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ORIGINAL ARTICLE

Epidemiological profile of newborns with retinopathy of prematurity at the university hospital of the federal university of maranhão

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Abstract

Objective: To describe the profile of premature newborns and exploratory analysis of factors associated with the development of retinopathy of prematurity (ROP) at the University Hospital of the Federal University of Maranhão (HU-UFMA). Methods: This is a cross-sectional study based on data from the medical records of premature newborns treated at the University Hospital of the Federal University of Maranhão (HU-UFMA), from 2015 to 2020. Possible statically significant associations for the development of ROP were evaluated: sex, gestational age, birth weight, length, head circumference, length of hospital stay, APGAR and others. The significance level adopted was 5% ($p<0.05$). Results: It was found that, in children with a confirmed diagnosis of ROP, the most prevalent sex was female (50.95%), the mean gestational age was 29.08 weeks, the most frequent outcome was hospital discharge (70, 71%), mean birth weight was 1,089 grams, mean hospital stay was 45.44 days, mean length was 35.73 cm, mean head circumference was 26.06, Apgar most prevalent in the first minute was in the range from 4 to 7 (43.32%) and in the fifth minute from 8 to 10 (56.40%). Conclusions: The prevalence of ROP cases was 61.40% among newborns followed up at a reference service in the state of Maranhão. It was observed that the lower the gestational age and birth weight, the greater the risk of developing ROP.

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INTRODUCTION

Retinopathy of prematurity (ROP) is a potentially serious disease that occurs in premature babies, which affects the blood vessels of the developing retina. ROP occurs as a result of the appearance of vascular shunts and neovascularization. In its most severe cases, there may be retinal traction and detachment[1]. This condition only affects premature babies with an immature retina and incomplete vascularization[2]. The main cause associated with ROP is inadequate administration of oxygen in delivery rooms or intensive care units (NICU) for premature newborns[3].

The main risk factors for the development of this retinopathy are low birth weight and prematurity. And there are other risk factors such as an Apgar score lower than 7, fluctuation in oxygen levels in the first weeks of life[4], the use of oxygen therapy, blood transfusion, the need for mechanical ventilation, patent ductus arteriosus[5], respiratory distress syndrome, low child weight for gestational age (SGA), perinatal asphyxia, intraventricular hemorrhage, multiple gestation, meningitis and sepsis[6,7].

ROP is one of the main pathologies that cause preventable blindness in children[8]. It can affect up to 34% of premature babies weighing less than 1,500 grams at birth, of which 6 to 27% will require treatment[9]. A systematic review identified the population prevalence of ROP in Latin America: Argentina (2010): 26.2% of all premature children; Bolivia (2002): 14.3%; Brazil (2010): 9.3%; Chile (2004): 12.3; Cuba (2010): 5.1%; Guatemala (2010): 13%, Nicaragua (2004): 23.8%; Peru (2007): 19.1%[10], reporting a prevalence of 9.4%[11]; Colombia (2016): reports a prevalence of 3.19% for every 10,000 live births[12].

Taking these factors into account, the World Health Organization (WHO), through its Vision 2020 program, includes the management of this entity within its priority policies to improve eye health and reduce the prevalence of avoidable blindness[13]. According to the current guidelines for carrying out the exam, the following are eligible: BW ≤1,500 grams and/or GA ≤32 weeks or newborns with the presence of one of these 5 risk factors: Respiratory distress syndrome; Sepsis; Blood transfusions; Multiple pregnancy or intraventricular hemorrhage. Remembering that the first exam must be carried out between the 4th and 6th week of life.

Low gestational age, low birth weight and quality of postnatal growth have more recently been identified as risk factors for ROP, revealing the important role of placental growth factors such as IGF-1 (insulin-like growth factor-1). and one of its transport proteins, IGFBP-3 (IGF-3 binding protein), in retinal vascular development[14].

