

# Any Concern About Delays in the Diagnosis of Childhood Cancers During the COVID-19 Pandemic?

Begüm Şirin Koç<sup>1</sup>, Funda Tekkeşin<sup>1</sup>, Elif Ezgi Haccaloğlu<sup>2</sup>, Büşra Beyter<sup>2</sup>, Selime Aydoğdu<sup>1</sup>, Suar Çakı Kılıç<sup>1</sup>

<sup>1</sup>Department of Pediatric Hematology and Oncology, University of Health Sciences, Ümraniye Research and Training Hospital, İstanbul, Turkey

<sup>2</sup>Department of Pediatrics, University of Health Sciences, Ümraniye Research and Training Hospital, İstanbul, Turkey

## What is already known on this topic?

- The lockdown precautions during the COVID-19 pandemic led to concerns about the delayed diagnosis of malignancies and this issue remains unclear for children.

## What this study adds on this topic?

- This study showed that the duration of complaint before diagnosis was longer during the pandemic, while this delay did not increase the metastasis rate at diagnosis in children with cancer.

## ABSTRACT

**Objective:** The lockdown precautions during the COVID-19 pandemic led to concerns about the delayed diagnosis of malignancies. This study aimed to compare the duration of complaints at home and the presence of metastasis at diagnosis during the pre-pandemic and pandemic period in children with cancer.

**Materials and Methods:** All children diagnosed with cancer and followed up in our clinic between 2017 and 2022 were included. Patients with a diagnosis of acute/chronic leukemia were excluded. Age, gender, cancer type, duration of complaints, and presence of metastasis at diagnosis of the children were recorded. The duration of complaints and presence of metastasis at diagnosis were compared statistically before and after March 11, 2020, the start point of the COVID-19 pandemic in our country.

**Results:** A total of 161 patients diagnosed with cancer were analyzed retrospectively; 61% of patients were males and 39% were females. These patients were diagnosed with brain tumors (23.6%), lymphomas (23%), neuroblastoma (13.7%), rhabdomyosarcomas (10.6%), Ewing's sarcoma (4.3%), osteosarcoma (3.7%), Wilm's tumor (3.7%), and germ cell tumors (3.1%). The duration of complaint was longer during the pandemic than before the pandemic (median: 45 days vs. 30 days) ( $P < .05$ ). The presence of metastases at diagnosis was 45.3% in the pre-pandemic period, while it was 40% during the pandemic with no statistical difference ( $P > .5$ ).

**Conclusion:** We concluded that the duration of complaint before diagnosis was longer during the pandemic, while this delay did not affect the metastasis rate at diagnosis in children with cancer. The high rates of distant metastases in newly diagnosed patients both before and during the pandemic suggest that more studies are needed to diagnose these patients earlier.

**Keywords:** Pandemic, cancer, children

## INTRODUCTION

According to 2016 data from the World Health Organization, approximately 300 000 children between the ages of 0 and 19 are diagnosed with cancer every year, and an average of 80 000 children die due to cancer.<sup>1</sup> Cancer, which is the most common cause of death in children in the USA according to 2019 data, ranks in the top 4 in developing countries such as ours.<sup>2</sup> The 5-year overall survival rate for all childhood cancers has been reported to be 84.1% in the USA and over 80% in Europe.<sup>3</sup> In our country, the 5-year survival rate is approximately 70%, according to TPOG (Turkish Pediatric Oncology Group) cancer records.<sup>4</sup> Through the new developments in diagnosis and treatment methods, mortality and morbidity rates in childhood cancers have decreased compared to previous years.<sup>5</sup> The most critical reasons for this situation can be listed as new imaging methods, the histopathological definition of new cancer types, genetic mutations detected in cancerous tissue, surgical

## Corresponding author:

Begüm Şirin Koç

✉ begumsirins@hotmail.com

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methods, targeted therapies in chemotherapy, new chemotherapy agents, and developments in the field of radiotherapy. Cancers in children differ from adults as they have a higher growth rate and are more aggressive.<sup>6</sup> Therefore, children may need urgent treatments. It is vital to detect cancer at an early stage since the early diagnosis of childhood cancers provides a higher chance of cure and a better prognosis. In the staging performed when the first diagnosis is made, the presence of distant metastases is considered an advanced-stage disease in all cancer types.

