Review Article

Risk factors for retinopathy of prematurity: integrative review

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ABSTRACT

To summarize the risk factors for retinopathy of prematurity in newborns admitted in the neonatal intensive care unit from primary studies published in databases. We conducted a integrative review in the following databases: SCOPUS, PubMed, Science Direct, Web of Science and CINAHL.Twenty-six studies composed the sample. We listed thematic categories with the risk factors for retinopathy of prematurity, known as: factors related to the clinical therapeutic, use of medications, comorbidities related to retinopathy of prematurity, neonatal characteristics, clinical characteristics associated to retinopathy of prematurity and, maternal factors. To know the risk factors implicates in early retinopathy detection through adoption of preventive measures as the oxygen therapy monitoring, mechanical ventilation and blood transfusions, besides the assessment of neonatal characteristics, to allow an ophthalmologic screening to impede the disease development, its sequelae and/or enable treatment in the initial phase of disease.

Descriptors: Risk Factors; Retinopathy of Prematurity; Intensive Care Units, Neonatal.

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INTRODUCTION

Retinopathy of prematurity (ROP) is a disease clinically characterized by the abnormal proliferation of vessels in the immature retina of premature and low weight at birth newborns[1]. According to the International Classification of ROP (ICROP), the disease can be classified according to its severity and growing order (stages 1-5), its localization (zones I, II and III), its extension in hours (between one and twelve hours) and the presence of an additional disease, a arteriole dilation and venous tortuosity, indicative characteristic of the disease activity[2].

ROP is considered one of the leading causes of avoidable blinding in childhood. It is estimated that about 400 children lose their vision annually because of it. The level of neonatal care of neonatal institutions through screening program, treatment and plans influence this context. Within them, there is the Global Action Plan for the Prevention of Avoidable Blindness and Visual Impairment 2014-2019, which the objectives are related with the reduction of avoidable visual impairment and guarantee access to rehabilitation services for all who need them[2-3].

The disease has a multi-factorial etiology as it is associated to many risk factors that increases its chance of occurrence. Since the neonatal intensive care unit (NICU) is a critical care sector and attends high complexity patients, it becomes an environment vulnerable for errors and adverse events when considering the susceptibility of these patients[4-5]. In the NICU, many professionals manipulate the patient, predisposing to an increased probability of suffering the consequences of an error/adverse event. Because they need many interventions for diagnosis and treatment, admission time tends to grow, resulting in more exposition to potential risks[6].

In this vulnerability context of patients admitted in the NICU, it becomes relevant to address the Patient's Safety National Program (PNSP). Its primary objective is the qualification of health care in all health establishments in the national territory, prioritizing the patient's safety in the sense of reducing errors/adverse events[7].

Our study becomes relevant, as the summarizing of risk factors will allow the reunion of all risk factors present in the literature predisposing ROP occurrence. Once knowing the factors, health professionals will have more information for early ROP detection, favoring the improvement of care quality and an assistance free of health risks.

Therefore, this study aimed to summarize ROP risk factors in newborns admitted in NICU from primary studies published in databases.

METHODS

We conducted a integrative literature review, characterized by a rigorous process to establish defined criteria about the research question conception, sampling and data collection, analysis and presentation of results based on a research protocol previously created. Our study aims to gather and synthesize results of primary studies about a particular theme or research question. Because it is a research method used in evidence-based practices, it allows incorporation of evidence in clinical conduct of many areas of health attention[8-11].

We organized this review study according to the following steps: identification of the research problem and guiding question; literature search guided by inclusion and exclusion criteria; data collection using a previously formatted instrument; data analysis and review presentation[9,12].

The guiding question to operationalize this review was: What are the risk factors to develop retinopathy of prematurity in neonates admitted in a neonatal intensive care unit?

We searched databases in September to December of 2015 using the licensed proxy by Rio Grande do Norte Federal University, through the Coordination for the Improvement of Higher Education Personnel (CAPES) (http://www.capes.gov.br/). We accessed it via CAPES Periodicals Portal (http://www-periodicos-capes-gov-br.ez18.periodicos.capes.gov.br/) the following databases: SCOPUS (Elsevier), Pubmed Central – PMC, Science Direct (Elsevier), Web of Science – Main Collection and Cumulative Index to Nursing and Allied Health Literature – CINAHL.

