



OPEN Analysis of full-term neonatal eye disease screening results and trends from 2016 to 2023

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To analyze the results and trends of common eye diseases from full-term neonatal eye screenings conducted between 2016 and 2023. A retrospective study was conducted on 17,378 full-term neonates screened for eye diseases at Cixi Maternity&Child Health Care Hospital from January 2016 to December 2023. Statistical analysis and Joinpoint regression were used to assess trends in eye disease incidence, measured by the Average Annual Percent Change (AAPC). Among 17,378 full-term neonates, 5,986 (34.45%) had abnormal eye screening results: Retinal hemorrhage (3,274 cases, 18.84%), white spots (1,440 cases, 8.29%), exudates (943 cases, 5.43%), pigment abnormalities (437 cases, 2.51%), and lesions resembling Familial Exudative Vitreoretinopathy (FEVR-like) (228 cases, 1.31%). Retinal hemorrhage ($\chi^2 = 1840.390$, $P = 0.000$) and exudates ($\chi^2 = 10.488$, $P = 0.001$) were more common in neonates born via vaginal delivery. From 2016 to 2023, the overall abnormality rate declined (AAPC = -6.9%, 95% CI: -12.1% to -1.5%, $P = 0.0211$). Trends included: Retinal hemorrhage (AAPC = -3.2%, 95% CI: -6.4% to 0.0%, $P = 0.0499$) and pigment abnormalities (AAPC = -25.4%, 95% CI: -42.8% to -3.0%, $P = 0.0342$). Other retinal abnormalities showed no significant trends (all $P > 0.05$). Eye disease due to fundus lesions From 2016 to 2023, The overall incidence of fundus lesions in full-term neonates showed a declining trend. Vaginal delivery is a risk factor for retinal hemorrhages and retinal exudation in full-term neonates. We found a strong association between cytomegalovirus infection and retinal exudation.

Keywords Full-term neonates, Neonatal eye disease screening, Incidence rate, Trends, Digital wide-field fundus imaging system

The necessity of eye disease screening for high-risk newborns has been widely recognized^{1–3}, however, whether universal ocular screening should be implemented for full-term neonates remains controversial. Current studies^{4,5}, have found that the most common abnormalities detected in eye disease screening of full-term neonatal include retinal hemorrhage, peripheral retinal exudation⁷ (or retinal white lesions), and familial exudative vitreoretinopathy (FEVR)-like^{9,10} fundus changes, among others. However, there have been no reports on the trends in the incidence of various retinal abnormalities. This study utilizes Chi-square tests and Joinpoint regression to analyze the results and incidence trends of eye disease screening abnormalities in full-term neonatal in Cixi City from 2016 to 2023, providing a scientific reference for the standardization of eye disease screening and follow-up for full-term neonatal.

Materials and methods

Screening subjects

A total of 17,378 full-term neonates born in our hospital from January 2016 to December 2023 were selected. The study was approved by the Clinical Research Ethics Committee of Cixi Maternity&Child Health Care Hospital (LCKY-L2024-64-02). All participants were screened in accordance with the ethical principles outlined in the Declaration of Helsinki for human research, and written informed consent was obtained from their guardians.

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Screening methods

For full-term neonatal with a willingness for eye disease screening, the screening is conducted after their guardians sign an informed consent form. full-term neonatal undergo examination and image interpretation within one week after birth by two professional pediatric ophthalmologists trained in pediatric retinal examination. If there is a diagnostic discrepancy, a senior reviewer is consulted.

The examination consists of two parts: anterior segment examination and fundus examination. Feeding and drinking are prohibited for 60 min before the examination. Before the examination, 0.5% Tropicamide Phenylephrine Eye Drops (Santen Pharmaceutical Co., Ltd., Japan) are used to dilate the pupils (four drops per eye, one drop every 10 min). After dilation (pupil diameter reaching 6–8 mm), the neonate is brought by the guardian to the eye screening room for examination. Before the examination, the examiner administers 0.5% Proparacaine Hydrochloride Eye Drops (Alcaine Eye Drops, Alcon Laboratories Inc., Fort Worth, TX, USA) for conjunctival and corneal surface anesthesia in both eyes.

Anterior segment examination

The neonate is placed in a supine position. The examiner first observes the eyelids, then inserts an eyelid speculum. A handheld slit lamp and penlight are used to examine the conjunctiva, cornea, iris, pupil, lens, and red reflex.

Fundus examination

Ofloxacin Eye Ointment (Shenyang Xingqi Eye Drops Co., Ltd., China) or Gatifloxacin Eye Gel (Shenyang Xingqi Eye Drops Co., Ltd., China) is applied to the conjunctival sac. A wide-field imaging system (PanoCam from Suzhou Visunex Company, January 2016 - March 2018; Orthocone RS-B002 from Guangzhou Nuoxunde Medical Technology Co., Ltd., April 2018 - December 2023) with a 130-degree lens is used to capture retinal images of the posterior pole, macula, optic disc, temporal, nasal, superior, and inferior regions for fundus examination.

Findings in full-term neonatal fundus images include:

- Retinal Hemorrhage⁶.
- Retinal Exudates⁷(The peripheral retina of the fundus presents white lesions with clear or slightly blurred boundaries, distributed in patchy (isolated or continuous), striped, clustered (scattered and fused dot-like), or ring-shaped patterns (involving one or multiple quadrants, or even 360° around the retinal periphery.)
- Retinal White spots^{7,8}(Scattered throughout the fundus, with a size similar to the diameter of a retinal arteriole. The spots are beige or pure white in color, or white with a slight yellowish tint, and appear as single or multiple well-defined punctate lesions on the retina.)
- Retinal Pigment abnormalities(This category included hypertrophy of retinal pigment, disordered retinal pigmentation, focal depigmentation, and retinal pigment nevi, all of which were collectively classified as retinal pigment abnormalities.)
- FEVR-like lesions^{9,10}(Defined by avascular areas in the peripheral retina of one or both eyes in full-term neonates. These could be accompanied or not accompanied by peripheral blood vessel thinning and rigidity. Additional findings included peripheral retinal neovascularization or exudative changes, vitreoretinal adhesion and traction, or retinal detachment.This retinopathy was described as FEVR-like lesions due to the absence of genetic confirmation required for definitive FEVR diagnosis.)

Additionally, data on the neonate's gender, gestational age, delivery method, and birth weight are collected. After the examination, Ofloxacin Eye Ointment or Gatifloxacin Eye Gel is applied to both eyes twice daily for three days to prevent infection.

Statistical analysis

An eye disease screening database was established using Excel 2019 to organize and extract all screening data for full-term neonates from 2016 to 2023. Statistical analysis was performed using SPSS 17.0. Categorical data were expressed as percentages (%), and group comparisons were conducted using the Chi-square (χ^2) test. Joinpoint regression analysis was performed using the Joinpoint Regression Program (version 4.8.0.1) developed by the U.S. National Cancer Institute. A significance level of $P < 0.05$ was considered statistically significant.