Upon the increase in the cases of atypical pneumonia due to the new type of coronavirus (SARS-CoV-2), which was first detected in Wuhan, China, in December 2019, the World Health Organization declared the disease as an emergency health problem on January 30, 2020, and named it as COVID-19. The outbreak caused by SARS-CoV-2 was defined as a pandemic by WHO on March 11, 2020.<sup>7</sup> The first COVID-19 case in our country was detected on March 11, 2020. Since then, quarantine measures have been taken in our country to prevent the spread of the virus. Especially, when the number of new cases increased in hospitals, emergency healthcare services for non-COVID-19 patients were disrupted, and most of the routine and elective interventions were interrupted in many hospitals. During the pandemic period, there have been patients who waited at home until the last minute, being afraid of the pandemic due to the "stay at home" call to prevent the spread of the virus all over the world and in our country, the overcrowding of the hospitals, and the fear of contracting the virus in the hospital. Among these patients, there are cancer patients who have not been diagnosed yet.<sup>8</sup>

Considering the general population, COVID-19 infection in children was not as severe as in adults.<sup>9</sup> Signs and symptoms of COVID-19 infection in children with cancer were similar to those without.<sup>10</sup> The number of newly diagnosed cancer cases has been demonstrated to decrease significantly in the studies, including adults, due to the postponement of cancer screenings throughout the COVID-19 pandemic.<sup>11,12</sup> Delays in hospital admissions and late diagnosis of cancer patients have been a concern, especially for adult patients, and this issue remains unclear for children. Routine screening tests are not used in childhood cancers. However, non-specific symptoms such as weight loss, fatigue, and pain are clues that require cancer research in children. It was thought that the families' refusal to go to hospitals due to the fear of COVID-19 may have caused them to bring their children to the hospital at a later period and to be diagnosed with cancer at an advanced stage. The present study aimed to compare the duration of complaints of children with newly diagnosed cancer in our clinic during the pandemic period (March 2020 to March 2022) and the presence of distant metastases at the time of diagnosis in terms of the advanced stage with the pre-pandemic period (May 2017 to March 2020).

## MATERIALS AND METHODS

Children aged 0-18 years who were diagnosed with malignant diseases in our center between May 2017 and March 2022 were included in our retrospective observational study. Patients with leukemia were excluded since there would be no delay in

admission for acute leukemia and there is no concept of distant metastases in the staging of leukemia. The patients' age, gender, cancer type, the time between the diagnosis and the onset of the complaints, and the presence of distant metastases in the staging performed at the time of the first diagnosis were recorded. Since staging systems differ according to each tumor type, only the presence of distant metastases was accepted as the criterion for advanced disease. The presence of distant metastases was indicated as stage IV for all diseases. The period from March 11, 2020, the start date of the COVID-19 pandemic in our country, to March 1, 2022, was considered the pandemic period (March 11, 2020, to March 1, 2022). The period before the pandemic was defined as the period between May 1, 2017, and March 10, 2020. Age and gender distribution and diagnoses of all patients included in the study were calculated proportionally. The time between diagnosis and the onset of complaints and whether there was distant metastasis at the time of diagnosis in children diagnosed with cancer during the pandemic period were statistically compared with the pre-pandemic period.

## Statistical Analysis

Descriptive statistical methods such as mean, standard deviation, frequency, ratio, and median values, as well as Mann-Whitney *U* test, and chi-square test were used for evaluating the study data.

For this study, COVID-19 Scientific Research Study Approval was obtained from the Ministry of Health on April 10, 2022, and at the same time, the approval numbered B.10.1.TKH.4.34.H.GP .0.01/137 was acquired from the ethics committee of University of Health Sciences, Umraniye Research and Training Hospital on April 21, 2022.