The severity of ROP is classified into five stages: ROP 1 – identification of a white, flat line that separates the vascular retina from the avascular retina; ROP 2 – widening of the demarcation line and presence of a high crest; ROP 3 – having fibrovascular proliferation, starting from the crest, leaving the plane of the retina; ROP 4 – having subtotal retinal detachment; and ROP 5 – total retinal detachment (open or closed funnel)[13].

The objective of this study was to describe the profile of premature newborns and analyze, on an exploratory basis, factors associated with the development of ROP in a University Hospital.

METHOD

This is a cross-sectional study carried out using data from medical records of patients treated at a University Hospital, which exclusively serves the Brazilian Public Healthcare System - SUS, a member of the Brazilian Neonatal Research Network (RBPN). RBPN is a voluntary, non-profit collaboration of neonatologists from Brazilian universities who, in an integrated and coordinated way, study and research the morbidity and mortality of newborns, together with the clinical practices applied in their care. Maternal and delivery data were collected by pediatricians and neonatologists working in the delivery room and in the NICU of the University Hospital.

Patient data were evaluated from 2015 to 2020. The study population was made up of newborns with birthweights less than or equal to 1,500 grams or with a gestational age of 22 to 37 weeks, who were admitted or died at the Hospital University, up to 28 days after birth and who underwent an eye fundus examination. The non-inclusion criteria were live births < 20 weeks and 0 days; weight greater than 1500 grams or unknown weight and GA >38 weeks, who did not undergo a fundus examination because they were discharged with less than 30 days to live or died, as well as those who did not have all the complete data in their medical records evaluated. Possible statically significant associations for the development of ROP were evaluated: sex, gestational age, birth weight, length, head circumference, length of hospital stay, APGAR and others.

The collected data were stored and analyzed in the SPSS, version 23 software. The significance level adopted was 5% ($p<0.05$), with a confidence interval (CI) of 95%. Continuous variables that presented normal distribution were described using mean ± standard deviation and categorical variables were described using frequency and percentage. Initially, the Kolmogorov-Smirnov test was applied to test the hypothesis that the data followed a normal distribution or not and assist in choosing between parametric and non-parametric tests. After checking the data normality, the parametric T-student test (for paired samples) and the non-parametric Mann-Whitney test were used for numerical variables, as well as the Fisher's exact test for categorical variables.

This study was approved by the Research Ethics Committee of the University Hospital, under protocol number 5,188,600, dated December 28, 2021.

RESULTS

We found 760 newborns in the University Hospital database, from 2015 to 2020. However, 26 medical records were excluded because they had incomplete information, totaling a final sample of 734 newborns.

Table 1 shows the clinical-epidemiological characterization of premature newborns admitted to the University Hospital. We found that the most prevalent sex was female (50.95%), the average gestational age was 29.08 weeks, the most common outcome was hospital discharge (70.71%), the average birth weight was 1,089 grams, the average length of hospital stay was 45.44 days, the average length was 35.73 cm, the average head circumference was 26.06, the most prevalent Apgar in the first minute was in the range from 4 to 7 (43.32%), and in the fifth minute from 8 to 10 (56.40%).

Table 02 describes the maternal and childbirth data of the sample analyzed in the study, in which it is observed that the maternal age group between 21 and 30 years was the most prevalent (45.05%), the predominant race was brown (78 .51%), 8 to 11 years of schooling was the most common (51%), 90.08% of pregnant women underwent prenatal care, only 36.11% were hypertensive and 4.23% diabetic, 89 .14% did not use drugs, only 1.35% had HIV, 16.87% had chorioamnionitis, 65.91% took antenatal steroids, 10.95% had hemorrhage and cesarean section was the most common (55, 28%).

When analyzing the prevalence of ROP among premature newborns evaluated between 2015 and 2020 at the University Hospital, through confirmation of the eye fundus examination, a positive result was obtained in 76 patients, which is equivalent to a prevalence 10% of the total number of patients initially identified. Of these, 66 (86.8%) patients were in stage 1; 5 (6.6%) in stage 2 and 5 (6.6%) in stage 3. No patients were diagnosed in stages 4 and 5. Graph 01 describes the number of confirmed cases in each year of the series analyzed.

