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Study on the Prevalence Risk factors and Outcome of Retinopathy of Prematurity

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Abstract

Retinopathy of prematurity (ROP) is an illness that affects the eyes of preterm newborns and can end in blindness if it is not detected and treated in a timely manner. However, due to improvements in neonatal care, the incidence of ROP has been on the rise. To estimate the prevalence of Retinopathy of prematurity (ROP), as well as its prognosis and the connection between premature birth and risk factors. This was a retrospective cohort study looked back at data collected from January 2016 through December 2019 at the NICU of the Shareyah Society in ltay El-Baroud, Al Beheira. We analyzed data from 312 preterm that were either born prematurely (GA ≤34 weeks) or had low birth weight (less than 2000 grams) Indirect ophthalmoscopy with a 28 D or 20D lens was utilized to examine the fundus. The overall prevalence of ROP was 40.7%. Out of the 312 screened preterm babies, 127(40.7%) cases had ROP, among whom 84 (66.2%) need injection, 64(50.4%) of them had type 1 ROP, 20 (15.7%) had aggressive posterior retinopathy. The Follow up examination was done through one month after the operation showed progression in 97.6% of examined cases. ROP was significantly associated with GA, BW, oxygen therapy, and sepsis, Length of hospital stay, thrombocytopenia and frequency of blood transfusions. There is a significant prevalence of ROP. There are a number of factors that have a significant role in the development of ROP, including low birth weight, short gestational age, oxygen administration, thrombocytopenia, blood transfusions, and length of hospital stay.

Keywords: Low birth weight, Low gestational age, Prevalence, Oxygen therapy, Retinopathy of prematurity.

1. Introduction

About a million infants every year lose their lives because of issues related to being born prematurely. Lifelong difficulties such as learning disabilities, vision loss, and hearing loss plague many survivors [1]. Premature newborns are more likely to

suffer from proliferative vitreoretinopathy known as (ROP) [2]. As a result of their immature lungs and respiratory distress syndrome (RDS), premature neonates tend to have abnormalities in the formation of the blood vessels in their retinas [3]. The administration of oxygen to premature infant's results in hyperoxia, which, in turn, leads to vasoconstriction, vascular obliteration, peripheral ischemia, and the irreversible termination of retinal vascular development. In many parts of the world, premature delivery is one of the main causes of death among infants. It also has the potential to induce an excess production of vascular endothelial growth factor (VEGF), which can lead to the development of various ROP problems and unwanted retinal neovascularization. This helps to justify the prevalence of ROP in preterm newborns (PTNB) who are exposed to higher concentrations of oxygen for an extended period of time [4]. Exposure to relative hyperoxia followed by hypoxia causes the release of (VEGF), which in turn causes aberrant blood vessel growth in the retina, which ultimately results in retinal detachment and significant visual impairments [5].

2. Patients and Methods

This was a retrospective cohort study From January 2016 to December 2019, researchers from the Shareyah Society's NICU in ltay El-Baroud, Al Beheira conducted a retrospective cohort analysis of preterm newborns admitted to the facility.

2.1 Inclusion criteria:

Screening for ROP should be performed on all preterm (newborns and L&W) born weighing less than 2000 grams or at a gestational age of ≤ 34 weeks. It should also be performed on a subgroup of infants born weighing between 1500 and 2000 grams or at a gestational age of ≤ 34 weeks who are believed to be at risk for ROP as a result of variables such as: newborns who were given oxygen supplementation for more than a few days (cut of point), infants who were given oxygen supplementation without saturation monitoring, and infants who suffered from hypotension severe enough to require inotropic support. [6]

2.2 Exclusion criteria

Full-term babies, infants with obvious congenital anomalies and patients who died before complete resolution of ROP or did not attend the outpatient clinic for follow-up examination

2.3 Medical records of preterm infant reviewed for the following

2.3.1 Physical Examination of the Newborn

Length (taken from the top of the head to the bottom of the heel) and weight (measured using a standard scale) are the most fundamental metrics. The new Ballard score uses physical and neuromuscular characteristics to pinpoint the gestational age.

