What Is Left After Resolution of Neonatal Retinal Hemorrhage: The Longitudinal Long-term Outcome in Foveal Structure and Visual Function

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• PURPOSE: **Neonatal retinal hemorrhage (NRH) is one of the most common neonatal fundus conditions. Hemorrhage resolves spontaneously; however, its long-term outcome is unknown yet. The current study explores the long-term role of NRH in foveal structure and visual function.**

• DESIGN: **Cohort study (a prospective longitudinal study, in which the participants were followed up for 4-6 years).**

• METHODS: **A total of 125 healthy newborns during 2013-2015, including 50 newborns with NRH and 75 newborns without NRH, were enrolled. The eyes with NRH were further categorized into the foveal hemorrhage (FH) group and non-FH group. A comprehensive ophthalmic examination including best-corrected visual acuity (BCVA) measurement, slit-lamp examination, refractive error measurement, scanning laser ophthalmoscopy, and spectral-domain OCT was performed. Total retinal thickness (TRT) and the inner and outer retinal layers in the fovea were measured and compared.**

• RESULTS: **The NRH was absorbed within 2.1 ± 0.98 weeks (median: 3 weeks). No difference was noted in the demographic characteristics between the groups; there was no significant difference in the logMAR BCVA ($P = .83$) or in the TRT. Subgroup analysis showed that TRT at the fovea in the FH group was significantly thicker ($P = .005$). Segmentation analysis showed a significantly thicker foveal outer nuclear layer (ONL) in the FH group ($P = .017$).**

• CONCLUSIONS: **Birth-related retinal hemorrhage, even FH, might not lead to obvious visual abnormalities at the age of 4 years, at least according to this study with relatively small sample size. However, a thicker fovea, mainly attributed to a wider ONL and a shallower foveal pit, is noted in our study.** **(Am J Ophthalmol 2021;226: 182–190. © 2021 Elsevier Inc. All rights reserved.)**

Birth-related neonatal retinal hemorrhage (NRH) is one of the most common neonatal retinal abnormalities. The incidence ranges from 2.6% to 50%,[1,2] depending on the circumstances of birth and the timing of the examination. It is mostly located in the intra-retina and occurs bilaterally within the first week after birth. Several studies have extensively explored the prevalence, risk factors, obstetric management, and resolution pattern.[3-6] The hemorrhage is mild and spontaneously resolves within a couple of weeks in the majority of cases.

However, hemorrhage involving the macula take longer to resolve and has raised significant concerns regarding its role in visual development.[6,7] Horton and Hocking reported that the visual cortex is most vulnerable to deprivation during the first weeks of life in monkeys.[8] These hemorrhages could obstruct the visual axis during the critical period and ultimately lead to ametropia or even deprivation amblyopia. Zwaan and associates studied long-term visual acuity in children aged about 10 years who had macular hemorrhage at birth. Of the 7 children examined, 6 had normal visual acuities. One had reduced vision in the eye with macular hemorrhage, possibly related to deprivation amblyopia secondary to slow resorption of the hemorrhage.[9] Crucial data regarding the long-term role of NRH on the structure and function of the fovea are still largely unknown.[10,11]

Currently, the question of whether neonatal retinal hemorrhage affects foveal development and visual function is certainly an area where information is lacking. In the current study, newborns with NRH and normal controls were recruited from birth and followed up for 6 years. Visual acuity, refractive error, and the macula architecture were measured at 4 years of age. The current study aimed to explore the long-term role of retinal hemorrhage in macular structure and visual function.

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FIGURE 1. Wide-field fundus photography in patients with neonatal retinal hemorrhage and normal controls. A. Extensive retinal hemorrhage with foveal involvement in right eye of a baby girl with gestational age (GA) 39 + 6 weeks and birthweight (BW) 2,500 g. High-magnification image was embedded. B. Retinal hemorrhages without the foveal involvement in left eye of a baby girl (GA 38 + 2 weeks, BW 3,100 g). C. No retinal hemorrhage was noted in a baby girl (GA 40 + 2 weeks, BW 3,600 g) in normal control.

