Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci

August 2022; 8(3):333-339

RESEARCH ARTICLE

DOI: 10.19127/mbsjohs.1072251

Impact of COVID-19 Outbreak on Retinopathy of Prematurity Screening

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Received: 11 February 2022, Accepted: 13 March 2021, Published online: 31 August 2022

Abstract

Objective: To evaluate the impact of COVID-19 outbreak on screening of premature babies for retinopathy of prematurity (ROP).

Methods: Medical records of infants who underwent ROP screening at Ordu University, Training and Research Hospital were reviewed, retrospectively. Sixty premature babies who were not brought into their follow-up visits and reported to the Child, Adolescent, Woman and Reproductive Health (CEKUS) unit between March 2020 and March 2021 were included. The patients were divided into 4 groups according to the timing of CEKUS reports; Group 1: March-May 2020, Group 2: June-August 2020, Group 3: September-November 2020, and Group 4: December 2020-February 2021.

Results: A total number of 60 babies were reported to the CEKUS unit between March 2020 and March 2021. While 18% of the patients were consulted from our neonatal intensive care unit (NICU), 82% of the infants were referred from other NICUs. The parents of only 17 (28%) of all patients were living in Ordu, additionally. Compared to the total number of patients reported to the CEKUS unit in the last year before the onset of the pandemic, a decrease in compliance with the appointments was observed after the announcement of the first COVID-19 case in Turkey ($p<0.001$). Adherence to the appointments increased in the period when COVID-19 patients decreased. When the COVID-19 cases began to rise again significantly after November (Group 4), the number of CEKUS reports increased correspondingly. However, there was no significant correlation between the number of CEKUS reports and the total number of COVID-19 cases in the groups ($p = 0.600$, $r = 0.400$).

Conclusion: In addition to the difficulty of screening for ROP since the onset of the COVID-19 outbreak, the follow up of babies who are not brought in has become a serious problem. A decrease in adherence to appointments was observed after the beginning of the COVID-19 pandemic. An institution such as our CEKUS unit may help the ophthalmologists and neonatologists to complete all screening sessions. Most babies that were not brought in to ROP screening, were also the ones referred from other NICUs and those who lived in neighboring cities, in our study. Therefore, increasing the number of ROP units may also prevent the non-adherence of the parents.

Keywords: COVID-19, premature, retinopathy of prematurity, screening

Suggested Citation: Keles Sahin A, Uzun A. Impact of COVID-19 Outbreak on Retinopathy of Prematurity Screening. Mid Blac Sea Journal of Health Sci, 2022;8(3):333-339.

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Note: This study was presented as oral presentation at 21st International Eastern Mediterranean Family Medicine Congress, 2022.

INTRODUCTION

Preterm infants with a low birth weight (BW) and small gestational age (GA) may develop a proliferative retinal vascular disorder which is known as retinopathy of prematurity (ROP), one of the leading causes of childhood blindness, worldwide (1). While patients lower than 1000 g of BW and 28 weeks of GA have an increased risk for severe ROP in high-income countries, the disease may be seen even in infants up to 2000 g of BW and up to 37 weeks of GA in developing areas (2). Regular eye examinations, timely screening and appropriate treatment are crucial to prevent severe visual loss in these babies.

Turkish Ophthalmological Association (TOA) and Turkish Neonatal Society (TNS) recommended that "all preterm babies smaller than 34 weeks or lower than 1700 g, and those bigger than 34 weeks and heavier than 1700 g receiving cardiopulmonary support and who were considered as risky by the attending clinician should be examined", in the revised National Guideline on ROP in 2021 (3). According to these national guidelines published by TOA and TNS, screening and follow-up of premature infants for ROP has been performed by the same experienced ophthalmologist at Ordu University, Training and Research Hospital since 2013. In 2019, we began to use a new protocol model for the follow up of babies who missed their visits at our hospital. When babies are not brought into their appointments, their families are reported to the Child, Adolescent, Woman and Reproductive Health (CEKUS) unit within the Provincial Health Directorate. The CEKUS unit informs the family physicians to refer the parents to the ROP unit. However, the use of this protocol is unfortunately not possible in all ROP units. Therefore, it is difficult to find parents who miss their babies' appointments. Especially in extraordinary situations such as pandemics, the importance of ensuring the continuity of ROP screening sessions and having a specific institution where premature infants can be reported when they are not brought into their appointments has emerged.

In the first year of the coronavirus disease (COVID-19) pandemic, elective examinations and surgeries were cancelled except for emergencies. In our ROP unit, screening and treatment for ROP continued in the same way, taking into account the principals recommended by the Infection Control Committee. Since the first case of COVID-19 was reported in Turkey, we have observed an increase in the number of patients reported to the CEKUS unit. In the current study, we aimed to evaluate the impact of COVID-19 outbreak on screening of premature babies for ROP.