2.3.2 All preterm baby systems examined included

2.3.2.1 Cardiorespiratory system

An infant's heart and lungs are checked at a period of relative calm. Rhythmic and without a murmur heartbeat (typical range, 100-160 bpm).

2.3.2. 2 The respiratory system

Breathing at a rate of 40–60 breaths per minute is considered normal.

2.3.2.3 Head and neck

Normal Head size and shape closed posterior fontanelle, anterior fontanelle opened and at the level. Eyes examined for the red reflex to exclude glaucoma, cataracts, or retinoblastoma. Normal neck with no abnormalities such as cystic hygromas, goiters, and branchial arch remnants.

2.3.2.4 Abdomen and pelvis

The abdomen is loose, symmetrical, and spherical without evidence of organomegaly.

2.3.2.5 Musculoskeletal system

There are no limb abnormalities such as malformations, amputations, contractures, or maldevelopment.

2.3.2.6 The Nervous system

Tone, attentiveness, limb movement, and reflexes are assessed in an infant. The Moro, sucking, and rooting responses are all typical in newborns. Skin Visible veins under the skin, lanugo (baby hair), an enlarged clitoris (in female infants), reduced body fat, a small, smooth scrotum devoid of ridges and undescended testicles at 28 gestational age (in male infants), and soft, pliable ear cartilage are all characteristics of infants' skin.

2.3.3 Laboratory Investigations

CBC, CRP and blood culture and sensitivity

2.3.4 Retinal examination

Using a binocular indirect ophthalmoscope with 20 or 28 diopter lenses, an ophthalmologist experienced in the examination of preterm newborns for ROP will examine the retinas of the infants.28D Look at the retina and its borders at less than 20D magnification. Each newborn was examined using a BIO and 20D lens in addition to a sterile lid speculum and scleral depress. Using a 20D lens and a careful examination of the eye, we started with the anterior portion. The peripheral retina with scleral depression was then checked, and finally the posterior pole. The follow-up was done one month after the operation.

2.4 Statistical analysis

SPSS 20.0, a statistical tool developed by IBM, was utilized in both the processing and analysis of the data. Armonk, New York location of IBM Corporation. There was no distinction made between the presentation of quantitative and qualitative data. The Kolmogorov-Smirnov test was utilized so that we could be certain that our sample was normally distributed. The quantitative data were characterized based on their minimum and maximum values, as well as their mean, standard deviation, median, and interquartile range (IQR). At the 5% significant relation level, the acquired results were declared to be significant.

3. Results

As shown in Table .1. the prevalence of ROP was high (40.7%). There was a highly significant relation between Length of hospital stay *&* ROP. As shown in Table .2. ROP was strongly linked with low birth weight & preterm birth. There is no correlation between delivery method, gender, or ROP. As shown in Table .3. There was a highly significant relation between sepsis, Thrombocytopenia, Blood transfusion, mechanical ventilation, duration of MV, CPAP, duration of CPAP and ROP. No significant relation between Respiratory distress, Apnea, Pneumothorax, Exchange transfusion, nasal cannula, duration of nasal cannula and ROP. As shown in Table .4. 299 of all cases came for follow-up with a percentage of 95.8% and progress while 13 cases did not come for follow-up and the outcome was missed.

Table (1): Relation between ROP and length of hospital stay (n = 312).

Length of hospital stay	Total (n = 312)	ROP		p
		Yes (n = 127)	No (n = 185)	
Min. – Max.	3.0 – 35.0	5.0 – 35.0	3.0 – 24.0	<0.001*
Mean ± SD.	12.96 ± 6.16	17.70 ± 5.85	9.71 ± 3.81	
Median (IQR)	12.0 (9.0 – 17.0)	17.0 (13.0 – 21.50)	9.0 (7.0 – 12.0)	

IQR: Inter quartile range, SD: Standard deviation, U: Mann Whitney test, P: P-value for comparing between, ROP and length of hospital stay, *: Statistically significant at $P \leq 0.05$.