Regarding the major risk factors analyzed, of the 76 patients with a confirmed diagnosis of ROP, all had complete data in their medical records; And, of the 734 patients who were part of the study sample, 658 were not diagnosed with ROP. Among patients with a positive diagnosis, 57.89% were females, the most prevalent gestational age was 24 to 29 weeks (63.15%), the most common outcome was hospital discharge (93.42%), weight average at birth was 1,023 grams, length of hospital stay of 85.31 days, average height of 34.7 cm, average head circumference of 25.3 cm, Apgar in the first minute predominated in the range of 4 to 7 (50%), Apgar in the fifth minute prevailed in the range of 8 to 10 (51.31%). There was a statistically significant difference ($p<0.05$) between patients with a confirmed diagnosis of ROP and those not confirmed in the following variables: gestational age, outcome, length of hospital stay, head circumference and Apgar in the first and fifth minutes.

DISCUSSION

With the improvement of human resources in the neonatal area, associated with technological advances and the increase in public policies aimed at the neonatal period, there has been an increase in the survival rate of newborns with increasingly lower birth weight and lower gestational age. Children are more vulnerable to suffer late repercussions from prematurity and intrauterine restriction.[15] Among these repercussions, ROP stands out[16], the focus of this study.

ROP represents one of the main causes of preventable blindness in children. Its increase is related to an increase in the survival rates of many premature babies monitored in neonatal intensive care units. In this study, the prevalence of ROP was observed in 10% of the newborns evaluated (Graph 01). It is important to highlight that the prevalence found was lower than that reported in the literature (between 20 and 27.73%)[17-19]. A possible explanation for this low prevalence is that at the University Hospital not all premature infants underwent a fundus examination because they were discharged with less than 30 days of life or died.

The female sex was prevalent among the newborns analyzed (50.95%) (Table 01). However, this variable did not demonstrate a significant relationship with the development of ROP, although some studies reported a tendency for females, as well as in the present study (57.89%) (Table 03). Shim et al. (2017)[20] showed in their study that men had a lower incidence of ROP with a P = 0.022 in contrast to a P = 0.026 for women; Schumann et al. (2010)[21] analyzed 73 premature newborns, of which 40 (54.8%) were females and 33 (45.2%) were males.

In this study, after analyzing the clinical profile of the newborns under investigation, they were premature, with an average of 29.08 weeks of gestational age and had low weight (average of 1,089 grams) (table 01). The variable related to gestational age proved to be relevant ($p<0.05$) when related to risk factors for ROP, since 100% of the records collected were from premature babies (Table 03).

After Theiss et al., (2016)[22] reported that 83.33 (n=45) and 79.4% (n=96) of the newborns who developed retinopathy, weighed less than 1,500 grams and had a gestational age of less than 32 weeks; respectively, stated that the lower the weight and gestational age, the greater the risk of developing the disease. Data also found in the

Table 01: Characteristics of premature newborns evaluated, 2015-2020.