METHODS

Medical records of infants who underwent screening for ROP at Ordu University, Training and Research Hospital were reviewed, retrospectively. Sixty premature babies who were not brought in to their appointments and reported to the CEKUS unit between March 2020 and March 2021 were included in the study. The demographics, BW and GA of patients, the timing of first examination and the neonatal intensive care unit (NICU) that consulted the infant were recorded. The clinical characteristics at last visit before discontinuation and at first visit after CEKUS report, and the interval between these two examinations were also reviewed, retrospectively. The patients were divided into 4 groups according to the timing of CEKUS reports; Group 1: March - May

2020, Group 2: June - August 2020, Group 3: September - November 2020, and Group 4: December 2020 - February 2021. The numbers of COVID-19 cases by groups were calculated by accessing the Ministry of Health COVID-19 Information Platform (4). The total number of patients reported to the CEKUS unit in the last year before the onset of the pandemic (between February 2019 and February 2020) was also recorded.

The study protocol was approved by Ordu University Clinical Research Ethics Committee (approval number: 2021/86), and the study procedures were conducted in accordance with the tenets of Helsinki Declaration. Since the study was performed based on retrospective data analysis, informed consent was not obtained.

Statistical analysis

All data were analyzed using the SPSS statistical software package, version 21.0 (SPSS Inc., Chicago, IL, USA). Data were expressed as means with ranges for continuous variables. Categorical variables were expressed as frequency (percentage) and compared using Pearson's chi-square test. A normality check was performed using the Kolmogorov–Smirnov test. The number of CEKUS reports in the groups was compared with the total number of COVID-19 cases in those months using the Spearman correlation coefficient. $P < 0.05$ was accepted as a statistically significant level.

RESULTS

A total number of 60 babies were reported to the CEKUS unit between March 2020 and March 2021. Demographics and clinical characteristics of all patients are given in Table 1. While 11 (18%) patients were consulted from our NICU, 49 (82%) patients were the ones who were referred from other NICUs in and around Ordu. Additionally, the parents of 17 (28%) babies were living in Ordu, and the parents of the remaining 43 (72%) infants were living in different cities.

As the total number of patients reported to the CEKUS unit in the last year before the onset of the pandemic was 14, a decrease in the adherence to the appointments was observed after the announcement of the first COVID-19 case in Turkey on March 10, 2020 ($p<0.001$). The number of CEKUS reports and COVID-19 cases according to the groups are given in Table 2. In the current study, there was no significant correlation between the number of CEKUS reports and the total number of COVID-19 cases in the groups ($p = 0.600$, $r = 0.400$). Most of the babies not brought in were the ones who were referred from other NICUs and those were living in neighboring cities. Adherence to the appointments increased in the period when COVID-19 patients decreased. However, as the COVID-19 cases began to rise again after November, the number of infants reported to the CEKUS unit increased correspondingly.

The mean postmenstrual ages at last visit before discontinuation and at first visit after CEKUS report were 39.3 (range: 35 - 47) weeks and 45.7 (range: 38-53) weeks, respectively. The interval between these two examinations was 6.1 (range: 3-10) weeks. Although in 46 (77%) of these babies, retinal vascularization reached temporal ora serrata at first visit following CEKUS report, retinal vascularization was still incomplete in 9 (15%) patients. Unfortunately, ROP was still persisting in 5 (8%) patients. None of the parents missed their baby's

appointments again. The patients whose retinal vascularization was completed, were referred to Pediatric Ophthalmology section for detailed ophthalmological evaluation.

Table 1. Demographics of patients (ROP: Retinopathy of prematurity, CEKUS: Child, Adolescent, Woman and Reproductive Health, PM: Postmenstrual)

Female / Male	31 patients (52%) / 29 patients (48%)
Gestational age	32.65 (range: 22 - 37) weeks
Birth weight	1971.2 (range: 730 - 3400) grams
The time of first examination (postpartum)	32.2 (range: 25 - 55) days
The time of last examination before CEKUS report (PM)	39.3 (range: 35 - 47) weeks
Retinal vascularization before CEKUS report	
Posterior to zone III	22 (37%) patients
Anterior to zone III	38 (63%) patients
The presence of ROP before CEKUS report	
No ROP	45 (75%) patients
Spontaneous regressed ROP	14 (23%) patients
ROP requiring treatment	1 (2%) patient

*Data are given as means with ranges (minimum–maximum) for continuous variables and as frequency (percentage) for categorical variables.