Table (2): Relation between ROP and demographic data (n = 312).

	Total (n = 312)	ROP		p
		Yes (n = 127)	No (n = 185)	
Gestational age (weeks)				
Min. – Max.	26.0 – 36.0	26.0 – 36.0	28.0 – 36.0	<0.001*
Mean ± SD.	32.48 ± 2.09	31.60 ± 2.12	33.09 ± 1.84	
Median (IQR)	33.0 (31.0 – 34.0)	32.0 (30.0 – 33.0)	33.0 (32.0 – 34.0)	
Birth weight (grams)				
Normal	2 (0.6%)	0 (0.0%)	2 (1.1%)	MCp= 0.004*
LBW	166 (53.2%)	57 (44.9%)	109 (58.9%)	
VLBW	141 (45.2%)	67 (52.8%)	74 (40.0%)	
ELBW	3 (1.0%)	3 (2.4%)	0 (0.0%)	
Min. – Max.	820.0 – 2600.0	820.0 – 2400.0	1100.0 – 2600.0	<0.001*
Mean ± SD.	1652.0 ± 389.8	1542.6 ± 366.7	1727.1 ± 388.3	
Median (IQR)	1595.0 (1335.0 – 1930.0)	1460.0 (1275.0 – 1770.0)	1700.0 (1400.0 – 2000.0)	
Mode of birth				
CS	264 (84.6%)	108 (85.0%)	156 (84.3%)	0.863
NVD	48 (15.4%)	19 (15.0%)	29 (15.7%)	
Time of exam (weeks)				
Min. – Max.	4.0 – 23.57	4.0 – 21.43	4.0 – 23.57	0.601
Mean ± SD.	4.79 ± 1.99	4.85 ± 2.02	4.76 ± 1.97	
Median (IQR)	4.29 (4.14 – 4.71)	4.29(4.29 – 4.79)	4.29(4.14 – 4.57)	
Gender				
Male	188 (60.3%)	82 (64.6%)	106 (57.3%)	0.197
Female	124 (39.7%)	45 (35.4%)	79 (42.7%)	

IQR: Inter quartile range, SD: Standard deviation, t: Student t-test, χ^2: Chi-square test, MC: Monte Carlo, U: Mann Whitney test, P: P-value for comparing between ROP and demographic data, *: Statistically significant at $P \leq 0.05$.

Table (3): The target SaO_2 and PaO_2 based on the infant's gestational age.

Infants	PaO_2	FiO_2	Saturation Range
Preterm Infants <32 weeks gestational	50 – 70 mmHg	25 – 80	87 – 92%
Preterm Infants ≥32 weeks gestational	60 – 75 mmHg	25 – 80	90 – 93%

Table (4): V- Table (4): Relation between ROP and different parameters (n = 312).

