Comparative Study on Optic Disc Features of Premature Infants and Term Infants

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Research article

Keywords: Premature infant, Term infant, Optic disc parameter, Shape of sclerotic ring and optic disc, Wide-Field Digital Pediatric Retinal Imaging

DOI: https://doi.org/10.21203/rs.3.rs-30626/v1

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Abstract

Background

To study optic disc features of premature infants and compare to that of term infants to explore the pattern and features of newborn optic disc development and provide the basis for the diagnosis of newborn optic disc disease.

Methods

This is a prospective clinical research. Newborns underwent newborn fundus disease screening from January 1st, 2016 to October 31st, 2016 in the neonatal ward of Ruian City Maternal and Child Health Hospital were selected. RetCam 3 Version6.1.25.0 Wide-Field Digital Pediatric Retinal Imaging System developed by Clarity Medical Systems, Inc was adopted to conduct fundus examination on both eyes, 130 degree wide-angle lens was used to film the images centering optic disc.

Results

For both premature infants and term infants, vertical diameter of the optic disc to lateral diameter of the optic disc ratio was > 1, and the shape of the optic disc was a vertical oval. The difference of each optic disc parameter between premature infants and term infants was not statistically significant (P > 0.05). There's a difference of constitution of sclerotic ring type on optic disc between premature infants and term infants. Among which, the proportion of single ring type and double ring type in premature infants was higher than that in term infants (P < 0.05). The proportion of no ring type in term infants was higher than that in premature infants (P < 0.05). The proportion of mixed type had no significant difference (P > 0.05) between premature infants and term infants.

Conclusions

We found that The proportion of mature types (single ring type and double ring type) in term infants was higher than that in premature infants. While there's no statistical difference of the proportion of mixed types between premature infants and term infants. Double ring type is a normal stage of the development of optic disc.

Background

The optic disc, also called the optic nerve head, is a reddish disc-shaped structure with a diameter of about 1.5 mm, about 3 mm from the macula lutea to the nasal side. The optic disc is the part of the retina where the optic fibers collect through the eye and the beginning of the optic nerve. The optic disc has no light sensation due to the lack of photoreceptor cell, therefore, forming a physiological blind spot in the
visual field. When seeing in eyes normally, the blind spots in one eye's field of view can be compensated by the visual field of the contralateral eye, so no blind spot would be felt in the field of vision.

The optic disc develops from the embryo's stalk. All the retinal ganglion cell axons and retinal blood vessels need to pass through the optic disc. Thus even minor optic disc injury may cause serious clinical consequences[1]. Any pathological influence of ganglion axon in anatomical path from the retina to the brain can cause characteristic visual field defects, regular optic disc disc loss and paleness. These characteristic changes contribute to clinical location of the lesion. Therefore, studies of the morphology of optic discs has always been the focus of researchers. Understanding of development is of great important for the diagnosis and treatment of certain diseases such as optic nerve disease, retinopathy, glaucoma. Neonatal eye diseases have their characteristics in anatomy, physiology, pathology, clinical manifestations, diagnosis, treatment methods and other aspects. The fundus data measured from normal adults is not suitable criterion for juvenile fundus screening. Therefore, it is necessary to establish a visual disc parameter system for newborns to provide reference and basis for the diagnosis and treatment of neonatal diseases.

Newborn group lack capacity of communication, cooperation with inspection, as well as equipments, only some relatively simple instruments were used for measurement, such as direct or indirect ophthalmoscope. This requires fairly skilled level of ophthalmic instrument operation of the physician to avoid omissions. For the recording of the optic disc, the examination results are usually recorded by pictures or description. There are differences in subjective description between different doctors, lack of objective diagnostic evidence, that would influence early diagnosis and monitoring of diseases, which may lead to delay in diagnosis and treatment.

In recent years, with the rapid development of digital imaging systems, especially the neonatal digital wide-area fundus imaging system (Retcam) developed by Clarity Medical Systems in the United States, has been widely used in screening for neonatal eye diseases. Retcam has the characteristics of instant imaging, real and clear image, as well as can accurately record and further analyzed the image, including the degree and extent of the lesion. In addition, that make it possible to quantify numerical structure of the neonatal fundus structure according to the conversion relationship between the pixels measured by the lens provided by the manufacturer and the actual millimeter value. More studies on the morphology and parameters of optic discs in neonates, especially premature babies appears recently. Compared with domestic studies, researches mainly focused on retinopathy of prematurity [2–4], while premature infants and full-term newborns reports on the study of pediatric optic disc morphology are very rare [5–7]. Therefore, we designed this research topic, by taking pictures of the fundus of premature and full-term newborns, observing the morphological characteristics of the scleral ring of the optic disc, then recording and converting the specific values of the optic disc parameters of premature and full-term neonates. After comparing and analyzing the optic disc characteristics of premature and full-term neonates, the specific values of optic disc parameters in premature and full-term neonates in China will be summarized, that could provide a diagnostic basis for optic disc diagnosis and treatment of neonatal optic nerve diseases as well as congenital glaucoma.
Methods

