Prevalence and Risk Factors for Retinopathy of Prematurity in China: A Systematic Review and Meta-Analysis

Qi Lumin

Dalian Medical University

Gu Ziyang

Dalian Medical University

Sun Xincheng (✉ czeyedoctor@stu.njmu.edu.cn)

Changzhou Second People's Hospital of Nanjing Medical University

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Abstract

Background

The etiology of retinopathy of prematurity (ROP) is thought to be related to genetic susceptibility and environmental exposure factors. The purpose of this article was to estimate the prevalence of ROP in mainland China and to attempt to summarize the environmental risk factors for ROP in Chinese infants.

Method

We searched 9 databases for articles that were published before May 29, 2021, and studies describing the prevalence and risk factors for ROP in Chinese infants were included. The fixed-effects model and the random-effects model were applied to the effect sizes (ES) and their 95% confidence intervals (CIs) with $I^2 \leq 50\%$ and $I^2 > 50\%$ in the heterogeneity tests, respectively.

Results

Twenty-two separate populations were included in the meta-analysis of the prevalence of ROP. The prevalence of ROP in mainland China was 9.284% (95% CI: 6.546-12.022%). It was negatively correlated with birth weight (BW) and gestational age (GA). Fifty independent meta-analyses were observed to be related to environmental exposure factors of ROP. Thirty of the 50 meta-analyses had results that were significant at p values less than 0.05. The first three risk factors with the largest combined effect size were $GA \leq 34$ w, bronchopulmonary dysplasia (BPD) and $BW \leq 2,000$ g.

Conclusions

Approximately one in ten immature infants suffered from ROP. More studies need to be included. Premature babies with diseases that cause hypoxia and irregular oxygen use should be paid more attention for ROP screening.

Introduction

Retinopathy of prematurity is a vascular proliferative retinal disease that occurs in immature infants. It almost always occurs in small for gestational age infants and a small number of low birth weights in the population of full-term newborns. Due to the fact that ROP is a disease that can be detected early through screening, neonatal fundus screening should be seriously considered. Standardized screening criteria need to be formulated based on the investigations of the prevalence and risk factors for ROP in different countries and regions.

Before 2010, research on ROP screening has been mostly concentrated in economically developed provinces, municipalities and capital cities in eastern coastal areas, such as Guangdong, Beijing, Zhejiang, Shandong, Jiangsu and Shanghai¹. When compared with developed countries, infants with larger birth weights and larger gestational ages were more likely to suffer from ROP in China, which were similar results observed in some developing countries (such as Vietnam)^{2,3}. In the past 10 years (2008-2018), the number of ROP screenings in the eastern coastal provinces and cities has further increased, and the number of studies in western and southwestern China has also significantly increased. However, reports in Northeast China are still few⁴.

It seems that reports on the prevalence of ROP in various regions in China are relatively scattered, and there are few reviews describing the prevalence of ROP in premature infants in China. Moreover, China's vast territory and economic and medical levels vary. Although the Chinese guidelines for screening for retinopathy of prematurity were formulated in 2014⁵, the screening standards of various provinces and cities still varied, which made the screening results of various regions less comparable. Therefore, it is necessary to update a review.

Some hypotheses have been proposed to explain the development of ROP, but its exact mechanism is still unclear. Lower birth weight and smaller gestational age are the most frequently mentioned risk factors for ROP. The long-term use of oxygen after birth is also an important factor in promoting the development of ROP; however, this relationship has not been verified. Polymorphisms in some genes (such as the gene encoding vascular endothelial growth factor) also partially explain the occurrence of ROP⁶. Other factors have been included by researchers in Chinese newborns, but the data are scattered, and some articles have obtained the opposite conclusion. Thus, a systematic review and quantitative meta-analysis need to be conducted.

This article introduces the development of retrieval strategies, the retrieval and screening of literature, literature quality evaluation, data extraction and merging and an analysis of the sources of bias. The innovations and shortcomings of this study will be discussed at DISCUSSION part of this article.