Results

Screening results for full-term neonatal eye diseases from 2016 to 2023

A total of 17,378 full-term neonates participated in eye disease screening. Among them, 9,178 were male (52.81%), and 8,200 were female (47.19%) (Table 1). Vaginal deliveries accounted for 9,988 cases (57.47%), while cesarean sections accounted for 7,390 cases (42.53%). Initial screening identified 11,392 normal cases, with a pass rate of 65.55%, and 5,986 abnormal cases, resulting in an abnormality rate of 34.45%. Among the abnormalities, the five most common conditions were: Retinal hemorrhage, (Fig. 1a) (3,274 cases, 18.84%), Retinal white spots, (Fig. 1b) (1,440 cases, 8.29%), Retinal exudates, (Fig. 1c) (943 cases, 4.53%), Retinal pigment abnormalities, (Fig. 1d)(437 cases, 2.51%), FEVR-like lesions, (Fig. 1e) (228 cases, 1.31%). Among the 3,274 cases with retinal hemorrhages, 489 involved macular hemorrhages, including 287 unilateral cases and 202 bilateral cases.Foveal hemorrhage was identified in 45 of the 489 cases with macular hemorrhage.This study also identified 18 cases of congenital cataracts and 275 cases of other ocular abnormalities. Excluding subconjunctival hemorrhages, 141 cases of relatively rare retinal abnormalities were observed, including: choroidal coloboma, (Fig. 1f)

Screening Year	2016	2017	2018	2019	2020	2021	2022	2023	Total
Number of Screenings	1044	948	1923	3355	2511	2698	2562	2337	17,378
Normal Screenings	599	637	984	2055	1630	1924	1799	1764	11,392
Abnormal Screenings									
Retinal Hemorrhage	249	188	418	569	478	472	475	425	3274
Retinal White Spots	115	49	248	478	238	130	118	64	1440
Retinal Exudation	52	54	173	227	185	104	111	37	943
FEVR-like Lesions	13	9	28	47	47	40	22	22	228
Retinal Pigment Abnormalities	30	27	203	95	21	19	26	16	437
Congenital Cataracts	0	1	0	5	0	3	6	3	18
Others	20	11	25	50	42	46	52	29	275

Table 1. Summary of fundus screening for Full-Term neonates (2016–2023) (n). Retinal Hemorrhage, any form of hemorrhagic foci present in the fundus of the retina; Retinal White Spots, single or multiple punctate retinal lesions, scattered in the fundus, with white or cream-colored appearance, well-defined borders, and sizes comparable to retinal arterioles; Retinal Exudation, well-defined or ill-defined white lesions in the peripheral retina, presenting as punctate, patchy (isolated or confluent patches), linear, clustered (coalesced scattered punctate lesions), or annular configurations (involving a single quadrant, multiple quadrants, or 360-degree circumferential distribution); FEVR-like Lesions, full-term neonates without genetic diagnosis present with avascular peripheral retina in one or both eyes, with or without peripheral vascular thinning and rigidity, Peripheral retinal neovascularization or exudative changes may be present, along with vitreoretinal adhesion, traction, or retinal detachment; Retinal Pigment Abnormalities, including various forms of retinal pigmentation, hypertrophy, depigmentation changes, or abnormal distribution of retinal pigment; Congenital Cataracts, Any form and any degree of lens opacity; Others, other abnormalities detected in neonatal eye disease screening;.

(n = 45), vitreous opacity (n = 29), tortuous retinal arteries without other retinal changes (n = 19), peripheral retinal avascular zone (1–2 disc diameters) without other retinal changes (n = 18), corneal opacity (n = 5), abnormal cup-to-disc ratio (n = 5), persistent pupillary membrane (n = 3), eyelid hemangioma (n = 3), persistent hyaloid artery remnant, (Fig. 1g) (n = 2), abnormal retinal arteriovenous anastomosis (n = 2), microphthalmos with microcornea (n = 2), blepharophimosis (n = 2), retinoblastoma (RB), (Fig. 1h) (n = 1), persistent fetal vasculature (PFV), (Fig. 1i) (n = 1), lenticonus (n = 1), optic disc drusen (n = 1), conjunctival polyp (n = 1), and vitreous hemorrhage (n = 1).

Screening results for full-term neonates by gender and delivery method from 2016 to 2023
During the study, ocular screening was performed on 9,178 male and 8,200 female full-term neonates. The screening results were normal in 5,984 (65.20%) males and 5,409 (65.96%) females, and abnormal in 3,194 (34.80%) males and 2,791 (34.04%) females. No significant difference in the abnormality rate was observed between male and female neonates ($\chi^2 = 1.120$, $P = 0.290$; Table 2). A total of 9,988 vaginally delivered full-term neonates were screened, with 5,581 normal (55.88%) and 4,407 abnormal (44.12%). For 7,390 neonates delivered via cesarean section, 5,812 were normal (78.65%) and 1,578 were abnormal (21.35%). The proportion of eye abnormalities was significantly higher in vaginal deliveries than in cesarean sections ($X^2 = 975.299$, $P = 0.000$, Table 2).

Retinal abnormalities in full-term neonates by delivery method from 2016 to 2023
A comparison of retinal hemorrhage, retinal white spots, and retinal exudates by delivery method is shown in Table 3. Among the 9,988 neonates delivered vaginally, 7,013 (60.25%) had no retinal hemorrhage, while 2,975 (29.79%) had retinal hemorrhage. Among the 7,390 neonates delivered via cesarean section, 7,091 (95.95%) had no retinal hemorrhage, while 299 (4.05%) had retinal hemorrhage. Retinal hemorrhage was more common in neonates born vaginally ($X^2 = 1840.390$, $P = 0.000$, Table 3).
Among the 9,988 neonates delivered vaginally, 9,171 (91.82%) had no retinal white spots, while 817 (8.18%) had retinal white spots. Among the 7,390 neonates delivered via cesarean section, 6,764 (91.53%) had no retinal white spots, while 626 (8.47%) had retinal white spots. There was no significant difference in the probability of retinal white spots between delivery methods ($X^2 = 0.473$, $P = 0.429$, Table 3). Among the 9,988 neonates delivered vaginally, 9,397 (94.08%) had no retinal exudates, while 591 (5.92%) had retinal exudates. Among the 7,390 neonates delivered via cesarean section, 7,036 (95.21%) had no retinal exudates, while 354 (4.79%) had retinal exudates. Retinal exudates were more likely to occur in vaginal deliveries than in cesarean section ($X^2 = 10.488$, $P = 0.001$, Table 3).

