)	R	2130	128	6	Apgar score	5
54	Zhang, et al. [77]	2016	Shaanxi, Ankang(N)	U	10,364	126	1.22	Apgar score	5
55	Zhang, et al. [78]	2016	Liaoning, Jinzhou(N)	U	2218	45	2	Apgar score	5
56	Wu, et al. [11]	2016	Zhejiang, Ruian(S)	U	18,819	135	0.7	Apgar score	6
57	Zhao, et al. [79]	2017	Sichuan, Chongzhou(S)	U	6023	150	2.49	Apgar score	7
58	Qu [80]	2018	Guangdong, Zhaoqing(S)	U	8395	68	0.81	Apgar score	5
59	Wu, et al. [12]	2018	Zhejiang, Taizhou(S)	U	3162	159	5.03	Apgar score	5
60	Xu, et al. [81]	2018	Jiangsu, Qunshan(S)	U	11,788	86	0.73	Apgar score	5
61	Wang, et al. [82]	2018	Gansu, Gannan(N)	R	1197	183	15.3	Apgar score	5
62	Guo, et al. [83]	2018	Henan, Xuchang(N)	U	1226	202	16.5	Apgar score	5
63	Liu, et al. [84]	2019	Sichuan, Leshan(S)	U	3400	299	8.79	Apgar score	5
64	Wu, et al. [85]	2019	Hubei, Enshi(S)	R	22,294	733	3.29	[a]Apgar score + PH	6
65	Yao [86]	2019	Shanxi, Taiyuan(N)	U	4547	102	2.24	Apgar score	5
66	Zhang, et al. [87]	2019	Zhejiang, Taizhou(S)	U	5989	174	2.91	Apgar score	5
67	Yuan [88]	2019	Jiangxi, Nanchang(S)	U	1175	67	5.7	Apgar score	5
68	Fu, et al. [89]	2020	Zhejiang, Hangzhou(S)	U	954	51	5.4	Apgar score	6
69	Jiang, et al. [90]	2020	Zhejiang, Hangzhou(S)	U	1200	62	5.17	Apgar score	5
70	Xing, et al. [91]	2020	Guangdong, Shenzhen(S)	U	27,439	127	0.46	Apgar score	5
71	Qiu, et al. [92]	2020	Hannan, Hankou(S)	U	2152	91	4.23	Apgar score	4
72	Han, et al. [93]	2020	Xizang, Lasa(N)	U	1873	262	13.99	Apgar score	5
73	Zeng [94]	2021	Guangdong, Guangzhou(S)	U	11,628	100	0.86	Apgar score	5
74	Guo [95]	2021	Hebei, Handan(N)	U	2814	215	7.64	Apgar score	5
75	Wu [96]	2022	Hubei, Jingzhou(S)	M	3911	272	6.95	[a]Apgar score + PH	6
76	Zhang [97]	2022	Anhui, Hefei(S)	U	26,328	228	0.88	Apgar score	4
77	Li [98]	2022	Zhejiang, Ningbo(S)	U	55,281	43	0.78	Apgar score	5
78	Li, et al. [99]	2022	Guangdong, Guangzhou(S)	U	40,319	1415	3.5	Apgar score	4
79	Zou, et al. [100]	2022	Jiangxi, Nanchang(S)	U	1024	52	5.08	[a]Apgar score + PH	4
80	Zou, et al. [101]	2023	Anhui, Huainan(S)	U	24,214	160	0.66	Apgar score	5

N north, *S* south, *U* urban, *R* rural, *M* mixed

[a] Diagnostic criteria included in the articles:

Chen, et al., 2009 [13]; ①1-min Apgar score ≤ 7 points; ②Umbilical artery blood pH < 7.20

Wu, et al.; 2012 [63]; ① Umbilical artery blood pH < 7.20, tested by the neonatal department using the GEM3000 blood gas analyzer produced by the American IL company; ② 1-min Apgar score ≤ 7 points, assessed by a neonatologist in the delivery room or operating room