Research population

Select newborns screened for neonatal fundus disease in the neonatal ward of Ruian Maternal and Child Health Hospital from January 1, 2016 to October 31, 2016. Including 60 premature infants (31.74 weeks to 36.86 weeks of gestational age, 33.57±1.11 weeks of average gestational age), and 60 full-term neonates (37.14 weeks to 40.85 weeks of gestational age, average gestational age 39.50±1.52 weeks). Among the premature babies, 30 (50%) males and 30 females (50%) received neonatal fundus screening within one week of birth (corrected gestational age 32.28 weeks to 37.71 weeks, mean corrected gestational age 34.19±0.70 weeks). In full-term neonates, 30 males (50%) and 30 females (50%) received neonatal fundus screening within 1 week (corrected gestational age 37.14 weeks to 41.71 weeks, mean corrected gestational age 39.97±1.52 weeks). All the guardians of the inspected were informed and signed the informed consent form. The study was approved by the Ethics Committee of the Eye Hospital of Wenzhou Medical University.

The inclusion criteria for preterm infants are (1) gestational age within 37 weeks; (2) within 1 week after birth; (3) physical condition can be matched with screening (4) delivery or laparotomy. The inclusion criteria for full-term neonates were (1) gestational age of 37 to 40 weeks; (2) birth weight over 2500 g; (3) within 1 week after birth; (4) delivery or laparotomy. Exclusion criteria are (1) birth injury and other major systemic diseases (such as abnormal brain development, cardiopulmonary disease, respiratory failure) and could not be screened for neonatal fundus; (2) eye infections and inflammation affect neonatal fundus screening operations; (3) eye disease affects the morphology of the optic disc; (4) optic disc congenital dysplasia affects the morphology of normal optic disc.

Retcam

Developed by Clarity Medical Systems, Retcam (Wide-Field Digital Pediatric Retinal Imaging System) V6.1.25.0 uses computer image acquisition software with five lenses to collect real-time dynamics of the anterior segment of the eye (including the cornea, anterior chamber angle, iris and lens) and the fundus (including the optic nerve and retina). Retcam instruments have advantages over traditional binocular indirect ophthalmoscopy [8]. Retcam is easy and convenient to operate and complete the inspection in few minutes. Retcam also has a wide range of 130°lens and high resolution, which can accurately determine the lesions and retinal vascularization. And Retcam generally takes 5 photos to complete the screening of neonatal eye disease (the posterior pole and 4 quadrants), can complete the fundus examination and diagnosis of the disease within a few minutes. In addition, photo images can be saved and exported in different formats for further analysis of the extent and extent of the lesion after the end of the examination. These images can also be used for ROP training, student teaching, and explaining the condition of the child's parents.

Fundus screening operation
Operation of each newborn is performed by the same experienced child ocular fund specialist. We drop the compound tropicamide eye drops to the eyes of the newborn 40 minutes before the test, waiting for the pupil to be fully dilated. We placed the newborn on the inspection table and fixed it with a wax bag. We added epiprene hydrochloride eye drops to the neonatal conjunctival sac for 3 minutes, and use the newborn-specific sputum to open the sputum and fully expose the eyeball after the surface anesthesia is fully effective. Dicorro ointment was used to make the RetCam probe couplant, then placed the lens vertically above the eye, gently touched the corneal surface, and followed the order of the posterior pole, the top, the temporal side, the lower side, and the nasal side, delete unclear pictures, clear fundus photos are saved and archived.

Data collection

We exported all the photos from the neonatal digital wide-area fundus imaging system instrument in jpg format without compression, and uniformly selected the right eye clear photos. We measured the video disc parameters using Markman v2.7.17, a professional measurement and annotation software developed by the Adobe AIR platform. All disc measurements and conversion of the optic disc were performed by the same researcher.