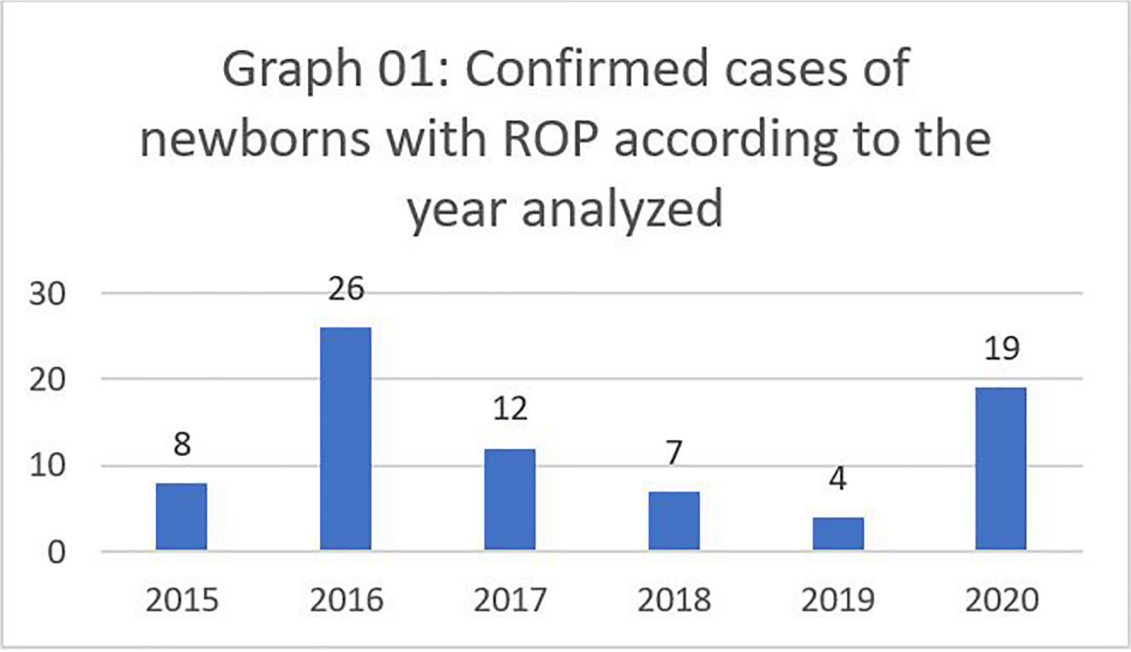
Variables	n(%)
Sex (n=734)	
Females	374 (50.95%)
Males	360 (49.05%)
Gestational age (weeks) (n=734)	29.08 ± 3.29
<24	40 (5.45%)
24 to 26	119 (16.21%)
27 to 29	229 (31.20%)
30 to 32	254 (34.60%)
33 to 35	82 (11.18%)
≥36	10 (1.36%)
Outcome (n=734)	
Discharge	519 (70.71%)
Transfer	5 (0.68%)
Death	209 (28.47%)
Remains hospitalized for up to 01 year	1 (0.14%)
Birth weight (grams) (n=734)	1089.27 ± 240.49
< 500	6 (0.82%)
500 to 749	107 (14.58%)
750 to 999	138 (18.81%)
1000 to 1249	195 (26.57%)
1250 to 1499	288 (39.22%)
Hospitalization duration (days) (n=734)	45.44 ± 35.96
<10	145 (19.75%)
10 to 49	314 (42.78%)
50 to 99	233 (31.74%)
100 to 149	34 (4.63%)
150 to 199	6 (0.82%)
200 to 249	1 (0.14%)
≥250	1 (0.14%)
Length (cm) (n=734)	35.73 ±3.47
<26	1 (0.14%)
26 to 30	65 (8.86%)
31 to 35	239 (32.56%)
36 to 40	391 (53.27%)
41 to 45	36 (4.90%)
≥46	2 (0.27%)
Head Circumference (cm) (n=734)	26.02 ± 2.77
<17	1 (0.14%)
17 to 20	24 (3.27%)
21 to 24	168 (22.88%)
25 to 28	417 (56.81%)
29 to 32	121 (16.49%)
≥33	3 (0.41%)
Apgar 1º min (n=734)	
0 to 3	218 (29.70%)
4 to 7	318 (43.32%)
8 to 10	198 (26.98%)
Apgar 5th min (n=734)	
0 to 3	74 (10.09%)
4 to 7	246 (33.51%)
8 to 10	414 (56.40%)

Source: Database of the Brazilian Neonatal Research Network – RBPN14

Table 02: Maternal and birth data from the analyzed sample, 2015-2020.