Referral cases from 2016 to 2023
This study recorded 8 cases of full-term neonates with significant ocular abnormalities identified during screening, which required referral to higher-level hospitals for further evaluation and treatment due to severe impact on visual development (Table 4). Among them: 1 case of bilateral retinoblastoma (RB): Detected on the second day after birth; following active treatment, the child's right eye had uncorrected visual acuity of 0.8, and the left eye retained light perception at the age of 5.1 case of familial exudative vitreoretinopathy (FEVR) like

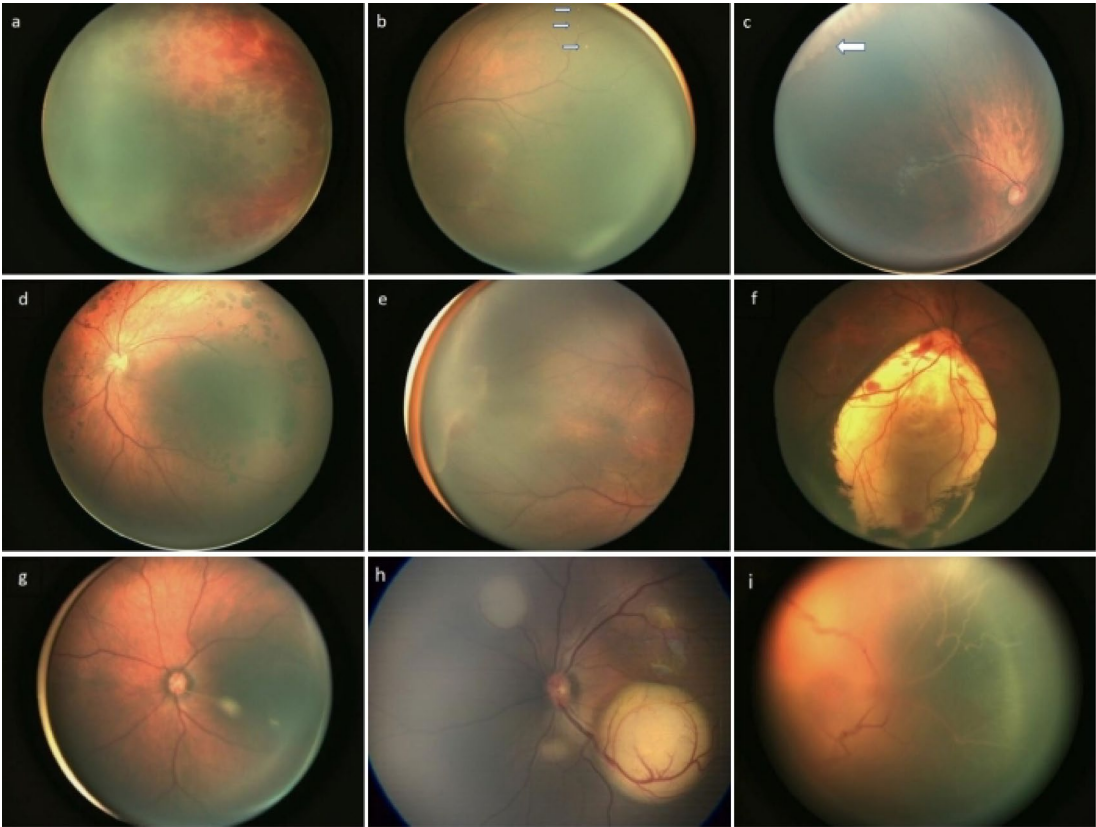


Fig. 1. Abnormalities in Eye Disease Screening among full-term neonatal **a:**Retinal hemorrhage. **b:**Retinal white spots (several white spots in the superotemporal retina, as indicated by the arrows). **c:**Retinal Exudates, (Grayish-white exudative lesions in the temporal peripheral retina, as indicated by the arrows). **d:**Retinal pigment abnormalities,(Congenital Hypertrophy of the Retinal Pigment Epithelium, CHRPE). **e:**Familial exudative vitreoretinopathy (FEVR)-like fundus changes. **f:**Choroidal coloboma (a large coloboma inferior to the optic disc in the right eye, accompanied by minor retinal hemorrhage). **g:**Persistent Hyaloid Artery. **h:**retinoblastoma (RB). **i:**persistent fetal vasculature (PFV).

		Normal	Abnormal	X ²	P Value*
Gender	Male	5984 (65.20)	3194 (34.80)	1.120	0.290
	Female	5409 (65.96)	2791 (34.04)		
Delivery Method	Vaginal Delivery	5581 (55.88)	4407 (44.12)	975.299	0.000
	Cesarean Section	5812 (78.65)	1578 (21.35)		

Table 2. Comparison of screening results by gender and delivery method (n, %). Normal, the neonatal eye disease screening result was normal; Abnormal, the neonatal eye disease screening result was abnormal; Gender, sex of term infants undergoing neonatal eye disease screening; Delivery Method, newborn’s delivery method,.

		Vaginal Delivery	Cesarean Section	X ²	P Value*
Retinal Hemorrhage	No	7013 (60.25)	7091 (95.95)	1840.390	0.000
	Yes	2975 (29.75)	299 (4.05)		
Retinal White Spots	No	9171 (91.82)	6764 (91.53)	0.473	0.429
	Yes	817 (8.18)	626 (8.47)		
Retinal Exudates	No	9397 (94.08)	7036 (95.21)	10.488	0.001
	Yes	591 (5.92)	354 (4.79)		

Table 3. Comparison of retinal abnormalities by delivery method (n, %).

Disease Name	Cases
Retinoblastoma (RB)	1
FEVR-like (Laqua Staging)	
Stage 3 A	1
Corneal Abnormalities	
Microcornea with Lens Opacity	1
Lens Abnormalities	
Bilateral Posterior Lens Capsule Opacity	3
Cone-Shaped Lens with Opacity	1
persistent fetal vasculature (PFV)	1
Total	8

Table 4. Summary of referred cases of diseases affecting visual development (2016–2023).

Category	AAPC(% <i>95</i> CI)	<i>P</i> -Value	Time Period (Years)	APC(% <i>95</i> CI)	<i>P</i> -Value	Time Period (Years)	APC(% <i>96</i> CI)	<i>P</i> -Value
Overall Abnormal Rate	−6.9(−12.1~−1.5)*	0.0211	2016–2023	−6.9(−12.1~−1.5)*	0.0211			
Retinal Hemorrhage	−3.2(−6.4~0.0)*	0.0499	2016–2023	−3.2(−6.4~0.0)*	0.0499			
Retinal White Spots	−15(−29.0~1.6)	0.0677	2016–2023	−15(−29.0~1.6)	0.0677			
Retinal Exudation	−14.3(−33.3~10.0)	0.2255	2016–2020	9.3(−30.9~72.9)	0.5818	2020–2023	−38.1(−70.0~27.9)	0.1260
FEVR-like Lesions	−2.5(−12.6~8.6)	0.5826	2016–2023	−2.5(−12.6~8.6)	0.5826			
Retinal Pigment Abnormalities	−25.4(−42.6~−3.0)*	0.0342	2016–2023	−25.4(−42.6~−3.0)*	0.0342			
Other Conditions	0.8(−7.3~9.60)	0.8271	2016–2023	0.8(−7.3~9.6)	0.8271			

Table 5. Trend analysis of abnormality rates in eye disease screening of Full-Term neonates (2016–2023). Statistically significant changes (*P* < 0.05).Average Annual Percent Change(AAPC). Annual Percent Change, (APC).

lesions: Classified as stage 3 A according to Laqua staging. 1 case of microcornea with lens opacity. Severe lens abnormalities:3 cases with bilateral total opacity of the posterior lens capsule, rendering the fundus unviewable. 1 case with unilateral cone-shaped lens and lens opacity.1 case of persistent fetal vasculature (PFV).