Disc measurement

The parameters of the optic disc, including the longitudinal diameter of the optic disc, the transverse diameter of the optic disc, the longitudinal diameter of the optic cup, the transverse diameter of the optic cup, the average diameter of the optic disc, the ratio of the cup to the pan and the cup to pan are measured in this study. The selected fundus photos were imported into the Markman V2.7.17 software (Fig.1a), ignoring the distortion and distortion produced by the camera system. Take the disc as the edge of the disc, according to the morphological characteristics of the neonatal disc, defined the vertical diameter of the optic disc as the longest diameter from 11 o'clock to 1 o'clock to 5 o'clock to 7 o'clock. The horizontal diameter refers to the shortest path from 8 o'clock to 10 o'clock to 2 o'clock to 4 o'clock. We use the same method to measure the vertical and horizontal diameters of the cup [9] (Fig.1b).

Unit conversion

According to the data provided by Retcam [10], this Retcam is the third generation instrument V6.1.25.0 version, with imaging pixels up to 1.92 million, of which the horizontal pixel is 1600 and the vertical pixel is 1200. By conversion, this Retcam instrument The conversion relationship between the pixel and the actual value is 0.0122 mm/pixel. According to the conversion relationship between pixels and millimeters, the longitudinal and transverse diameters of the optic disc and the optic cup are converted from pixel units to millimeter units, and the average diameter of the optic disc is then calculated.

Statistical analysis

Statistical data were analyzed with SPSS 22.0 (IBM. Armonk, NY, USA). Statistical analysis was performed on all data collected, and the optic disc morphology, optic disc scleral ring type and optic disc
parameters of premature and full-term neonates were summarized. The chi-square test was used to compare the differences between the four different types of optic discs in premature and full-term neonates. An independent sample $t$-test was used to compare the differences between disc diameter, disc diameter, cup diameter and cup diameter in premature and full-term neonates, $P<0.05$ (* or #) was considered statistically significant.

**Results**

**Basic information of the research subjects**

120 newborns (120 eyes), including 60 premature infants (30 males and 30 females), 60 full-term newborn (30 males and 30 females) were chosen in our study. Newborns are screened for neonatal fundus within one week after birth. The average gestational age, corrected gestational age, birth weight of premature and full-term neonates are shown in Table 1. The gestational age, corrected gestational age, and specific distribution of birth weight are represented by box plots (Fig.2a-c). The correlation between birth weight and birth gestational age as well as between birth weight and corrected gestational age are represented by scatter plots (Fig.2d, e).

The birth weight, gestational age and corrected gestational age of premature and full-term newborns measured by the experiment were found normally distributed by nonparametric test (single sample K-S test). Result of $t$ test showed that the birth weight, corrected gestational age and birth gestational age were the same in the two groups, indicating that the three indicators have the characteristics of variance and homogeneity. The birth weight was tested by $t$ test. The difference between the two groups was statistically significant ($t=-20.515, P=0.000$). It can be considered that the birth weight levels between the two groups were different, and the second group was significantly higher than the first group. The corrected gestational age was statistically significant between the two groups ($t=-32.887, P=0.000$), indicating that the difference between the two groups was statistically significant, and the second group was significantly higher than the first group. The difference in gestational age between the two groups was statistically significant ($t=-33.351, P=0.000$), indicating that the difference between the two groups was statistically significant, and the second group was significantly higher than the first group.

**Video disc parameters**

Average disc length, optic disc transverse diameter, optic disc longitudinal diameter/optical disc transverse diameter, optic disc average diameter, cup longitudinal diameter, cup transverse diameter, cup-and-panel longitudinal ratio, cup-to-disk lateral ratio of premature and full-term neonates were shown in Table 2. The distribution of the longitudinal diameter and transverse diameter of the optic disc in premature and full-term infants, the longitudinal diameter and the transverse diameter of the cup are compared using a box diagram (Fig.3a-d). The disc longitudinal diameter, optic disc transverse diameter, visual cup longitudinal diameter and visual cup transverse diameter of premature and full-term neonates measured by the experiment were found to be normally distributed by nonparametric test (single sample K-S test). The longitudinal diameter and transverse diameter of the optic disc, as well as the longitudinal
diameter and the transverse diameter of the optic cup in premature and full-term neonates by two independent sample \( t \)-tests, the results showed that \( P>0.05 \), indicating that premature and full-term neonates were there is no difference in optic disc parameters.

