Research Square

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Wide-field Digital Retinal Photography in 10,330 Newborns: Prevalence, Risk Factors and Clinical Implications in a Large Chinese Cohort

Chunjuan Wang
Lishui Maternity and Child Health Care Hospital
Lixing Zhou
Wenzhou Medical University
Shuzheng Chen
Lishui Maternity and Child Health Care Hospital
Chunhong Ye
Lishui Maternity and Child Health Care Hospital
Qunda Shan
Lishui Maternity and Child Health Care Hospital
Jiao Liu
66198172@qq.com

Lishui Maternity and Child Health Care Hospital

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Abstract

Objective

To characterize the prevalence and spectrum of fundus abnormalities in a large newborn cohort and to evaluate the association of these abnormalities with perinatal immaturity, a novel composite neonatal morbidity index, and a composite maternal high-risk index.

Design:

Retrospective, single-center cohort study.

Participants:

A total of 10,330 consecutive newborns who underwent universal wide-field digital retinal photography (WFDRP) screening within 72 hours of birth.

Methods

Two novel aggregated indices—the Neonatal Risk Count (summing complications across four domains: baseline risk, respiratory support, feeding/gastrointestinal issues, and hematologic/metabolic issues) and the Maternal High-Risk Count (summing peripartum risk factors)—were constructed. Fundus findings were classified as normal or abnormal. Univariable and multivariable logistic regression were used to assess associations, with multicollinearity assessed by variance inflation factors (VIF).

Main Outcome Measures:

Prevalence of any fundus abnormality; adjusted odds ratios (OR) for the association between abnormal fundus status and key predictors including birth weight, gestational age, Neonatal Risk Count, and Maternal High-Risk Count.

Results

Fundus abnormalities were detected in 3,079 infants (29.8%). Retinal hemorrhage was the most common finding (60.1% of abnormalities). In the final multivariable model, a higher Neonatal Risk Count (OR 1.42 per additional risk, 95% CI 1.23–1.63, $p < 0.001$), lower birth weight (OR 1.00 per gram, $p < 0.001$), and lower gestational age (OR 0.96, 95% CI 0.93–1.00, $p = 0.05$) were independent predictors of abnormal findings. The Maternal High-Risk Count showed a significant inverse association (OR 0.80,

95% CI 0.76–0.84, p < 0.001). Other neonatal clinical domain counts and sex were not significant. All VIFs were < 2.

Conclusions

In this large cohort, nearly one-third of newborns had detectable fundus abnormalities on WFDRP. Cumulative neonatal morbidity burden and perinatal immaturity were significant risk factors, while a higher aggregated maternal risk score was associated with lower odds of abnormality. These findings support the utility of WFDRP in universal newborn screening and highlight the importance of neonatal systemic health in ocular outcomes.

1. Introduction

The early detection of ocular abnormalities during the neonatal period is crucial for the prevention of lifelong visual impairment and for facilitating timely interventions during the critical phase of visual development. Numerous neonatal retinal disorders originate from factors such as perinatal stress, hypoxia, prematurity, metabolic instability, or vascular dysregulation, and may remain asymptomatic without systematic examination. Although the red reflex test is recommended as the universal initial ocular screening tool, it exhibits limited sensitivity in detecting peripheral or subtle posterior-segment abnormalities, including small hemorrhages, vascular anomalies, or pigmentary changes[1,2]. In contrast, wide-field digital retinal photography (WFDRP) allows for high-resolution visualization of the posterior pole and ora serrata, demonstrating excellent feasibility and diagnostic utility in large-scale neonatal screening programs[3–5].

Retinal hemorrhage (RH) is consistently identified as the most prevalent neonatal fundus abnormality, with prevalence estimates ranging from approximately 10% to over 30%, depending upon the timing of imaging, delivery practices, and population characteristics[5–10]. While the majority of RHs resolve spontaneously, dense macular, multilayer, or fovea-involving hemorrhages have been associated with an increased risk of amblyopia, refractive error, and strabismus in later childhood[3,9]. Studies utilizing WFDRP have also revealed a broad spectrum of non-hemorrhagic abnormalities, including immature vascularization, retinal white-spot lesions, retinal pigment anomalies, optic disc variations, congenital cataract, persistent pupillary membrane (PPM), and vascular disorders such as familial exudative vitreoretinopathy (FEVR), many of which may be overlooked during conventional examinations[3,4,10–12].

Perinatal and maternal factors are critically influential in the development of neonatal retinal findings. Vaginal delivery, particularly spontaneous vertex delivery, is significantly associated with RH due to mechanical compression and alterations in venous pressure during labor.[6,13]. Lower gestational age and low birth weight are correlated with delayed retinal vascular maturation, rendering the neonate more susceptible to hemorrhage or persistent vascular anomalies[14,15]. Neonatal systemic instability, including conditions such as respiratory distress, sepsis, metabolic derangements, and hypoxia, can disrupt retinal

vascular autoregulation, thereby increasing the likelihood of fundus abnormalities[16–18]. Furthermore, maternal complications, including hypertensive disorders, gestational diabetes, and placental insufficiency, can impair fetal oxygenation and angiogenic signaling. These disruptions may alter retinal and choroidal vascular development, thereby elevating the risk of adverse neonatal retinal outcomes[19–21].

Despite the increasing implementation of WFDRP[22], there remains a paucity of large-scale studies that integrate both perinatal characteristics and maternal risk factors. The majority of existing research in China and other regions primarily focuses on descriptive epidemiology, with sample sizes ranging from several hundred to several thousand, and often lacks comprehensive multivariable risk modeling[3,4,12]. Consequently, the relative contributions of perinatal immaturity, neonatal morbidity burden, and maternal high-risk status to various types of fundus abnormalities are not well characterized. To address these gaps, we conducted a retrospective study involving 10,330 newborns who underwent universal WFDRP screening at our center. Our objectives were to: (1) characterize the prevalence and spectrum of neonatal fundus abnormalities; (2) evaluate the associations between abnormal fundus findings and key perinatal variables (such as gestational age, birth weight, and mode of delivery), neonatal morbidity burden (Neonatal Risk Count), and maternal risk burden (Maternal High-Risk Count); and (3) develop a predictive model for abnormal fundus outcomes and assess its stability and reliability.

These findings aim to support evidence-based risk stratification and inform neonatal ocular screening pathways.

2. Methods

2.1 Study design and participants

We conducted a retrospective review of all liveborn neonates at Maternal and Child Health Hospital in Lishui City between March 2019 and September 2025 who underwent WFDRP within 72 hours after birth. Exclusion criteria included poor-quality imaging, missing perinatal data, or major congenital ocular malformations diagnosed prenatally.

