Analysis of differences in screening results of neonatal ophthalmopathy between Neonatal Intensive Care Unit and Mother-infant Room Ward

Gang Wang  
Zhongshan City People's Hospital

Lu-Bo Fan  
Zhongshan City People's Hospital

Nai-Yang Li (zslee6@qq.com)  
Zhongshan City People's Hospital

Research Article

Keywords: Eye screening, Neonate intensive care unit (NICU), Mother-infant Room Ward (Control Group), Wide-field fundus imaging system

Posted Date: October 12th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2128511/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Objective: To compare and analyze the differences in the results of neonatal ocular diseases screening in the Intensive Care Unit, and the Mother-infant ward in the same room of a general hospital.

Methods: The eye screening data of newborns were collected in Zhongshan City People's Hospital, from December 2018 to December 2021, using a digital wide-field fundus imaging system (RetCam3). The neonates were divided into Neonatal Intensive Care Unit group (NICU) and Mother-infant Ward group (Control Group) according to the ward in which the neonates were located. The differences in the results between the two groups were analyzed in the same manner. Results: A total of 7239 neonates completed eye examinations, of which 1200 (16.58%) had abnormal eyes. In the Control Group 5481 cases were screened. The result showed that 1000 cases (18.24%) with ocular abnormalities; 976 cases (17.80%) with retinal hemorrhage; and 24 cases (0.44%) with other abnormalities. 1758 cases in the NICU group were screened. Out of which 200 cases with ocular abnormalities (11.37%), 165 cases (9.38%) of retinal hemorrhage, 19 cases (1.10%) of retinopathy of prematurity (ROP), 6 cases of ROP were treated with intravitreal injection, and 16 cases (0.91%) of other abnormalities.

Conclusion: The rate of retinal hemorrhage was significantly lower in the NICU group than in the Control Group, but other congenital ocular abnormalities accounted for greater proportion of children in theNICU group. General newborn screening is conducive to the early detection and treatment of various eye diseases, reducing the missed diagnosis of eye diseases. For high-risk neonates in the NICU group, eye disease screening is more imperative.

Introduction

Neonatal ophthalmopathy has its own characteristics in terms of pathogenesis, development, and outcome. Missing the optimal treatment time window may cause irreversible visual dysfunction. This can even be life-threatening to a child. If more neonatal eye diseases children can receive timely and accurate treatments, the visual function of more children can be saved. Hence, the long-term quality of children's lives can be improved. In a natural environment the heavy burden on children's families and society can be reduced. The effective method for the prevention of neonatal eye disease is through routine screenings of neonatal eye conditions and timely treatments of the early lesions found in the children. However, there are still some discrepancies in the screening methods and in the treatments of the screenings for neonatal ophthalmopathy at this time. The screening is mainly aimed at low-weight, low-gestational age babies instead of full-term babies. In addition, it is more necessary to carry out neonatal eye screening disease for children in the neonatal intensive care unit (NICU). Studies such as Teow [3] found that eye diseases such as retinopathy and retinoblastoma still exist in full-term newborns and NICUs that threaten children's vision.

Zhang Jin [4] and others compared the results of the examinations performed on children with neonatal eye disease in the same ward of NICU and in the Control Group. It was found that eye abnormalities accounted for 14.18% in NICU children, 8.34% in the Control Group. The risk of eye abnormalities of high-risk patients in NICU was also significantly higher than that of normal newborns in the Control Group.

Given the presence of eye diseases in both NICU and the Control Group neonates that may threaten the children's vision. The eye screening data of 7,239 newborns in Zhongshan People's Hospital from December 2018 to December 2021 using a digital wide-field fundus imaging system (RetCam3) was reviewed. This review compared the proportion and types of abnormal ocular findings in the neonates in NICU and the Control Group, to provide a reference for the necessity of universal screening of neonatal eye disease which can reduce the rate of missed diagnosis of neonatal eye diseases.