**Disc shape**

The average visual disc longitudinal diameter/opic disc transverse diameter of preterm infants included in this study was \( 1.29\pm0.01 \), and the full-length neonatal disc longitudinal diameter/opic disc transverse diameter was \( 1.27\pm0.01 \), and the ratio was higher than 1. Therefore, the optic discs of premature and full-term neonates were vertical oval discs, and no transverse elliptical discs were found in this study. In addition, the color of the optic disc is mostly pink or reddish, because some of the premature infants have residual vitreous primitive arteries, covering the surface of the optic disc, which may affect the observation of some cases of physiological depression. The optic disc borders of premature and full-term neonates are blurred compared to adult optic discs, and the borders are relatively irregular.

**Optic disc scleral ring morphology**

Most of the optic discs are surrounded by a scleral ring which presents four types, including acyclic (Fig.4a), single ring (Fig.4b), double ring (Fig.4c) and mixed (Fig.4d, Fig.4e) types. Mixed type is divided into single-ring double-ring hybrid, single-ring double-ring hybrid. Melanin filling can be observed in part of the optic disc and the scleral ring, which is especially evident in the double scleral ring. The distribution of optic disc scleral rings in preterm and term neonates is shown in Table 3.

Chi-square test showed the proportion of optic disc scleral ring morphology in preterm and full-term neonates was not the same (\( \chi^2=26.075, P=0.000 \)). Further, through the layered chi-square test, it was found that there was a significant difference between the two groups in the single-ring type of the scleral ring of the optic disc (\( \chi^2=5.058, P=0.025 \)). The scleral ring of the optic disc and the bicyclic pattern of the optic disc scleral ring also had a statistically significant difference between the two groups (\( \chi^2=19.863, P=0.000; \chi^2=9.755, P=0.002 \)). The irregular shape of the optic disc scleral ring was not statistically significant between the two groups (\( \chi^2=0.170, P=0.680 \)). Through the composition ratio of the optic disc scleral ring in the premature infant group and the full-term neonate group, the monocyclic type of the optic disc scleral ring has a higher proportion in preterm infants, and the proportion of the double ring of the optic disc scleral ring is significantly higher in preterm infants than in term newborns. The acyclic form of the optic disc scleral ring is significantly higher in term newborns, and the irregular shape of the optic disc scleral ring weren't significant difference between the two groups.

**Discussion**

The optic disc is the beginning of the optic nerve, is traversed by the retinal ganglion axon fibers in the nerve fiber layer and converges to the optic disc following the fine structure of the retina. All retinal ganglion axons pass through the optic disc. The optic disc consists of the front area of the screen
(between the screen and the glass body), the screen area and the rear area of the screen. The blood circulation of the optic disc is mainly from choroid around the optic disk which supplied by the Haller-Zinn arterial ring and the posterior ciliary artery. Since the structure of the optic disc includes all retinal ganglion cell axons and retinal blood vessels, even relatively small optic disc damage can cause serious clinical consequences. Any case in the anatomical pathway from the retina to the brain would affects the ganglion axons, causing a characteristic visual field defect. Therefore, many researchers have paid great attention and enthusiasm to the study of the morphology of optic discs over the years.

Understanding the characteristics and developmental rules of normal optic disc is of great significance for the diagnosis and treatment of diseases such as optic nerve disease, retinopathy and glaucoma. The size and shape of the optic disc in normal healthy eyes may vary greatly in different regions, races, stages of development and age, the appearance may be extremely asymmetric. Therefore, before identifying the pathological changes of the optic disc, it is necessary to grasp the morphological characteristics and developmental rules of the optic disc of the normal eye, so as to avoid missed diagnosis and misdiagnosis. The morphological characteristics of adult optic discs are significantly different from those of infants and young children, the size of optic disc and optic nerve at birth is 75% of that of adults. Neonatal eye disease has special characteristics in anatomy, physiology, pathology, clinical manifestations, diagnosis and treatment methods, as well as other aspects [11–13].

Previous studies mostly focused on the characteristics of adult optic discs. Fundus data measured from normal adults are not suitable screening criteria for neonatal fundus screening. Therefore, to establish a visual disc parameter system for newborns is of necessity, which provides a reference and basis for the diagnosis of neonatal fundus diseases, especially for the diagnosis and treatment of optic nerve diseases and glaucoma.