Table 2. Number of CEKUS reports and COVID-19 cases according to the groups (*Taken from: "https://covid19.saglik.gov.tr/TR-66935/genel-koronavirus-tablosu.html")

	Number of reports (%)	**Number of COVID-19 cases***	**P[a]**
Group 1	17 (28%)	163.941	0.600
Group 2	13 (22%)	106.191	
Group 3	8 (13%)	230.732	
Group 4	22 (37%)	2.200.724	
Total	**60 (100%)**	**2.701.588**	

*Data are given as frequency (percentage) for categorical variables. [a] Spearman correlation analysis

DISCUSSION

All premature babies smaller than 34 weeks of GA or lower than 1700 g of BW, and those bigger than 34 weeks and heavier than 1700 g receiving cardiopulmonary support and who were considered as risky by the attending clinician should be screened for ROP as recommended by TOA and TNS. Before the COVID-19 outbreak, screening and treatment of preterm infants for ROP in Ordu was relatively uneventful. Nevertheless, parents who miss their babies' appointments have always been a challenging issue for ophthalmologist in terms of medicolegal concerns. There is also no specific institution where premature infants can be reported when they are not

brought in to their appointments. However, the CEKUS unit within the Provincial Health Directorate taking responsibility in Ordu province works in coordination with the ROP unit and family physicians. Once a premature infant is missed from follow-up, the ophthalmologist reports the parents to CEKUS unit that informs the family physicians to refer the parents to the ROP unit.

During the COVID-19 pandemic, the screening, follow-up and treatment of ROP have been reported as urgent procedures by both the American Academy of Ophthalmology and TOA (5,6). In addition to the difficulty in ROP screening since the beginning of COVID-19 outbreak, failure in compliance with the appointments has become a serious problem. Katoch, et al discussed the impact of the COVID-19 pandemic on ROP services and found a decrease in the number of infants screened for ROP, consequently (7). The excess recommendation to reduce unnecessary hospital admissions, the lockdowns, travel restrictions, lack of transport facilities and the concerns of parents about their newborns and themselves seem to be causing these problems. Correspondingly, the parents of 72% of the infants were living in different cities, in our study. More than 80% of the babies who missed their appointments were the ones referred from other NICUs in and around Ordu, additionally.

The use of a virtual technology, telemedicine, has drawn significant attention during the COVID-19 pandemic (8,9). Ravindran et al screened 356 preterm babies in a 2-months period using a RetCam shuttle and reported that 57 infants had ROP and 6 of them underwent treatment for ROP (10). Guo et al reported that completing percentage of total online ROP screening appointments assisted by telemedicine network was higher than that of total face-to-face appointments during COVID-19 pandemic (11). Isaac et al defined that telemedicine screening for ROP is an economically feasible option depending on the location and the number of infants screened (12). Unfortunately, we could not use teleophthalmology due to the lack of technical infrastructure. Therefore, ROP screening procedures continued in the same way according to the recommendations of the Infection Control Committee during the outbreak.

There was a decrease in compliance with the appointments as the number of COVID-19 cases increased, in the current study. This non-adherence rate was higher in the parents of babies who were living in different cities and those referred from other NICUs. On the other hand, the absence of an institution where premature babies can be reported when they are not brought in to their appointments has become an even more important problem during the pandemic. However, the CEKUS unit in Ordu continued to work in coordination with the ROP unit and family physicians. That coordination between all these units during the first year of COVID-19 pandemic resulted in screening of all preterm babies, albeit late.

The present study also had some limitations. Although the CEKUS unit meticulously followed the infants who were not brought into their appointments, we did not evaluate why the parents missed these follow-ups. The study period was also limited to the first year of the pandemic. We ended the study after the first year for two reasons. First, it was accepted that the pandemic would continue, and the restrictions

were lifted. Second, vaccination against COVID-19 began after the first year.

CONCLUSION

In addition to the difficulty of ROP screening since the onset of the COVID-19 outbreak, the follow up of babies who are not brought in has become a serious problem. A specific institution that can follow up the babies may help the ophthalmologists and neonatologists to complete all screening sessions. Our protocol model between ROP and CEKUS units may serve as an example for other hospitals. Additionally, increasing the number of ROP units or having at least one ophthalmologist experienced in ROP in all hospitals with NICUs may prevent the non-adherence of the parents.

Acknowledgments

First, we would like to thank our nurse of ROP unit, Merve Şura Yayla, for her great sacrifice in the operation of the CEKUS reports. We would also like to thank the director of Public Health Services of Ordu Provincial Health Directorate dealing with the CEKUS unit, Fatih Aydın, MD, for taking responsibility for the follow up of babies that were not brought in. Finally, we would like to thank all the CEKUS team and family physicians who ensured the referral of all patients to the ROP unit.

Ethics Committee Approval: Ethics committee approval was received for this study from Ordu University Clinical Research Ethics Committee (2021/86)

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: A.K.S, A.U, Design: A.K.S, A.U, Literature search: A.K.S, A.U, Data Collection and Processing: A.K.S, A.U, Analysis or Interpretation A.K.S, A.U, Writing: A.K.S, A.U.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors also decline any financial support neither from any pharmaceutical company, nor from a company that provides or produces medical instruments and materials.

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