METHODS

This prospective study was approved by the Institutional Review Board of Zhongshan Ophthalmic Center and 2 community hospitals. All investigations followed the tenets of the Declaration of Helsinki. Informed consent was obtained from the parents or legal guardians of all participants. All participants received universal newborn eye screening within 48 hours of birth in 1 of 2 community hospitals.

A total of 125 systemically healthy newborns during 2013-2015 were included in this study. The inclusion criteria were as follows: (1) gestational age $\geq$ 37 weeks; (2) birthweight > 2,000 g; (3) Apgar score $\geq$ 7. Any neonate with congenital eye disease or family history of any ocular disease or who presented for other diseases or evidence of any condition that might affect visual acuity or macular development was excluded. Bilateral external ocular examination, red reflex test, handheld slit-lamp examination, and wide-angle funduscopy (RetCam III; Clarity Medical Systems, Pleasanton, California, USA) was performed in each neonate within 48 hours after birth. According to the presence of NRH, all newborns were categorized into the NRH group (50 patients; 8 unilateral, 42 bilateral) and the control group (75 patients) (Figure 1). The newborns in the NRH group were followed up once a week until hemorrhage was completely resolved in both eyes. After that, all the participants were followed by telephone once a year. In the fifth year, all participants were invited to an in-person examination. A comprehensive ophthalmic examination was performed, including best-corrected visual acuity (BCVA), slit-lamp examination, refractive error, Optos scanning laser ophthalmoscopy (Optomap 200Tx; Optos pls. Dunfermline, UK), and spectral-domain OCT (Cirrus 5000 AngioPlex; Carl Zeiss, Dublin, California, USA). Refraction was measured with cycloplegia (0.5% tropicamide), and the spherical equivalent was calculated. Ocular alignment was assessed by the cover-uncover test and the corneal light reflex test for strabismus.[12] Amblyopia was defined by BCVA visual acuity tests as in previous study.[13]

The spectral-domain OCT was performed using the 6 × 6-mm raster scan mode or a 6-mm (or 12-mm) radial scan mode. Total retinal thickness (TRT), the thickness of the entire retina from the inner boundary of the inner limiting membrane to the base of the retinal pigment epithelium (RPE),[14] was measured by 2 independent investigators (L.S. and Z.J.) at the central foveola (central retinal thickness; CRT) and 500 μm temporal, nasal, superior, and inferior from the fovea, indicated as TRT_{T500}, TRT_{N500}, TRT_{S500}, and TRT_{I500} (Supplemental Table; Supplemental Material available at AJO.com). According to the prior studies,[14-14] the retina between the fovea and optic disc is critical to the visual function; thus, TRT 1,000 μm, 1,500 μm, and 2,000 μm temporal, nasal, superior, and inferior from the fovea were also measured (Supplemental Table). Additionally, the inner retinal layers (IRL) were defined from the inner boundary of the inner limiting membrane to the outer border of the inner nuclear layer (INL); the outer retinal layers were defined from the outer border of the INL to the outer border of the RPE.[12] Photoreceptor outer segment (OS) thickness was measured from the ellipsoid zone to the inner border of the RPE.[15] The outer nuclear layer (ONL) ratio was defined as the ratio of the ONL to the external limiting membrane–RPE thickness at the fovea[16] (Figure 2).

All the parameters were measured twice by each observer. The intra- and interobserver agreements were high. Intraclass correlation coefficient ranged from 0.876 to 0.991, demonstrating great repeatability for both observers. Since all the data met normal contribution, Pearson correlation was done to identify whether the results of these 2 investigators could make an agreement. The r values in all the measured parameters, including retinal thickness 500, 1,000, 1,500, and 2,000 μm to fovea superiorly, inferiorly, temporally, and nasally; thickness of IRL, outer retinal layer, and OS; ONL ratio; and K values ranged from 0.825 to 0.986 (all *P* values less than .001), showing trends toward a high