Methods

We conducted this review based on the preferred reporting items for systematic review and meta-analysis (PRISMA) protocols.

Search strategy

The retrieved literature originated from nine English and Chinese databases, including PubMed, the Cochrane Library, Embase, Medline, Web of Science, SinoMed, China National Knowledge Infrastructure (CNKI), VIP Database for Chinese Technical Periodicals (VIP) and Wanfang databases. The search strategy was a combination of subject terms, such as "premature infant", "retinopathy of prematurity", "ROP", "prevalence", "morbidity", "risk factors" and free words.

This section contains five parts: search strategy, the inclusion and exclusion criteria of the studies, the quality assessment of studies, data extraction and statistical analysis. Each step was separately performed by two researchers without interference. Any inconsistent results between the two researchers were submitted to the third researcher to obtain an agreement.

Inclusion and exclusion criteria

Inclusion criteria

- 1) Prevalence of ROP: ☐ newborns with gestational ages less than 37 weeks or gestational ages greater than 37 weeks but with birth weights less than 2,500 g were included in this study; ☐ the population that was studied included infants from mainland China; and ☐ the included studies must have described the prevalence of ROP and its 95% confidence intervals (CIs) or other forms of data that can be transformed into CIs.
- 2) Risk factors for ROP: ☐ the restrictions on the study population were the same as previously described; and ☐ the included studies must have clearly described the exposure factors, outcome indicators, relative risk (RR) values or

odds ratio values, as well as their 95% CIs. Other data that can be transformed into these values were also accepted.

Exclusion criteria

The following studies were excluded: ☐ studies that were not representative in the population, such as studies that were conducted only in infants with a certain disease and studies that were conducted only in the NICU, among other cases; ☐ reviews, comments, conference abstracts and case reports, among other types; ☐ articles that only reported the prevalence (i.e., the incidence) of newly diagnosed ROP; and ☐ duplicate reports.

Quality assessment of studies

We used the Agency for Health Care Research and Quality (AHRQ) scale to evaluate cross-sectional studies. Those studies with a score of ≥ 8 were classified as being high-quality studies, and those studies with a score of 4-7 and less than 3 were of medium-quality and low-quality, respectively. Newcastle–Ottawa Scale (NOS) was used to assess cohort studies and case-control studies. Studies with scores of no less than 6 were classified as being high-quality studies.

Data extraction

The extracted information included the first author, publication year, survey year, survey area, sample size, number of patients and other data containing demographic characteristics.

Statistical analysis

We used STATA software (Version 16.0; Stata Corporation) to analyze the extracted data. The Cochran's Q test and I^2 index were used to test the heterogeneity of the studies. Studies with lower heterogeneity (I^2 less than 50%, $p > 0.05$) used a fixed-effects model to combine the effect values. In contrast, other studies used a random-effects model. A subgroup analysis, sensitivity analysis, cumulative meta-analysis and meta-regression were used to analyze the sources of heterogeneity. The publication bias was analysis by funnel plot and Egger's test.

Results

Search results and characteristics

This review included all of the eligible studies that were published as of May 29, 2021, and unpublished studies were not involved. A total of 3,868 articles were retrieved, and 22 and 30 articles describing ROP prevalence and ROP risk factors, respectively, that met the criteria were finally included (Fig. 1). Among the 22 studies describing the prevalence of ROP, there were 6 high-quality studies, 15 medium-quality studies and only one low-quality study. Among the 30 studies included in the analysis of ROP risk factors, data extracted from 28 studies could be meta-analyzed. 24 of these studies were of high-quality.

Prevalence of ROP

We extracted and merged data with a sample size of 30,118 from 22 studies⁷⁻²⁸ and concluded that the prevalence of ROP in mainland China was 9.284% (95% CI: 6.546-12.022%). The highest prevalence was 20.34% (95% CI: 10.07-30.61%), which was reported in Jiang YR (1994)⁷, and the lowest prevalence was 1.10% (95% CI: 0.53-1.68%), which was mentioned in Tian N (2014)²⁰ (Fig. 2).

