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Retinopathy of Prematurity (ROP) a Cross-Sectional Study in Basra 2022-2023

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Abstract

Preterm labor is characterized by the commencement of labor before reaching 37 weeks of pregnancy based on gestational age: "extremely preterm" for births before 28 weeks, "very preterm" for births between 28 and 32 weeks, and "moderate to late preterm" for births occurring between 32 and 37 weeks. One complication of preterm which is very important is ROP. because it effect on quality of life is a primary contributor to preventable blindness in children. It is a multifaceted condition that affects premature infants, partly caused by incomplete or abnormal development of retinal blood vessels. Worldwide, approximately 50,000 children under 15 are affected by blindness due to ROP-related complications. Aim of the study To assess the presence of ROP in premature neonate. 2- Study the presence of ROP in relation to some neonatal characteristics. In this study we follow up preterm babies after discharge from intensive care unit and send them for ophthalmology from October 2022_october2023 total preterm 77 was male 62. 1% & 47was girl 37.9% total 124 preterm . Most preterm patients suffering from ROP in the study patient less than wight 1000 gram 3. 2% and preterm those need more than 1 week duration of admission in neonatal word. Larger scale study (national) is needed with a larger study group sample. With more detailed assessment of the neonatal course and the timing of screening and assesment for the ROP. Try to implement neonatal screening programs to assist in early detection of ROP and prevent blindness. Help to provide a

screening criteria that is more fit for Iraq. Provide the instruments and the training needed for the doctors in the hospitals were neonatal care units are present to facilitate the screening of neonates before discharge.

Keywords: Retinopathy of Prematurity (ROP), premature infants, neonatal care, oxygen therapy, ROP screening and diagnosis.

1. Introduction

Preterm labor is defined as the onset of labor before 37 weeks pregnancy. The preterm birth rate in developed countries is usually less than 10 percent. Considering a UK example the rate is approximately 7% whereas in the USA it varies between 9 and 12 depending on the region and ethnic background. Conversely, preterm birth rates in many low-income countries are over 15%. No research could be located which mentions the number of cases of preterm births in Iraq and/or in Basra in particular. Over 75% of all perinatal deaths are due to preterm births(1).

The World Health Organization distinguishes between different types of preterm births, according to gestational age: extremely preterm births below 28 weeks old, very preterm births between 28 and 32 weeks old, moderate and late preterm births between 32 and 37 weeks old (2).

Developmental immaturity affects several organ systems causing a wide range of complications that can have a long term effect on the health, growth and development of infants with developmental immaturity.

Surfactant starts to be produced in the lungs at about 30 to 32 weeks of gestation. But babies born prior to 28 to 30 weeks lack the development of alveoli and use terminal bronchioles and primitive air sacs to breathe. This immaturity may result in respiratory distress syndrome, an acute disease that is treated with respiratory support like oxygen, positive airway pressure, ventilation or surfactant. The symptoms usually improve after 2 to 4 days and end after 7 to 14 days. There is another complication that is called apnea and it happens because of the immaturity of the respiratory control mechanism. (3)

Chronic lung disease or bronchopulmonary dysplasia is a chronic condition resulting in inflammation, injury and scarring of the airways and alveoli. This syndrome is associated with growth deficits, medical problems and neurodevelopmental disabilities during childhood(4).

The underdevelopment of the gastrointestinal system is a common complication of preterm babies leading to feeding intolerance as the digestion process becomes difficult. Babies with a premenstrual age less than 34 or 35 weeks tend to have uncontrolled sucking, swallowing and breathing, and require tube feeding to feed adequately.

(5)

Necrotizing enterocolitis (NEC) is a critical disease with acute damage to small or large intestines resulting in inflammation, dysbiosis and ischemia necrosis of the bowel mucosa. It mostly occurs in those babies whose gestation time is less than 32 weeks and with very low birth weight

more than normal (6).

Infants born at 22 to 25 weeks of gestation usually have a skin that is weak and gelatinous and is very prone to tears when touched. It permits too much lost of fluid and does not offer sufficient protection against infections. Fluid and electrolyte needs in the initial days following birth may be unpredictable and differ widely until the skin matures. Also, regular medical checks and intravenous line invasion tend to leave several scars on preemies (7).Preemies also lack the development of an immune system, which leaves them without the ability to fight bacteria, viruses, and other infectious diseases. Consequently, this makes them susceptible to severe infections, and some of the major problems associated with this include pneumonia, sepsis, meningitis, and urinary tract infections to mention a few (8).

