

LETTER TO THE EDITOR

Retinoblastoma management during the COVID-19 pandemic: A report by the Global Retinoblastoma Study Group including 194 centers from 94 countries

To the Editor:

In December 2019, cases of pneumonia of unknown origin were reported in Wuhan, Hubei, China.¹ Investigations showed that the cause was a novel RNA virus belonging to the Coronaviridae family. Since the first reported cases, the disease, termed Corona virus disease 2019 (COVID-19), has spread widely resulting in the World Health Organization, on January 30, 2020, declaring COVID-19 a Public Health Emergency of International Concern.²

As of the last week of March 2020, many countries are under lockdown, medical services are changing priorities and policies, and healthcare resources have been shifted to focus on outbreak management. These new circumstances, which continue to evolve, may impact negatively on the treatment of other diseases. Of particular interest is the effect on oncology patients,³ and more specifically pediatric oncology patients,⁴ where disease poses a threat to life.

Retinoblastoma is the most common ocular malignancy of childhood.⁵ Early diagnosis and treatment have improved the prognosis for children with retinoblastoma in high-income countries, now reaching > 90% disease-free survival rate.^{6,7} We aimed to investigate the impact of the COVID-19 pandemic on retinoblastoma management in treatment centers across the world, and indirectly on patients' prognosis. This information is important for policy and healthcare planning at national and international levels, during the pandemic, and for better preparation in the future.

A survey focusing on retinoblastoma management during the pandemic was sent on March 29, 2020, to members of the Global Retinoblastoma Study Group.⁸ Participants were asked to return the completed survey before April 4, 2020. During this week, daily COVID-19 data at country and global levels were retrieved from the World Health Organization database.⁹

Overall, 194 centers from 94 countries were included in the analysis. Of the participating centers, 73 (37.6%) were from Asia, 34 (17.5%) from Europe, 40 (20.6%) from Africa, 6 (3.1%) from Australasia, 17 (8.8%) from Latin America and the Caribbean, and 24 (12.4%) from North America.

Globally, the total number of COVID-19-positive patients reported on March 29 and April 4, 2020, respectively, was 723 390 and 1 201 483, and reported deaths were 34 065 and 64 690. The total

number of reported COVID-19-positive patients in the 94 participating countries on March 29 and April 4, 2020, respectively, was 702 559 (97.1%) and 1 165 380 (97.0%), and reported deaths were 33 660 (98.8%) and 63 720 (98.5%) (Supporting Information Figure S1).

Supporting Information Table S1 shows the COVID-19 data per participating country during the study period, data on travel restrictions, and policy for retinoblastoma patients. In 51 countries (54.3%), there were fewer than 100 COVID-19-positive cases per average day; in 30 countries (31.9%), there were between 100 and 999 new positive cases; and in 9 (9.6%) countries, there were between 1000 and 10 000 new positive cases per day. In terms of deaths, no cases were reported in 23 (24.5%) of the participating countries; in 50 (53.2%) countries, there were 1 to 9 deaths per day on average; and in 17 (18.1%) countries; there were between 10 and 499 deaths per day on average. In France, Italy, Spain and the United States, there were 500 to 1000 new deaths on average per day in each country.

Of the 194 participating centers, 82 (42.3%) reported that families are restricted from traveling to the retinoblastoma center. Most centers (170 [87.7%]) reported that they accept new referrals for examination and treatment, and most (185 [95.4%]) reported that they continue treating active cases. Of the 194 participating centers, 112 (57.7%) reported a policy of deferring stable cases. Six (3.1%) centers reported that they are not providing any services.

Overall, 16 (8.3%) centers reported that retinoblastoma management was disrupted due to personnel being quarantined or sick (i.e., COVID-19 positive), 11 (5.7%) due to personnel being needed elsewhere, 7 (3.6%) due to equipment being needed elsewhere/missing, 40 (20.6%) due to a combination of factors, and 120 (61.9%) reported no disruption.

Table 1 shows the modalities available in treatment centers before and during the pandemic. Examinations under anesthesia (EUAs), enucleation, intravenous chemotherapy (IVC), and intra-arterial chemotherapy (IAC) were available in 186 (95.9%), 193 (100.0%), 187 (96.9%), and 96 (49.7%), respectively, of the centers before the outbreak. During the pandemic, EUAs were fully available in 107 (55.2%) of the centers. In terms of treatment modalities, enucleation was available in 173 (89.6%), IVC in 181 (93.8), and IAC in 73 (37.8) of the centers.

Overall, 104 (53.6%) of the centers have reported that changes and restrictions outside or within the center due to the COVID-19 pandemic are potentially affecting the lives of retinoblastoma patients.

Abbreviations: COVID-19, Corona virus disease 2019; EUAs, examinations under anesthesia; IAC, intra-arterial chemotherapy; IVC, intravenous chemotherapy

TABLE 1 Modalities available in 194 retinoblastoma treatment centers before and during the Covid-19 pandemic (March 29–April 4, 2020)

Modalities ^a	Availability before pandemic (%)	Availability during pandemic (%)	Number decrease (%)
Examination under anesthesia	Available: 186 (95.9) Unavailable: 8 (4.1)	Available: 107 (55.2) Partly available: 66 (34.0) Unavailable: 21 (10.8)	79 (42.5) ^b
Enucleation	Available: 193 (100.0)	Available: 173 (89.6) Unavailable: 20 (10.4)	20 (10.4)
Intravenous chemotherapy	Available: 187 (96.9) Unavailable: 6 (3.1)	Available: 181 (93.8) Unavailable: 12 (6.2)	6 (3.2)
Intra-arterial chemotherapy	Available: 96 (49.7) Unavailable: 97 (50.3)	Available: 73 (37.8) Unavailable: 120 (62.2)	23 (24.0)

^aData on treatment modalities (i.e., enucleation, intravenous chemotherapy, and intra-arterial chemotherapy) were available for 193 centers.