2.2 Imaging procedure

After topical mydriasis, wide-field retinal images were acquired (RetCam III), covering posterior pole and peripheral fields (superior, inferior, nasal, temporal). Images were reviewed independently by two pediatric ophthalmologists; discrepancies resolved by consensus.

2.3 Data collection

Perinatal variables collected included gestational age (weeks), birth weight (grams), delivery mode (vaginal, cesarean, assisted delivery), and sex. Neonatal clinical variables encompassed complications such as respiratory distress, gastrointestinal issues, metabolic and hematologic disturbances, sepsis, asphyxia, need for resuscitation, and NICU admission.

To facilitate analysis, we developed aggregated indices by summing predefined risk factors. The Neonatal Risk Count was calculated by summing selected neonatal complications categorized into four domains: (1) Neonatal Risk, which includes premature birth, very low birth weight, low birth weight, and small for gestational age (SGA); (2) Respiratory Support, encompassing history of oxygen therapy, continuous positive airway pressure (CPAP), noninvasive ventilation, and invasive mechanical ventilation; (3) Feeding/Gastrointestinal Issues, which comprises gastric lavage, food allergies, necrotizing enterocolitis (NEC), gastroesophageal reflux disease (GERD), and transient neutropenia; and (4) Hematologic/Metabolic Issues, including hypoglycemia, hypocalcemia, hypomagnesemia, hypokalemia, anemia, polycythemia, and transient coagulopathy. Similarly, the Maternal High-Risk Count was determined by summing maternal peripartum risk factors such as preeclampsia, gestational diabetes, maternal anemia, chorioamnionitis, uterine scar, endometriosis, puerperal infection, cervicitis, uterine fibroids, placental abruption, intrahepatic cholestasis, liver dysfunction, Group B Streptococcus (GBS) carrier status, oligohydramnios, postpartum hypothyroidism, immediate hemorrhage, paddle-shaped placenta, and cord torsion. These aggregated counts were used in subsequent statistical analyses to evaluate their association with neonatal retinal outcomes.

2.4 Statistical analysis

Continuous variables summarized as mean ± SD or median (IQR), categorical as counts (percent). Univariable and multivariable logistic regression models were built to estimate odds ratios (OR) and 95% confidence intervals (CI) for predictors of abnormal fundus status. Multicollinearity assessed via variance inflation factors (VIF); VIF < 5 considered acceptable. Trend/dose–response between all the risk count and abnormal fundus prevalence evaluated visually via scatter+jitter and by regression; stratified analyses by delivery mode performed. Statistical significance defined as two-sided $p < 0.05$. All analyses performed in R 4.4.1.

3. Results

3.1 Cohort characteristics and fundus findings

A total of 10,330 neonates fulfilled the inclusion criteria, of which 5,043 (48.82%) were male. The mean gestational age was 38.58 ± 1.67 weeks, the mean birth weight was 3,241.71 ± 526.72 g, and the mean maternal age was 29.49 ± 4.86 years (Table 1). Fundus imaging revealed abnormal retinal findings in 3,079 infants (29.81%), while 7,251 infants (70.19%) exhibited normal retinal appearances.

Table 1
Summary of Basic Information of the Participants

Parameter	Values
Gender (%)	
Male	5043 (48.82%)
Female	5287 (51.18%)
Gestation Age (weeks)	38.58 ± 1.67
Birth Weight (g)	3241.71 ± 526.72
Maternal Age (years)	29.49 ± 4.86
Funds Image (%)	
Normal	7251 (70.19%)
Abnormal	3079 (29.81%)
Distribution of Abnormal Fundus Disease Count (%)	
1 category	2798 (90.87%)
2 categories	258 (8.38%)
3 categories	21 (0.68%)
4 categories	2 (0.06%)

3.2 Spectrum and frequency of abnormalities

Among those with abnormal findings, the majority (2,798; 90.87%) presented with a single category of abnormality; 258 infants (8.38%) exhibited two categories, 21 infants (0.68%) had three categories, and 2 infants (0.06%) had four categories of abnormalities (Table 1). Retinal hemorrhage was the most prevalent lesion, identified in 1,850 infants (60.08% of those with abnormal findings) (Table 2). Other frequent abnormalities included punctate pigmentation (384 infants; 12.47%), peripheral retinal white spots (324 infants; 10.52%), immature retina (277 infants; 9.00%), and pigment abnormality (132 infants; 4.29%). Less common but clinically significant findings comprised punctate choroidal defect (101 infants; 3.28%), vascular underdevelopment (61 infants; 1.98%), FEVR-like patterns (56 infants; 1.82%), unclear optic disc (52 infants; 1.69%), congenital cataract (29 infants; 0.94%), and retinopathy of prematurity (ROP) (19 infants; 0.62%) (Table 2 and Fig. 4).

Table 2
Prevalence of Abnormal Fundus Findings Among the Participants

Disease	Count	Percent (%)
Retinal Hemorrhage	1850	60.08
Punctate Pigmentation	384	12.47
Peripheral Retinal White Spots	324	10.52
Immature Retina	277	9.00
Pigment Abnormality	132	4.29
Punctate Choroidal Defect	101	3.28
Vascular Underdevelopment	61	1.98
FEVR	56	1.82
Unclear Optic Disc	52	1.69
Congenital Cataract	29	0.94
Vascular Dysplasia	23	0.75
Persistent Pupillary Membrane	21	0.68
ROP	19	0.62
Albinism	14	0.45
PHPV	12	0.39
Vascular Dilatation	12	0.39
Vitreous Opacity	8	0.26
Iris Posterior Synechia	5	0.16
Vascular Tortuosity	4	0.13
Bilateral Punctate Lesions	1	0.03

3.3 Group comparisons

Infants presenting with abnormal fundus findings exhibited significantly lower gestational ages (38.33 ± 2.04 weeks compared to 38.68 ± 1.47 weeks; $t = 8.69$; $P < 0.001$) and reduced birth weights (3,148.30 ± 531.56 g versus 3,281.38 ± 519.63 g; $t = 11.72$; $P < 0.001$) relative to those with normal fundus findings, as detailed in Table 3. Although maternal age showed a marginal statistical difference ($P < 0.001$), the mode of delivery demonstrated significant variation ($\chi^2 = 568.53$; $P < 0.001$). Specifically, vaginal delivery was predominant among the group with abnormal findings (69.54% compared to 44.26%), whereas

cesarean delivery was more prevalent in the group with normal findings (54.12% compared to 28.65%), as illustrated in Table 4.