1 Data And Methods

1.1 Clinical Information
The retrospective study was conducted on 7239 cases of neonatal screening data collected at Zhongshan People's Hospital from December 2018 to December 2021. The newborns were, according to the wards where they were, divided into Intensive Care Unit group (NICU) and Mother-Infant Room group (Control Group). The main risk factors in the NICU group included, in addition to low weight and premature birth, some diseases such as mothers with diabetes mellitus and difficult pregnancy etc., and infants with such as ischemic hypoxic encephalopathy, inhalation pneumonia and other diseases. The Control Group consisted of full-term newborns.

Among them in the Control Group 5,481 newborns (2,821 boys and 2,660 girls), Gestational age (39.1 ± 1.2) weeks; Birth mass (3249.6 ± 381.2) g; 1758 newborns in NICU group (982 boys and 776 girls), Gestational age (36.9 ± 3.1) weeks; Birth mass (2753.7 ± 994.6) g; The examination was be undertaken by the Chief Physician of the Ophthalmology department and the senior physician with the title of Attending Physician or higher rank. The research was approved by the Ethics Committee of Zhongshan People's Hospital, and all participants were given an Informed Consent form. They must sign the Informed Consent Form for Neonatal Eye Disease Screening.

1.2 Screening method

To ensure the safety of the infants' lives, screening for the neonates from the NICU group was carried out under the guardianship of NICU specialists. The newborns included in the screening were prohibited from breastfeeding for 30 minutes prior to the screening. One hour before the examination the participating newborns were given compound topicamine eye drops to dilate the pupils; then one drop every ten minutes thereafter for a total of three drops. After a minimum of 6mm pupillary dilation was achieved the screening began. The screening was done in the special neonatal eye disease screening room for both the neonatal care unit (NICU) and the Mother-child ward (Control Group). Topical anaesthetic eye drops propemecaine hydrochloride 0.5% was applied to anaesthetise the eyes. Using RetCam3 reference to the Expert Consensus on Fundus Screening for Newborns of the Child Eye Screening Group of the Child Eye Care Professional Committee of the China Maternal and Child Health Association. The whole retina would be imaged by a five-way photography. Retinal images were collected in order of posterior pole, temporal side, upper side, nasal side and lower side of the fundus optic papilla. In addition, care was given to observe the front section and the glass cavity. The results were recorded in detail. Eye drops of tobramycin were administered at the end of the examination in a timely fashion.

1.3 Statistical analysis

Data was explored and analyzed using SPSS software version 23.0. and the normal distribution data was presented using mean ± standard deviation(±s). The counting data was presented as frequency and percentage and the χ² test was used for inter-group comparison. statistical significance was defined by a P value of less than 0.05.

2 Results

2.1 General Information

A total of 7,239 newborns completed eye screening. They were divided into neonatal intensive care units (NICU Group) and Mother-infant ward group (Control Group). 1758 in the NICU group and 5481 in the Control Group. Basic neonatal information including sex, birth weight, gestational age, birth mode, etc., was recorded in detail in Table 1.

Table 1 General information on two groups of newborns Number (%)
### Group Statistics

<table>
<thead>
<tr>
<th>Group</th>
<th>Gender</th>
<th>Birth weight</th>
<th>Mode of delivery</th>
<th>Birth weight</th>
<th>Single multiple births</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>(\geq) Week</td>
<td>Week</td>
<td>Natural birth</td>
<td>Cesarean section</td>
</tr>
<tr>
<td>Control Group</td>
<td>2821</td>
<td>2660</td>
<td>5343</td>
<td>138</td>
<td>3647</td>
<td>1834</td>
</tr>
<tr>
<td>NICU Group</td>
<td>982</td>
<td>776</td>
<td>1055</td>
<td>703</td>
<td>866</td>
<td>892</td>
</tr>
</tbody>
</table>

Note: Control group = mother-child ward; NICU group = neonatal intensive care unit

### 2.2 Overall situation of eye abnormalities in two groups

A total of 7,239 neonatal eye screenings, 14,478 eyes and 1,200 neonatal eye abnormalities accounting for 16.58% of the total, were completed through the development of relevant screening projects and standards. A statistically significant difference between the Control Group and NICU group \((P < 0.05)\), as shown in Table 2.