Preterm babies are vulnerable to a number of cardiovascular conditions, such as congenital heart disease and heart failure. Such problems can develop because of the immaturity of the heart or as a consequence of other complications like sepsis and inflammation.

(9,10)

Prenatal bleeding, fetomaternal bleeding or fetal hemolysis can cause congenital anemia in preterm infants. The most frequent hematologic complication in preemies is, however, the anemia of prematurity (11).

Hearing disorders that are present at birth, or those acquired during newborn time, occur in 1-3 per 1000 newborns. But the prevalence among at-risk infants, such as preterm infants, is 10 to 50 times greater, with an approximate prevalence of 3 to 6 per 100. Although most hearing impairments are attributable to hereditary causes, a combination of in utero and neonatal diseases, including infections, prematurity, asphyxia, ototoxic medications, and hyperbilirubinemia, have also been cited as risk factors. Also, infants who are ventilated are more at risk of developing otitis media. (12)

The most prevalent eye disorder among preterm infants is retinopathy of prematurity (ROP), which is caused by eovascular retinal disorder, which in turn is caused by various risk factors the first factor being preterm infant immaturity of the retina. In premature babies, and in intraventricular hemorrhage, severe types of ROP, principally the threshold type, are commonly associated with chronic lung disease. Gestational age and birth weight are associated with an increase in the incidence of ROP. (13) Other complications related to vision in preterm infants include refractive disorders such as myopia, strabismus, amblyopia, optic nerve atrophy, cataracts, and cortical visual impairment. Long-term eye issues may include angle-closure glaucoma, retinal detachment, and phthisis. (14)

White matter around the ventricles and the highly vascular germinal matrix is especially vulnerable to damage in preterm babies. The situation is complicated by difficulties with the auto-regulation of cerebral blood flow. Ischemia, hypoxia, and inflammation are all involved in the damage of the central nervous system in preterm infants, with the relative importance of each factor being controversial. The retina is a vascular coating on the back of the eye that translates light into electrical impulses to the brain. It is among the later organs that gets vascularized in the fetus. Optic grooves are the first part of the eye to develop in a fetus, and they grow out of the neuroectoderm of the forming forebrain during week three of gestation. After this, the optic vesicle is developed, the neural tube folds and the optic groove evaginates. These optic vesicles are hollow vessels that extend through the mesenchyme around them to the surface ectoderm. Four weeks into gestation, an invagination of the optic vesicle forms the optic cup which will further differentiate into the retina. Grooves called retinal (or choroid) fissures run along the ventral surface of the optic cup and stalk, through which the hyaloid artery and vein pass. They create hyaloid vessels that get incorporated into the optic nerve when optic cup closes around them forming the central retinal artery and vein in the end (16). Retinal vasculogenesis is a hypoxia process which is initiated by the migration of many spindle-shaped mesenchymal precursor cells out of the optic disc. These cells multiply and

differentiate into cords of endothelial cells and this process is controlled by vascular endothelial growth factor (VEGF). An early (14-21 weeks of gestational age) stage of retinal vessel formation, vasculogenesis, forms an immature vascular plexus in the inner retinal layers, centred around the optic disc. The second stage, angiogenesis, increases the vascularity of this primitive complex and expands it peripherally and temporally of the pre-existing blood vessels. This is done between the 25th and 26th gestation time. At 27 weeks, the retina is only vascularized in 70 percent of cases, however, as the pregnancy progresses, at 36 weeks, the retina is generally completely vascularized on the nasal side and at 40 weeks, the temporal side of the retina is also vascularized (in most cases) (17).

Physiologic in-utero hypoxia is reduced at birth and the newborn is subjected to a period of hyperoxia, with atmospheric oxygen and additional oxygen. Also, insulin-like growth factor 1 (IGF1) levels are low at this age. The combination of these two factors leads to poor retinal vascularization and the capillaries enter into reflex vasoconstriction and later vaso-obliteration which forms Phase 1 of retinopathy of prematurity (ROP). Phase 2 ROP development starts with angiogenesis pathology. Hypoxic injury occurs in the peripheral avascular retina, and the maturing retinal neurons releases angiogenic factors such as vascular endothelial growth factor (VEGF) into the vitreous. They also increase effects of VEGF on angiogenesis of the retina as serum IGF1 levels also increase. The growth of abnormal blood vessels is originating in the retina and moves towards the high VEGF levels in the vitreous. Purpose of this study To determine the existence of ROP in premature babies. Intended also, to Investigate the occurrence of ROP in relation to certain features of the neonate.