Table 3
Comparison of Gestation Age, Birth Weight, and Maternal Age Between Infants with Normal and Abnormal Fundus Findings

Variable	Mean ± SD (95%CI)	t	P
Gestation Age		8.69	< 0.001
Normal	38.68 ± 1.47 (38.65–38.71)		
Abnormal	38.33 ± 2.04 (38.26–38.40)		
Birth Weight		11.72	< 0.001
Normal	3281.38 ± 519.63 (3269.41–3293.33)		
Abnormal	3148.30 ± 531.56 (3129.51–3167.08)		
Maternal Age		−1.72	< 0.001
Normal	29.44 ± 4.85 (29.33–29.55)		
Abnormal	29.62 ± 4.89 (29.45–29.79)		

Table 4
Comparison of Delivery Method Between Infants With Normal and Abnormal Fundus Findings

Delivery Method	Count (%)	χ^2	P
Assisted		568.53	< 0.001
Normal	118 (1.63)		
Abnormal	56 (1.82)		
C Section			
Normal	3924 (54.12)		
Abnormal	882 (28.65)		
Vaginal			
Normal	3209 (44.26)		
Abnormal	2141 (69.54)		

3.4 Regression Results and Visualization

Both simple and multivariable logistic regression analyses produced consistent estimates, as detailed in Table S1. In the final multivariable model (Table 5), the Neonatal Risk Count emerged as the most robust

independent predictor of abnormal fundus findings, with an odds ratio (OR) of 1.42 (95% confidence interval [CI] 1.23–1.63, p < 0.001). Conversely, the Maternal High-Risk Count exhibited a significant inverse relationship (OR 0.80, 95% CI 0.76–0.84, p < 0.001). Birth weight maintained significance, albeit with a minimal per-gram effect (OR 1.00, p < 0.001), while gestational age demonstrated borderline significance (OR 0.96, 95% CI 0.93–1.00, p = 0.05). Other neonatal clinical factors and sex were not significant predictors.

Table 5
Multiple Logistic Regression Model of Studied Variables

Variable	OR (95%CI)	P
(Intercept)	6.89 (1.88–25.28)	< 0.001
Birth Weight	1.00 (1.00–1.00)	< 0.001
Gestation Age	0.96 (0.93–1.00)	0.05
Neonatal Risk Count	1.42 (1.23–1.63)	< 0.001
Maternal High-Risk Count	0.80 (0.76–0.84)	< 0.001
Hematologic Metabolic Count	0.95 (0.82–1.09)	0.45
Respiratory Support Count	0.93 (0.82–1.05)	0.26
Feeding GI Issues Count	1.05 (0.88–1.24)	0.58
Gender	1.06 (0.97–1.16)	0.17
Note: AUC = 0.6 for multiple logistic regression.		

A forest plot was constructed to depict all regression coefficients and their 95% CIs, thereby illustrating the relative contribution of each variable (Fig. 2). Additionally, the scatter-jitter plots in the figure reveal distinct dose-response patterns: the prevalence of abnormal fundus findings shows a monotonically increasing trend with higher Neonatal Risk Counts. In contrast, a slight negative correlation trend is observed for Maternal High Risk Counts, indicating a modest decrease in the prevalence of abnormal fundus findings as the risk count increases (Fig. 3). These visual patterns were entirely consistent with the regression estimates. Model diagnostics confirmed good stability.

The model diagnostics demonstrated satisfactory stability, as evidenced by all variance inflation factors (VIFs) being less than 2,, as detailed in Table S2, indicating an absence of problematic multicollinearity. Sensitivity analyses employing penalized logistic regression for rare outcomes yielded results that were directionally consistent with the primary model, thereby reinforcing its robustness.

4. Discussion

In this large cohort of 10,330 neonates undergoing universal wide-field digital retinal photography (WFDRP), nearly one-third (29.81%) exhibited abnormal fundus findings. This prevalence is comparable to that reported in large-scale neonatal screening programs from China, India, Malaysia, and New Zealand, where abnormal posterior segment findings ranged from approximately 20% to 30%[5,12,23,24]. The high detection rate underscores that a substantial proportion of neonatal fundus abnormalities would likely remain unrecognized without systematic imaging-based screening.

The spectrum of abnormalities observed in this study was dominated by retinal hemorrhage (RH), accounting for approximately 60% of all abnormal findings, followed by punctate pigmentation, peripheral retinal white spots, immature retina, and pigment abnormalities. This distribution closely mirrors prior WFDRP-based studies, in which RH consistently emerged as the most prevalent lesion among term and near-term infants[5,9,10,12]. RH in neonates is widely regarded as a manifestation of delivery-related mechanical stress, perinatal hypoxia, and abrupt changes in intracranial and ocular venous pressure. Ji et al. demonstrated that ocular compression during delivery—particularly with vacuum or forceps assistance—plays a major etiologic role in the development of RH[17]. Although the majority of RH cases are intraretinal and self-limited, resolving spontaneously within weeks, their high prevalence reinforces the value of early documentation and follow-up to distinguish benign transient findings from lesions requiring surveillance[9,25,26].

Beyond RH, the detection of vascular developmental variants, FEVR-like patterns, punctate choroidal defects, and rare congenital anomalies highlights the broader clinical value of universal screening. Large neonatal fundus-screening initiatives have consistently shown that WFDRP enables early identification of uncommon but potentially vision-threatening conditions, facilitating timely referral and intervention[3,6]. The presence of multiple categories of abnormalities in a subset of infants in our cohort further suggests that neonatal fundus pathology often reflects a cumulative burden of perinatal stress rather than isolated ocular events.

Group comparisons revealed that infants with abnormal fundus findings had significantly lower gestational ages and birth weights than those with normal findings. These observations are consistent with extensive prior literature demonstrating that both gestational maturity and fetal growth are critical determinants of retinal vascular development[3,6,10,12]. Tang et al., in a multicenter study involving nearly 200,000 newborns, reported a clear gradient effect of birth weight on the prevalence of retinal abnormalities[6]. Current evidence links low birth weight and intrauterine growth restriction (IUGR) with abnormal retinal vascular development[27]. Studies have linked these conditions with long-term alterations in retinal vessel morphology, indicating that IUGR may disrupt normal vascular programming[28]. This disruption could predispose the retina to hemodynamic instability, potentially explaining a higher susceptibility to conditions such as retinal hemorrhage and optic disc anomalies.

The biological plausibility of these associations is well supported. Retinal and choroidal vascularization continues through late gestation and into the early postnatal period, rendering the immature vasculature

particularly vulnerable to fluctuations in oxygenation and perfusion[29]. Prior studies have shown that lower birth weight and younger gestational age are associated with abnormal retinal vessel morphology in moderately preterm infants[30], delayed choroidal thickening[31], and long-term alterations in macular vessel density and foveal avascular zone characteristics[32]. Collectively, these findings support the inclusion of birth weight and gestational age as key parameters in neonatal ocular risk stratification.