#### Table 2 Overall situation of two groups of neonatal eye disease screening  Number (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Number of normal cases</th>
<th>Number of abnormal cases</th>
<th>(\chi^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>5481</td>
<td>4481</td>
<td>1000</td>
<td>18.25</td>
<td>45.405</td>
</tr>
<tr>
<td>NICU Group</td>
<td>1758</td>
<td>1558</td>
<td>200</td>
<td>11.38</td>
<td></td>
</tr>
</tbody>
</table>

Note: Control group = mother-child ward; NICU group = neonatal intensive care unit

### 2.3 Distribution of eye abnormalities in two groups

A total of 1,200 children with congenital eye abnormalities were found, accounted for 16.58% of the total number of newborns. Abnormalities of 1000 in 5481 cases of Control Group, accounted for 18.24% and haemorrhage 976 cases, accounted for 17.80% of the Control Group. In the 1758 cases of NICU group there were 200 cases of abnormalities which accounted for 11.37%. 165 Bleeding cases which accounted for 9.38%. The vast majority of abnormality was retinal haemorrhage. Mentoring parents to have early detection, early diagnosis and early treatments can help to shorten the course of development on eye disease with positive therapeutic significance such as retinopathy of prematurity, congenital retinoblastoma, congenital cataracts, etc. For some congenital eye abnormalities less intense therapeutic significance such as retinal degeneration, corneal leukoplasia, etc., the children's families should be informed promptly so as not to cause psychological burden and other contradictions. The detection of congenital eye abnormalities in the Control Group and NICU group is shown in Table 3.

#### Table 3 Abnormalities in Screening for Neonatal Eye Diseases in Two Groups  Number (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>RH</th>
<th>ROP</th>
<th>ROP-like</th>
<th>RB</th>
<th>PHPV</th>
<th>Retinal degeneration</th>
<th>Congenital cataracts</th>
<th>Pupillary residual membrane</th>
<th>Corneal leukoplasia</th>
<th>Others</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>976</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>1000</td>
</tr>
<tr>
<td>NICU Group</td>
<td>165</td>
<td>19</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>200</td>
</tr>
</tbody>
</table>

Note: RH = retinal hemorrhage; ROP = retinopathy of prematurity; ROP-like = retinopathy of similar premature infants found in full-term infants; RB = congenital retinoblastoma; PHPV = persistent hyperplasia of primary vitreous; Others: albino fundus, optic papillary pigmentation, peripheral white spot, peripheral exudative retinopathy and other lesions.
2.4 Two Groups of Eye Abnormalities Prognostic and outcome

Among 1200 newborns with abnormal screening results, the most common abnormality was RH, which was eventually absorbed without any treatment. In children with ROP and ROP-like, 5 cases of them had a one-time anti-VEGF injection treatment. Another one case had a two-time anti-VEGF injection (Ranibizumab) treatment. After that the retinal spine gradually decreased and eventually subsided. In 2 cases of congenital cataract newborns, one case was transferred to an upper-level hospital for further treatment without surgery. They are under a follow-up plan. Another newborn is currently 10 months old and is in our hospital's follow-up plan. Two cases of RB neonates were transferred to an upper-level hospital for diagnosis and care. Surgeries were completed. Among them, one case of neonatal diagnosis of binocular RB. The left eye was more severe than the right eye. After surgical treatment the left eye lost its function. The vision of the right eye was at 0.5. A higher-level hospitals recommended that regular follow-up and surgery again if necessary. In another case, RB was diagnosed in the right eye, the left eye was normal. The right eye extraction had been performed and the life of the two newborns described above was not threatened after the surgery. In addition, retinal degeneration, permanent primitive vitreous hyperplasia, pupillary residual membrane, corneal leukoplakia and other abnormalities have not been surgically treated. They are to be followed up.