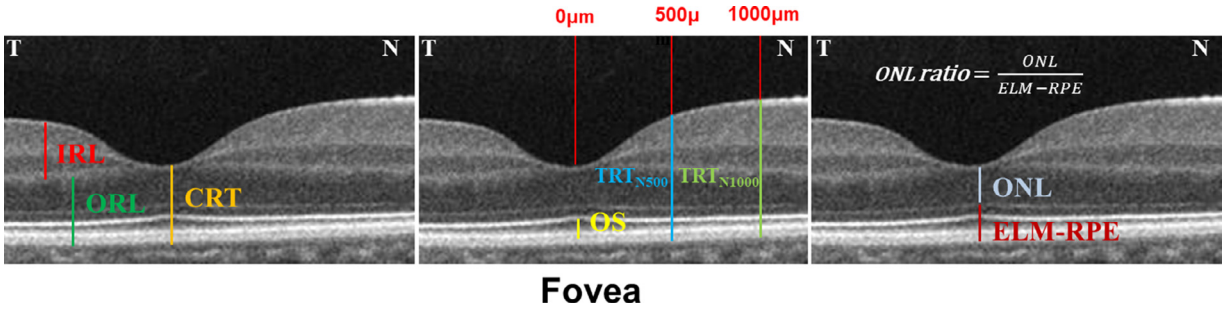

FIGURE 2. Definition and measurement of spectral-domain OCT parameters used in this study. Total retinal thickness (TRT) is the entire retinal thickness from inner boundary of the inner limiting membrane to the base of the retinal pigment epithelium (RPE). Central retinal thickness (CRT) is TRT at the foveola. TRT_{N500} is TRT at 500 μm in the nasal side from the fovea on horizontal OCT scan. TRT_{N1000} is TRT at 1,000 μm in the nasal side from the fovea on horizontal OCT scan. The inner retinal layers (IRL), the outer retinal layers (ORL), photoreceptor outer segment (OS), and the calculation of outer nuclear layer (ONL) ratio were shown. ELM = external limiting membrane

interobserver agreement. The mean values were employed in the statistical analysis.

• **STATISTICAL ANALYSIS:** All statistical analyses were performed using GraphPad Prism (GraphPad Software, San Diego, California, USA) or Stata 13.1 (StataCorp, College Station, Texas, USA). The data were presented as mean ± standard deviation (SD). Analyses of continuous variables were performed by 2-tailed Student *t* test or Mann-Whitney test when appropriate. Between-group comparisons for dichotomous variables were performed with Pearson χ^2 test (or Fisher exact test when appropriate). The level of significance was set at $P = .05$.

RESULTS

• **DEMOGRAPHIC AND CLINICAL CHARACTERS IN EYES WITH NEONATAL RETINAL HEMORRHAGE:** The NRH was absorbed within 2.1 ± 0.98 weeks (median: 3 weeks). At least 1 parent of each child received a minimum of 1 follow-up via telephone. A total of 38 children were followed up at least once, between 4 and 6 years of age, from the NRH group (including 6 unilateral and 32 bilateral), and 37 were followed up from the control group. The overall follow-up rate was 60% (75/125); follow-up rate was 76% (38/50) and 49% (37/75) in the 2 groups, respectively. The loss of follow-up was owing to the family moving (3, 2), loss of contact (5, 7), and subject request (4, 29) in the NRH and control groups, respectively.

No difference was noted in the demographic characteristics between the NRH and control groups. The mean gestational age was 273.1 ± 7.8 days in the NRH group vs 272.8 ± 7.5 days in the control group ($P = .83$), with a parallel mean age of 5.06 ± 0.74 years vs 5.04 ± 0.63 years ($P = .84$), and parallel sex ratio ($P = .49$). According to the presence of NRH, 70 eyes (38 children) in the NRH group and 74 eyes (37 children) in the control group were included in the analysis. The mean axial length was 22.09 ± 0.74 mm vs 21.91 ± 0.84 mm, respectively ($P = .18$). The median spherical equivalent was 1.00 diopter in both groups ($P = .60$) (Table 1).