	Total (n = 312)		ROP				p
			Yes (n = 127)		No (n = 185)		
	No.	%	No.	%	No.	%	
Respiratory distress	311	99.7	127	100.0	184	99.5	$^{FE}p=1.000$
Apnea	19	6.1	8	6.3	11	5.9	0.898
Sepsis	150	48.1	75	59.1	75	40.5	0.001*
Pneumothorax	1	0.3	0	0.0	1	0.5	$^{FE}p=1.000$
Thrombocytopenia	50	16.0	30	23.6	20	10.8	0.002*
Blood transfusion	75	24.0	41	32.3	34	18.4	0.005*
Exchange transfusion	3	1.0	1	0.8	2	1.1	$^{FE}p=1.000$
Phototherapy	165	52.9	74	58.3	91	49.2	0.115
MV	162	51.9	87	68.5	75	40.5	<0.001*
Duration of MV (days)	(n = 162)		(n = 87)		(n = 75)		
Min. – Max.	3.0 – 17.0		4.0 – 17.0		3.0 – 12.0		<0.001*
Mean ± SD.	8.16 ± 3.98		10.41 ± 3.79		5.55 ± 2.21		
Median (IQR)	7.0 (5.0 – 12.0)		10.0 (7.50 – 13.0)		5.0 (4.0 – 6.0)		
Cpap	208	66.7	107	84.3	101	54.6	<0.001*
Duration of cpap (days)	(n = 208)		(n = 107)		(n = 101)		
Min. – Max.	2.0 – 16.0		2.0 – 16.0		2.0 – 10.0		0.001*
Mean ± SD.	5.59 ± 2.47		6.18 ± 2.75		4.96 ± 1.95		
Median (IQR)	5.0 (4.0 – 7.0)		6.0 (4.0 – 7.0)		5.0 (3.0 – 6.0)		
Nasal cannula	306	98.1	126	99.2	180	97.3	$^{MC}p=0.41$
Duration of Nasal(days)	(n = 306)		(n = 126)		(n = 180)		
Min. – Max.	2.0 – 17.0		2.0 – 17.0		2.0 – 12.0		0.454
Mean ± SD.	5.05 ± 2.65		5.40 ± 3.19		4.80 ± 2.18		
Median (IQR)	4.0 (3.0 – 6.0)		4.0 (3.0 – 6.0)		4.0 (3.0 – 6.0)		

IQR: Inter quartile range, SD: Standard deviation, U: Mann Whitney test, χ^2: Chi-square test, FE: Fisher Exact, MC: Monte Carlo, P: p-value for comparing between ROP and different parameters, *: Statistically significant at $P \leq 0.05$.

Table (5): Percentage of injection and laser in ROP patient (n = 127)

Injection	No.	%
No	43	33.9
Yes	84	66.1
Type 1 ROP	64	50.4
Agerssive posterior ROP (APROP)	20	15.7

Table (6): Outcome of ROP patient (n = 312)

	Total (n = 312)		ROP				p
			Yes (n = 127)		No (n = 185)		
	No.	%	No.	%	No.	%	
Follow up							
No	13	4.2	3	2.4	10	5.4	0.186
Yes	299	95.8	124	97.6	175	94.6	
Outcome progress							
Missed	13	4.2	3	2.4	10	5.4	0.186
Yes	299	95.8	124	97.6	175	94.6	

χ^2: Chi-square test, P: P-value for comparing between ROP and outcome.

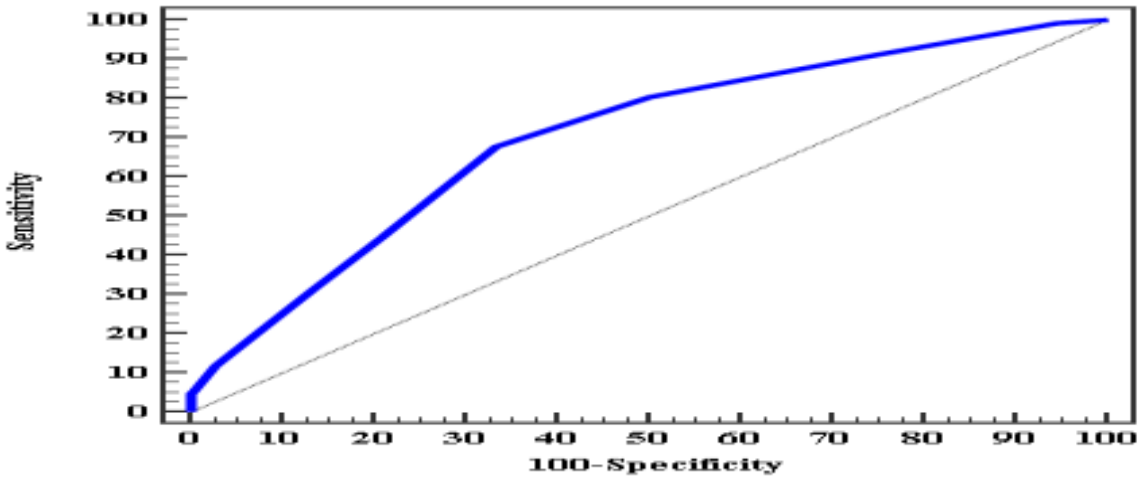

Figure (1): ROC curve for gestational age (weeks) to prognoses ROP patients (n = 127 vs. 185).