Cytomegalovirus testing results in children with peripheral retinal exudation

From 2016 to 2023, 943 cases of retinal exudation abnormalities were identified. Among them, 174 cases consented to CMV-IgG and CMV-IgM testing. The results showed:145 cases (83.33%) were CMV-IgG(+)/CMV-IgM(-),23 cases (13.22%) were CMV-IgG(+)/CMV-IgM(+),6 cases (3.45%) were CMV-IgG(-)/CMV-IgM(-). This suggests a strong association between cytomegalovirus infection and retinal exudation.

Trend analysis of eye diseases in full-term neonates

Joinpoint regression results from 2016 to 2023 showed the following: The overall abnormal rate in eye disease screenings exhibited a downward trend (AAPC = −6.9%, 95% CI: −12.1% to −1.5%, *P*=0.0211, Table 5; Fig. 2). The incidence of retinal hemorrhage showed a significant downward trend (AAPC = −3.2%, 95% CI: −6.4% to 0.0%, *P*=0.0499, Table 5; Fig. 3).

The incidence of retinal white spots showed a downward trend (AAPC = −15%, 95% CI: −29.0% to 1.6%, *P*=0.0677, Table 5; Fig. 4), but the trend was not statistically significant. The incidence of retinal exudation showed a downward trend (AAPC = −14.3%, 95% CI: −33.3% to 10.0%, *P*=0.2255, Table 5; Fig. 5), with an increasing trend from 2016 to 2020 (APC=9.3%, 95% CI: −30.9% to 72.9%, *P*=0.5818, Table 5; Fig. 5) and a decreasing trend from 2020 to 2023 (APC = −38.1%, 95% CI: −70.0% to 27.9%, *P*=0.1260, Table 5; Fig. 5), neither of which was statistically significant. The incidence of retinal FEVR-like lesions showed a downward trend (AAPC = −2.5%, 95% CI: −12.6% to 8.6%, *P*=0.5826, Table 5; Fig. 6), but the trend was not statistically significant. The incidence of retinal pigment abnormalities showed a significant downward trend (AAPC = −25.4%, 95% CI: −42.8% to −3.0%, *P*=0.0342, Table 5; Fig. 7).

The incidence of other abnormalities showed an upward trend (AAPC=0.8%, 95% CI: −7.3% to 9.6%, *P*=0.8271, Table 5; Fig. 8), but the trend was not statistically significant.

Discussion

In recent years, an increasing number of countries and regions have adopted digital wide-field retinal imaging systems for neonatal eye disease screening, with retinal hemorrhage being the most prevalent ocular condition identified in neonates^{4,11,12}.Early studies have identified vaginal delivery as a significant factor contributing to neonatal retinal hemorrhage, with neonates delivered vaginally being more prone to this condition compared to those delivered via cesarean section, consistent with the findings of this study. In addition to a history of vaginal delivery, other studies have identified low birth weight⁴,prolonged labor⁴,advanced maternal age, and maternal

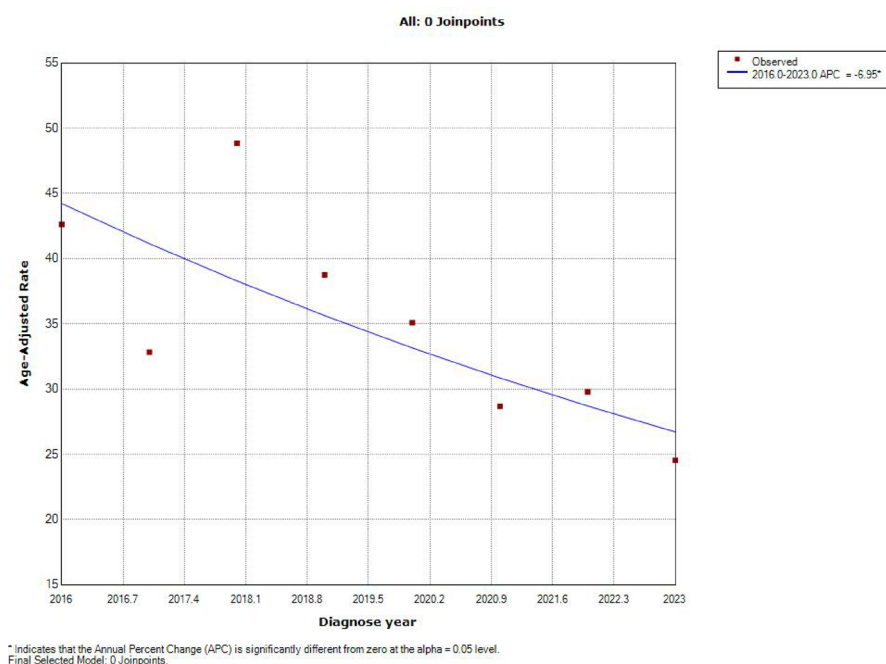


Fig. 2. Trend of Abnormal Findings in Eye Disease Screening of Full-Term Neonates from 2016 to 2023.