2. Methodology

This is a cross-sectional study which was conducted at the outpatients clinic at Al-Basra maternity and children hospital between the months of October of 2022 and October of 2023 (one year period). This study included all preemies born below or at 36 gestational weeks of age with a birth weight of up to or below 2500 gm and caught in the neonatal care unit or visited on an outpatient basis.

Neonates with inborn visual defects (or died before first ophthalmologic assessment) were not included, as well as neonates with kernicterus.

Upon admission, the babies were examined by neonatologists and any medical conditions treated. The gestational age was determined using Ballard score; the first day of last menstrual period of the mother and physical examination of the baby. They weighed the babies naked at birth on a basinet to the nearest 50g.

Due to the absence of the screening program of the preterm newborns in Iraq, it meant that all of the study patients were screened for the first time, between 50 days to 6 months of age.

The eye was dilated using 0.5 percent tropicamide. The babies were studied following instillation of a topical anesthetic, 0.5% proparacaine. The peripheral retina was visualized with a lid speculum and scleral indentator. Each patient had his or her examination performed by an ophthalmologist depending on the geographical location of the family home of the patient and not by one individual ophthalmologist.

2.1. Statistical Analysis

Data were analyzed using statistical package Stata version 24. Qualitative variables were presented as absolute numbers (%). Fisher's exact test was used to compare Qualitative variables. A P value of less than 0.05 was accepted as significant.

3-Results

3.1. Description of the neonatal characteristics

The results demonstrated in table (3-1) in numbers and percents of some of the neonatal features including sex, gestational age, weight at birth devided into groups**.**

Table (3-1) : Demographic characteristics of the neonates

(No. = 124)		
	Number	**Percent**
Sex		
Male	77	62.1%
Female	47	37.9%
Gestational age		
≥34	27	21.8%
32-34	42	33.9%
28-32	42	33.9%
<28	13	10.5%
Weight at birth		
ELBW	26	21%
VLBW	29	23.4%
LBW	69	55.6%

This table shows that the majority of the study group are males, most of neonates are between 28-34 week gestational age, and more than half of them with a birth weight between 1500- 2500 gm.
Some other neonatal features of the study group demonstrated in table (3-2)

Table (3-2) : Demographic characteristics of the neonates			
	Minimum	**Maximum**	**Mean ±SD**
Gestational age (wk)	25	36	31.44±2.78
Weight (gm)	700	2500	1460±380
Admission duration in neonatal care unit	1	38	12.41±8.7

In table (3-2), it describes that the mean gestational age ranging between 29 –34 week, with a minimum of 25. the highest weight at birth is 2500 gm with a mean of 1460 gm. While the duration of admission of the neonates ranged from 1 – 38 days with a mean of 12.41 days, this depends on the conditions that develop in the neonates from respiratory distress syndrome, sepsis, oxygen or ventilator need, or until appropriate weight gain and feeding to be discharged.

3.2. Frequency of ROP in the affected group according to sex

table (3-3) describes the number of patients affected with ROP, and was compared according to the sex.

Table (3-3) : Number of patients affected with ROP According to Sex					
Sex	**Normal (No)**	**Normal (%)**	**ROP (No)**	**ROP (%)**	**P value**
Male	71	57.3%	6	4.8%	0.709
Female	45	36.3%	2	1.6%	
Total	116	93.5%	8	6.5%	124

This table is showing that most of the affected patients are males (6 (4.8%)). Eight (6.5%) affected patients out of the total 124.

3.3. Frequency of ROP in the affected group according to neonatal weight groups

This table describes the number and percents of affected patients by ROP, devided according to their weight at birth into three groups.

Table (3-4) : Patients affected by ROP according to Weight at birth					
Weight groups	**Normal (No)**	**Normal (%)**	**ROP (No)**	**ROP (%)**	**P value**
≤1000 gm	22	17.7%	4	3.2%	0.067
1000 – 1499gm	27	21.8%	2	1.6%	
1500- 2500 gm	67	54%	2	1.6%	
Total	116	93.5%	8	6.5%	124
Fisher's exact test					

Table (3-4) shows that most of the affected patients by ROP are within the weight group of less than 1000 gm (4 (3.2%), while this group represent only 20.9% of the total study group.