The prevalence of boys and girls for ROP was 12.063% (95% CI: 8.225-15.902%) and 10.603% (95% CI: 5.811-15.395%), respectively (Table 1).

N, number; CI, confidence interval; GA, gestational age; BW, birth weight; Premature infants, infants with gestational age less than 37 weeks; Full-term infants with low birth-weight, infants whose gestational age over 37 weeks but whose birth weight less than 2,500 grams.

Sensitivity analysis for prevalence

A sensitivity analysis of the prevalence of ROP (Fig. 3) showed that the exclusion of each study one by one did not have a significant impact on the overall combined results, thus suggesting good stability of the results. The cumulative meta-analysis of ROP prevalence sorted by publication year is shown in Fig. 3.

Subgroup analysis of ROP prevalence based on geographic region

We conducted a subgroup analysis of the prevalence of ROP in eastern, western and central China based on the survey area of each study. The results showed that the prevalence of ROP was the highest in central China at 12.083% (95% CI: 9.838-14.328%), whereas the prevalence of ROP in western China was the lowest at 4.339% (95% CI: 0.822-7.855%). The prevalence of ROP in central China was observed to be located the two previous prevalences at 9.112% (95% CI: 6.526-11.699%). However, there was no significant difference in the prevalence between South and North China (Table 1).

The prevalence of ROP based on gestational age

When grouped by gestational age, the combined results of ROP prevalence are shown in Table 1. In newborns with a gestational age of less than 30 weeks, the prevalence of ROP was as high as 44.541% (95% CI: 17.808-71.275%), which was only 3.207% (95% CI: 0.962-5.451%) in newborns with a gestational age of more than 34 weeks. With the increase of gestational age, the prevalence of ROP showed a downward trend.

The prevalence of ROP based on birth weight

The prevalence of ROP (as calculated by birth weight grouping) is shown in Table 1. According to the data of 3 included studies, the prevalence of ROP in infants with BW<1,000 g was up to 42.470% (95% CI: 3.616-81.324%). Ten studies reported the prevalence of ROP in infants with BW>2,000 g, which was only 4.503% (95% CI: 2.537-6.469%). The prevalence of ROP in infants with BW<1,500 g, BW between 1,500 and 2,000 g, BW between 2,000 and 2,500 g and BW>2,500 g was 37.866% (95% CI: 28.214-47.519%), 16.444% (95% CI: 10.205-22.682%), 4.270% (95% CI: 1.778-6.762%) and 3.298% (95% CI: -2.510-9.106%), respectively. The prevalence exhibited a significant downward trend with increasing birth weight.

Meta regression

The meta-regression analysis of ROP prevalence is shown in Fig. 4. The regression model showed that the prevalence of ROP decreased with increasing publication year, and the relationship was significantly different (meta-regression coefficient: -0.600, 95% CI: -1.152 to -0.0487, $p=0.034$). However, the variation between the studies was relatively large ($\text{Tau}^2=28.37$), the 98.75% residual variation could be explained by the heterogeneity ($I^2=98.75\%$) and the covariate that was included in the model (the year of publication) could only be responsible for 14.5% of the total variation (Adj R-squared= 14.5%).