## RESULTS

The files of 161 patients followed up with a cancer diagnosis (all non-leukemia malignant patients) between May 1, 2017, and March 1, 2022, were retrospectively reviewed. Of all the patients participating in the study, 61% were male, and 39% were female. The median age of the patients was 89 months (2 months-18 years). While the median age of the patients who applied before the pandemic was 95 months, it was 79.8 months during the pandemic period. There was no statistically significant difference between the 2 groups regarding age ( $P > .5$ ). While the number of newly diagnosed patients before the pandemic was  $n = 59$ , it was  $n = 102$  during the pandemic period. The distribution of diagnoses of these patients consisted of brain tumor (23.6%), lymphoma (23%), neuroblastoma (13.7%), rhabdomyosarcoma (10.6%), Ewing's sarcoma (4.3%), osteosarcoma (3%), Wilms tumor (3.7%), and germ cell tumors (3.1%) (Table 1). While the median duration of complaints before diagnosis was 45 days during the pandemic period, it was 30 days in those diagnosed in the pre-pandemic period. When the pre-pandemic and pandemic period were compared, a statistically significant difference was determined between the 2 groups in terms of duration of complaints ( $P < .05$ ) (Table 2). There was distant metastasis (stage IV) at the time of diagnosis in 42.3% of all patients presenting before and during the pandemic. While the rate of stage IV disease at the first diagnosis was 45.3% in the pre-pandemic period, it was 40% during

**Table 1.** Demographic Characteristics and Diagnosis Distribution of the Patients

|                      |                      | n   | %    |
|----------------------|----------------------|-----|------|
| <b>Gender</b>        | Boy                  | 98  | 60.9 |
|                      | Girl                 | 63  | 39.1 |
| <b>Period</b>        | Pre-pandemic         | 59  | 36.6 |
|                      | Pandemic             | 102 | 63.4 |
| <b>Diagnoses</b>     | Brain tumor          | 38  | 23.6 |
|                      | HL                   | 22  | 13.7 |
|                      | NBL                  | 22  | 13.7 |
|                      | RMS                  | 17  | 10.6 |
|                      | NHL                  | 15  | 9.3  |
|                      | Germ cell tumor      | 9   | 5.6  |
|                      | Ewing's sarcoma      | 7   | 4.3  |
|                      | Wilms' tumor         | 6   | 3.7  |
|                      | Osteosarcoma         | 6   | 3.7  |
|                      | Non-RMS              | 6   | 3.7  |
|                      | Nasopharynx          | 4   | 2.5  |
|                      | Tumor of Gis origin  | 3   | 1.9  |
|                      | Adrenocortical       | 2   | 1.2  |
|                      | Clear cell carcinoma | 1   | 0.6  |
|                      | Over carcinoma       | 1   | 0.6  |
| Malignant melanoma   | 1                    | 0.6 |      |
| Neuroendocrine tumor | 1                    | 0.6 |      |

HL, Hodgkin Lymphoma; NBL, Neuroblastoma; RMS, Rhabdomyosarcoma; NHL, Non-Hodgkin Lymphoma.

the pandemic. There was no statistically significant difference between the pre-pandemic and the pandemic period in terms of the presence of distant metastases at the time of admission ( $P > .5$ ) (Table 3).

**DISCUSSION**

Due to the quarantine restrictions during the COVID-19 pandemic, routine pediatric control visits of children were also