• **RETINAL STRUCTURAL AND FUNCTIONAL RESULTS IN NEONATAL RETINAL HEMORRHAGE CHILDREN AND NORMAL CONTROLS:** Overall, no statistical differences were noted in the retinal thickness between the 2 groups, including CRT (203.0 ± 16.0 μm vs 203.3 ± 12.8 μm, $P = .90$), TRT_{T500} (277.7 ± 16.6 μm vs 278.7 ± 22.6 μm, $P = .63$), TRT_{N500} (283.7 ± 21.4 μm vs 282.7 ± 24.2 μm, $P = .78$), TRT_{S500} (302.1 ± 22.8 μm vs 296.4 ± 19.9 μm, $P = .27$), and TRT_{I500} (290.4 ± 21.8 μm vs 286.2 ± 17.0 μm, $P = .23$). Persistence of the IRL was detected in 1 eye in the control group, but not in the NRH group. In addition, there was no significant difference in logMAR BCVA between the 2 groups (median 0.097 [SD 0.13] vs 0.097 [SD 0.11], $P = .83$) (Table 1). All children were referred for a complete eye examination to confirm that there was no subject with obvious strabismus or amblyopia among the 2 groups.

• **SUBGROUP ANALYSIS IN NEONATAL RETINAL HEMORRHAGE CHILDREN AND NORMAL CONTROLS:** According to the presence of foveal hemorrhage (FH), 70 eyes with NRH were further categorized into 2 subgroups: FH group (14/70, 20%) (including 12 unilateral and 2 bilateral) and non-FH group (56/70, 80%). There was no statistical difference in the demographic characteristics between the 2 subgroups (Table 2). The median resolution time was 3 weeks in the FH group and 2 weeks in the non-FH group. Although no statistical difference was identified (logMAR, median 0.10 [SD 0.14] vs 0.26 [SD 0.11], $P = .10$), the median BCVA in the non-FH group was numerically better compared with that of the FH group.

TABLE 1. Demographic and Clinical Characteristics in Children With Neonatal Retinal Hemorrhage and Normal Controls

	Children With Neonatal Retinal Hemorrhage	Normal Controls	*P*
Number of patients	38	37	
Number of eyes	70	74	
Male/female, n	14/24	17/20	.49
Age, y	5.06 (0.74) [4.91,4.05-6.85]	5.04 (0.63) [4.97, 4.11-6.55]	.84
SE, D	1.01 (1.02) [1.00, -2.75 to 3.50]	1.14 (1.74) [1.00, -3.63 to 3.25]	.60[a]
Axial length, mm	22.09 (0.74) [22.20, 20.24-23.57]	21.91 (0.84) [21.85, 20.35-24.56]	.18
logMAR visual acuity	0.15 (0.13) [0.097, -0.08 to 0.52]	0.13 (0.11) [0.097, 0.00-0.40]	.83[a]
GA, day	273.1 (7.8) [273, 259 to 289]	272.8 (7.5) [273, 258-288]	.83
CRT, μm	203.3 (12.8) [205, 171-228]	203.0 (16.0) [206, 145-231]	.90
TRT_{N500}, μm	282.7 (24.2) [279.5, 216-348]	283.7 (21.4) [282, 238-340]	.78
TRT_{T500}, μm	278.7 (22.6) [279, 233-339]	277.7 (16.6) [275, 249-323]	.62
TRT_{S500}, μm	296.4 (19.9) [296, 252-342]	302.1 (22.8) [298, 265-383]	.27
TRT_{I500}, μm	286.2 (17.0) [288, 244-314]	290.4 (21.8) [290, 242-367]	.23
IRL persistence, n (%)	0 (0%)	1 (1.4%)	-

CRT = central retinal thickness (total retinal thickness at the foveola); D = diopter; GA = gestational age; IRL = inner retinal layer; SE = spherical equivalent; TRT = total retinal thickness.

TRT_{N500}, TRT_{T500}, TRT_{S500}, and TRT_{I500} refer to the total retinal thickness at, respectively, 500 μm nasal, temporal, superior, and inferior to the fovea.

Results are shown as mean (SD) [median, range] unless stated otherwise;

[a]Mann-Whitney test.