Delivery mode differed markedly between infants with and without abnormal fundus findings, with vaginal delivery being substantially more common in the abnormal group, while cesarean delivery predominated among infants with normal fundus appearances. This pattern is concordant with previous reports linking vaginal delivery to a higher incidence of RH, likely due to increased mechanical compression of the globe and transient elevations in venous pressure during labor and delivery[9,17]. In contrast, cesarean delivery may mitigate these mechanical forces, thereby reducing the risk of birth-related retinal hemorrhage. Although delivery mode was not included as an independent variable in the final regression model, its strong univariate association highlights the importance of perinatal mechanical factors in shaping neonatal fundus outcomes.

Multivariable logistic regression analysis further clarified the relative contributions of perinatal and systemic factors. Neonatal systemic burden, quantified by the Neonatal Risk Count, emerged as the strongest independent predictor of abnormal fundus findings. This result aligns with prior evidence linking systemic neonatal illness—including sepsis, asphyxia, respiratory failure, and metabolic instability—to retinal vascular injury through inflammatory pathways, impaired autoregulation, and altered perfusion[33–35]. Notably, neonatal sepsis has been proposed as an oxygen-independent contributor to retinopathy of prematurity in both cohort studies and narrative reviews[33]. The clear dose–response relationship observed between increasing Neonatal Risk Count and abnormal fundus prevalence in our cohort further supports a cumulative-risk model, in which systemic illness amplifies retinal vulnerability.

In contrast, the Maternal High-Risk Count demonstrated a significant inverse association with abnormal fundus findings. Although this observation may appear counterintuitive, it is consistent with a growing body of literature suggesting that certain maternal complications do not uniformly increase neonatal ocular risk. In very-low-birth-weight infants, maternal preeclampsia has been associated with a reduced risk of ROP (adjusted OR = 0.65)[36], with similar protective trends reported in other cohorts[37]. Conversely, in full-term infants, pregnancy-related hypertension has been linked to increased RH and other fundus abnormalities[38], underscoring the heterogeneity of maternal risk effects.

In our cohort, the aggregated maternal high-risk variable likely encompassed diverse conditions with differing pathophysiologic implications. The observed protective association may reflect intensified prenatal surveillance, planned delivery strategies (including higher rates of cesarean section), and optimized neonatal care among high-risk pregnancies. Such measures may reduce fetal hypoxia, hemodynamic instability, and birth trauma—key contributors to RH and retinal vascular abnormalities. These findings suggest that aggregated maternal risk scores may obscure condition-specific effects and

highlight the need for future studies to disaggregate maternal risk subtypes and incorporate perinatal management variables when modeling neonatal retinal outcomes.

Other neonatal clinical factors, including hematologic/metabolic abnormalities, respiratory support frequency, feeding or gastrointestinal issues, and sex, were not independently associated with abnormal fundus findings after adjustment. The similarity between simple and multivariable regression estimates, together with low variance inflation factors, indicates minimal confounding and limited multicollinearity among predictors, supporting the stability of the model. Sensitivity analyses using penalized regression approaches for rare outcomes yielded directionally consistent results, further reinforcing the robustness of the observed associations.

Although the discriminative performance of the multivariable model was modest (AUC = 0.60), this finding should be interpreted in the context of the study objective. The primary aim was etiologic inference and population-level risk stratification rather than individual-level prediction. In neonatal screening research, particularly when outcomes are heterogeneous and largely transient, moderate AUC values are common and do not preclude clinical relevance[39,40]. Importantly, the model demonstrated internally consistent effect estimates, biologically plausible directions of association, and clear dose–response patterns for key predictors, such as Neonatal Risk Count and Maternal High-Risk Count (Figs. 1–2). These features suggest that the model captures meaningful population-level relationships even if its standalone predictive accuracy is limited. Future studies incorporating longitudinal outcomes and additional perinatal variables may further improve predictive performance.

From a clinical and public health perspective, these findings provide additional support for universal WFDRP screening in neonates. Prior programs in India (KIDROP) and China have demonstrated that systematic imaging improves early detection, reduces missed diagnoses, and facilitates longitudinal monitoring of retinal health[10,20,41]. Clare O et al. emphasized that many neonatal and infantile ocular conditions are reversible if identified early, whereas delayed diagnosis may result in permanent visual impairment[42]. The present results indicate that even term infants without overt clinical risk factors may harbor fundus abnormalities linked to subtle perinatal and systemic stressors, arguing against overly restrictive, risk-based screening strategies in high-volume birth settings.

The strengths of this study include its large sample size, the use of validated WFDRP technology, comprehensive characterization of neonatal and maternal risk factors, and consistent findings across multiple analytic approaches. Nevertheless, several limitations warrant consideration. The single-center design may limit generalizability, and the absence of long-term follow-up precludes confirmation of lesion resolution or long-term visual sequelae. Important obstetric variables, such as labor duration and detailed delivery mechanics, were unavailable, and inter-operator variability in image acquisition may have introduced measurement heterogeneity. In addition, the moderate discriminative performance of the regression model likely reflects the heterogeneous and largely transient nature of neonatal fundus findings rather than inadequate modeling. Future multicenter, longitudinal studies incorporating detailed

perinatal management data, serial imaging, and long-term visual outcomes are needed to better delineate the natural history of neonatal fundus abnormalities and to refine screening strategies.

5. Conclusion

Our findings confirm that neonatal posterior segment abnormalities are common and significantly influenced by birth weight, gestational age, neonatal systemic morbidity, and perinatal conditions. Universal WFDRP screening is feasible, safe, and clinically valuable for early identification of both transient and potentially vision-threatening lesions. These results support broader adoption of neonatal eye screening programs, particularly in regions with higher risk profiles and limited access to pediatric ophthalmology.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Lishui Maternity and Child Health Care Hospital (NO.2020030), and it is in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. For participants under 16 years of age, parental or legal guardian consent was additionally secured prior to enrollment.

Consent for publication

Not applicable.

Availability of data and materials

The datasets are not publicly available due to patient privacy concerns but can be provided by the corresponding author upon reasonable request and approval from the institutional ethics committee.

Competing interests

The authors declare no competing interests.

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Authors' contributions

Chunjuan Wang contributed to data collection and assisted in revising the manuscript. Lixing Zhou drafted the manuscript, led the writing of the article, and participated in data interpretation as well as

table and figure preparation. Chunhong Ye and Shuzheng Chen was involved in the entire process of data collection and quality management. Qunda Shan and Jiao Liu served as corresponding authors. Chunjuan Wang and Lixing Zhou contributed equally to this work. All authors reviewed and approved the final manuscript and agree to be personally accountable for their own contributions and to ensure the integrity of the work.

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used DeepSeek (an AI language model by DeepSeek Company) for language polishing, grammar checking, and improving the clarity and fluency of the text. After using this tool, the authors thoroughly reviewed and edited the content as needed and take full responsibility for the content of the published article.