For searches in databases, we used the indexed descriptors and its respective synonyms in the Medical Subject Headings (MeSH):

- **1#** ("Premature Birth" OR "Birth, Premature" OR "Births, Premature" OR "Premature Births" OR "Preterm Birth" OR "Birth, Preterm" OR "Births, Preterm" OR "Preterm Births" OR " Infants, Premature" OR "Premature Infant" OR "Preterm Infants" OR "Infant, Preterm" OR "Infants, Preterm" OR "Preterm Infant" OR "Premature Infants" OR "Neonatal Prematurity" OR "Prematurity, Neonatal"),
- **2#** ("Risk Factors" OR "Factor, Risk" OR "Factors, Risk" OR "Risk Factor"),
- **3#** ("Retinopathy of Prematurity" OR "Prematurity Retinopathies" OR "Prematurity Retinopathy" OR "Retrolental Fibroplasia" OR "Fibroplasia, Retrolental" OR "Fibroplasias, Retrolental" OR "Retrolental Fibroplasias")
- **4#** ("Intensive Care Units", "Neonatal OR Neonatal ICU" OR "Neonatal Intensive Care Units" OR "Newborn Intensive Care Units" OR "Newborn Intensive Care Units (NICU)" OR "ICU, Neonatal" OR "ICUs, Neonatal" OR "Neonatal ICUs" OR "Newborn ICU" OR "ICU, Newborn" OR "ICUs, Newborn" OR "Newborn ICUs").

It is important to note that we used synonyms with the objective to identify the more substantial number possible of publications related to the study theme. The crossings in the databases occurred using the operator AND, being: 1# AND 3# AND 4# and 2# AND 3# AND 4#.

We considered as inclusion criteria: full articles available in databases and articles addressing ROP risk factors in neonates admitted in NICU. We excluded editorials, letter to editors, abstracts, opinion of specialists, other reviews, correspondences, reviews, book chapters, theses and dissertations. We did not establish a temporal cut aiming to explore the most publications possible about the proposed subject.

We screened the studies through reading of titles, abstracts and applying the relevance test (composed by inclusion and exclusion criteria). We excluded duplicated articles in databases and after, we conducted full-reading of texts that we selected for the sample.

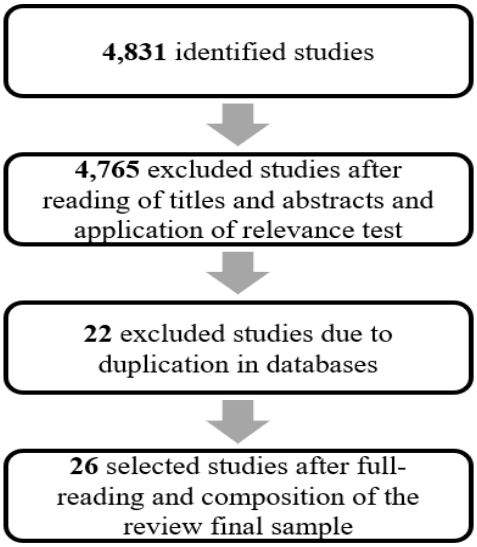
For analysis and data extraction, we created an instrument with the following data: publication identification (article title, indexed databases, authors, country, language and, year of publication), name of the scientific journal, methodological aspects (methods applied, type of approach and objective or investigation question), risk factors, limitations and, conclusions.

For the critical assessment, we identified the type of evidence from the Collaborative Center Joana Briggs Institute (JBI). It classifies evidence according to method design (Level I – Evidence from systematic reviews of randomized controlled trials; Level II – Evidence from randomized controlled trial; Level III.1 – Evidence from well-

designed non-randomized controlled trial; Level III.2 – Evidence from well-designed cohort or case-control; Level III.3 – Evidence from multiple temporal series, with or without intervention and dramatic results in non-controlled experiments and Level IV – Reports of respected authorities, based on clinical criteria and experience, descriptive studies or committee reports of specialists)[13]. The categories arose from the thematic synthesis of data, these were grouped and named by similarity of risk factors associated with the ROP development[10].

The search resulted in a total of 4,831 articles. From those, we selected 26 to compose the final sample of the review. Figure 1 represents the selection of the studies. We presented results descriptively and in tables.

Figure 1: Synthesis of the selection of studies process.



RESULTS

We distributed the studies according to country, year of publication, language, periodical, applied method, type of approach and level of evidence, as demonstrated in Table 1. Within the publication countries of the 26 selected studies, the United States of America (USA) were in 23.1% of articles. The studies published in the last five years added a total of 65.4% of the sample. All articles were available in English.