Because of the lack of neonatal fundus examination equipment, previous study of neonatal fundus was to analyzed the optic disc shape of children over 10 years old, and to evaluate the relationship between optic disc parameter morphology and birth gestational age or birth weight in the past. Fledelius et al. [14] noted that children with birth weight less than 2000 g had significantly greater disc C/D than full-term infants, but there was no significant difference between children born less than 2000 g and children born less than 1500 g. Hellstrom et al. [15, 8] reported that children at the age under 7 years had an average premature birth of 27 weeks, the optic disc and disc area were significantly smaller compared with full-term birth, and there was no difference in the C/D area between the two groups. In a study of 12-year-old children, Samarawickrama et al. [16] indicated that infants with intrauterine growth retardation had significantly greater optic disc C/D ratios than the normal group. It is suggested that intrauterine growth retardation may be a risk factor of glaucoma. Other studies also reported a significant increase in optic disc C/D ratio in infants with ischemic brain injury [17, 18]. However, these studies analyzed the disc shape of premature or full-term children over 7 years of age and did not represent the optic disc characteristics of the neonatal period.
In our study, 60 preterm infants were at a chronological gestational age of 31.74 to 36.86 weeks, with an average gestational age of 33.57 ± 1.11 weeks, average corrected gestational age of 34.19 ± 0.70 weeks, and the average birth weight of 2110.5 ± 106.07 g. The full-term gestational age of 60 full-term newborns ranged from 37.14 weeks to 40.85 weeks. The average gestational age was 39.50 ± 1.52 weeks, the average corrected gestational age was 39.97 ± 1.52 weeks, and the average birth weight was 3646.68 ± 106.67 g. Neonatal fundus screening was performed within one week of birth. There were significant differences in gestational age, corrected gestational age, and birth weight between the preterm and term newborns. Disc parameters of premature infants showed that longitudinal diameter of the optic disc is 1.43 ± 0.00 mm, the transverse diameter of the optic disc is 1.11 ± 0.04 mm, the longitudinal diameter of the optic cup is 0.44 ± 0.01 mm, the transverse diameter of the optic cup is 0.40 ± 0.01 mm, the ratio is 0.31 ± 0.01, and the transverse cup-to-disk ratio is 0.36 ± 0.01. Full-term neonatal optic disc parameters showed that longitudinal diameter of the optic disc is 1.42 ± 0.11 mm, the transverse diameter of the optic disc is 1.13 ± 0.05 mm, the longitudinal diameter of the optic cup is 0.44 ± 0.03 mm, the transverse diameter of the optic cup is 0.40 ± 0.05 mm, longitudinal the cup-to-disk ratio is 0.31 ± 0.05, and the transverse cup-to-disk ratio is 0.35 ± 0.03.

The neonatal optic disc parameters obtained in this study were compared with those of normal adults. Typical adult optic disc is elliptical with an average longitudinal diameter (1.9 mm) that is slightly larger than the average horizontal diameter (1.7 to 1.8 mm). In this study, we found that the visual disc longitudinal diameter/transverse diameter ratio was 1.29 in preterm infants and 1.27 in full-term infants, indicated the morphology of optic disc was vertical elliptical and the number of transverse elliptical optic disc was 0. This may indicate that the visual system in the neonatal period is at the beginning of development. The shape of the optic disc is mainly larger than the transverse diameter, and is mainly vertical and elliptical. The development of the eyeball and the development of the transverse diameter of the optic disc are accelerated with age, some may exceed the longitudinal diameter and develop into a transverse elliptical optic disc.

Current study of neonatal optic discs mainly focus on optic discs in preterm infants in different premature stages of preterm infant development, including premature infants with fixed eyeballs in formalin due to premature death [1, 19], birth babies [20, 21] and premature birth children [15, 18, 8, 22]. Different methods have also been introduced into analytical research. Binoculars and other methods [15, 17, 20, 21, 23] were used in some studies and the in vivo digital images used in this study all measured higher value than those measured by Rimmmer at autopsy. This may due to use of formalin fixation by Rimmmer and Liu, that may reduce the actual optic disc, or the amplification effect of the digital image in vivo.

In our study, we analyzed that birth weight and gestational age have no statistical significance on optic disc parameters at the gestational age of 31 to 40 weeks, which may indicate that the optic disc has developed to full-term birth levels around 31 weeks, which is related to JW Park [23]. In this study, the longitudinal cup-to-disk ratio and transverse cup-to-disk ratio of premature and full-term neonates were not statistically significant, with the values of 0.3 to 0.4.
In view of the fact that Hellstrom et al. pointed out that during childhood (at the age of 7 years) [14], the area of the edge of the optic disc was born 27 weeks before the child was significantly smaller than the full moon. This may due to premature infants, the degree of retinal maturity is different from normal newborns. In the last month of pregnancy, full-term infants are in a relatively stable environment in the mother's womb. However, premature babies are in different environments at the corresponding time, and may therefore change their physiology and metabolism. This change would lead to the optic nerve to increase to the maximum diameter at the age of 2 years, interfering with the natural apoptosis of the optic axon leading to excessive axonal apoptosis [24]. Therefore, the lower weight of premature babies, the lower the gestational age, the larger the cup and the smaller the area along the disc they will have after 2 years old.