References

1. Subhi Y, Schmidt DC, Al-Bakri M, Bach-Holm D, Kessel L. Diagnostic Test Accuracy of the Red Reflex Test for Ocular Pathology in Infants: A Meta-analysis. JAMA Ophthalmol. 2021;139(1):33–40. 10.1001/jamaophthalmol.2020.4854.
2. da Cunha LP, Cavalcante Costa MAA, de Miranda HA, et al. Comparison between wide-field digital imaging system and the red reflex test for universal newborn eye screening in Brazil. Acta Ophthalmol (Copenh). 2021;99(7):e1198–205. 10.1111/aos.14759.
3. Goyal P, Padhi TR, Das T, et al. Outcome of universal newborn eye screening with wide-field digital retinal image acquisition system: a pilot study. Eye Lond Engl. 2018;32(1):67–73. 10.1038/eye.2017.129.
4. Ma Y, Deng G, Ma J, Liu J, Li S, Lu H. Universal ocular screening of 481 infants using wide-field digital imaging system. BMC Ophthalmol. 2018;18(1):283. 10.1186/s12886-018-0943-7.
5. Teow Kheng Leong K, Abu Kassim SNA, Sidhu JK, et al. Neonatal eye screening for 203 healthy term new-borns using a wide-field digital retinal imaging system. BMC Ophthalmol. 2021;21(1):128. 10.1186/s12886-021-01882-x.
6. Tang H, Li N, Li Z, et al. Fundus examination of 199 851 newborns by digital imaging in China: a multicentre cross-sectional study. Br J Ophthalmol. 2018;102(12):1742–6. 10.1136/bjophthalmol-2018-312366.
7. Fei P, Liu Z, He L, et al. Early detection of ocular abnormalities in a Chinese multicentre neonatal eye screening programme-1-year result. Acta Ophthalmol (Copenh). 2021;99(3):e415–22. 10.1111/aos.14586.

8. Sitorus RS, Pambudy IM, Rohsiswatmo R, Barliana JD, Yulia DE, Widyahening IS. 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 Vitr. 2021;7(1):67. 10.1186/s40942-021-00337-1.
9. Callaway NF, Ludwig CA, Blumenkranz MS, Jones JM, Fredrick DR, Moshfeghi DM. Retinal and Optic Nerve Hemorrhages in the Newborn Infant: One-Year Results of the Newborn Eye Screen Test Study. Ophthalmology. 2016;123(5):1043–52. 10.1016/j.ophtha.2016.01.004.
10. Yang T, Hu R, Chen J, et al. Prevalence, Characteristics, and Risk Factors of Retinal Hemorrhage among Full-Term Neonates in Southern China. Int J Environ Res Public Health. 2022;19(21):13927. 10.3390/ijerph192113927.
11. Yaoyao S, Kaixin D, Xiaoxin L, et al. Analysis of non-retinopathy of prematurity (ROP)-related fundus hemorrhage in preterm infants in China. Front Pediatr. 2022;10:985268. 10.3389/fped.2022.985268.
12. Liu D, Zheng J, Lu Y. Fundus Examination of 23,861 Newborns by Digital Imaging in Ningbo. J Ophthalmol. 2021;2021:6620412. 10.1155/2021/6620412.
13. Baptista FI, Ambrósio AF. Tracing the influence of prenatal risk factors on the offspring retina: Focus on development and putative long-term consequences. Eur J Clin Invest. 2024;54(10):e14266. 10.1111/eci.14266.
14. Ungersma R. Practicing Ophthalmologists Curriculum Pediatric Ophthalmology/Strabismus.
15. Modrzejewska M, Kulik U, Lubiński W. Iris rubeosis, severe respiratory failure and retinopathy of prematurity–case report. Ginekol Pol. 2014;85(1):70–3. 10.17772/gp/1695.
16. Schenker JG, Gombos GM. Retinal hemorrhage in the newborn. Obstet Gynecol. 1966;27(4):521–4. 10.1097/00006250-196604000-00014.
17. Ji MH, Ludwig CA, Callaway NF, Moshfeghi DM. Birth-related subconjunctival and retinal haemorrhages in the Newborn Eye Screening Test (NEST) Cohort. Eye Lond Engl. 2019;33(11):1819. 10.1038/s41433-019-0523-y.
18. Besio R, Caballero C, Meerhoff E, Schwarcz R. Neonatal retinal hemorrhages and influence of perinatal factors. Am J Ophthalmol. 1979;87(1):74–6. 10.1016/0002-9394(79)90194-6.
19. Athikarisamy SE, Lam GC, Cooper MN, Strunk T. Retinopathy of prematurity and placental histopathology findings: A retrospective cohort study. Front Pediatr. 2023;11:1099614. 10.3389/fped.2023.1099614.
20. Opara CN, Akintorin M, Byrd A, Cirignani N, Akintorin S, Soyemi K. Maternal diabetes mellitus as an independent risk factor for clinically significant retinopathy of prematurity severity in neonates less than 1500g. Lewin AS, ed. *PLOS ONE*. 2020;15(8):e0236639. 10.1371/journal.pone.0236639
21. Villamor-Martinez E, Cavallaro G, Raffaeli G, et al. Chorioamnionitis as a risk factor for retinopathy of prematurity: An updated systematic review and meta-analysis. PLoS ONE. 2018;13(10):e0205838. 10.1371/journal.pone.0205838.
22. Athikarisamy SE, Lam GC, Ross S, et al. Comparison of wide field imaging by nurses with indirect ophthalmoscopy by ophthalmologists for retinopathy of prematurity: a diagnostic accuracy study.

BMJ Open. 2020;10(8):e036483. 10.1136/bmjopen-2019-036483.