Table 1. Prevalence of ROP based on GA, BW, year, region and gender of studies								
Variable		Studies(N)	Sample(N)		Heterogeneity		Prevalence(%)	95% CI
			Total	Cases	I^2	P-value		
GA	≥30w	6	253	102	96.40%	0.000	44.541	17.808-71.275
	30-34w	6	900	131	94.30%	0.000	17.344	8.335-26.352
	≥34w	6	1550	60	89.30%	0.000	3.207	0.962-5.451
	≤32w	8	8623	1889	91.40%	0.000	27.609	20.99-34.228
	≥32w	8	13802	1092	96.40%	0.000	8.369	5.11-11.629
BW	≥1,000g	3	103	51	94.00%	0.000	42.470	3.616-81.324
	≥1,500g	12	10282	2438	94.50%	0.000	37.866	28.214-47.519
	1,500-2,000g	10	1632	230	94.50%	0.000	16.444	10.205-22.682
	≥2,000g	10	2783	128	91.40%	0.000	4.503	2.537-6.469
	2,000-2,500g	6	1824	87	93.00%	0.000	4.270	1.778-6.762
	≥2,500g	2	380	14	90.50%	0.001	3.298	-2.51-9.106
Year	2014-2018	9	4485	356	94.90%	0.000	7.725	4.742-10.707
	1990-2013	12	25025	3037	99.20%	0.000	10.552	6.346-14.759
Region	Southern	12	26057	3117	99.30%	0.000	8.962	4.989-12.936
	Northern	10	4061	326	86.50%	0.000	8.782	6.418-11.146
	Eastern	14	66846	7371	95.90%	0.000	9.112	6.526-11.699
	Western	3	2105	88	94.90%	0.000	4.339	0.822-7.855
	Central	5	21403	2870	84.30%	0.000	12.083	9.838-14.328
Gender	Male	7	12379	1590	93.90%	0.000	12.063	8.225-15.902

Female	6	9722	1271	96.10%	0.000	10.603	5.811-15.395
Premature infants	6	2980	306	97.60%	0.000	11.556	5.422-17.691
Full-term infants with low birth-weight	2	298	2	0.00%	0.506	1.071	-0.591-2.732

Publication bias

A funnel chart was used to test for publication bias (Fig. 5), and the Egger's test results ($t=0.46$, $p=0.652$) showed that the funnel chart was symmetrical, thus suggesting that the possibility of publication bias in this study was unlikely.

Meta-analysis of risk factors for ROP

The meta-analysis of the univariate analysis of 50 risk factors for ROP in the Chinese population is shown in Table 2.

* $p \leq 0.05$; ** $p \leq 0.01$; N, number; ES, combined effect size (OR or RR); CI, confidence interval; GA, gestational age; w, weeks; BW=birth weight; g, grams; RDS, respiratory distress syndrome; PDA, patent ductus arteriosus; ART, artificial reproductive technology; IVF, in vitro fertilization; PROM, premature rupture of membranes; d, days; HIE, hypoxic-ischemic encephalopathy; BPD, bronchopulmonary dysplasia; CHD, congenital heart disease; Random, random effects model; Fixed, fixed effects model.

The results showed that smaller GA, $GA \leq 28$ w, $GA \leq 32$ w, $GA \leq 34$ w, $BW \leq 750$ g, $BW \leq 1,500$ g, $BW \leq 2,000$ g, the male sex, oxygen therapy, cesarean sections, uses of alveolar surfactant, mechanical ventilation, RDS, pneumonia, PDA, apnea, PROM, placental abruption, the prenatal use of steroids, the neonatal use of steroids, oxygen therapy time > 5 d, anemia, blood transfusion, neonatal hypoglycemia, neonatal hyperglycemia, acidosis, cholestasis of pregnancy, septicemia, BPD and congenital heart disease (a total of 30 variables) were significantly related to the occurrence of ROP ($p < 0.05$). Among them, the two variables of cesarean section (OR: 0.735, 95% CI: 0.571-0.947) and cholestasis of pregnancy (OR: 0.404, 95% CI: 0.212-0.770) had protective effects on the occurrence of ROP. The other 28 variables were risk factors for the occurrence of ROP ($OR > 1$).

Other risk factors for ROP

In addition, risk factors that were not included in the meta-analysis were mentioned in some articles (Table 3).

* $p \leq 0.05$; ** $p \leq 0.01$; N, number; ES, combined effect size (OR or RR); CI, confidence interval.