Wu, et al., 2019 [85]; Mild asphyxia: Apgar score ≤ 7 points in 1 min or 5 min, with umbilical artery blood pH < 7.2. Severe asphyxia: Apgar score ≤ 3 points in 1 min or ≤ 5 points in 5 min, with umbilical artery blood pH < 7.0. Hospitals that are unable to perform umbilical artery blood gas analysis will still use the Apgar score for diagnosis

Wu, 2022 [96]; Mild asphyxia: Apgar score ≤ 7 points for 1 or 5 min, with umbilical artery blood pH < 7.2; Severe asphyxia: Apgar score ≤ 3 points for 1 min or ≤ 5 points for 5 min, with umbilical artery blood pH < 7.0. Hospitals that are unable to perform umbilical artery blood gas analysis will still use the Apgar score for diagnosis, i.e. mild asphyxia: 4 points ≤ 1 min Apgar score ≤ 7 points, or 1 min Apgar score > 7 points but 5 or 10 min Apgar score ≤ 7 points; severe asphyxia: 1 min Apgar score < 3 points, or 5 min Apgar score ≤ 5 points

Zou, et al., 2022 [100]; Apgar score ≤ 7 at 1 or 5 min after birth, umbilical artery blood pH < 7.2

Labor factors

A total of 9 risk factors related to labour factors were identified from the articles, and meta-analysis revealed that 5 risk factors, namely, breech delivery, assisted breech delivery, caesarean section, assisted delivery, prolonged second stage of labour, and malpresentation, were statistically significant.

Discussion

On the basis of the 80 studies included in the present meta-analysis (a total of 17,140 newborns), the pooled prevalence of neonatal birth asphyxia in China was 4.8%. An evaluation of potential risk factors associated with neonatal asphyxia in China revealed statistically significant associations with the following fourteen factors:

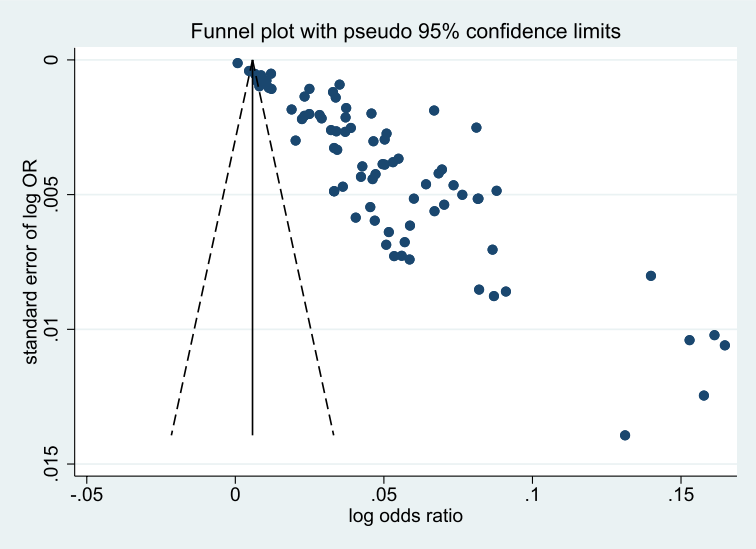

Fig. 3 Funnel plot of the enrolled studies

Table 2 Subgroup analyses of the prevalence of birth asphyxia

Subgroup	No. of studies	birth asphyxia among neonates				
		n/N	Prevalence (%)	95%*CI*	I^2	*P* value
Geographical setting						
North	32	7508/181484	5.1	4.1—6.3	99.3	0.000
South	48	9632/420244	4.1	3.3—5.1	99.5	0.000
Study setting						
Urban	74	13,948//531246	4.2	3.4—5	99.5	0.000
Rural	14	2645/61101	6	4.6—7.4	97.7	0.000
Mixed	2	547/9381	5.8	5.3—6.3	-	-
Diagnostic criteria						
Apgar score	75	15,546/552867	4.6	3.8—5.4	99.5	0.000
Apgar score wit Umbilical artery blood pH	5	1594/48861	3.7	2.2—5.7	98.9	0.000
Simple size						
> 5000	30	10,376/487188	2.2	1.6—3	99.6	0.000
≤ 5000	50	6764/114540	6.2	5.5—7.1	96.8	0.000
Study period						
1995–2016	55	11,704/314576	4.9	4.2—5.6	98.8	0.000
2017–2023	25	5436/287152	3.7	2.6—5	99.6	0.000