3 Discussion

Early, accurate and comprehensive eye examination of newborns is a crucial step in prevention and treatment of blindness in children's vision care and in the society as a whole. Facilitating timely and effective intervention in all types of eye diseases in newborns within the optimal time window plays a key role in the physical and mental health of newborns [1]. Digital Wide Area Fundus Imaging System (RetCam3) is well imaged, easy to operate and can record the eye situation objectively and accurately. The device has been widely used in many hospitals around the world and is important for neonatal eye screening [7].

The study collected 7,239 cases of neonatal eye disease screening data, and results showed that the abnormal rate was 16.58% (1200 cases). Among them the highest rate was retinal hemorrhage (RH) which accounted for 95.08% of all abnormalities. The results are basically consistent with those of Zhao Peiquan [1]. We found that the main reason why the overall ocular abnormality rate was lower in the NICU group (11.37%) than in the Control Group (18.24%) was that the positive rate of retinal bleeding (9.38%) was lower in NICU group than in the Control Group (17.80%). The reason was that children in NICU were hospitalized for longer periods of time. The intervals between screenings was usually more than one week while most mild and moderate retinal haemorrhage would be generally absorbed within 1 to 2 weeks, leaving no trace, making some children with haemorrhage absorbed during screening. Therefore, the data obtained do not represent the actual onset of the disease. There were other eye abnormalities except retinal bleeding 35 cases in NICU group (17.5%), 24 cases (2.4%) in the Control Group. The abnormal rate of NICU group was significantly higher than that of the Control Group. The threat of optic function was more serious for those children. Therefore, it is more necessary to carry out screenings to newborns with risk factors in NICU for eye disease. The results of this study show that screening neonatal eye disease with the same device (RetCam3) support, and comparative analysis of the proportions and types of eye abnormalities in the NICU and Control Groups found that both groups had congenital ophthalmopathy that seriously affected visual function and even threatened the children's lives. Such as fundus bleeding, retinopathy of prematurity, congenital retinoblastoma, etc., a total of 19 cases of retinopathy in premature infants were detected in the NICU group. There were no stage III and lesions in the 19 ROPs. 13 cases of phase I lesions in region III and 6 cases of phase II lesions in region III. The 6 children were diagnosed thoroughly. Their families were given an Informed Consent to sign before the emergency injection of anti-vascular endothelial growth factor in the vitreous cavity (VEGF) (Ranibizumab) was administered. Anti-VEGF therapy not only can reduce the formation and development of uncontrolled retinal neovascular vessels, it can also vascularize vasculature without blood vessels, including neural and vascular development that supports the retina [8]. The peripheral retina was vascularized after 1 to 2 injections of anti-VEGF drugs in 6 infants with ROP. Five of them were successfully treated by one surgery. The cure rate was 83.4%, the recurrence rate was 16.6%. The recurring condition of a child was under control after a second injection. The results were, primarily, consistent with those of Xiong WeiWei [9] et al. In recent years, with the promotion of internet medicine, artificial intelligence has played an important role in the screening and diagnosis of eye diseases. Artificial intelligence has significantly increased the sensitivity and specificity of ROP diagnosis [10, 11]. Enabling early detection, early diagnosis and treatment of children with ROP in the optimal time window is a great boon for
children with critical NICU patients. ROP-like fundus changes may also occur in healthy full-term children of the Control Group. In this study, 3 cases of ROP-like in the Control Group were 0.3% and 3 cases of ROP-like in NICU group were 1.5%. None of the six cases of ROP-like disease progression met the standard of intervention, and the retinal spine gradually diminished and eventually subsided. The factors of ROP-like lesions are similar with those of premature infants. That is, oxygen supply, low birth mass, multiple births, etc., which can make irreversible visual impairment [12–14]. Why the incidence of ROP-like in NICU was significantly higher than in the control group was perhaps mainly associated with a history of oxygen inhalation of the three children. More attention should be paid to the children with NICU with a history of oxygen inhalation. One case of RB was found in the Control Group and NICU group respectively. Both cases were transferred to the upper-level hospital for diagnosis and surgery as needed. As a result, the lives of the two newborns were not threatened. There was a newborn's older brother who had been diagnosed RB. The family history was verified but showed no significant abnormalities were seen during the newborn's follow-up examination. Further follow-up was ongoing. Studies such as Liu Yue [15] found that the misdiagnosis rate of RB was as high as 3.91%. All cases of misdiagnosis have progressed to the advanced stage at the time of final diagnosis and were treated with eye extraction. The common types of clinical misdiagnosis include Coats disease, intraocular inflammation, and confusion with other tumors in the eye. While promoting mass screenings, we should also pay attention to improving the accuracy of diagnosis.