TRT was then analyzed between the 2 subgroups. CRT was 211.7 ± 10.8 μm in the FH group, which is significantly thicker compared to 201.2 ± 12.5 μm in the non-FH group ($P = .005$). A significantly thicker retina was also identified at TRT_{T500}, TRT_{N500}, TRT_{S500}, and TRT_{I500} in the FH group vs the non-FH group (respectively, 291.6 ± 21.6 μm vs 276.6 ± 22.1 μm, $P = .025$; 303.2 ± 17.3 μm vs 282.7 ± 24.3 μm, $P = .002$; 314.7 ± 14.7 μm vs 292 ± 18.5 μm, $P = .000$; 298 ± 12.2 μm vs 283.4 ± 16.8 μm, $P = .004$). TRT_{N1000}, TRT_{T1000}, TRT_{S1000}, and TRT_{I1000} were also analyzed and significantly thicker retina was identified at TRT_{N1000} in the FH group (359.1 ± 34.2 μm vs 339.4 ± 25.9 μm, $P = .038$), but no differences in TRT_{T1000}, TRT_{S1000}, and TRT_{I1000} (respectively, 332.3 ± 26.7 μm vs 318.5 ± 18.4 μm, $P = .06$; 352.9 ± 14.4 μm vs 347.7 ± 15.7 μm, $P = .28$; 346 ± 14.3 μm vs 337.2 ± 15 μm, $P = .059$) were noted between the subgroups. However, a significant difference in mean TRT 500 μm and 1,000 μm temporal, nasal, superior, and inferior from the fovea (TRT_{500}, TRT_{1000}) was found ($P < .001$, $P = .001$). The mean TRT_{1500} in the FH group was thicker than that in the non-FH group, with a borderline significance ($P = .065$), while the mean TRT_{2000} was similar in both groups. TRT at 1,500 and 2,000 μm temporal, nasal, superior, and inferior from the fovea are listed in Table 2.

Considering retinal segmentation, the foveal architecture was measured. No persistence of the IRL was noted in both groups. Foveal ONL thickness was identified to be thicker in the FH group (111.3 ± 12.9 μm) compared with the non-FH group (101.0 ± 14.4 μm, $P = .017$). The average ONL ratio was 1.12 ± 0.20 in the FH group, which is significantly higher than that in non-FH eyes (1.00 ± 0.17, $P = .02$). However, OS thickness was parallel between the 2 groups (100.4 ± 8.2 μm in the FH group vs 100.2 ± 9.6 μm in the non-FH group, $P = .93$) (Table 2, Figure 3).

TABLE 2. Demographic and Clinical Characteristics in Non–Foveal Hemorrhage and Foveal Hemorrhage Groups

	FH Group	Non-FH Group	*P*
Number of eyes	14	56	
Age, y	4.93 (0.96) [4.82, 3.68-6.85]	5.06 (0.71) [4.92, 3.56-6.39]	.57
SE, D	1.30 (1.27) [1.00, -0.50 to 3.50]	0.92 (0.99) [1.00, -2.75 to 2.88]	.65[a]
Axial length, mm	22.23 (0.60) [22.23, 21.37-23.49]	22.03 (0.77) [22.13, 20.24-23.57]	.36
logMAR visual acuity	0.21 (0.11) [0.26, 0.00-0.30]	0.14 (0.14) [0.10, -0.08 to 0.52]	.10[a]
GA, day	271.4 (6.1) [270, 261-283]	273.2 (8.4) [274, 258-288]	.43
CRT, μm	211.7 (10.8) [212, 188-223]	201.2 (12.5) [203.5,171-228]	.005
TRT_{500}, μm	301.7 (18.5) [302.5, 270-352]	283.6 (21.3) [284.5, 216-348]	.000
TRT_{1000}, μm	347.5 (26.7) [342.5, 304-449]	335.6 (22.0) [337, 281-493]	.001
TRT_{1500}, μm	342.7 (23.6) [340, 300-436]	336.2 (18.7) [334, 291-339]	.065
TRT_{2000}, μm	320.4 (24.6) [316.5, 278-420]	315.6 (21.5) [314, 268-396]	.15
ILM to ELM, μm	100.4 (12.9) [113.5, 91-131]	101.0 (14.4) [100.5, 75-149]	.017
ELM to RPE, μm	100.4 (8.2) [100, 87-113]	100.2 (9.6) [99.5, 51-124]	.93
ONL ratio (ILM to ELM / ELM to RPE)	1.12 (0.20) [1.09, 0.82-1.51]	1.00 (0.17) [1.01, 0.67-1.49]	.02

CRT = central retinal thickness (total retinal thickness at the foveola); D = diopter; ELM = external limiting membrane; FH = foveal hemorrhage; GA = gestational age; ILM = inner limiting membrane; ONL = outer nuclear layer; RPE = retinal pigment epithelium; SE = spherical equivalent; TRT = total retinal thickness.