placental abruption, placenta previa, advanced maternal age, primigravida, premature birth, intrauterine distress, stained amniotic fluid, macrosomia, foetal abnormalities, breech delivery, assisted breech delivery, caesarean section, assisted delivery, prolonged second stage of labour, and malpresentation.

Despite global declines in neonatal mortality, significant differences remain between regions and countries [102]. In developed countries, the prevalence of perinatal asphyxia is 2 per 1,000 births, whereas in developing countries with limited resources, the rate is as high as 10 times, making it one of the leading causes of infant death and complications [103, 104]. Although the neonatal mortality rate of China, a developing country, has declined with the advancement of medicine, a meta-analysis revealed that the main causes of neonatal death in China are asphyxia, respiratory distress syndrome, and infection [105]. A Chinese study in

Table 3 Pooled risk factors of birth asphyxia

Risk factors		Number of included studies	OR	95%*CI*	I^2	*P* value
Maternal factors	Placental abruption	9	5.00	3.08–8.13	65.4%	0.003
	Placenta previa	8	2.57	1.84–3.58	51.9%	0.042
	Gestational diabetes	2	4.27	1.41–12.98	52.9%	0.145
	Gestational hypertension	5	2.62	1.81–3.81	25.2%	0.253
	Maternal anemia	5	1.69	1.43–1.99	13.9%	0.325
	Placental anomalies	3	3.05	1.94–4.79	33.8%	0.221
	Advanced maternal age	3	3.94	1.46–10.62	85.3%	0.001
	Primigravida	2	5.33	0.41–68.71	97.2%	0.000
	Antepartum bleeding,	2	4.10	2.50–6.71	0	0.630
Fetal factors	Preterm birth	14	3.36	2.61–4.32	63.9%	0.001
	Intrauterine distress	15	4.48	3.47–5.80	70.7%	0.000
	Birth weight	4	2.57	1.89–3.50	0	0.923
	Gestational age	3	3.29	1.96–5.54	0	0.806
	Amniotic fluid contamination	13	2.90	2.47–3.40	24.2%	0.199
	Stained amniotic fluid	5	3.28	2.25–4.79	73%	0.005
	Umbilical cord abnormalities	10	2.20	1.79–2.70	42.9%	0.072
	Emergency delivery	2	3.66	2.36–5.68	0	0.467
	Male infant	2	2.04	1.56–2.68	0	0.952
	Nuchal cord	7	2.31	1.82–2.93	26.8%	0.224
	Twin pregnancy	2	4.76	1.81–12.51	63.5%	0.098
	Macrosomia	2	6.30	0.61–65.22	92.6%	0.000
	Foetal malformation	2	7.44	1.46–38.02	76.6%	0.038
Labor factors	Breech birth	3	2.42	1.24–4.73	67.4%	0.047
	Breech aissisted delivery	2	29.03	9.20–91.63	0	0.327
	Forceps delivery	3	4.50	2.35–8.60	63.3%	0.066
	Prolonged labor	5	2.58	1.80–3.71	0	0.589
	Caesarean section	5	1.72	0.91–3.24	87.6%	0.000
	Assisted delivery	2	13.62	5.50–33.73	80.4%	0.024
	Prolonged second stage of labor	2	1.43	0.68–3.01	87.3%	0.005
	Inadequate contractions	3	2.97	1.97–4.49	0	0.884
	Malpresentation	4	4.20	2.21–7.99	75.4%	0.007