postponed or canceled. Even in emergencies such as appendicitis and diabetic ketoacidosis, higher rates of complications have been reported due to late admissions.<sup>13,14</sup> Significantly in periods when full lockdown processes are prolonged, the fact that patients do not go to the hospital unless it is very urgent, which causes the progression of many diseases, and the postponement of cancer screenings (such as mammography, colonoscopy, cervical cytology) that are recommended for adults at certain ages, has reduced the number of cases diagnosed at an early stage.<sup>15-17</sup> It has been reported that the number of applications to pediatric oncology outpatient clinics decreased during the pandemic, and fewer patients were diagnosed with cancer.<sup>18-20</sup> Although routine screening tests are not used to detect cancer early in childhood, there have been concerns about delays in hospital admissions and delayed diagnosis due to the fear of COVID-19 in families of children with non-specific symptoms. A study performed in Italy revealed that the number of newly diagnosed patients in terms of pediatric tumors decreased significantly during the 8-week full closure period applied during the pandemic. Again, the same study demonstrated that the number of newly diagnosed pediatric solid tumors increased when the coronavirus cases decreased and the full closure measures were lifted; however, they were diagnosed late.<sup>18</sup> Nevertheless, when the pre-pandemic years (2017-2020) and the 6 months of the pandemic period were compared in a study performed in Canada, no statistically significant difference was observed in childhood cancers.<sup>21</sup> The same study also reported no increase in metastatic disease and early mortality during the pandemic period. The present study determined that the number of newly diagnosed patients during the pandemic increased by 2 times compared to the pre-pandemic period, but similar to other studies, the application times were prolonged. In the pre-pandemic period, our clinic was newly established, and the number of patients was few in the first years (started in 2017). Then, the number of patients increased exponentially. The reasons for the increase in the number of patients who applied to us during the pandemic period were considered to be the uninterrupted service of our pediatric oncology clinic under pandemic conditions; the fact that the pediatric surgery performed operations on children with cancer without delay and the continuation of the in-hospital and out-of-hospital pediatric tumors council on the internet without interruption. Despite the pandemic, our team, consisting of pediatric oncology, pediatric surgery, neurosurgery, radiology, and radiation oncology, performed the diagnosis and treatment of these patients without delays.

The results of this study revealed that the pre-admission period of children with cancer was 15 days later on average, and therefore, they were diagnosed later. The effect of the pandemic and the "fear of catching the COVID-19 virus from the hospitals" of the families were considered to play a role in this delay. Also, the rapid global report for the COVID-19 pandemic mentioned that many late diagnoses of childhood cancers can be expected from the limited access to healthcare services related to the pandemic and the fear of infection that prevents parents from seeking early medical evaluation of their child's symptoms.<sup>22</sup> In addition, the major problem was the interruption and delay in treatment for children with cancer due to COVID-19. Cancer treatment was delayed in 62.7% of the

**Table 2.** Comparison of Patients' Admission Age and Duration of Complaints During and Before the Pandemic

|                               | Pre-pandemic Period |       | Pandemic Period |       | Z      | P    |
|-------------------------------|---------------------|-------|-----------------|-------|--------|------|
|                               | Median              | IQR   | Median          | IQR   |        |      |
| <b>Age (months)</b>           | 95.0                | 145.9 | 79.8            | 145.8 | -0.496 | .620 |
| <b>Duration of complaints</b> | 30.0                | 46.0  | 45.0            | 100.0 | -2.356 | .018 |

Mann-Whitney U test is used to compare differences between two independent groups when the dependent variable is either ordinal or continuous, but not normally distributed.  
IQR, interquartile range.

**Table 3.** Comparison of Patients Diagnosed with Advanced Stage (Stage IV) with the Pandemic Period and Before

|              |          | Pre-pandemic Period |      | Pandemic Period |      | X <sup>2</sup> | P    |
|--------------|----------|---------------------|------|-----------------|------|----------------|------|
|              |          | n                   | %    | n               | %    |                |      |
| <b>Stage</b> | Stage IV | 24                  | 45.3 | 28              | 40.0 | 0.162          | .687 |
|              | Others   | 29                  | 54.7 | 42              | 60.0 |                |      |

Chi-square test

patients and delayed with a median of 15 (3-45) days in the nationwide study in Turkey. And, 11% of these patients were just at diagnosis.<sup>23,24</sup>

Although a decrease in the number of newly diagnosed patients and delays in admission was reported in previous studies,<sup>18-20</sup> there was no statistical difference in a comprehensive study performed in Canada.<sup>21</sup> It is known that these delays in cancer diagnosis are more common in adults during the pandemic period. According to the results of our study, although the admission time of newly diagnosed patients was 15 days later during the pandemic period, it was observed that this delay period did not increase the rate of advanced disease. The rate of distant metastases at the time of presentation was high in childhood cancers both before and during the pandemic (45.3% vs. 40%). Biologic factors also influence the duration to develop distant metastasis; however, delays in diagnosis may lead to advanced stages of the disease. Considering that the duration of the complaint is 30 days in the pre-pandemic period, it may be sufficient time for distant metastasis in most cancer types in children. The high rate of advanced disease in both periods has been a finding indicating that childhood cancers have an aggressive course, independent of the effect of the pandemic.