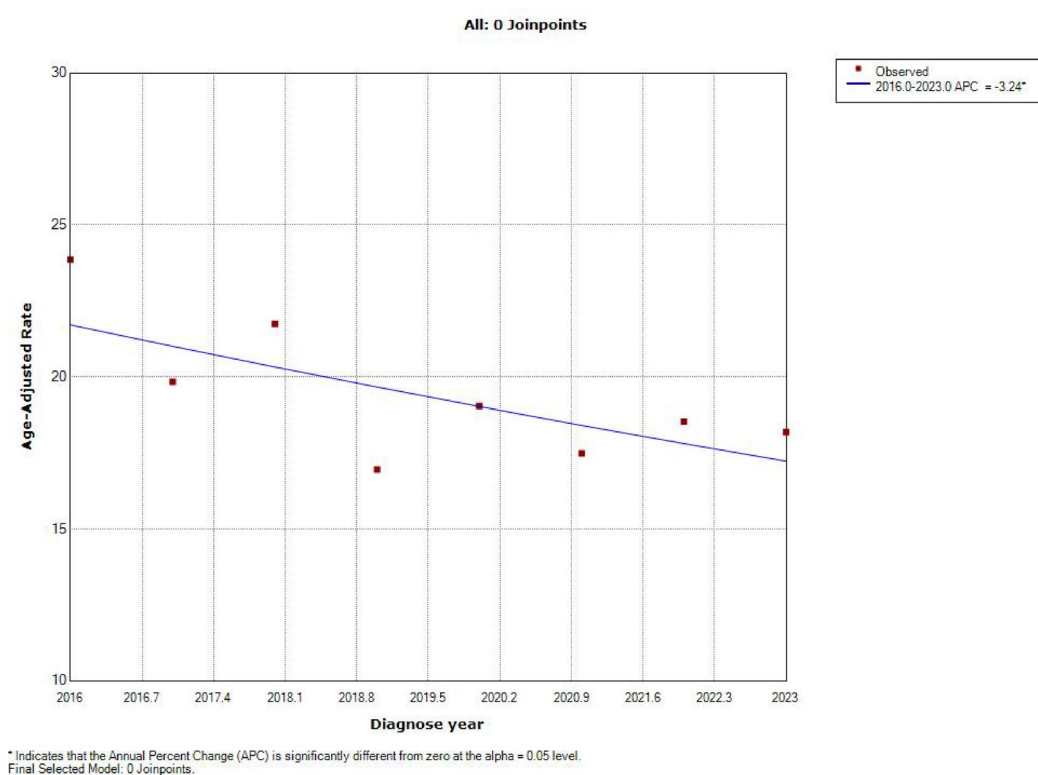


Fig. 3. Trend of Retinal Hemorrhage in Full-Term Neonates from 2016 to 2023.

anemia¹⁴ as risk factors for neonatal retinal hemorrhage. Further research into retinal hemorrhage, such as that conducted by Coste et al. has revealed that underdeveloped retinal vascular walls in neonates provide the pathological basis for retinal hemorrhage¹⁵. During vaginal delivery, compression in the birth canal significantly increases neonatal intracranial pressure, impairs venous return, and causes rupture of the optic disc capillary network, leading to retinal hemorrhage. Most retinal hemorrhages resolve spontaneously¹⁶, typically within 4

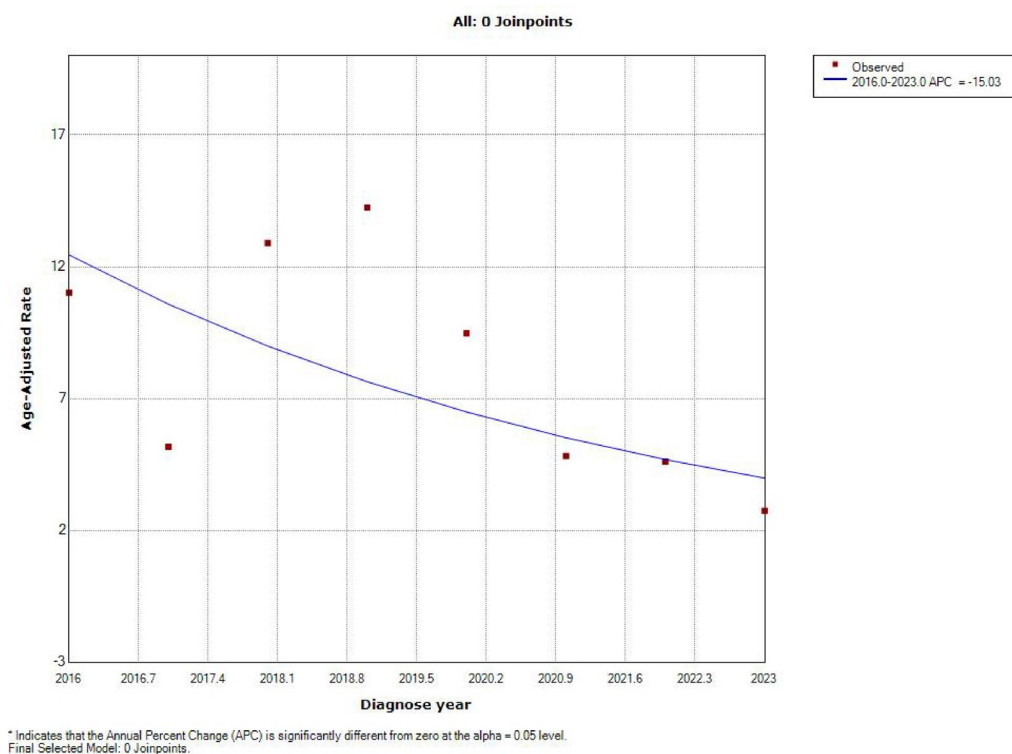


Fig. 4. Trend of Retinal White Spots in Full-Term Neonates from 2016 to 2023.

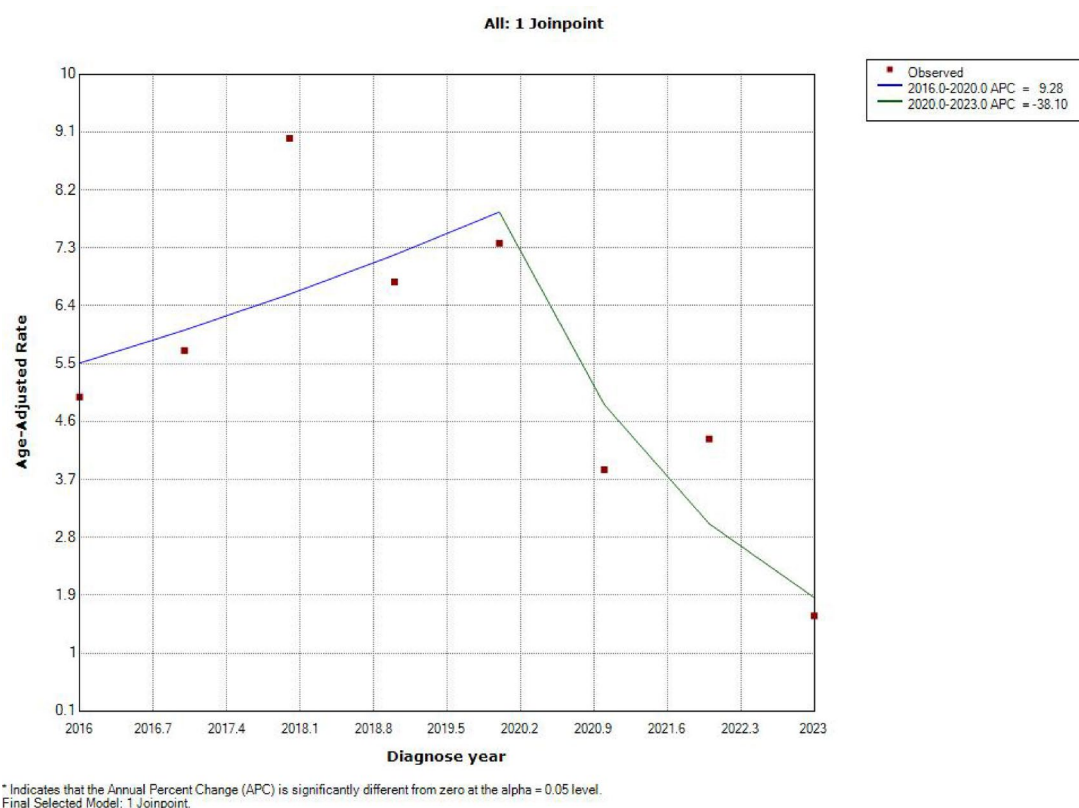


Fig. 5. Trend of Retinal Exudates in Full-Term Neonates from 2016 to 2023.