TRT_{500}, TRT_{1000}, TRT_{1500}, and TRT_{2000} refer to the mean TRT at 500 μm, 1,000 μm, 1,500 μm, and 2,000 μm nasal, temporal, superior, and inferior to the fovea.

Results are shown as mean (SD) [median, range] unless stated otherwise.

[a]Mann-Whitney test.

DISCUSSION

NRH is one of the most common neonatal fundus abnormalities. Although the retinal hemorrhage is mild and resolves spontaneously in the majority of cases, the long-term effects on macular structural and functional development are still unknown.[1,6] To our knowledge, this is the first prospective cohort study with long-term follow-up on macular structural and functional effects of NRH. We believe this study will provide important data for future screening strategy and help us to understand the mechanism of macular maturing.

In this study, all the children received visual assessment as early as possible. We selected the age of 4 years for at least 2 reasons. First, it is well documented that the fovea develops as early as 22 weeks postmenstrual age and continues into childhood, with most anatomic changes occurring by approximately 17 months postmenstrual age.[17,18] Good-quality OCT imaging is difficult to obtain when handheld devices are lacking. Precise visual and structural tests can be used on children beginning at 4 years of age. Second, the fovea in a 4-year-old child is morphologically similar to that in a 13-year-old. In addition, the cone has achieved a parallel density to that of adults.[19,20] Previous studies show that hemorrhage is located in the intraretina via funduscopy or RetCam, but little is known about the microstructural changes in the retina.[6,21] Spectral-domain OCT imaging in children is a new field that has expanded our understanding of the developing retina through longitudinal, in vivo analysis of the macular microstructure.[11,17]

It was well documented that visual deprivation in early infancy owing to various factors is likely to cause depriva-