Variable	Value (n=734)
Age (years) (n=734)	27.71 ± 2.12
>15	33 (4.36%)
15 to 20	131 (17.31%)
21 to 30	341 (45.05%)
31 to 40	236 (31.18%)
≥41	16 (2.11%)
Race (n=734)	
White	98 (13%)
Black	61 (8.09%)
Yellow	1 (0.13%)
Brown	592 (78.51%)
Indian	2 (0.27%)
Schooling (n=734)	
None	9 (1.2%)
From 1 to 3 years	3 (0.4%)
From 4 to 7 years	163 (21.65%)
From 8 to 11 years	384 (51%)
From 12 years of age or more	194 (25.76%)
Pre-natal (n=734)	
No	75 (9.92%)
Yes	681 (90.08%)
Hypertension (n=734)	
No	483 (63.89%)
Yes	273 (36.11%)
Diabetes (n=734)	
No	724 (95.77%)
Yes	32 (4.23%)
Use of Drugs (n=734)	
No	681 (89.14%)
Tobacco	25 (3.27%)
Alcohol	39 (5.1%)
Cocaine	1 (0.13%)
Crack	9 (1.18%)
Marihuana	8 (1.05%)
Other	1 (0.13%)
HIV (n=734)	
No	362 (98.64%)
Yes	5 (1.36%)
Chorioamnionitis (n=734)	
No	626 (83.13%)
Yes	127 (16.87%)
Prenatal steroid (n=734)	
No	256 (34.09%)
Yes	495 (65.91%)
Hemorrhage (n=734)	
No	667 (89.05%)
Yes	82 (10.95%)
Type of delivery (n=734)	
Vaginal	339 (44.72%)
C-section	419 (55.28%)

Source: Database from the Brazilian Neonatal Research Network - RBPN14



Source: Database of the Brazilian Neonatal Research Network - RBPN14

study by Silva et al., (2016)[23], in which the average weight was less than 1,500g and gestational age of 29.4 weeks.

Low birth weight and prematurity are the most important risk factors for infant mortality. On the other hand, technological advances have provided new care practices that favor an increase in the survival rate of premature and low birth weight newborns who require advanced neonatal care.[24]

The data found also revealed that the average age among mothers was 27.71 years; the predominant race was mixed race (78.51%); education of 8 to 11 years of study was the most common (51%); 90.08% of pregnant women underwent prenatal care (Table 02). This is relevant data, as it reflects that adherence to care during childbirth is increasing and that more women are having access to assistance. The study also demonstrated a high number of cesarean deliveries (52.28%) (Table 01).

Similar results were found in a study that aimed to investigate whether restricting the ROP criteria to <31 weeks and < 1,300g would be adequate to identify cases of more severe ROP effectively and safely with therapeutic indication, where of the 91 newly premature births analyzed, 76.9% were born by cesarean section[25]. A cesarean section is a surgical procedure with the aim of removing the fetus via a high route, through an incision in the uterine and abdominal walls; and its indication is intended to prevent or treat maternal and/or perinatal complications.[26]

In the present study, there was a prolonged hospital stay of 85.31 days in the group of patients with ROP (Table 03). Although it is fundamental and extremely important, advances in neonatology, although it has enabled a reduction in neonatal mortality, it has also brought an increase in complications in newborns, related to prematurity itself, considering the prolonged length of hospital stay, risking infections and exposure to invasive, painful procedures and increased stress levels in newborns[27]. The majority of patients in our study (65.91%) used antenatal steroids. In the study by Nunes and Colvero[28], only 47.3% of the patients used antenatal steroids. Failure to use antenatal steroids is considered a minor risk factor for ROP.

The low growth and head circumference observed (table 03) suggest that factors involved in the growth and development of the newborn are implicated in the etiology of this pathology. Studies carried out in animals, based on clinical findings, points to insulin-like growth factor-1 (IGF-1), which is already known to be important in fetal growth and development, as a fundamental participant in retinal vascular formation. Serum IGF-1 level correlates with fetal growth. Therefore, a lower expression of this factor would contribute to a fetus with reduced weight and, therefore, a greater risk for ROP.[29]

It is important to highlight that the risk factors were corroborated between univariate and multivariate analysis in some studies. In the study by Silva et al.,[23] different from gestational age, birth weight, Apgar score in the 1st and 5th minutes were not independent risk factors for the development of ROP in multivariate logistic regression analyses. The findings of this study and existing incidence data suggest that despite the preventable and reversible nature of ROP, the risk factors for this condition deserve further investigation in order to mitigate long-term consequences.