In addition, our study observed that the scleral ring morphology of the optic disc has four forms, including acyclic, monocular, bicyclic, and irregular. Among the 60 eyes of premature infants, 8 were acyclic (10.0%), 22 were monocular (36.7%), 17 were bicyclic (28.3%), and 15 were irregular (25.0%). In the full-term neonates, the scleral ring morphology of the optic disc was acyclic (46.7%), monocular (18.3%), bicyclic (6.7%), and irregular (28.3%). The data showed that the ratio of the scleral ring monocyclic and bicyclic in the optic disc is significantly higher in the preterm infant group than in the full-term neonate group, while the acyclic ring ratio of the optic disc in the full-term neonatal group, significantly more than the proportion of premature infants. Among them, the double ring sign is considered to be a characteristic manifestation of optic nerve hypoplasia [25, 26]. Optic nerve hypoplasia is regarded as abnormal development of the optic nerve, characterized by a decrease in the number of optic nerve fibers in the optic nerve [27] and a small disc morphology [25], which may be only 1/3 – 1/2 of normal, and may be small or nearly normal. Comparing the proportion of the scleral ring bicyclic and monocular in the optic disc in premature and full-term neonates, we believe that the optic disc scleral ring bicyclic and monocular is a relatively early naive stage in the development of the optic disc during neonatal development.

Objects in our study ranged from premature to full-term neonates, from 31.74 weeks to 40.85 weeks of gestational age, and the proportion of double-rings decreased from 28.3–6.7% with increasing gestational age. This suggests that due to leaving the relatively stable uterus environment early in the final stages of pregnancy, oxygenation of the placenta changed to pulmonary oxygenation, fetal circulation of premature infants also changed. Oxygen saturation rises from mixed venous blood levels to arterial blood levels, while fetal lungs are still immature and do not perform the oxygen transport process well. These altered functions and metabolic requirements may have certain effects on the morphological development of the optic disc, slowing down the process of maturation of the scleral ring of the optic disc. Therefore, further follow-up studies are necessary for postnatal neonatal optic disc development.

In recent years, development of digital imaging technology, especially the neonatal digital wide-area fundus imaging system made it possible to conduct screening for neonatal eye diseases in ophthalmic hospitals [28, 29]. Neonatal digital wide-area fundus imaging systems overcome some of the shortcomings of traditional inspection equipment. Retcam takes only few minutes and could reduce the
impact of crying on newborns, especially those with poor general conditions. Screening and recording of fundus diseases can be completed with a minimum of 5 photos for the entire examination (posterior pole and 4 quadrants). However, Retcam also has limitations: 1) The lens design is more suitable for smaller infants than infants with larger months. 2) Preparation for dilation before the examination of neonatal fundus diseases would cause the time consuming. 3) Children with poor fit need fundus examination under general anesthesia. The cumbersome procedure and invasive anesthesia examination limit the fundus examination of older children.

**Conclusions**

In conclusion, our study showed that neonatal digital wide-area fundus imaging system (Retcam3) can not only provide clear fundus imaging images, but also data measurement and analysis of optic disc parameters. The morphology of the optic discs in premature and full-term neonates observed in this study was longitudinally elliptical. There was no statistically significant difference between the longitudinal diameter of the optic disc, the transverse diameter of the optic disc, the longitudinal diameter of the optic cup, and the transverse diameter of the optic cup.

The types of scleral rings of premature and full-term neonatal optic discs can be divided into four types: acyclic, single-ring, double-ring, and hybrid. Among them, the acyclic form represents the mature type of the optic disc scleral ring; the monocyclic type, the bicyclic type and the mixed type represent the naive type of the optic disc scleral ring. In premature infants, the naive type of optic disc scleral ring type (monocyclic and bicyclic) is higher than in term infants. The mature type of optic disc sclera (acyclic) is higher in term newborns than in preterm infants. The optic disc scleral ring hybrid type did not differ between preterm and term newborns. The scleral ring double loop sign of the optic disc is a normal stage of optic disc development.