In addition to risk factors such as BW and GA, a study by Liu Q et al.²⁹ (with a sample size of 1,614 cases) also showed that acid-base imbalance, maternal cold, hypoproteinemia, erythropoietin, encephalopathy of preterm infants, myocardial injury, coagulation dysfunction and vasoactive substances were also risk factors for ROP ($OR > 1$, $p < 0.05$). Yau GS et al.³⁰ showed that hypotension, cardiotonic use, NSAID use, thrombocytopenia and light therapy were also risk factors for ROP ($OR > 1$, $p < 0.05$) in another study. A 5-year cohort study by Yang Q et al.³¹ suggested that 1 min Apgar < 4 points was a risk factor for ROP ($RR > 1$, $p < 0.05$). Furthermore, oxygen therapy during pregnancy and intravascular hemolysis were mentioned as being risk factors for ROP^{32,33}. Vitamin A supplementation in infants was found to reduce the incidence of ROP in very premature infants ($RR=0.601$, 95% CI: 0.465-0.775,

Table 2. Meta-analysis for risk factors of ROP in China

Variable	Studies (N)	Sample(N)		Heterogeneity		Model	ES	95% CI	P-value
		Total	Cases	I ² (%)	P-value				
Smaller GA	18	26407	-	97.90	0.000	Random	1.851	1.112-3.081	0.018*
GA≤26w	5	14195	5475	92.90	0.000	Random	2.214	0.637-7.692	0.211
GA≤28w	8	11740	2150	78.30	0.000	Random	4.844	3.286-7.142	0.000**
GA≤32w	9	9986	1796	83.90	0.000	Random	3.526	2.382-5.219	0.000**
GA≤34w	4	7915	1380	77.30	0.004	Random	11.536	3.732-35.663	0.000**
Lower BW	17	17728	-	97.20	0.000	Random	1.009	0.995-1.022	0.205
BW≤750g	5	5302	1319	0.00	0.918	Fixed	2.361	1.683-3.313	0.000**
BW≤1,000g	5	9091	2796	92.60	0.000	Random	2.518	0.975-6.502	0.056
BW≤1,500g	7	6529	1048	74.80	0.001	Random	4.374	2.968-6.445	0.000**
BW≤2,000g	6	9824	1737	0.00	0.577	Fixed	6.265	5.331-7.362	0.000**
Male	15	21078	-	0.00	0.540	Fixed	1.108	1.03-1.191	0.006**
Multi birth	14	18909	-	75.10	0.000	Random	1.194	0.971-1.469	0.093
Oxygen therapy	8	12807	-	92.40	0.000	Random	1.816	1.063-3.104	0.029*
Cesarean section	9	15101	3001	84.40	0.000	Random	0.735	0.571-0.947	0.017*
Use of alveolar surfactant	7	6843	-	86.50	0.000	Random	2.234	1.28-3.898	0.005**
Mechanical Ventilation	8	10290	-	87.00	0.000	Random	2.564	1.547-4.248	0.000**
Invasive mechanical ventilation	2	1017	-	93.60	0.000	Random	3.875	0.923-16.266	0.064
RDS	8	7719	-	73.30	0.000	Random	1.881	1.278-2.77	0.001**
pneumonia	6	6064	-	44.00	0.112	Fixed	1.967	1.623-2.384	0.000**