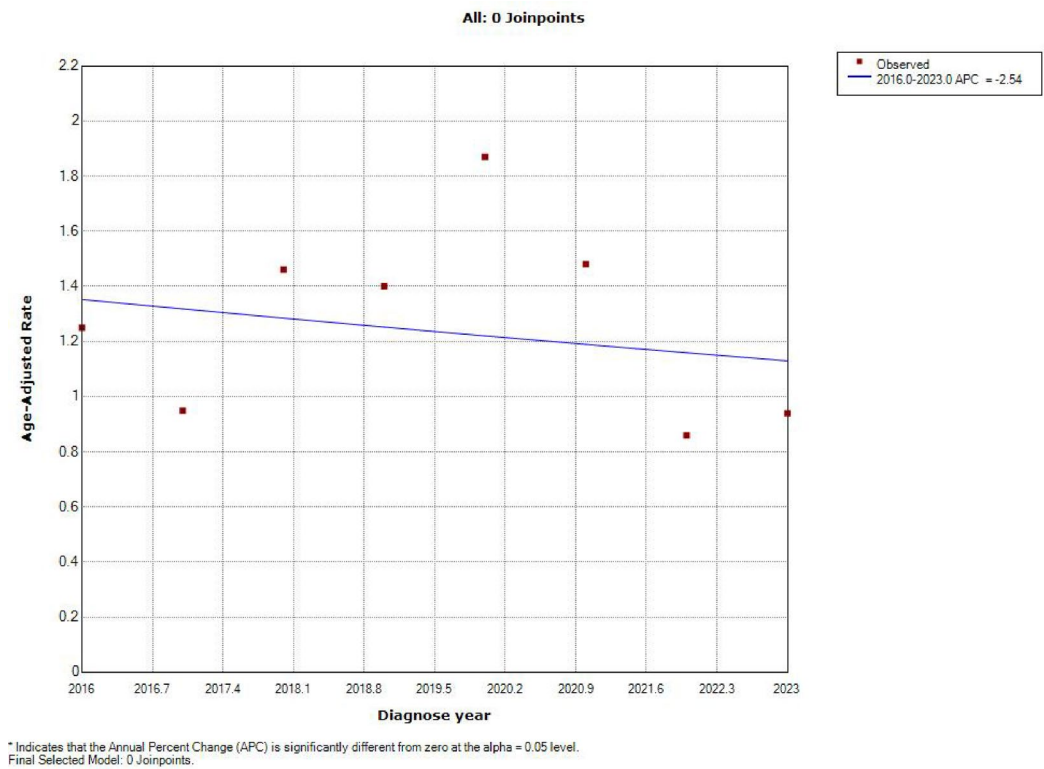


Fig. 6. Trend of Retinal FEVR-like Lesions in Full-Term Neonates from 2016 to 2023.

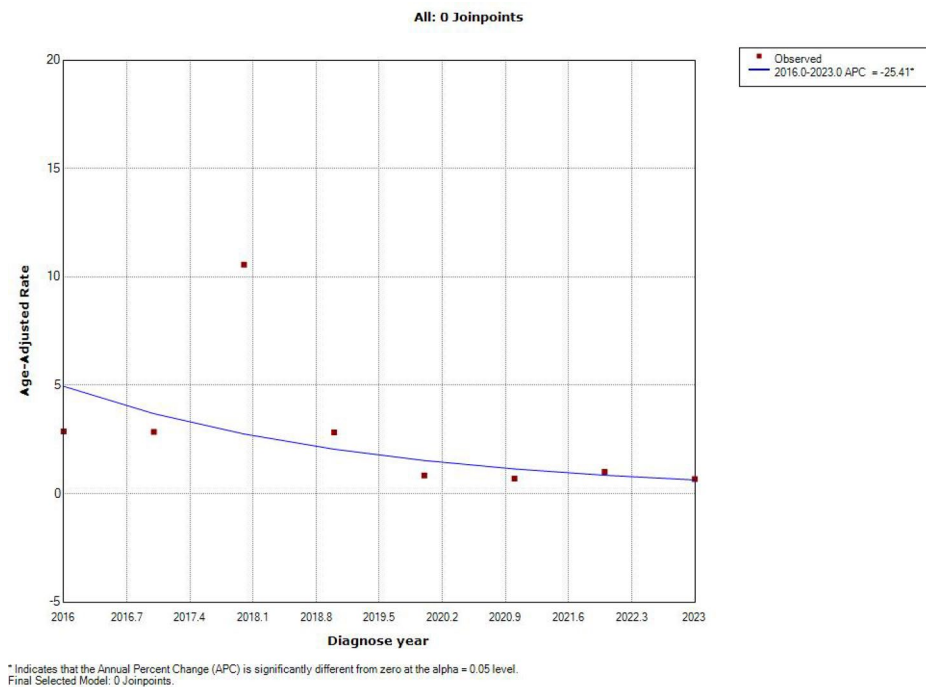


Fig. 7. Trend of Retinal Pigment Abnormalities in Full-Term Neonates from 2016 to 2023.

weeks¹⁴. However, neonates with hemorrhage involving the foveal center may require long-term follow-up to monitor visual development and potential functional impairments¹⁷.