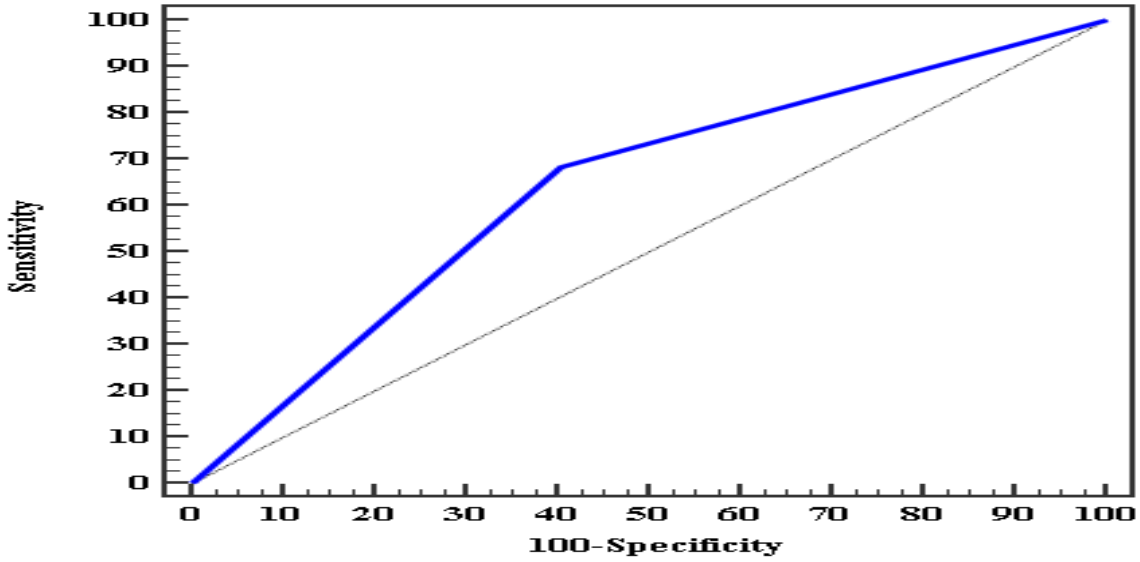

Figure (2): ROC curve for MV to prognoses ROP patients (n = 127 vs. 185).

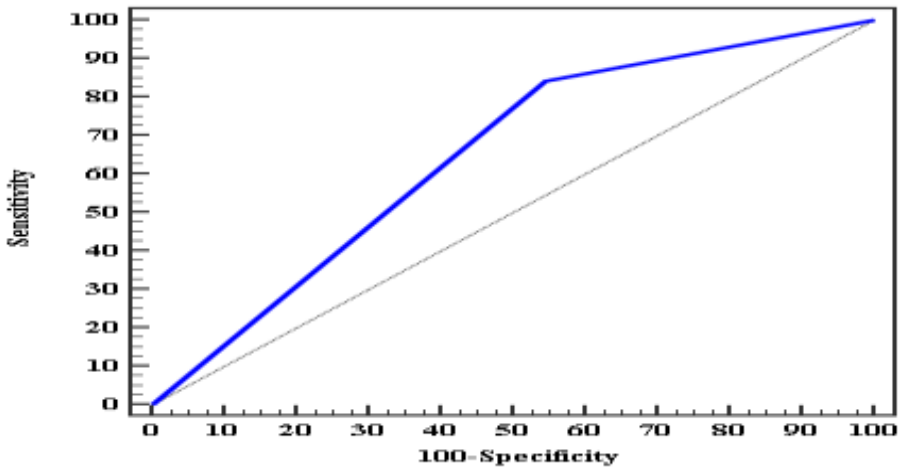

Figure (3): ROC curve for Cpap to prognoses ROP patients (n = 127 vs. 185).