The higher frequency of publications was in the Journal of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) with three studies (11.5%), followed by the Brazilian Journal of Ophthalmology, Introducion Journal of Ophthalmology and Iran Journal Pediatrics with two (7.8%) studies each. Regarding study methods, cohort studies were predominant (76.9%), followed by case-control studies (15.3%).

Regarding the type of approach, all studies of the sample were quantitative. In 23 (88.4%) articles, the level of evidence was III.2, in two (7.8%) studies it was IV and, in one (3.8%) it was III.3.

After the analysis, we conducted the thematic data synthesis and we organized the results in categories to characterize the risk factors for ROP in the neonatal intensive care environment. We classified the risk factors in categories were by the number of studies addressing them, according to Table 2.

Table 1: Distribution of studies according to country, year, language, periodical, applied methodology, type of approach and level of significance. Natal, RN, Brazil, 2016.

Variables	Frequency	%
Country of publication		
United States of America (USA)	6	23.1%
China	5	19.2%
Iran	3	11.5%
Brazill	2	7.8%
Egypt	2	7.8%
Turkey	2	7.8%
Saudi Arabia	1	3.8%
Greece	1	3.8%
India	1	3.8%
Italy	1	3.8%
Mexico	1	3.8%
Romania	1	3.8%
Total	**26**	**100%**
Year of publication		
2011	6	23.1%
2012	3	11.5%
2014	3	11.5%
2015	3	11.5%
2007	2	7.8%
2010	2	7.8%
2013	2	7.8%
2002	1	3.8%
2004	1	3.8%
2006	1	3.8%
2008	1	3.8%
2009	1	3.8%
Total	**26**	**100.0%**
Language		
English	26	100%
Total	**26**	**100%**
Periodical		
Journal of AAPOS	3	11.5%
Brazilian Journal of Ophthalmology	2	7.8%
Introducion Journal of Ophthalmology	2	7.8%
Iran Journal Pediatrics	2	7.8%
The Journal of Maternal-fetal and Neonatal Medicine	1	3.8%
Journal of Perinatology	1	3.8%
Graefes Archives Clinical Exp Ophthalmology	1	3.8%
The Journal of Pediatrics	1	3.8%
Indian Journal Pediatrics	1	3.8%
China Medical Journal	1	3.8%
Journal of Pediatrics Ophthalmology and Strabismus	1	3.8%
Revista de Investigación Clínica	1	3.8%
Clinical Ophthalmology	1	3.8%
American Journal of Ophthalmology	1	3.8%
Early Human Development	1	3.8%
Ophthalmology	1	3.8%
São Paulo Journal of Medicine	1	3.8%
Pediatrics International	1	3.8%
Middle East African Journal of Ophthalmology	1	3.8%
Pediatrics and Neonatology	1	3.8%
World Journal of Pediatrics	1	3.8%
Total	**26**	**100.0%**

[continue...]

Table 1: Distribution of studies according to country, year, language, periodical, applied methodology, type of approach and level of significance. Natal, RN, Brazil, 2016. [continue]

Variables	Frequency	%
Applied methodology		
Cohort	20	76.9%
Case-control	4	15.3%
Cross-sectional	2	7.8%
Total	**26**	**100.0%**
Approach		
Quantitative	26	100%
Total	**26**	**100%**
Level of evidence		
III.2	23	88.4%
IV	2	7.8%
III.3	1	3.8%
Total	**26**	**100.0%**

Table 2. Categories of risk factors for retinopathy of prematurity in neonatal intensive care unit (n=26). Natal, RN, Brazil, 2016

Risk factors	N	%
Related to clinical therapeutic		
Oxygen therapy[14-17,18-22]	9	34.6%
Mechanical ventilation[16-17,19-21,23-25]	8	30.7%
Blood transfusion[15-16,19,21-22,24,26]	7	26.9%
High permanence in NICU[17,23]	2	7.6%
Related to use of medications		
Use of recombinant human erytropoietin[21,27]	2	7.6%
Use of steroids after birth[25]	1	3.8%
Inhalation of nitric oxide[23]	1	3.8%
Use of surfactant[19]	1	3.8%
Comorbidities related to ROP*		
Compromised pulmonary function[19,24,28-29]	4	15.3%
Intraventricular hemorrhage[24-25,30]	3	11.5%
Anemia[22,31]	2	7.6%
Candidemia[32]	1	3.8%
Neonatal characteristics		
LWB**[14-15,18-26,28-31,33-35]	17	65.3%
Low GA***[14-15,17-19,21-25,28,30,31,33-36]	17	65.3%
Sepsis[15,16,19,24-25]	5	19.2%
PDA****[19,24-25]	3	11.5%
Non-black race[37]	1	3.8%
Male sex[37]	1	3.8%
Clinical characteristics associated to ROP*		
Hyperglycemia[17,24,38-39]	4	15.3%
Hypotension[17,19,25]	3	11.5%
Apnea[17,19,31]	3	11.5%
Post-natal Hypoxia[22]	1	3.8%
Low Apgar score[25]	1	3.8%
Maternal factors		
Maternal pre-eclampsia[14,17,25]	3	11.5%
Placental abruption[31]	1	3.8%
Multiple pregnancies[17]	1	3.8%