Currently, there is no specific research on the causes and pathogenesis of neonatal retinal white spots. In studies on the etiology of multiple evanescent white dot syndrome (MEWDS) in adults, Jampol et al. suggested

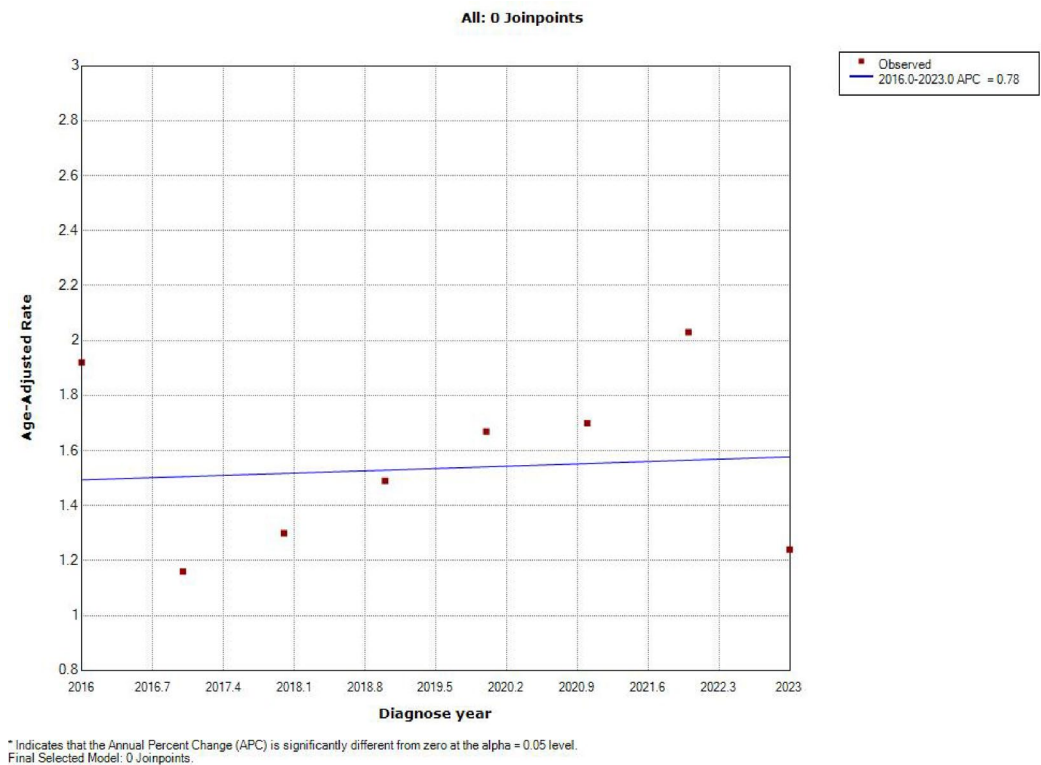


Fig. 8. Trend of Other Retinal Abnormalities in Full-Term Neonates from 2016 to 2023.

that retinal white spots are an immune-related disease associated with genetic susceptibility and infection¹⁸. On the other hand, research by Gross NE et al. proposed that inflammation or circulatory disturbances in the choroidal capillaries could be a potential cause of retinal white spot lesions, which resolve spontaneously after inflammation subsides or perfusion improves¹⁹. In our study, a total of 1,440 cases of retinal white spots were identified, with an incidence rate of 8.29%. During follow-up, some of these lesions resolved spontaneously, while others showed no morphological changes even after 3 to 6 months of observation. Ma Yan et al. found that in most cases, retinal white spot-like, patch-like, or streak-like changes in infants and young children resolved spontaneously within 12 months, suggesting that such changes may be physiological in nature⁷.

In the study of the causes of neonatal retinal exudates, Ma Yan et al. conducted an eye disease screening of 481 full-term newborns and found that factors such as the neonate gender, family history of high myopia, preterm birth, low birth weight, macrosomia, intrauterine fetal distress, umbilical abnormalities, neonatal asphyxia, meconium aspiration syndrome, neonatal anemia, maternal delivery method, abnormal labor process, amniotic fluid contamination, thyroid disease, preeclampsia, and gestational diabetes were not risk factors for retinal white lesions⁷. Ying Xiafen et al. studied 2,612 full-term neonates and found that retinal exudative-like changes in full-term neonates were associated with factors such as gestational diabetes, umbilical cord twisting, and nuchal cord abnormalities²⁰.

Additionally, early research discovered that cytomegalovirus (CMV) could migrate to the retina via leukocytes in peripheral blood²¹. CMV crosses the retinal vascular endothelium through endocytosis, replicates within cells, disrupts the integrity of the blood-retinal barrier, and ultimately involves retinal pigment epithelial cells, forming retinal white or yellow-white lesions. It was observed in our study that vaginal delivery was associated with an increased incidence of retinal exudate-like lesions in full-term newborns. Among 174 cases of retinal exudates from 943 identified cases, 168 (96.55%) had evidence of cytomegalovirus infection, with CMV-IgG(+). This study identified vaginal delivery as a risk factor for retinal exudates, differing from previous research. This discrepancy may be due to the larger sample size in this study, which exposed this factor. The extremely high prevalence of CMV-IgG(+) in cases of retinal exudates further supports a significant association between retinal exudates and cytomegalovirus infection. Previous studies have demonstrated that neonates with immature vascular wall development are susceptible to retinal capillary rupture during vaginal delivery, which compromises the integrity of the blood-retinal barrier (BRB)¹⁵. BRB impairment may further facilitate CMV penetration through the vasculature, enabling viral invasion of retinal pigment epithelial (RPE) cells. This study observed that retinal exudation in full-term neonates delivered vaginally is associated with CMV infection, suggesting that a compromised ocular barrier enhances viral tropism for RPE cells. Neonates with vascular immaturity may thus represent a high-risk population, making CMV screening potentially necessary.

When analyzing the incidence trends of eye diseases in full-term neonates from 2016 to 2023, we found a significant downward trend in both the overall abnormality rate and specifically in retinal pigment abnormalities. This overall improvement may be attributed to advancements in the diagnosis and treatment of obstetric,

gynecologic, and pediatric disorders, which have contributed to a reduction in perinatal complications among newborns²². Similarly, the incidence of retinal hemorrhage also showed a notable decline. We speculate that this reduction may be related to our hospital's adoption of the moderate perineal protection method during delivery in recent years, which alleviates compression of the fetal head in the birth canal.

Although the incidence rates of retinal white spots, retinal exudates, and FEVR-like lesions also exhibited a downward trend, and other abnormalities showed a slight upward trend, none of these changes were statistically significant. This indicates that retinal white spots, retinal exudates, and FEVR-like lesions may have stable incidence rates in full-term neonates.

In summary, retinal hemorrhage remains the most common eye disease in full-term neonates, and we must pay attention to the impact of foveal hemorrhage on visual development. Vaginal delivery is significantly associated with retinal hemorrhage and exudation in full-term neonates, and cytomegalovirus infection may be an important cause of retinal exudation. Fortunately, thanks to advancements in modern medical technology and early neonatal screening, the overall incidence of neonatal eye diseases is declining. This progress encourages further research into quantifying specific interventions, such as early pregnancy screening for ocular malformations or remote monitoring of retinopathy, to improve visual outcomes in neonates.

Data availability

The data used to support the findings of this study are available from the corresponding author/s upon request.