4. Discussion

ROP is the major cause of retinal vasculopathy in preterm and low birth weight infants [7]. This issue is also one of the most common reasons why preterm and low birth weight newborns go blind in their early years.

ROP may have a variety of causes [8]. Numerous potential risk factors have been identified in studies, such as intraventricular hemorrhage (IVH), necrotizing enterocolitis, sepsis, supplemental oxygen, gestational age, prolonged mechanical ventilation, Apgar score, and pulmonary complications. [9].

The main aim of this study was to establish the number of preterm infants who are susceptible to develop retinopathy of prematurity as a Screening during the observed time period to know the relation among the risk factors & development of ROP. Follow up examination to ROP cases and detect the outcome.

This retrospective cohort study of 312 preterm infants admitted to NICU of shareyah society in ltay El-Baroud, Al Beheira, Egypt during the period from January 2016 to December 2019.

The study's findings indicated that the incidence of the ROP in the studied preterm infants was 40.7%, 97.6% of them were followed up and 97.6% have progress.

Similar to our findings, Dwivedi et al. [10] conducted a retrospective investigation on 763 screened infants and found that 30% had ROP. There were 59 cases of classic ROP and 30 cases of APROP, for a total prevalence of 14.2%.

In another retrospective cohort study with 602 neonates, Freitas et al. [11] found that the overall incidence of ROP was 33.9% & that of type 1 prethreshold ROP was 5.0%.

As well a Prospective Observational Study by Gezmu et al., [12] investigated 200 premature infants 22 of them were identified with ROP with an occurrence of 11percent. It was discovered that 3.5% of patients had type 1 ROP, which is a sight-threatening kind.

In addition, the retrospective study conducted by Leng et al., [13] evaluated a total of 436 preterm newborns who were consecutively screened for ROP. Of these premature infants, 138 (31.6%) were found to have ROP, and 61 (13.99%) were treated for it.

According to our findings, retinopathy of prematurity was significantly associated with longer hospital stays.

Our results are constant with those of Ali et al. [14], who also showed that longer initial hospital admissions were linked to greater ROP incidence. However, it is possible that the correlation between hospitalization duration and ROP results from the fact that

longer hospitalizations are necessary for sicker infants.

Moreover, van Sorge et al. [15] corroborated our findings by reporting that a longer-than-28-day stay in a neonatal critical care unit was linked with an increased risk of retinopathy of prematurity (OR 1.6, 95% CI 1.1-2.6, P =.03).

Wani et al. [16] also found that a longer-than-15-day stay in the intensive care unit was associated with a higher risk of developing any ROP (OR 2.25, 95% CI 1.05-4.85; P = 0.033).

Regarding the relation between ROP and demographic data, our results revealed that there was high significant relation between birth weight, gestational age and retinopathy of prematurity. No significant relation between mode of birth, gender and ROP.

In agreement with our study Dwivedi et al., [10] reported that there was significant relationship among ROP and birth weight, gestational age (p<.05) while there was no statistically significant relationship among ROP and sex (p>.05).

Also, in line with our results Freitas et al., [11] stated that there was high significant relation between birth weight, gestational age and ROP (p<.001). No significant relation between mode of birth, gender and ROP (p>.05).

Furthermore, there was an agreement with our results and Leng et al., [13] as they reported that there was high significant relation between birth weight, gestational age & ROP (p<.001) & there was a significant relation between gestational age and ROP (p<.05), while no significant relation between gender and ROP (p>.05).

In line with our results, Celebi et al. [17] found a correlation between advanced maternal age & retinopathy of prematurity onset (p<.001) & between blood transfusion, advanced maternal age, and a low birth weight and the development of severe ROP (p<.05).

Logistic regression analysis indicated that gestational age was an independent risk factor for ROP (p= 0.034), according to the study by Hu et al. [18]. When comparing birth weight among the 2 groups, a statistically significant difference was not found; nonetheless, the P value was close to being significant (P=0.073).