23. Padhi TR, Bhunia S, Das T, et al. Outcome of real-time telescreening for retinopathy of prematurity using videoconferencing in a community setting in Eastern India. Indian J Ophthalmol. 2024;72(5):697–703. 10.4103/IJO.IJO_2024_23.
24. Yehiam SZ, Simkin SK, Al-Taie R, Wong M, Battin M, Dai S. Incomplete peripheral retinal vascularisation in retinopathy of prematurity: is it the consequence of changing oxygen saturation? Front Pediatr. 2023;11:1203068. 10.3389/fped.2023.1203068.
25. Laghmari M, Skiker H, Handor H, et al. [Birth-related retinal hemorrhages in the newborn: incidence and relationship with maternal, obstetric and neonatal factors. Prospective study of 2,031 cases]. J Fr Ophtalmol. 2014;37(4):313–9. 10.1016/j.jfo.2013.06.005.
26. Hughes LA, May K, Talbot JF, Parsons MA. Incidence, distribution, and duration of birth-related retinal hemorrhages: a prospective study. J AAPOS Off Publ Am Assoc Pediatr Ophthalmol Strabismus. 2006;10(2):102–6. 10.1016/j.jaapos.2005.12.005.
27. Kandasamy Y, Smith R, Wright IMR. Retinal microvascular changes in low-birth-weight babies have a link to future health. J Perinat Med. 2012;40(3):209–14. 10.1515/JPM.2011.116.
28. Maria Ortega-Molina J, De Larraya A, SP A, SM et al. Risk Factors of Retinopathy of Prematurity Associated with Delayed Retinal Vascular Development. *Iran J Pediatr*. 2017;In Press(In Press). 10.5812/ijp.7642
29. Lutty GA, McLeod DS. Development of the hyaloid, choroidal and retinal vasculatures in the fetal human eye. Prog Retin Eye Res. 2018;62:58–76. 10.1016/j.preteyeres.2017.10.001.
30. Allvin K, Hellström A, Dahlgren J, Andersson Grönlund M. Birth weight is the most important predictor of abnormal retinal vascularisation in moderately preterm infants. Acta Paediatr Oslo Nor 1992. 2014;103(6):594–600. 10.1111/apa.12599.
31. Mangalesh S, Toth CA. Preterm infant retinal OCT markers of perinatal health and retinopathy of prematurity. Front Pediatr. 2023;11:1238193. 10.3389/fped.2023.1238193.
32. Czeszyk A, Hautz W, Jaworski M, Bulsiewicz D, Czech-Kowalska J. Morphology and Vessel Density of the Macula in Preterm Children Using Optical Coherence Tomography Angiography. J Clin Med. 2022;11(5):1337. 10.3390/jcm11051337.
33. Dammann O, Stansfield BK. Neonatal sepsis as a cause of retinopathy of prematurity: An etiological explanation. Prog Retin Eye Res. 2024;98:101230. 10.1016/j.preteyeres.2023.101230.
34. Choi YJ, Jung MS, Kim SY. Retinal hemorrhage associated with perinatal distress in newborns. Korean J Ophthalmol KJO. 2011;25(5):311–6. 10.3341/kjo.2011.25.5.311.
35. Ying GS, Quinn GE, Wade KC, et al. Predictors for the development of referral-warranted retinopathy of prematurity in the telemedicine approaches to evaluating acute-phase retinopathy of prematurity (e-ROP) study. JAMA Ophthalmol. 2015;133(3):304–11. 10.1001/jamaophthalmol.2014.5185.
36. Yu XD, Branch DW, Karumanchi SA, Zhang J. Preeclampsia and retinopathy of prematurity in preterm births. Pediatrics. 2012;130(1):e101–107. 10.1542/peds.2011-3881.

37. Huang HC, Yang HI, Chou HC, et al. Preeclampsia and Retinopathy of Prematurity in Very-Low-Birth-Weight Infants: A Population-Based Study. PLoS ONE. 2015;10(11):e0143248. 10.1371/journal.pone.0143248.
38. Chen LN, He XP, Huang LP. A survey of high risk factors affecting retinopathy in full-term infants in China. Int J Ophthalmol. 2012;5(2):177–80. 10.3980/j.issn.2222-3959.2012.02.12.
39. Jin C, Yu X, Lei M, Deng P, Li X, Jiang W. A simple nomogram tool for predicting fetal chromosomal abnormalities based on ultrasound soft markers: a research note. BMC Res Notes. 2025;18:453. 10.1186/s13104-025-07512-9.
40. Tonyali NV, Sarsmaz K, Bayraktar B, et al. Delta neutrophil index (DNI) as a potential biomarker for fetal growth restriction: insights from maternal hematological changes and neonatal outcomes. BMC Pregnancy Childbirth. 2024;24:655. 10.1186/s12884-024-06853-w.
41. Vinekar A, Jayadev C, Mangalesh S, Shetty B, Vidyasagar D. Role of tele-medicine in retinopathy of prematurity screening in rural outreach centers in India - a report of 20,214 imaging sessions in the KIDROP program. Semin Fetal Neonatal Med. 2015;20(5):335–45. 10.1016/j.siny.2015.05.002.
42. Stocks CO, Carson RA. Newborn and infant vision screening in primary care: A clinical review. J Spec Pediatr Nurs JSPN. 2024;29(1):e12421. 10.1111/jspn.12421.