Footnotes: * ROP (retinopatia da prematuridade); **LWB (low weight at birth); ***GA (gestational age); **** PDA (patent ductus arteriosus).

DISCUSSION

We observed most studies that approached risk factors for ROP in NICU were published in the past five years. It demonstrated the relevance of the debate nowadays. However, the level of evidence classification points the need to broaden and deepen studies in the field, to promote practice based in high-level evidence.

We highlight that all studies addressing risk factors for ROP in NICU included in our review grounded the thematic data synthesis. Thus, the discussion is based on established categories.

Related to clinical therapeutic

The category oxygen therapy was discussed in 34.6%[14-22] of studies. The oxygen effect in the premature newborn retina occur in two phases: vasoconstrictive and vaso-proliferative phases. In the first, the retinal hyperoxia triggers a suppression of the normal proliferation of vases and vasoconstriction. While in the vaso-proliferative phase, when the oxygen moves to the air, the levels of endothelial growth factors in the vessels increase and provoke an abnormal vaso-proliferation.[40] The number of oxygen therapy days was also significantly associated to the development of any ROP phase[41]. A retrospective study[42] conducted in England, that examined the incidence of the disease and the politics for oxygen supplementation in five NICUs showed that babies born before 28 weeks of pregnancy who used supplementary oxygen developed ROP.

Mechanical ventilation was present in 30.7% of selected studies[16-17,19-21,23-25]. Its association with the ROP development still is unclear and one study highlighted this lack of association could be due to the limited use of oxygen supplementation in premature babies during the study period[43]. It also highlights the intense exposure to oxygen levels under high pressure being the real mechanical ventilation issue for ROP development[43]. On the other hand, another study[15] did not find significant association between ROP occurrence and mechanical ventilation duration.

Most NICU neonates need some oxygen intervention due to pulmonary immaturity. Thus, it is indicated to investigate in more detail if the ROP risk factor is the oxygen or if it is the condition that leads to its use.

Blood transfusion, as a therapy-related factor, represented 26.9%[15-16,19,21-22,24,26] of articles from the sample. One study[44] revealed the volume of transfusions being an independent factor for the ROP incidence increase. Blood transfusion causes an increase of growth factor levels similarly to insulin; this factor ends up stimulating a retina neovascularization and ROP development. Besides, repetitive transfusions with adult hemoglobin can cause hyperoxia due to its low affinity with oxygen and cause oxidative loss in retinal vessels[44-46].

About the long permanence in the NICU[17,23], besides the lack of studies demonstrating the relationship of this factor with ROP, one of the selected studies[23] showed days in the NICU having a significant association with retinopathy occurrence, especially when the permanence was longer than 28 days[17].

Related to use of medications

We identified the use of recombinant human erythropoietin in 7.6% of the sample[21,27]. This medication is administered in premature with the objective of being a neuroprotector agent, targeting the neurological compromise of these newborns[47]. Few studies demonstrated that oxygen can induce the association between erythropoietin use and severe ROP[48-49]. In a model with transgenic mice, it was seen that erythropoietin promoted an intravitreal angiogenesis, which could lead to ROP development[50].

We found use of steroids after birth in 3.8% of the sample[25]. It is common in premature babies, as it helps to mature the lungs, but its use should be cautious[43]. The literature is scarce about mechanisms triggered by the use of steroids in ROP development, however, studies revealed that its use relates to the pathology[25,43].

A study[23] described inhalation of nitric oxide (iNO) as a new risk factor for ROP. The relationship between iNO and ROP is because nitric oxide increases the oxygen saturation and causes hyperoxia. It causes harms in the retinal vessels and leads to an incomplete vascularization in the premature retina[51]. Although it is considered a risk factor for ROP development, the treatment with iNO is a new choice for newborns with pulmonary hypertension who do not respond to mechanic ventilation, to reduce respiratory insufficiency, as it causes pulmonary vasodilation and as consequence, it improves oxygenation[41,52].