3.4. Frequency of ROP in the affected group according to neonatal gestational age groups

This table describes the number and percent of the affected patients according to their gestational age groups.

Table (3-5) : patients affected by ROP according to the gestational age					
Gestational age groups	**Normal (No)**	**Normal (%)**	**ROP (No)**	**ROP (%)**	**P value**
≤28 wk	10	8.1%	3	2.4%	**0.025**
28-32 wk	38	30.6%	4	3.2%	
>32 -34 wk	40	33.1%	1	0.8%	
>34-36 wk	27	21.8%	0	0%	
Total	116	93.5%	8	6.5%	124
Fisher's exact test					

This table (3-5) shows that the most affected groups are within the gestational age of less than 32 week (5.6%) with a statistical significant result.

3.5. Frequency of ROP in the affected group according to duration of admission to the neonatal care unit groups

In the following table, patients who are affected by ROP are shown in number and percentile, with the duration of admission used to compare.

Table (3-6) : Patients affected by ROP according to the duration of admission in neonatal care unit					
Duration of admission in days	**Normal (No)**	**Normal (%)**	**ROP (No)**	**ROP (%)**	**P value**
≤ 7	48	38.7%	2	1.6%	0.473
>7	68	54.8%	6	4.8%	
Total	116	93.5%	8	6.5%	124
Fisher's exact test					

It is shown here that most of the patients affected with ROP are within the group of the neonates with the longest duration of admission more than 7 days (6 (4.8%)), propably with a more complicated course and with smaller gestational age or weight at birth.

4-Discussion

Retinopathy of prematurity (ROP) is an abnormal retinal vascularization, if left untreated can progress to blindness. This Cross sectional study, was carried out at Al-Basra maternity and children hospital outpatients clinic and neonatal care unit, for the neonates who were admitted in it's neonatal care unit. Sample size that was obtained was 140 neonate, about 15 lost due to lack of follow up or wrong contact information, and one excluded due to kernicterus. The remaining 124 patient that was involved, only 8 showed ROP, most of which were blind at diagnosis.

Also is noted in this study that most of the affected are males (6 out of 8) with mean gestational age of (28.38±2.39 week), minimum 25 week and maximum of 32 week. Which is a finding that is consistent with many other studies in developed and developing countries as a study done by Abdulsahib AM et al.(19) in Iraq at 2023 showing a mean gestational age of 31.3 ± 2.2 weeks, with 9.3% aged less than 28 weeks which is similar to this study (10.5%). another study done in India at 2005 showing he mean gestational age was 29.6 weeks (26 - 36 weeks).(25) and similarly in Sweden higher incidence in neonates with a gestational age of less than 28 weeks.(20)

While mean of the weigh within affected group is (1140 ± 314 gm), with minimum weight of 700 gm and maximum of 1600 gm. Which is smaller in comparison to the study done in Iraq by Abdulsahib AM et al.(24) showing a birth weight of 1558.7 ± 476.8 grams. In India the birth weight of 115 babies ranged from 710 - 2000 gm (with a mean of 1254.5 ± 280.8 gm).(25) Also in US the CRYO-ROP Group Study reported that 66% of infants affected by ROP are with a birth weight of less than 1,250 g and 82% of infants with a birth weight of less than 1,000 gm. (54) and as in this study it is shown in sweden that incidence is more common in neonates with a birth weight of < 1000 gm.(20)

And most (6 out of 8) of these affected patients had an admission duration in the neonatal care unit of more than 7 days, with the maximum length of stay was 38 days. Which is expected to have more neonates affected by ROP who had a prolonged neonatal course with more complications as respiratory distress, sepsis, with prolonged oxygen therapy use or mechanical ventilation use, as shown in the Iraqi study (19) T1ROP was significantly associated with low gestational age (16% of cases aged < 28 weeks), respiratory distress syndrome (20%), and low birth weight (21.4% in cases with birth weight less than 1051 g).

4.Conclusion and Recommendation

Larger scale study (national) is needed with a larger study group sample. With more detailed assessment of the neonatal course and the timing of screening and assesment for the ROP. Try to implement neonatal screening programs to assist in early detection of ROP and prevent blindness. Help to provide a screening criteria that is more fit for Iraq. Provide the instruments and the training needed for the doctors in the hospitals were neonatal care units are present to facilitate the screening of neonates before discharge.

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