Figures

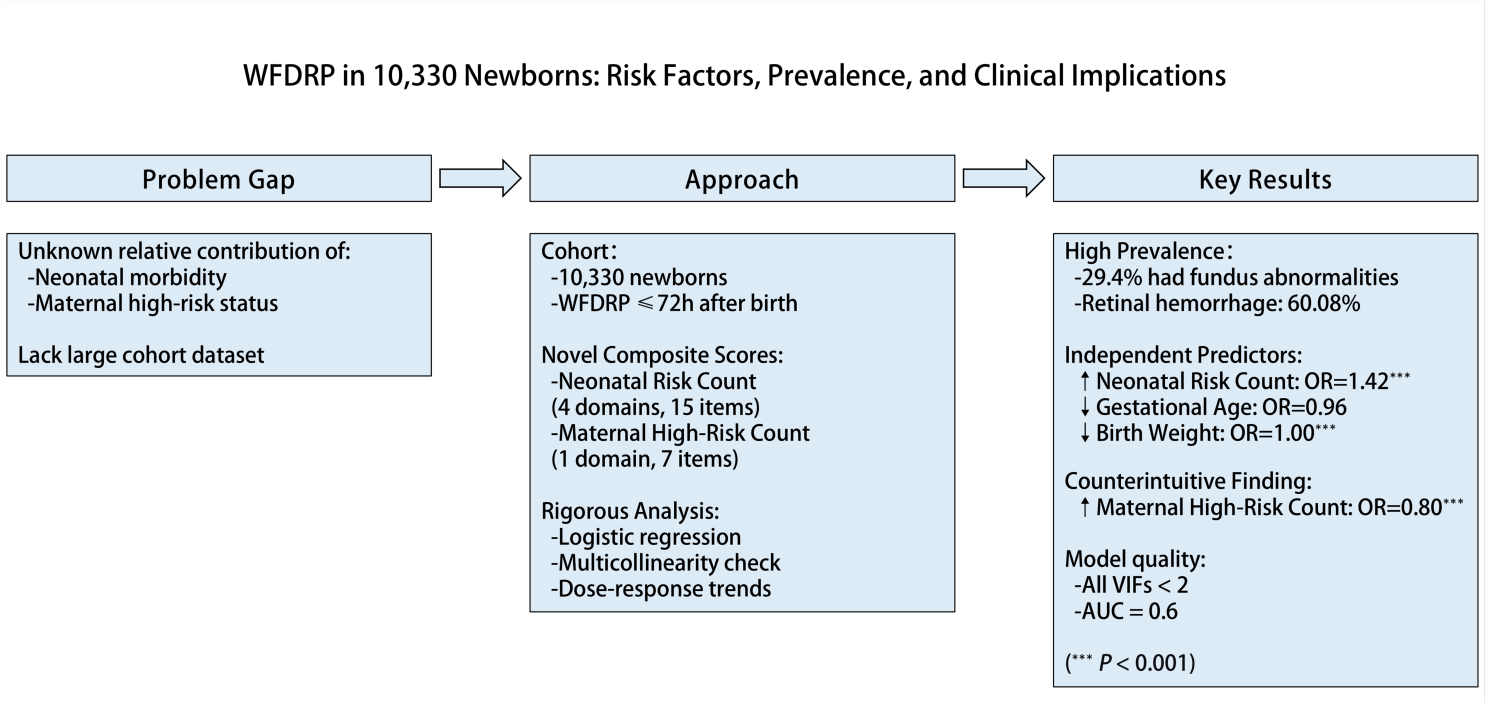


Figure 1

Graphical Abstract: A Visual Summary of the Study

Note: This schematic summarizes the study rationale, methodology, principal results, and clinical implications. Abbreviations: WFDRP, wide-field digital retinal photography; OR, odds ratio; VIF, variance inflation factor; AUC, area under the curve.