**Abbreviations**

None.

**Declarations**

**Ethics approval and consent to participate**

The study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of the Eye Hospital of Wenzhou Medical University. Written, informed-consent of patients was obtained from a parent or guardian for participants under 16 years old.

**Acknowledgements**

None.
Authors’ contributions

XFF, JG and FC designed the study. XFF and QL collected the data.

CX, JDP and RTZ analysed the data, and XFF drafted the manuscript. XFF, JG, QL, LYZ, and FC were all involved in the interpretation of the results and were major contributors to the writing of the manuscript. All authors approved the final version of the paper for submission.

Funding

This study was supported by the Science and Technology Program of Wenzhou (Y20180729 to XFF). The funding offered support in the design of the study and collection, analysis, interpretation of data, and publication fee.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

All authors agreed on the manuscript.

Competing interests

The authors declare that they have no competing interests.

References

1. Rimmer S, Keating C, Chou T, et al. Growth of the human optic disk and nerve during gestation, childhood, and early adulthood. Am J Ophthalmol. 1993;116(6):748–53.
2. Wilson C, Theodorou M, Cocker KD, et al. The temporal retinal vessel angle and infants born preterm. Br J Ophthalmol. 2006;90(6):702–4.
3. Jonas JB, Bergua A, Schmitz-Valckenberg P, et al. Ranking of optic disc variables for detection of glaucomatous optic nerve damage. Invest Ophthalmol Vis Sci. 2000;41(7):1764–73.
4. Robb RM. Increase in retinal surface area during infancy and childhood. J Pediatr Ophthalmol Strabismus. 1982;19(4):16–20.
5. Kandasamy Y, Smith R, Wright IM, et al. Optic disc measurements in full term infants. Br J Ophthalmol. 2012;96(5):662–4.
6. Provis JM, van Driel D, Billson FA, et al. Human fetal optic nerve: overproduction and elimination of retinal axons during development. J Comp Neurol. 1985;238(1):92–100.

7. Mansour AM. Racial variation of optic disc parameters in children. Ophthalmic Surg. 1992;23(7):469–71.

8. Hellstrom A, Hard AL, Svensson E, et al. Ocular fundus abnormalities in children born before 29 weeks of gestation: a population-based study. Eye (Lond). 2000;14(Pt 3A):324–9.

9. McLoone E, O’Keefe M, Donoghue V, et al. RetCam image analysis of optic disc morphology in premature infants and its relation to ischaemic brain injury. Br J Ophthalmol. 2006;90:465–71.

10. Tucker SM, Enzenauer RW, Levin AV, et al. Corneal diameter, axial length, and intraocular pressure in premature infants. Ophthalmology. 1992;99(8):1296–300.

11. Wikstrand MH, Hard A-L, Niklasson A, et al. Birth weight deviation and early postnatal growth are related to optic nerve morphology at school age in children born preterm. Pediatr Res. 2010;67:325–9.

12. Stritzke A, Kabra N, Kaur S, Robertson HL, Lodha A. Oral propranolol in prevention of severe retinopathy of prematurity: a systematic review and meta-analysis. J Perinatol. 2019 Sep 30.

13. Tsang JKW, Liu J, Lo ACY. Vascular and Neuronal Protection in the Developing Retina: Potential Therapeutic Targets for Retinopathy of Prematurity. Int J Mol Sci. 2019;20(17).

14. Fledelius H. Optic disc cupping and prematurity. Large cups as a possible low birth weight sequel. Acta Ophthalmol (Copenh). 1978;56(4):563–73.

15. Hellstrom A, Hard AL, Chen Y, et al. Ocular fundus morphology in preterm children. Influence of gestational age, birth size, perinatal morbidity, and postnatal growth. Invest Ophthalmol Vis Sci. 1997;38(6):1184–92.

16. Samarawickrama C, Huynh SC, Liew G, et al. Birth weight and optic nerve head parameters. Ophthalmology. 2009;116(6):1112–8.

17. Jacobson L, Hard AL, Svensson E, et al. Optic disc morphology may reveal timing of insult in children with periventricular leukomalacia and/or periventricular haemorrhage. Br J Ophthalmol. 2003;87(11):1345–9.

18. Jacobson L, Hellstrom A, Flodmark O. Large cups in normal-sized optic discs: a variant of optic nerve hypoplasia in children with periventricular leukomalacia. Arch Ophthalmol. 1997;115(10):1263–9.