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References

1. Azad, A. D. et al. The utility of universal newborn eye screening: A review. *Ophthalmic Surg. Lasers Imaging Retin.* **52** (S2), S6–S16. <https://doi.org/10.3928/23258160-20211115-02> (2021).
2. Al-Abaiji, H. A. et al. Evaluating the feasibility of a Telescreening program for retinopathy of prematurity (ROP) in Denmark. *J. Personalized Med.* **14** (10), 1020. <https://doi.org/10.3390/jpm14101020> (2024).
3. Nayak, S., Padhi, T. R., Mettla, A. L. & Khanna, R. C. Universal eye screening: perinatal risk factors and ocular abnormalities in 1795 newborns not meeting retinopathy of prematurity criteria. *Eye (London England)*. **38** (11), 2216–2223. <https://doi.org/10.1038/s41433-024-03162-6> (2024).
4. Sitorus, R. S. et al. Retinal abnormalities in universal eye screening of healthy, full-term newborn infants in Jakarta. The incidence and its risk factors: a pilot study. *Int. J. Retina Vitreous*. **7** (1), 67. <https://doi.org/10.1186/s40942-021-00337-1> (2021).
5. Cho, I. H., Kim, M. S., Heo, N. H. & Kim, S. Y. Birth-related retinal hemorrhages: the Soonchunhyang university Cheonan hospital universal newborn eye screening (SUCH-NES) study. *PLoS One*. **16** (11), e0259378. <https://doi.org/10.1371/journal.pone.0259378> (2021).
6. Egge, K., Lyng, G. & Malt, J. M. Effect of instrumental delivery on the frequency and severity of retinal hemorrhages in the newborn. *Acta Obstet. Gynecol. Scand.* **60** (2), 153–155 (1981).
7. Ma, Y. et al. Universal ocular screening of 481 infants using wide-field digital imaging system. *BMC Ophthalmol.* **18** (1), 283. <https://doi.org/10.1186/s12886-018-0943-7> (2018).
8. FUCHS A. White spots of the fundus combined with night blindness and xerosis (Uyemura's syndrome). *American journal of ophthalmology*, 48(1, Part 1), 101–103. (1959).
9. Pendergast, S. D. & Trese, M. T. Familial exudative vitreoretinopathy. Results of surgical management. *Ophthalmology*, 105(6), 1015–1023. (1998). [https://doi.org/10.1016/S0161-6420\(98\)96002-X](https://doi.org/10.1016/S0161-6420(98)96002-X)
10. Kashani, A. H. et al. Diversity of retinal vascular anomalies in patients with Familial exudative vitreoretinopathy. *Ophthalmology* **121** (11), 2220–2227. <https://doi.org/10.1016/j.ophtha.2014.05.029> (2014).
11. Liu, D., Zheng, J. & Lu, Y. Fundus examination of 23,861 newborns by digital imaging in Ningbo. *J. Ophthalmol.* **2021** (6620412). <https://doi.org/10.1155/2021/6620412> (2021).
12. Teow, K. et al. Neonatal eye screening for 203 healthy term new-borns using a wide-field digital retinal imaging system. *BMC Ophthalmol.* **21** (1), 128. <https://doi.org/10.1186/s12886-021-01882-x> (2021).
13. Yang, T. et al. Prevalence, Characteristics, and risk factors of retinal hemorrhage among Full-Term neonates in Southern China. *Int. J. Environ. Res. Public Health*. **19** (21), 13927. <https://doi.org/10.3390/ijerph192113927> (2022).
14. Hemalatha, B. C. et al. Retinopathy of prematurity screening and retinal hemorrhages - Our experience among Indian babies. *Indian J. Ophthalmol.* **69** (8), 2147–2150. https://doi.org/10.4103/ijo.IJO_3616_20 (2021).
15. Coste, V., Paya, C. & Korobelnik, J. F. Retinopathy of prematurity evolution after laser treatment: Retcam findings. *JAMA Ophthalmol.* **133** (1), e141808. <https://doi.org/10.1001/jamaophthalmol.2014.1808> (2015).
16. Simkin, S. K., Misra, S. L., Battin, M., McGhee, C. N. J. & Dai, S. Prospective observational study of universal newborn eye screening in a hospital and community setting in New Zealand. *BMJ Paediatrics open*. **3** (1). <https://doi.org/10.1136/bmjpo-2018-000376> (2019). bmjpo-2018-000376.
17. Wood, E. H. et al. Referable macular Hemorrhage-A clinically meaningful screening target in newborn Infants. Position statement of the association of pediatric retina surgeons. *Ophthalmic Surg. Lasers Imaging Retin.* **53** (1), 3–6. <https://doi.org/10.3928/23258160-20211214-01> (2022).
18. Jampol, L. M. & Becker, K. G. White spot syndromes of the retina: a hypothesis based on the common genetic hypothesis of autoimmune/inflammatory disease. *Am. J. Ophthalmol.* **135** (3), 376–379. [https://doi.org/10.1016/s0002-9394\(02\)02088-3](https://doi.org/10.1016/s0002-9394(02)02088-3) (2003).
19. Gross, N. E. et al. Multiple evanescent white Dot syndrome. *Archives Ophthalmol. (Chicago Ill. : 1960)*. **124** (4), 493–500. <https://doi.org/10.1001/archophth.124.4.493> (2006).
20. Ying, X. F., Tao, J. W., Zhao, S. X. & Chen, Y. Q. Clinical analysis of retinal peripheral exudative changes in full-term neonates. *Modern Practical Medicine* vol. **30**(02):234–236. (2018). Chinese.
21. Thorne, J. E. et al. Effect of cytomegalovirus retinitis on the risk of visual acuity loss among patients with AIDS. *Ophthalmology* **114** (3), 591–598. <https://doi.org/10.1016/j.ophtha.2006.08.008> (2007).
22. Zhao, Q. et al. Birth-related retinal hemorrhages in healthy full-term newborns and their relationship to maternal, obstetric, and neonatal risk factors. *Graefes Archive Clin. Experimental Ophthalmol. = Albrecht Von Graefes Archiv Fur Klinische Und Experimentelle Ophthalmologie*. **253** (7), 1021–1025. <https://doi.org/10.1007/s00417-015-3052-9> (2015).

Author contributions

Qi.C.X. wrote the main manuscript text, prepared Figs. 1, 2, 3, 4, 5, 6, 7 and 8; Table 5. Lei.C. Data analysis and interpretation, prepared Table 1, and 2. Wen.J.W. Data analysis and interpretation, prepared Table 3. Jia.H. Data

analysis and interpretation, prepared Table 4.Xiao.X.L.Data analysis and interpretation, Conceptualization and design.All authors reviewed the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

The study was approved by the Clinical Research Ethics Committee of CiXi Maternity&Child Health Care Hospital (LCKY-L2024-64-02). All participants were screened in accordance with the ethical principles outlined in the Declaration of Helsinki for human research, and written informed consent was obtained from their guardians.

Consent to participate

Not applicable.

Consent to publish

Not applicable.

Additional information

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