Surfactant use was in 3.8%[19] of studies composing the final sample. The exogenous surfactant is used in newborns with respiratory anguish, as it increases the levels of oxygen in the body and its relationship with ROP is given to that, as the oxygen relates to the ROP pathogenesis[52]. A retrospective study[41] revealed that the surfactant therapy in premature babies is associated with ROP.

The use of medications, as erythropoietin, steroids, nitric oxide and surfactant also relates to the nurse's assessment and conduct applied to its handling and rigorous administration control of these medications, considering the high prevalence of these procedures in neonates and for being directly proportional to the presence of retinopathy in prematurity.

Comorbidities related to ROP

The compromised pulmonary function was discussed in 15.3% of studies[19,24,28-29]. This category included the respiratory distress syndrome (RDS) and other chronic pulmonary diseases. Newborns with RDS presented variations in oxygen saturation and this instability can predispose to ROP[49].

Three studies presented intraventricular hemorrhage[24-25,30]. These revealed that ROP can happen in conjunct with this comorbidity. About anemia category, present in 7.6% of studies[22,31], one of them[31] conducted with 639 newborns showed that 10.8% developed ROP and anemia was significantly associated.

The candidemia category was addressed in 3.8% of the sample as a risk factor for ROP. One study[32] defined candidemia as the isolation of the *Cândida* species in at least one hemoculture. This finding corroborates with another study[53] that found an increasing relationship of the threshold ROP incidence in children with *Cândida*. The supposed connection between candidiasis and ROP presumes that the infection can stimulate the production of cytokines and angiogenic factors from the retina[32]. However, there are few actual studies about the theme describing the causal relationship between candidemia and ROP development.

The upbringing of comorbidities related to ROP shows the importance of complete prenatal assistance as an essential preventive component for the development of retinopathy of prematurity, besides highlighting the nursing role in the care for the pregnant woman, and consequently, the neonate.

Neonatal characteristics

Within neonate factors, we found LWB in 65.3% of studies[14-15,18-26,28-31,33-35], which related LWB being significantly associated with ROP development, within main disease risk factors. A study conducted in the Clinics

Hospital of the Uberlândia Federal University, in the southeast Brazilian region, concluded that the ROP development was inversely proportional to WB[54]. There are variations of the mean weight at birth to be considered as a risk factor among studies. A retrospective study conducted in Cuba found a higher frequency of individuals with ROP among those weighing between 1351 and 1700 grams at birth[43]. Nowadays, the low weight at birth in premature babies persisting for six weeks after delivery has been accepted as a risk factor for ROP development[40].

The low gestational age was the second most representative category within the studies[14-15,17-19,21-25,28,30-31,33-36]. From those, 65.3% demonstrated that GA lower than 30 weeks constitute a risk factor for ROP. The lower the gestational age, the higher is the retinal immaturity and the lower is the vascular development[55]. In consonance, another study reported that the GA < 28 weeks was associated with 100% of ROP cases in premature babies[54].

Still about these factors, sepsis was in 19.2% of selected studies[15-16,19,24-25]. The infection presence was associated to severe ROP, possibly due to systemic inflammation that acts in synergy with hyperoxia[56-58]. However, a retrospective study[30] that aimed to determine the incidence and risk factors for ROP did not identify the significant relationship between sepsis and the ROP occurrence.

Regarding the category patent ductus arteriosus (PDA), 11.5% of studies[19,24-25] approached this condition as a potential risk factor for the ROP occurrence. It is notable the few studies explaining the relationship between this factor and the retinopathy, but it is believed that this association is due to PDA clinical characteristics like: altered retinal perfusion and abnormalities in the blood flow to the retina[59].

Non-black race and male sex were variables discussed in 3.8% of studies[37]. This same study[37] found an increased ROP occurrence in individuals who were of another race that not black, but this was a moderate evidence, according to this type of study. The same study found that male newborns had a higher ROP incidence, however, its association with ROP was not clear and new studies should be conducted in this sense.

Clinical characteristics associated to ROP

The variable hyperglycemia was discussed in 15.3% of articles[17,24,38-39]. High blood glucose concentrations in newborns also increase the risk to develop ROP, mild to severe forms, because high levels of growth factor similarly to insulin type 1 (IGF-1) increase the levels of endothelial growth factor, which is the main determinant for ROP[41].