2000 reported that the prevalence of neonatal asphyxia ranged from 4.7% to 8.9% [106]. To the best of our knowledge, the present study is the first meta-analysis to explore the prevalence of neonatal birth asphyxia in China. According to the present meta-analysis results, the pooled prevalence of neonatal birth asphyxia in China is 4.8%, which is consistent with the findings of earlier studies. This pooled prevalence is lower than that reported in previous studies in underdeveloped regions of East Africa, Ethiopia (19.3%, 24.06%) [107], and sub-Saharan Africa (17.28%) [108] but higher than that reported in developed regions of the Netherlands (0.85%) [109], Iceland (0.94%) [110], and the Edinburgh region of the United Kingdom (0.09%) [111]. In addition, the present subgroup analysis revealed that the prevalence of neonatal birth asphyxia in China changed by region, study setting, diagnostic standards, sample size, and study year.

In China, hospitals in rural areas lag behind urban hospitals in terms of both standards and economic development, with limited training and promotion of resuscitation techniques [96, 112]. In addition, the education level of mothers in rural areas is mostly lower than that of mothers in cities [113]. In some remote rural areas, maternal and child health care is relatively underdeveloped because of influences from polytherapy, outdated customs, and family cultural beliefs about childbirth [114]. These factors explain why the neonatal asphyxia prevalence in rural China (6%) was higher than that in urban areas (4.2%) in the present study.

The present study revealed that the prevalence of neonatal asphyxia in the northern region (5.1%) was greater than that in the southern region (4.1%). A previous survey covering low Apgar scores in newborns in China reported that the northeastern region has the highest incidence of low Apgar scores [115]. Moreover, earlier research surveys in China also revealed that the prevalence of neonatal asphyxia is greater (4.3%) in northern areas than in southern areas [116]. In South China, the prevalence of neonatal asphyxia is relatively low. A previous survey revealed that the prevalence of neonatal asphyxia in Central and South China was 3.78% in 2005 [117], and the prevalence of neonatal asphyxia in Huainan was 0.66% between 2018 and 2022 [101]. Although the prevalence rates in different regions vary greatly in these studies, the prevalence of neonatal asphyxia in northern China is higher than that in southern China, which is consistent with the results of the present study.

These findings highlight the importance of reducing the incidence of birth asphyxia, bridging the urban–rural gap, and advancing regional maternal and infant health care management. In China, neonatal resuscitation has been a focus of attention. In April 2004, the Department of Maternal and Child Health and Community Health of the former Ministry of Health launched the Neonatal Resuscitation Program (NRP) in China, which has effectively reduced the incidence of neonatal asphyxia [118, 119]. However, given the vast territory and significant regional disparities in China, the implementation of the program in some rural areas has been suboptimal [120–122], which is largely due to the limited health care resources in rural areas, where the quality of resuscitation often falls short of that in secondary and higher level hospitals. To address this issue, experts should be stationed in rural towns and counties to help improve neonatal resuscitation capabilities [123]. Additionally, establishing regional critical neonatal care centres and building a post-resuscitation treatment system remain important areas of focus for hospitals in China [119].

The present subgroup analysis revealed that when the sample size exceeded 5,000, the prevalence of asphyxia was lower (2.2%), although some studies have reported different findings [124]. Additionally, the present analysis revealed that the use of the Apgar score alone yielded a greater incidence of asphyxia (4.6%) than the combination of the Apgar score with blood gas analysis (3.7%). This difference may also be related to earlier study periods when China relied solely on the Apgar score for diagnosis. Since 1996, the United States has incorporated umbilical artery blood gas analysis into its neonatal asphyxia criteria, with strict requirements that all four criteria be met [125–127]. However, many international scholars have not fully adopted these stringent standards [128, 129], and Chinese researchers have suggested that this approach may lead to missed asphyxia diagnoses [130]. As a result, China updated its neonatal asphyxia diagnostic criteria in 2016 to prevent reliance solely on the Apgar score [2]. The present analysis revealed a higher asphyxia incidence before 2016 (4.9%) than after 2017 (3.7%), highlighting the subjectivity and limitations of using only the Apgar score, which may have led to overestimates in earlier studies. Moreover, even with the updated criteria, some studies in the present analysis used a low Apgar score as the only diagnostic criterion, indicating that combined diagnostic methods need further clinical promotion. This conclusion aligns with the consensus of related studies both domestically and internationally [131–134].