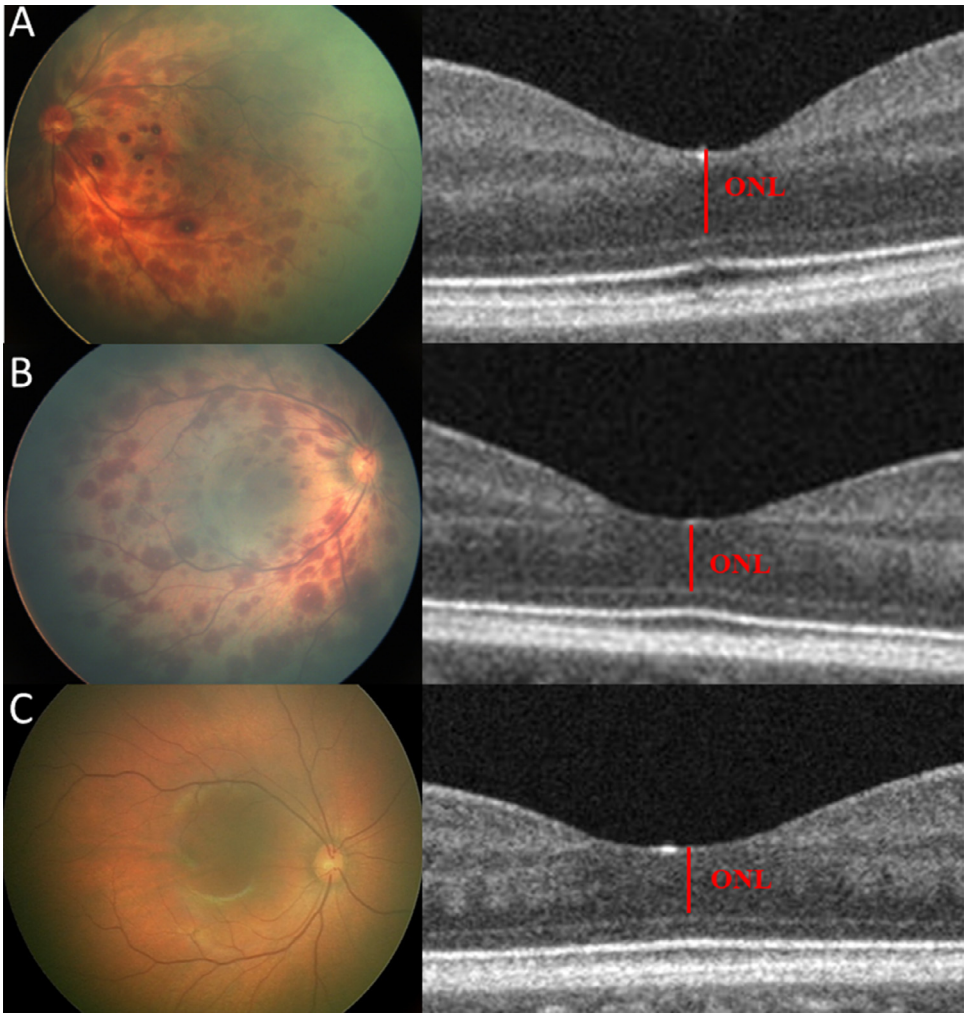

FIGURE 3. Representative OCT in neonatal retinal hemorrhage (NRH) patients with and without foveal hemorrhage (FH) and normal controls. The central retinal thickness is 218 μm (A, 4.8-year-old), 200 μm (B, 5.2-year-old), and 189 μm (C, 4.7-year-old) in patient with FH, patient with NRH but no FH, and normal control, respectively.

tion amblyopia, which is mainly attributed to the block of normal retinal input and the following disconnection between the deprived eye and the cortical circuits.[22-24] Thus, it is reasonable to hypothesize that macula-involved hemorrhage might be one of the causes of deprivation amblyopia or even secondary strabismus in children. Our current study is the first long-term cohort study longitudinally comparing the visual function in children with NRH to the normal control group.

Very interestingly and reassuringly, our study showed that visual acuity and macular structural appearance in NRH children is comparable to healthy controls. We have not found any visual functional abnormalities in these children. For this, we would like to highlight 3 possible explanations. First, in the current study, retinal hemorrhage is mostly resolved within 2 weeks, which is perhaps under the threshold of permanent damage to visual development. The complete absorption left clear refractive media for a continuous input of visual stimulation. Similar normal visual acuity was found in neonates with oculomotor nerve palsy, which resolved within 6 weeks, although oculomotor nerve palsy was confirmed as a potent predictable cause of amblyopia.[8,25] Second, FH does not lead to absolute scotoma and does not deprive the visual stimulation absolutely. We suggest this is different from the eye patch, which deprives visual stimulation completely. The degree of deprivation faded with the absorption of the FH. Third, the macular structural and functional recovery capacity is potentially stronger in children, compared with adults.[26,27]

Notably, the fovea in FH children is thicker than that in non-FH children in our subgroup analysis (Figure 4). The retinal thickness at the slope of the fovea, including 500 μm and 1,000 μm from the fovea in the FH eye, was higher than that in non-FH eyes, thus contributing together to a