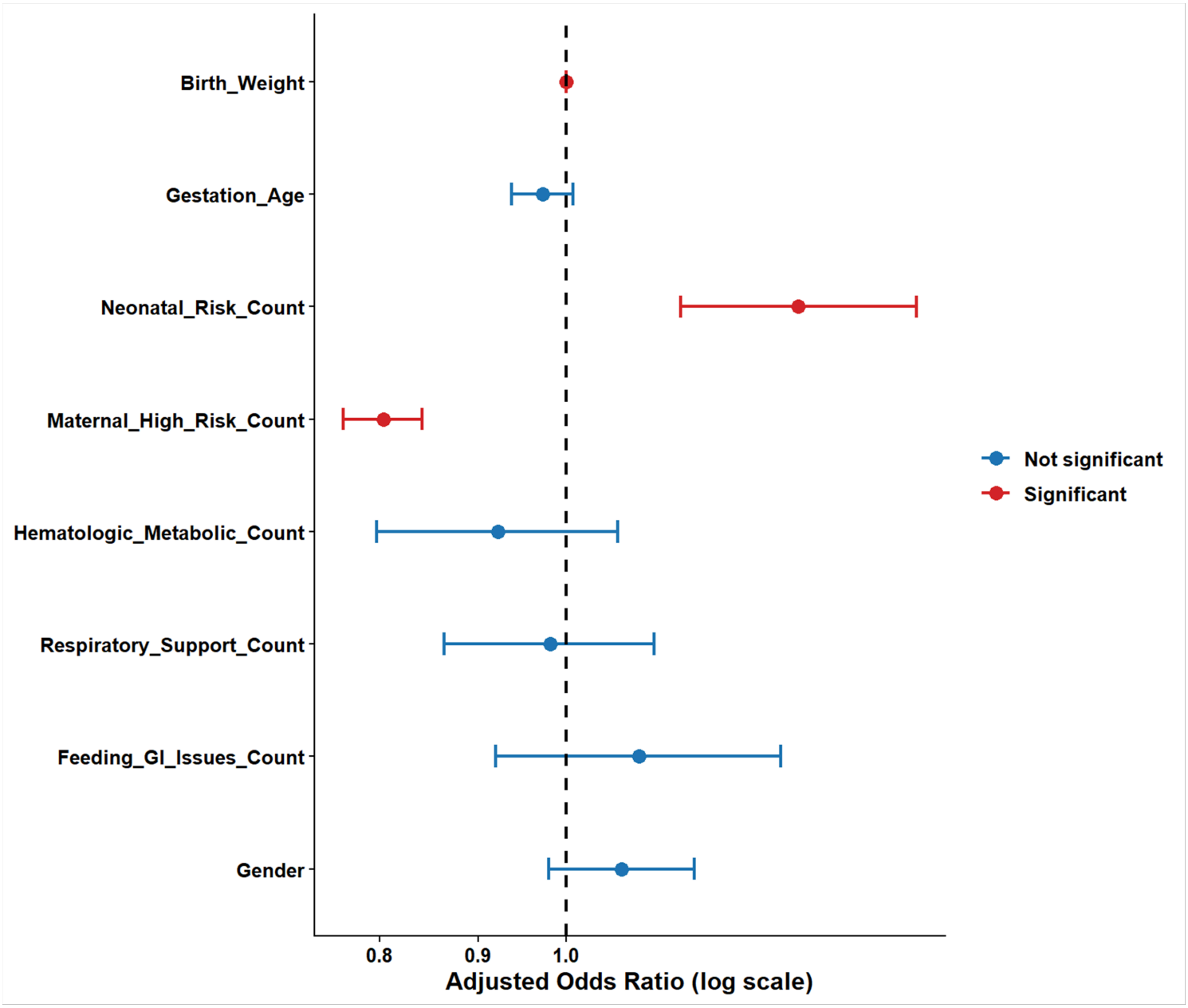


Figure 2

Forest Plot of Studied Variables

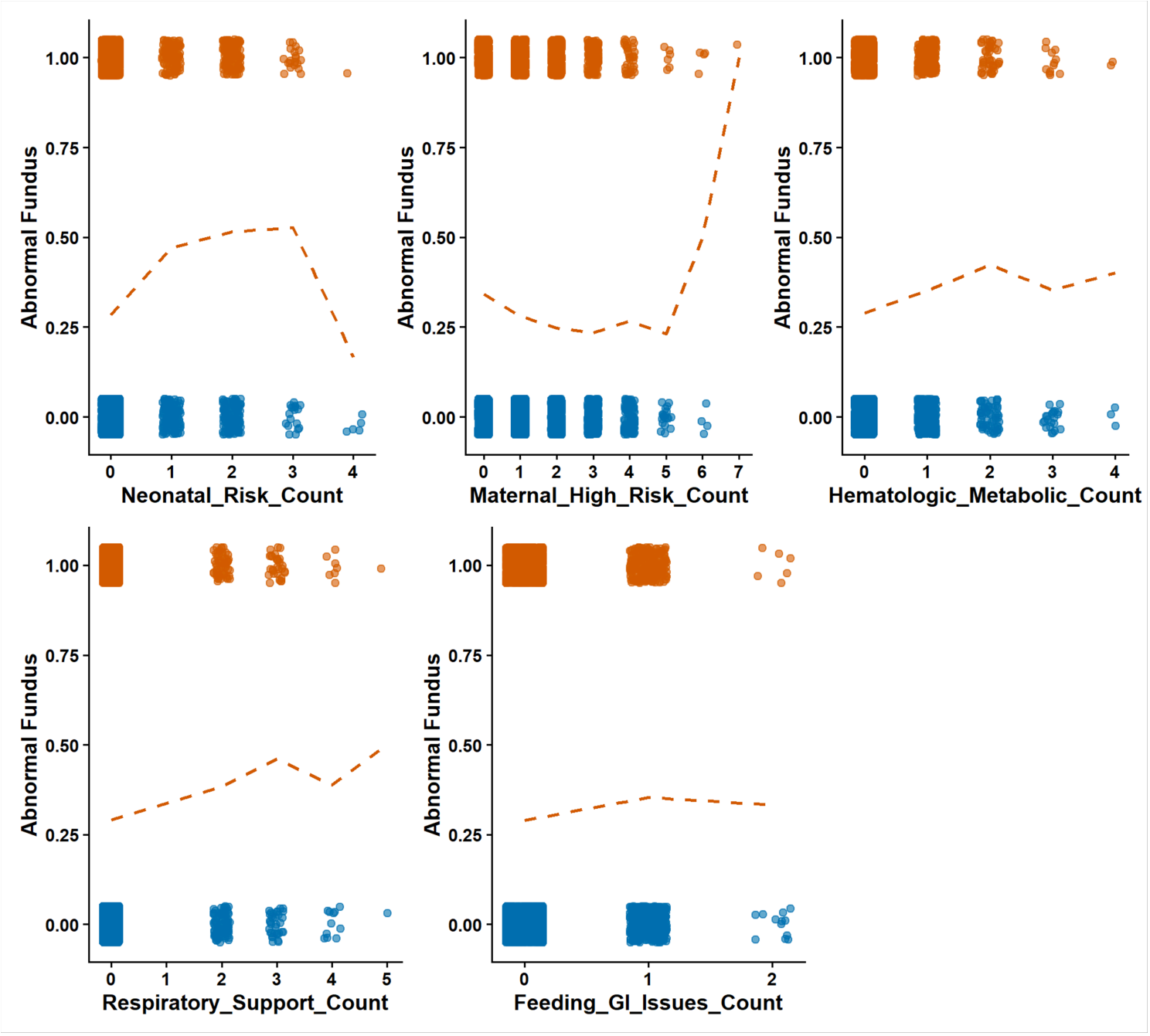


Figure 3

Association of Multiple Risk Factors with Abnormal Fundus in Neonates.

Note: Scatter-jitter plots with dashed lines indicating the proportion of abnormal fundus findings across increasing risk counts.

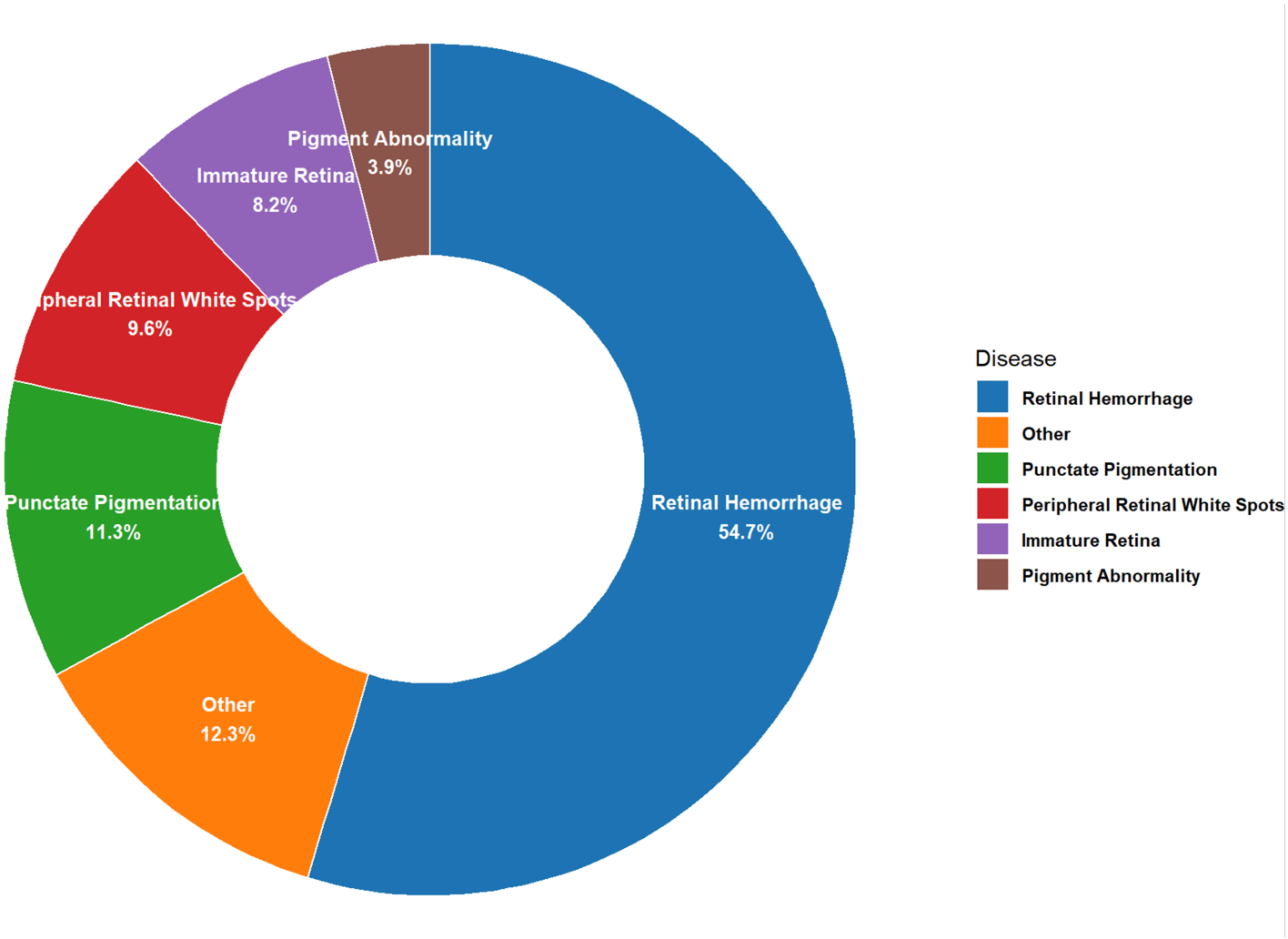


Figure 4

Prevalence of Abnormal Fundus Findings Among Participants

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