In the present study, the main maternal factors affecting neonatal asphyxia were placental abruption, placenta previa, advanced maternal age, and primigravida. Placental abruption is closely related to neonatal asphyxia [135]. An analysis of 285 newborns revealed that placental abruption accounts for 14% of children with asphyxia, and a multivariate analysis revealed that placental abruption is an independent risk factor for neonatal asphyxia [136]. Similarly, placenta previa can also affect the occurrence of birth asphyxia in newborns [89]. Placental factors, such as placenta previa, can cause maternal prepartum haemorrhage, reduce foetal blood perfusion, and lead to hypoxia and ischaemia [137]. Furthermore, the incidence of adverse pregnancy outcomes for both mothers and children increases with maternal age [138–140]. Advanced maternal age is identified as one of the risk factors for neonatal asphyxia [141] because age is an important factor that affects fertility and pregnancy outcomes [142]. Additionally, there is a growing focus in current research on primigravida childbirth. This is because there are high expectations for childbirth but little knowledge about childbirth, and increased negative emotions caused by a lack of childbirth experience can also affect the occurrence of neonatal asphyxia [143].

From the perspective of the foetus, the present study revealed that preterm birth, intrauterine distress, stained amniotic fluid, macrosomia, and foetal malformation were influencing factors for neonatal birth asphyxia. As the number of gestational weeks increased, the incidence of neonatal asphyxia gradually decreased ($P < 0.05$), indicating a close association between premature birth and birth asphyxia [144, 145]. Additionally, existing research suggests that intrauterine distress is an independent risk factor for neonatal birth asphyxia [146]. In a retrospective case analysis, Aslam et al. [147] reported that intrauterine distress increases the risk of birth asphyxia in normal newborns by 1.69 times. Zhang Youjun analysed newborns with intrauterine distress and reported

a 5.975-fold greater risk of asphyxia in these newborns than in normal newborns [97]. Furthermore, several factors, such as stained amniotic fluid, may also lead to foetal inhalation of affected amniotic fluid, triggering respiratory distress syndrome and birth asphyxia, especially when pregnant women experience irregular contractions or reduced amniotic fluid, which may exacerbate foetal hypoxia [19]. Previous studies have also indicated that the degree of amniotic fluid contamination is related to the incidence of neonatal asphyxia [148, 149]. Notably, the results of the present study revealed that macrosomia is also a risk factor for birth asphyxia, which was consistent with the findings of previous studies, showing that macrosomia increases the risk of neonatal asphyxia [150, 151]. However, another study revealed that infants with macrosomia do not have an increased risk of asphyxia at 1 min postpartum (OR = 1.43; 95% CI: 0.94–2.17, $P = 0.10$) [152]. This may be because infants with macrosomia develop more fully in the mother's body, with better organ function, and appropriate preventive measures are taken during delivery to reduce the risk of birth asphyxia. Additionally, foetal malformation is characterized by abnormalities in overall development, which may lead to organ dysfunction [153]. Particularly when the foetus has severe structural abnormalities, especially those involving the respiratory system, the risk of the newborn facing challenges in breathing and oxygenation may be intensified, thereby increasing the likelihood of asphyxia [154, 155].