A particular advantage of the study was the large number of cases, the use of the same screening criteria, the same screening equipment, fixed ophthalmology screening physicians, and the summary and analysis of the results of the screening for NICU and the Control Groups showed that general ophthalmopathy screening for all newborns in NICU and Maternal and Child Rooms (Control Group) may be widely applicable.

4 Conclusion

Combined with the newborn's own characteristics and screening process specifications, Comprehensive screening for neonatal eye diseases in general hospitals is essential. Where conditions exist, both neonates in the intensive care units and those in the same ward as mother and child should be included in universal screening for neonates. In order to facilitate early detection and treatment of various eye diseases, reduce the rate of missed diagnosis and blindness of caused by eye diseases, eye screening is most important for high-risk newborns in the Neonatal Intensive Care units.

Abbreviations

Control group = mother-child ward; NICU group = neonatal intensive care unit; RH = retinal hemorrhage; ROP = retinopathy of prematurity; ROP-like = retinopathy of similar premature infants found in full-term infants; RB = congenital retinoblastoma; PHPV = persistent hyperplasia of primary vitreous; Others: albino fundus, optic papillary pigmentation, peripheral white spot, peripheral exudative retinopathy and other lesions.

Declarations

Acknowledgements

The authors thank all doctors and nurses of Zhongshan People's Hospital and Medical Assistants. We also sincerely thank all patients and their families for their participation.

Authors' contributions

Gang Wang designed the study, analyzed the relevant data, drafted and revised the manuscript. Lu-Bo Fan helped complete eye disease screening and took charge of data collection and quantity control in the data ophthalmology center. Prof. Nai-yang Li conceptualised the study while Gang Wang contributed to the design of the work and was a major contributor in writing the manuscript. All the authors reviewed the manuscript rigorously.

Funding
Research Grant of Key Laboratory of Regenerative Medicine, Ministry of Education, Jinan University(No ZSYXM202109); Major Project of Zhongshan People’s Hospital (Dengfeng Plan).

**Availability of data and materials**

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**Declarations**

**Ethics approval and consent to participate**

Ethical approval was obtained from the Ethics Committee of Zhongshan People’s Hospital. This study adhered to the tenets of the Declaration of Helsinki and Expert consensus on fundus screening for newborns from Child Eye Screening Group of the Child Eye Care Professional Committee of the China Maternal and Child Health Association.

A written informed consent for Neonatal Eye Disease Screening was obtained from the parents/legal guardians of the minors included in this study, who participated.

**Consent for publication**

Consent to publish was provided in writing from the appropriate parents or legal guardians of the minors included in the study, as well as the minor used in an image within the consent forms attached to the manuscript.

**Competing interests**

The authors declare no conflict of interest.

**Author details**

1 Eye Centre, Zhongshan City People’s Hospital, 528403, Zhongshan, P.R. China

2 Guangdong Medical University, Zhanjiang, 524000, P.R. China

Correspondence to: Nai-Yang Li, Eye Centre, Zhongshan City People’s Hospital, 528403, Zhongshan, P.R. China, Email: zslee6@qq.com

**References**