^bNumber decrease from available to partly or unavailable.

A summary of the impact of the COVID-19 pandemic on retinoblastoma management as reported by the participating centers is shown in <https://retinoblastoma.world/>.

Findings of the present survey indicate that, according to most centers, changes and restrictions related to the COVID-19 pandemic potentially risk the lives of retinoblastoma patients. Approximately 40% of the participating centers reported that families are restricted from reaching a retinoblastoma center. Moreover, nearly 40% of centers reported disruption in retinoblastoma management during the outbreak related to personnel or equipment.

Enucleation can save lives. IVC can save lives and result in globe salvage when patients are diagnosed and treated before extraocular spread.^{10,11} During the study period, most centers were able to continue to provide these life-saving treatment modalities. Conversely, the availability of IAC reduced to just over one third of the centers from about half of the centers pre-COVID-19. Although IAC can be useful for globe salvage,¹² as a treatment modality it is not as critical as IVC or enucleation surgery for survival. However, continued provision of any treatment modalities is irrelevant if patients are precluded from reaching the treatment center.

In summary, findings of the present survey from 194 treatment centers, which was conducted while the pandemic escalates across the world, indicate that, globally, management of children with retinoblastoma is compromised, jeopardizing their lives. There is a delicate balance of risk management during a global pandemic. Treating patients, especially children, with a highly curable disease but potentially fatal when no treatment is delivered, remains a priority even in the face of a dangerous global viral outbreak. Decision makers should be aware of the effects of broad sweeping policies and take them into account when weighing all the risks and benefits of the situation.

AUTHOR CONTRIBUTIONS

Ido Didi Fabian had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

All the authors comply with ICMJE criteria for authorship. The authors are listed in alphabetical order. STUDY CONCEPT AND DESIGN Ido Didi Fabian. ACQUISITION, ANALYSIS OR INTERPRETA-

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CONFLICTS OF INTEREST

We declare no competing interests relevant to the present work.

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REFERENCES

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:P497-506.
- World Health Organization. WHO Director General's opening remarks at the media briefing on COVID-19, March 11, 2020. [Internet]. Available from: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19%201411-march-2020> [Accessed April 1, 2020].
- The Lancet Oncology. COVID-19: global consequences for oncology. *Lancet Oncol*. 2020;21:467.
- Bouffet E, Challinor J, Sullivan M, Biondi A, Rodriguez-Galindo C, Pritchard-Jones K. Early advice on managing children with cancer during the COVID-19 pandemic and a call for sharing experiences. *Pediatr Blood Cancer*;n/a:e28327. <https://onlinelibrary.wiley.com/doi/abs/10.1002/pbc.28327>.
- Kivelä T. The epidemiological challenge of the most frequent eye cancer: retinoblastoma, an issue of birth and death. *Br J Ophthalmol*. 2009;93:1129-1131.
- Fernandes AG, Pollock BD, Rabito FA. Retinoblastoma in the United States: a 40-year incidence and survival analysis [Internet]. *J Pediatr Ophthalmol Strabismus*. 2017;55:182-188.
- MacCarthy A, Birch JM, Draper GJ, et al. Retinoblastoma: treatment and survival in Great Britain 1963 to 2002 [Internet]. *Br J Ophthalmol*. 2009;93:38-39. <http://bjoo.bmj.com/cgi/doi/10.1136/bjo.2008.139626>.
- Global Retinoblastoma Study Group. Global retinoblastoma presentation and analysis by National Income Level [Internet]. *JAMA Oncol*. 2020;6:1-12. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32105305>. [Accessed March 1, 2020].
- World Health Organization. Coronavirus disease (COVID-19) outbreak. [Internet]. Available from: <https://who.sprinklr.com/> [Accessed April 1, 2020].
- Fabian ID, Stacey AW, Johnson KP, et al. Primary intravenous chemotherapy for group D retinoblastoma: a 13-year retrospective analysis. *Br J Ophthalmol*. 2017;101:82-88. <http://www.ncbi.nlm.nih.gov/pubmed/27965263>. [Accessed February 8, 2017].
- Shields CL, Bas Z, Tadepalli S, et al. Long-term (20-year) real-world outcomes of intravenous chemotherapy (chemoreduction) for retinoblastoma in 964 eyes of 554 patients at a single centre. *Br J Ophthalmol*. 2020. doi: [10.1136/bjophthalmol-2019-315572](https://doi.org/10.1136/bjophthalmol-2019-315572).
- Suzuki S, Yamane T, Mohri M, Kaneko A. Selective ophthalmic arterial injection therapy for intraocular retinoblastoma: the long-term prognosis. *Ophthalmology*. 2011;118(10):2081-2087.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.