Breech birth, malpresentation, prolonged second-stage labour, caesarean section, and assisted delivery are factors affecting neonatal birth asphyxia. Abnormal foetal positions include breech, occiput posterior, occiput transverse, face presentation, and shoulder presentation [19]. These abnormal foetal positions may lead to difficult labour during delivery, resulting in acute hypoxia for the foetus, thereby increasing the risk of birth asphyxia. Research has shown that the probability of neonatal asphyxia in foetuses with abnormal positions is 3.01 times greater than that in foetuses with normal positions (AOR = 3.014; 95% CI = 1.206–7.526) [83]. Moreover, when abnormal foetal positions are combined with various factors, such as uterine contraction weakness, maternal pelvic narrowing, or an abnormal birth canal, prolonged labour, slowed cervical dilation, and obstructed descent of the foetal head may occur. This can ultimately result in foetal compression or neonatal asphyxia, increasing the risk of adverse outcomes for the newborn [156]. In particular, a prolonged second stage of labour increases the risk of complications in newborns [157].

Caesarean section is a major risk factor for birth asphyxia, and the rate of asphyxia is closely related to the rate of caesarean section [158, 159]. In particular, when women who undergo vaginal delivery undergo an emergency caesarean section, the rate of neonatal asphyxia increases due to a prolonged second stage of labour [160, 161]. Notably, assisted delivery is also a risk factor for neonatal birth asphyxia. Compared with women undergoing natural childbirth, assisted delivery procedures carry a greater risk of facial compression and abrasion for the newborn, leading to a higher incidence of asphyxia [162]. Furthermore, assisted delivery procedures themselves can cause physical harm to the mother, such as severe perineal tears.

Strengths and limitations

To our knowledge, the present study is the first systematic review and meta-analysis of the prevalence and risk factors for neonatal asphyxia in China. First, a comprehensive search was conducted across eight databases, including English and Chinese publications, via a robust methodology. Second, most studies included in this meta-analysis were in Chinese, which may make these data valuable to non-Chinese readers and future research in neonatal asphyxia resuscitation and related fields. Third, many participants were reviewed to ensure the statistical power and accuracy of the estimates. However, some potential limitations should be noted. The present findings were limited by significant heterogeneity across studies, which may result from various factors, such as differences in study locations, designs, and sample characteristics. Even within regional subgroup analyses, considerable heterogeneity remained, as heterogeneity is often difficult to avoid in epidemiological research [163]. Additionally, despite efforts to minimize publication bias, some publication biases may still influence the results, as the present analysis included only studies published in Chinese, which may also be a source of bias. Future research should aim to address these limitations and build upon the present findings to further advance the management of neonatal asphyxia and improve neonatal health worldwide.

Conclusion

The present results establish that the prevalence of neonatal birth asphyxia in China is 4.8%, which is higher than that in undeveloped countries but lower than that in developed countries. The risk factors affecting neonatal birth asphyxia in China are mainly placental abruption, placenta previa, advanced maternal age, primigravida, preterm birth, intrauterine distress, stained amniotic fluid, macrosomia, foetal malformation, breech birth, malpresentation, prolonged second stage of labour, caesarean section, and assisted delivery.

The disparities between the southern and northern regions, as well as among the study settings, highlight the need to further advance resuscitation techniques for newborns in different areas. Furthermore, the use of different diagnostic criteria across years is also a factor influencing the incidence of neonatal birth asphyxia in China. Future clinical health care professionals should further refine the diagnostic procedures for birth asphyxia to minimize misdiagnosis. Finally, the integrated risk factors identified in the present study can provide guidance and reference for the early identification of neonatal birth asphyxia in subsequent research.

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Study concept and design: Yujie Su, Yueming Peng, Zhangbin Yu. Acquisition of data: Yujie Su, Wei Liu, Yueming Peng,. Analysis and interpretation of data: Yujie Su, Wei Liu, Yueming Peng, Ruirui Xing, Weixiang Luo, Zhangbin Yu. Drafting of the manuscript: Yujie Su. Revising it for intellectual content: Xinglei Yujie Su, Yueming Peng, Ruirui Xing, Wei Liu, Weixiang Luo, Zhangbin Yu. Final approval of the completed manuscript: Yujie Su, Yueming Peng, Ruirui Xing, Wei Liu, Weixiang Luo, Zhangbin Yu.. All authors read and approved the final manuscript.

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Data availability
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Declarations

Ethics and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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