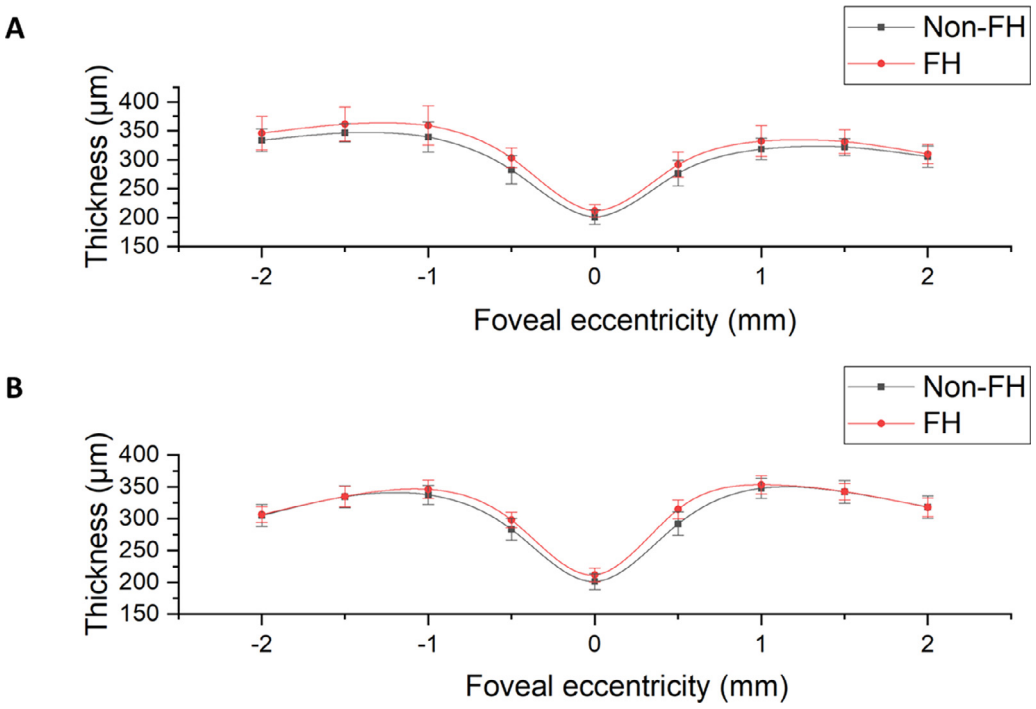

FIGURE 4. Mean thickness of retina in non-foveal hemorrhage (FH) and FH eyes. A. Mean total retinal thickness at 500 μm, 1,000 μm, 1,500 μm, and 2,000 μm nasal and temporal to the fovea. B. Mean total retinal thickness at 500 μm, 1,000 μm, 1,500 μm, and 2,000 μm inferior and superior to the fovea.

shallower pit in FH eyes. The change of macular architecture was further confirmed by the parallel thickness at 1,500 and 2,000 μm from the fovea in FH and non-FH groups. Shallow fovea was reported in several pediatric retinal diseases, such as retinopathy of prematurity, familial exudative vitreoretinopathy, and Stickler syndrome.[16,28,29] Usually, fovea shallowing is attributed to persistence of the IRL, retardation of INL extrusion, or elongation of cone outer segment.[20,30] Persistence of the IRL was previously reported in retinopathy of prematurity children as owing to possible arrest of foveal development, particularly affecting the centrifugal IRL migration and sparing photoreceptor maturation.[18,31]

However, segmentation analysis in our current study showed a 100% regression of IRL, presence of INL extrusion, and parallel outer segment length with the non-FH eyes ($P = .93$). INL extrusion in the fovea was fulfilled in all NRH children, no matter the presence of FH or not. A wider ONL in the FH eyes was noted compared to the non-FH eyes (111.3 ± 12.9 μm vs 101.0 ± 14.4 μm, $P = .017$). ONL consists of a single layer of cone photoreceptors underlying the developing pit up to birth; cone cell bodies reach approximately 8 layers by 3.8 years. The underlying mechanism of ONL widening is not yet clear. We suggest the possible explanation as (1) a blood clot in the ONL may induce a relaxed arrangement of the cones, or (2) retinal abnormalities in the NRH infant in very early life might induce the centripetal force of the cone, and thus thicken the ONL height.

Our study has some limitations. The sample size of the FH group is small owing to the nature of the low incidence of this condition; a larger sample size is needed to confirm our results. Second, foveal development is not completed at the age of 4 years. Variability in foveal morphologic structure was reported even among age-matched individuals. An extended and more prolonged investigation is warranted for the results of this current 5-year follow-up. Third, owing to the lack of handheld devices in 2013, OCT was not performed at the baseline or during hemorrhage resolution. The classification of hemorrhage according to the location in the retina was not assessed. Another prospective study to evaluate NRH resolution dynamically and macular architecture changes would be very helpful.

Overall, after 6 years of follow-up, children with a history of NRH achieved parallel visual acuity and reflective status with normal children; children with FH achieved parallel visual acuity and reflective status with the non-FH children. Birth-related retinal hemorrhage, even foveal hemorrhage, might not lead to obvious visual abnormalities at the age of 4 years, at least according to this study with relatively small sample size. None of the patients developed deprivation amblyopia or visual loss owing to macular abnormality. However, thicker fovea, mainly attributed to the ONL widening with unknown causes, is noted in our study.

A longer-term follow-up is needed to confirm our current findings and to explore the role in visual development.

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