In addition, ROP was significantly related with Sepsis, Thrombocytopenia, and Blood Transfusion , but not with Respiratory Distress, Apnea, Pneumothorax, Exchange Transfusion, or Phototherapy.

Our findings, which are similar with the findings of Dwivedi et al. [10], indicate that there is no relation between ROP and respiratory distress, thrombocytopenia, or apnea.

In addition, Freitas et al. [11] showed that there was a strong association between ROP and Sepsis, pulmonary illnesses, oxygen therapy, CPAP, mechanical ventilation, and the number of blood transfusions, all of which corroborated our findings.

Furthermore, there was an agreement with our results and Leng et al., [13] as they reported that there was high significant relation between ROP and Mechanical ventilation.

Also, Lundgren et al., [19] reported that there was significant relation between ROP and Sepsis.

Additionally, Zarei et al. [20] shown that only gestational age, birth weight, and transfusion were significant on multivariate analysis, whereas ARDS, oxygen therapy, sepsis, intubation, and IVH were significant risk factors on univariate analysis. This is so because the risk of IVH was only influenced by gestational age, birth weight, and transfusion. Risk factors such as advanced maternal age (P = 0.010), low newborn weight (P< 0.0001), and intraventricular hemorrhage (P = 0.028) were found in individuals who required therapy for ROP.

While the Study by Gezmu et al., [12] as they stated that there was significant relation between ROP and Frequency of Blood Transfusion, but there was no significant relation between ROP and Sepsis, Respiratory distress.

As regard Outcome of ROP patient, our results revealed that 299 of all 312 cases come for follow up with a percentage of 95.8% and progress while 13 cases not come for follow up and the outcome missed.

The results of our analysis of the ROC curve for gestational age (weeks) to prognosticate ROP patients presented an area under the curve of 0.701, (P.001; 95% CI 0.643 - 0.760), a cutoff of gestational age 32 weeks, sensitivities of 67.72% and 66.49%, specificities of 58.1% and NPVs of 75.0%.

Eckert et al. [9] found similar results: an area under the ROC curve of 0.69 (P0.001; 95% CI 0.63-0.75) for gestational age in predicting ROP, and an area under the ROC curve of 0.79 (P0.001; 95% CI 0.69-0.88) for predicting severe ROP.

Consistent with our findings, Ojaghi et al. [21] indicated that a GA cutoff of 32.5 weeks (sensitivity 69%, specificity 72%) was the best for predicting preterm newborn retinopathy. Birth at a gestational age of < 32.5 weeks was associated with a 5.9-fold greater incidence of ROP (95% CI: 3.619-9.519, P 0.001).

We used the ROC curve for Mechanical Ventilation to predict ROP outcomes and found an area under the curve of 0.64 (95% CI, 0.577 to 0.702), sensitivities of 68.50 and specificities of 59.46%, and positive and negative predictive values of 53.70 and 73.33%, respectively. In addition, CAPAP's sensitivity and specificity for ROP prognosis prediction were 84.25 and 45.41%, respectively; its PPV and NPV were 51.44 and 80.77%, respectively; and its area under the curve was 0.648 (P.001; 95% CI 0.587-0.709).

In a retrospective study, Katsan and Adakhovska [22] discovered that low gestational age (OR, 0.52; 95% CI, 0.45-0.60; p< 0.001), mechanical ventilation (OR, 2.9; 95% CI, 1.4-5.6; p = 0.003), blood transfusion (OR, 1.23; 95% CI, 1.03-1.49; p = 0.02), and thrombocytopenia (OR, 0.72; 95% CI, 0.60 – 0.87; p < 0.001).

5. Conclusion

It The prevention of blindness and overall improvement in a child's development can be achieved with the timely diagnosis of retinal impairment and the commencement of suitable treatment. ROP is connected with a wide variety of other risk factors and co-morbidities, which can only be discovered through additional research. A timely retinal screening of high-risk preterm as well as collaboration between neonatal doctors and competent ophthalmology subspecialists are essential for preventing the progression of ROP to an advanced stage.

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