19. Mao J, Luo Y, Liu L, Lao J, Shao Y, Zhang M, et al. Automated diagnosis and quantitative analysis of plus disease in retinopathy of prematurity based on deep convolutional neural networks. Acta Ophthalmol. 2019 Sep 27.

20. De Silva DJ, Cocker KD, Lau G, et al. Optic disk size and optic disk-to-fovea distance in preterm and full-term infants. Invest Ophthalmol Vis Sci. 2006;47(11):4683–6.

21. McLoone E, O’Keefe M, Donoghue V, et al. RetCam image analysis of optic disc morphology in premature infants and its relation to ischaemic brain injury. Br J Ophthalmol. 2006;90(4):465–71.
22. Jandeck C, Kellner U, Lorenz B, et al. Guidelines for ophthalmological screening of premature infants in Germany]. Klin Monbl Augenheilkd. 2008;225(2):123–30.

23. Park JW, Park SW, Heo H. RetCam image analysis of the optic disc in premature infants. Eye (Lond). 2013;27(10):1137–41.

24. Lambert SR, Hoyt CS, Narahara MH. Optic nerve hypoplasia. Surv Ophthalmol. 1987;32(1):1–9.

25. Novak JM, McLaren P. Optic nerve hypoplasia. J Am Optom Assoc. 1987;58(2):122–6.

26. Beuchat L, Safran AB. Optic nerve hypoplasia: papillary diameter and clinical correlation. J Clin Neuroophthalmol. 1985;5(4):249–53.

27. Zeki SM, Dutton GN. Optic nerve hypoplasia in children. Br J Ophthalmol. 1990;74(5):300–4.

28. Al-Khaled T, Mikhail M, Jonas KE, Wu WC, Anzures R, Amphonphruet A. Training of Residents and Fellows in Retinopathy of Prematurity Around the World: An International Web-Based Survey. J Pediatr Ophthalmol Strabismus. 2019;56(5):282–7.

29. Naldi A, Pivetta E, Coppo L, Cantello R, Comi C, Stecco A. Ultrasonography Monitoring of Optic Nerve Sheath Diameter and Retinal Vessels in Patients with Cerebral Hemorrhage. J Neuroimaging. 2019;29(3):394–9.

Tables

Table 1 Basic information on premature and full-term neonates.

|                      | Premature baby | Full-term newborn |
|----------------------|----------------|-------------------|
| Number of cases (eye)| 60             | 60                |
| Average birth gestational age (week) | 33.57±1.11    | 39.50±1.52        |
| Average corrected gestational age (week) | 34.19±0.70    | 39.97±1.52        |
| Average birth weight (g) | 2110.5±106.07 | 3466.68±106.67    |

Table 2 Value table of specific parameters of premature and full-term neonatal optic discs. (n=120)
Table 3  Distribution of scleral ring types in optic discs in premature and full-term neonates.

| Scleral ring type of optic disc | Total |
|--------------------------------|-------|
| Acyclic type (%)               |       |
| Single ring type (%)           |       |
| Double ring type (%)           |       |
| Hybrid (%)                     |       |
| Premature baby                 |       |
| 6(10.0)                        |       |
| 22(36.7)                       |       |
| 17(28.3)                       |       |
| 15(25.0)                       | 60    |
| Full-term newborn              |       |
| 28(46.7)                       |       |
| 11(18.3)                       |       |
| 4(6.7)                         |       |
| 17(28.3)                       | 60    |

Figures
Figure 1

Equipment and methods. a MarkMan V2.7.17. b Measurement of the optic disc (in pixels).
Figure 2

Basic information of the research object. a Comparison of gestational age distribution between premature and full-term neonates. b Comparison of corrected gestational age distribution between premature and full-term neonates. c Comparison of birth weight distribution between premature and full-term neonates. d Scatter plot of birth weight and gestational age in preterm and term newborns. e Scatter plot of birth weight and corrected gestational age in preterm and term newborns.
Figure 3

Disc parameter. a Comparison of longitudinal diameter distribution of optic disc in premature and full-term neonates. b Comparison of transverse diameter distribution of optic disc in premature and full-term neonates. c Comparison of longitudinal diameter distribution of premature infants and full-term neonates. d Comparison of transverse diameter distribution of premature infants and full-term neonates.
Figure 4

The shape of optic disc and optic disc scleral ring. a Optic disc scleral ring acyclic. b Optic disc scleral ring single ring. c Optic disc scleral ring double loop. d Disc sclera hybrid ring (single-double). e Disc scleral ring hybrid (single-none).