PDA	3	1769	-	84.60	0.002	Random	2.725	1.341-5.534	0.006**
ART	5	8992	-	66.80	0.017	Random	1.328	0.969-1.819	0.077
IVF	4	6789	-	69.40	0.020	Random	1.333	0.84-2.116	0.222
Apnea	6	3748	-	67.50	0.009	Random	2.069	1.32-3.242	0.002**
Gestational hypertension	5	7040	1302	32.30	0.206	Fixed	0.926	0.774-1.109	0.403
Pre-eclampsia	3	1485	-	86.40	0.001	Random	0.920	0.329-2.572	0.873
Gestational diabetes	6	7923	-	36.20	0.166	Fixed	1.020	0.785-1.325	0.882
Intrauterine infection	2	2707	498	0.00	0.942	Fixed	1.150	0.902-1.466	0.259
Intrauterine distress	4	5037	-	0.00	0.665	Fixed	1.051	0.843-1.309	0.659
Respiratory distress	2	2143	253	93.10	0.000	Random	1.707	0.498-5.852	0.395
PROM	7	13084	-	22.60	0.257	Fixed	1.317	1.118-1.552	0.001**
Placental abruption	3	2252	355	0.00	0.537	Fixed	2.002	1.011-3.963	0.046*
Placenta previa	4	2418	449	0.00	0.614	Fixed	1.080	0.601-1.941	0.797
Prenatal use of steroids	5	5058	-	0.00	0.662	Fixed	1.388	1.139-1.691	0.001**
Neonatal use of steroids	3	1070	206	0.00	0.369	Fixed	3.254	1.86-5.692	0.000**
asphyxia	6	4059	-	74.20	0.002	Random	1.515	0.862-2.66	0.148
Oxygen therapy time _{0-5d}	2	850	-	0.00	0.718	Fixed	2.683	1.97-3.653	0.000**
anemia	7	4952	-	66.70	0.006	Random	3.286	2.227-4.847	0.000**
Blood transfusion	7	4796	-	86.60	0.000	Random	2.470	1.452-4.201	0.001**
Neonatal hypoglycemia	4	3184	-	0.00	0.622	Fixed	1.740	1.189-2.546	0.004**
Neonatal hyperglycemia	3	2284	431	11.40	0.324	Fixed	2.262	1.559-3.282	0.000**
Acidosis	2	1256	-	0.00	0.382	Fixed	1.364	1.042-	0.024*

								1.788	
Cholestasis of Pregnancy	2	2118	337	0.00	0.869	Fixed	0.404	0.212-0.77	0.006**
Artificial feeding	2	3436	-	79.50	0.027	Random	1.227	0.232-6.481	0.809
septicemia	9	6027	-	42.20	0.086	Fixed	2.114	1.682-2.658	0.000**
IHE	4	2073	324	48.30	0.122	Fixed	1.049	0.665-1.655	0.837
Intracranial hemorrhage	6	3424	-	70.10	0.005	Random	1.473	0.905-2.397	0.119
BPD	3	1183	-	23.00	0.273	Fixed	7.281	5.003-10.596	0.000**
Hyperbilirubinemia	7	4872	-	59.00	0.023	Random	1.254	0.863-1.822	0.235
CHD	4	3968	-	0.00	0.525	Fixed	1.861	1.422-2.435	0.000**
Pulmonary hemorrhage	2	1780	300	0.00	0.981	Fixed	1.996	0.866-4.603	0.105

p=0.000)³⁴.

Discussion

In this meta-analysis, 50 separate populations from more than 21 provinces and cities were included, with 22 of those populations describing the prevalence of ROP. More than half (14) of these studies originated from provinces and cities in eastern China, with Guangdong possessing the most studies (4), followed by Shandong (3) and Beijing (3). There were only 3 studies mentioning the prevalence of ROP in western China from Inner Mongolia (1), Ningxia (1) and Guizhou (1) provinces. Only one study from Northeast China with a sample size of 60 was included in this meta-analysis.

Although the included populations had the same GA and BW characteristics, considerable differences were still identified in the prevalence of ROP among the studies, especially in studies from different regions. In addition, the different proportions of very low birth weight infants and very premature infants in the studies may also be one of the reasons for this difference.

As early as the last century, lower birth weight and smaller birth gestational age were found to be two important risk factors affecting the development of ROP. In this review, we re-confirmed this view and found that $GA \leq 34$ w (OR: 11.536, 95% CI: 3.732-35.663, p=0.000) and $BW \leq 2,000$ g (OR: 6.265, 95% CI: 5.331-7.362, p=0.000) seemed to be most relevant of all risk factors. Furthermore, we also clarified that some diseases that affect ventilatory function and that cause chronic hypoxia in newborns, such as BPD (OR: 7.281, 95% CI: 5.003-10.596, p=0.000), PDA (OR: 2.725, 95% CI: 1.341-5.534, p=0.000) and anemia (OR: 3.286, 95% CI: 2.227-4.847, p=0.000), also promoted the occurrence of ROP. However, it was not obvious whether there was an interaction between these factors.