Neonatal hypotension[17,19,25] was described in 11.5% of the sample. It is believed that its association with ROP is due to the decrease in oxygen levels that affect the retinal vessels in premature babies[25].

Apnea was discussed in 11.5% of selected studies[17,19,31]. Despite other studies not treating this as a risk factor for ROP, it was seen in selected studies that apnea represents a significant risk factor for ROP development, especially when the respiration suspension becomes longer than 20 seconds[19,31]. Post-natal hypoxia was present in only 3.8% of the sample[22]. Its discussion in the literature still is scarce.

Apgar index is used during postpartum to assess the newborn's adaptation to the extrauterine life. Besides, it is essential to evaluate physiological conditions and to identify the need for reanimation or another special care[60]. Based on this, 3.8% of selected studies[25] referred low Apgar Index as a risk factor associated to ROP.

Other studies[41,61] identified that low Apgar scores between the first and fifth minutes of life being significantly associated with ROP, considering that premature babies tend to present low Apgar scores.

Besides, there is a score that assess the newborn's clinical risk, the Index of Clinical Risk for Babies, calculating from six variables measured during the first 12 hours after birth: weight at birth, gestational age, congenital malformation, excess of basis and adequate fraction of inspired oxygen. The higher this index, the higher the risk of ROP development[32].

Maternal factors

These factors are still little discussed in the literature and their association with ROP still is not very clear, it would be important for new studies to be proposed in this sense. Maternal pre-eclampsia was addressed by 11.5% of the sample[14,17,25]. In the vascular level, pre-eclampsia is characterized by a conjunct of changes in the maternal-fetal vascularization, with ischemic changes, infarcts and even the placental abruption[62]. Such conditions can lead to inadequate oxygen supply to the fetus and to cause vascular harms in the retina[14]. One of the studies reported maternal pre-eclampsia as a significant protective factor for ROP[30].

The category placenta abruption was present in one study[31], which reinforces the need of new studies in this field to better explain the role and relationship of this condition with ROP. A study[31] assessed maternal and neonatal risk factors for ROP and found the placental abruption as a maternal factor with independent influence for ROP occurrence.

Regarding the category multiple pregnancies, only 3.8% of studies[17] approached this variable as a risk factor for ROP occurrence. Its association with ROP is not clear.

CONCLUSION

This review contributed with the knowledge about main risk factors for ROP development in neonatal intensive care units. Through this study, we verified two risk factor categories subjacent to all other presented ones: risk factors related to clinical therapeutic and neonatal characteristics. Such fundament questions oxygen therapy monitoring, use of mechanical ventilation and blood transfusions as preventive measures directly conducted by nursing.

In addition, when identifying non-modifiable risk factors especially related to low weight at birth and low gestational age, nursing can significantly contribute to guarantee the reduction of other risk factors associated to health assistance, and to allow ophthalmologic triage to impede disease development, its sequelae and/or to enable treatment in the initial phase of disease.

Therefore, the survey of comorbidities and neonatal characteristics show the importance of complete pre-natal assistance as crucial preventive component for the development of retinopathy of prematurity, besides highlighting the nursing role in the newborn healthcare.

Still, the use of medications, as erythropoietin, steroids, nitric oxide and surfactant are related to the nursing assessment and conduct applied to the handling and rigorous administration control of these medications, considering that the high frequency of these procedures in neonates can be directly proportional to the presence of retinopathy during prematurity.

Besides, equally pertinent, we verified the need to broaden the number of studies related to maternal factors, which results showed gaps in knowledge production related to health attention of pregnant woman focused in preventive and diagnostic measures for retinopathy of prematurity. Thus, we believe that through evidence-based practice, such measures can be applied in the future and contribute in reducing this disease.

Additionally, most studies included in our review correspond to articles published in the last six years, which shows the theme being actual. However, we highlight the importance to conduct other studies with other designs representing higher levels of evidence, to confirm the importance to know and act about ROP risk factors for disease prevention.

The knowledge about risk factors is important to adhere preventive measures, impeding the ROP development and its possible sequelae, as well as, to qualify neonatal health care and an assistance free of health risks. This knowledge contributes for the early retinopathy detection, as well as, its treatment in initial disease phase. Therefore, this study becomes pertinent for summarizing these information and present as categories, identifiable, foreseen and controlled risk factors. Once armed with this information, health professionals will be able to act avoiding and minimizing the occurrence of this phenomenon.

Therefore, we reached the study objective as it was a broad pertinent literature search and selection, which allowed the gathering of risk factors available in the literature.

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