Table 03 Major risk factors associated with the diagnosis of ROP, 2015-2020.

Variables	ROP	p-value	
	Yes (n=76)	No (n=658)	
Sex (n=734)			
Females	44 (57.89%)	331 (47.26%)	<0.22F
Males	32 (42.11%)	327 (52.74%)	
Gestational age (weeks) (n=734)			
<24	2 (2.63%)	33 (5.02%)	
24 to 26	24 (31.58%)	96 (14.59%)	
27 to 29	24 (31.58%)	205 (31.16%)	<0.001M
30 to 32	23 (30.26%)	232 (35.25%)	
33 to 35	2 (2.63%)	87 (13.22%)	
≥36	1 (1.32%)	5 (0.76%)	
Outcome (n=734)			
Discharge	71 (93.42%)	448 (68.09%)	
Transfer	2 (2.63%)	3 (0.46%)	<0.0001F
Death	2 (2.63%)	207 (31.45%)	
Remains hospitalized up to 01 year	1 (1.32%)	0 (0%)	
Birth weight (grams) (n=734)			
< 500	0 (0%)	17 (2.58%)	
500 to 749	15 (19.74%)	87 (13.22%)	
750 to 999	23 (30.26%)	210 (31.91%)	0.46M
1000 to 1249	17 (22.37%)	176 (26.75%)	
1250 to 1499	21 (27.63%)	168 (25.54%)	
Hospital stay length (days) (n=734)			
<10	0 (0%)	144 (21.88%)	
10 to 49	16 (21.05%)	291 (44.23%)	
50 to 99	37 (48.68%)	199 (30.24%)	
100 to 149	17 (22.37%)	21 (3.2%)	<0.008M
150 to 199	6 (7.9%)	0 (0%)	
200 to 249	0 (0%)	2 (0.3%)	
≥250	0 (0%)	1 (0.15%)	
Height (cm) (n=734)			
<26	0 (0%)	1 (0.15%)	
26 to 30	6 (7.9%)	58 (8.81%)	
31 to 35	37 (48.68%)	203 (30.86%)	0.06M
36 to 40	30 (39.47%)	360 (54.71%)	
41 to 45	3 (3.95%)	34 (5.17%)	
≥46	0 (0%)	2 (0.3%)	
Head circumference (cm) (n=734)			
<17	0 (0%)	1 (0.15%)	
17 to 20	0 (0%)	24 (3.65%)	
21 to 24	25 (32.89%)	143 (21.73%)	0.02M
25 to 28	45 (59.21%)	372 (56.54%)	
29 to 32	5 (6.58%)	116 (17.63%)	
≥33	1 (1.32%)	2 (0.3%)	
Apgar 1st min (n=734)			
0 to 3	25 (32.89%)	193 (29.33%)	
4 to 7	38 (50%)	280 (42.55%)	0.008T
8 to 10	13 (17.11%)	185 (28.12%)	
Apgar 5th min (n=734)			
0 to 3	6 (7.9%)	67 (10.18%)	
4 to 7	31 (40.79%)	215 (32.68%)	0.003T
8 to 10	39 (51.31%)	376 (57.14%)	

Caption: Student's t-test; Mann-Whitney test; Fisher's Exact Test
Source: Database of the Brazilian Neonatal Research Network – RBPN14

CONCLUSIONS

The prevalence of ROP cases in the time frame from 2015 to 2020 was 10% among newborns monitored at a reference clinic in the state. The lower the gestational age and birth weight, the greater the risk of developing ROP. These findings indicate the need for teams working in neonatal intensive care units to adopt protocols for diagnosing and preventing ROP early, in order to avoid its progression and the visual sequelae resulting from its onset.

The cross-sectional design can be considered a limitation, as it presents a time frame in which the analysis of a period of occurrences was demonstrated, as well as the profile of a specific region. However, this type of study is necessary to understand the reality of the clinics and to provide support for planning and improving the quality of care in these locations, with the aim of preventing an increase in ROP occurrences.

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