The most important point from this paper is that we used rigorous inclusion criteria in the included population;

Table 3. Other risk factors of ROP in China

Variable	Sample (N)	ES	95%CI	Type of ES	P-value
Maternal supplemental oxygen administration	468	6.090	2.200 - 16.880	OR	0.000**
Intravascular hemolysis	436	3.095	2.037 - 4.701	OR	0.000**
Acid-base imbalance	1614	2.197	1.491 - 3.192	OR	0.000**
Maternal cold	1614	1.630	0.983 - 2.615	OR	0.036*
Hypoproteinemia	1614	3.122	2.023 - 4.742	OR	0.000**
Erythropoietin	1614	2.178	1.112 - 4.041	OR	0.009**
Encephalopathy of preterm infants	1614	2.755	1.986 - 3.804	OR	0.000**
Myocardial injury	1614	1.655	1.158 - 2.341	OR	0.003**
Coagulation dysfunction	1614	1.919	1.299 - 2.795	OR	0.000**
Vasoactive substances	1614	3.161	2.187 - 4.529	OR	0.000**
Vitamin A supplement	262	0.601	0.465 - 0.775	RR	0.000**
Apgar score 1 min<4	4977	2.152	1.758 - 2.633	RR	0.000**
Postnatal hypotension	513	6.760	4.120 - 11.160	OR	<0.001**
Inotrope use	513	7.700	4.460 - 13.390	OR	<0.001**
NSAID use	513	6.530	3.940 - 10.860	OR	<0.001**
Thrombocytopenia	513	2.870	1.630 - 4.990	OR	<0.001**
Phototherapy	513	2.980	1.360 - 7.890	OR	<0.001**

specifically, babies who were born with a gestational age less than 37 weeks and full-term babies who were born with a gestational age greater than or equal to 37 weeks (but with a birth weight less than 2,500 g), were analyzed. The vast majority of babies who may have ROP were included in this meta-analysis. The GA and BW of the population of each included study were the same, in order to obtain a more stable result.

The limitations of this review included the fact that the number of included studies describing the prevalence of ROP is low, some of which are low- and medium-quality studies. Data from northeastern and western China are sparse. When regarding ROP risk factors, the data that we extracted were unadjusted OR (or RR) values of the univariate analysis because the confounding factors in each study were not the same. Some risk factors are only mentioned in 3 or fewer articles. Furthermore, we didn't include any unpublished studies in this systematic review and meta-analysis.

As mentioned above, the prevalence of ROP in China is generally lower than was previously reported and will further decrease in the future and obtain a relatively stable level. There is not much difference in risk factors for ROP

between China and other countries. More data, especially data from economically underdeveloped provinces, are urgently needed.

Declarations

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Author contributions QL conceived the study design and did the data collection, data extraction, data analysis and data interpretation. She wrote the main manuscript text and prepared the tables and figures. She wrote the main manuscript text and prepared the tables and figures. GZ did the data collection and data extraction. SX conceived the study design, supervised the data collection and data analysis and critically revised the manuscript.

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Registration information This review was not registered.

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Figures

Figure 1

PRISMA flowchart for the selection of studies

Figure 2

Forest plot for meta-analysis of ROP prevalence

a

b

Figure 3

(a) A sensitivity analysis of ROP prevalence; (b) Cumulative meta-analysis sorted by year of publication in ROP prevalence

Figure 4

Meta-regression of ROP prevalence based on publication year of studies (Coefficient: -0.600, 95% CI: -1.152 to -0.0487, P= 0.03)

Figure 5

Funnel chart of ROP prevalence