Ensuring that the patients apply to pediatric oncology outpatient clinics before 1 month may reduce the rate of metastasis when these patients are diagnosed with cancer. Early diagnosis is vital as patients without metastases have a much higher chance of being cured. Therefore, increasing the awareness of primary care family physicians and general pediatricians about cancer is critical in the early diagnosis of childhood cancers.

## CONCLUSION

The duration of complaints was concluded to be longer in children with cancer diagnosed during the pandemic, but this 15-day delay did not significantly affect the rate of distant metastases. Biologic factors also influence the duration to develop distant metastasis; however, delays in diagnosis may lead to advanced stages of the disease. Due to the high rate of distant metastases in newly diagnosed patients both during and before the pandemic, we believe that studies to increase cancer awareness are needed for the earlier diagnosis of childhood cancers.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of Health Sciences of University, Umraniye Research and Training Hospital (Approval No: B.10.1.TKH.4.34.H.GP.0.01/137, Date: 21.04.2022).

**Informed Consent:** Verbal informed consent was obtained from the patients who agreed to take part in the study.

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## REFERENCES

- Johnston WT, Erdmann F, Newton R, Steliarova-Foucher E, Schüz J, Roman E. Childhood cancer: estimating regional and global incidence. *Cancer Epidemiol.* 2021;71(B):101662. [CrossRef]
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424. [CrossRef]
- Kaatsch P. Epidemiology of childhood cancer. *Cancer Treat Rev.* 2010;36(4):277-285. [CrossRef]
- Kutluk MT, Yeşilipek A. Pediatric cancer registry in Turkey 2009-2018 (TPOG & TPHD). *J Clin Oncol.* 2019;37(15\_suppl):e21510. [CrossRef]
- Kebudi R, Alkaya DU. Epidemiology and survival of childhood cancer in Turkey. *Pediatr Blood Cancer.* 2021;68(2):e28754. [CrossRef]
- Miller KD, Fidler-Benaoudia M, Keegan TH, Hipp HS, Jemal A, Siegel RL. Cancer statistics for adolescents and young adults, 2020. *CA Cancer J Clin.* 2020;70(6):443-459. [CrossRef]
- Abrams EM, Greenhawt M. Risk communication during COVID-19. *J Allergy Clin Immunol Pract.* 2020;8(6):1791-1794. [CrossRef]
- Graetz D, Agulnik A, Ranadive R, et al. Global effect of the COVID-19 pandemic on paediatric cancer care: a cross-sectional study. *Lancet Child Adolesc Health.* 2021;5(5):332-340. [CrossRef]
- Rodríguez MS. COVID-19. The pandemic and the children. *Arch Argent Pediatr.* 2020;118(5):302-303. [CrossRef]
- Moreira DC, Millen GC, Sands S, Kearns PR, Hawkins DS. The care of children with cancer during the COVID-19 pandemic. *Am Soc Clin Oncol Educ Book.* 2021;41:1-10. [CrossRef]
- Ijzerman M, Emery J. Is a delayed cancer diagnosis a consequence of COVID-19? Victoria (AU). Melbourne: The University of Melbourne. Available at: <https://pursuit.unimelb.edu.au/articles/is-a-delayed-cancer-diagnosis-a->. Accessed March 31, 2021.
- Lai AG, Pasea L, Banerjee A, et al. Estimated impact of the COVID-19 pandemic on cancer services and excess 1-year mortality in people with cancer and multimorbidity: near real-time data on cancer care, cancer deaths and a population-based cohort study. *BMJ Open.* 2020;10(11):e043828. [CrossRef]
- Cherubini V, Gohil A, Addala A, et al. Unintended consequences of COVID-19: remember general pediatrics. *J Pediatr.* 2020;223:197-198. [CrossRef]
- Snipiri O, Rosenberg Danziger C, Krause I, et al. Delayed diagnosis of paediatric appendicitis during the COVID-19 pandemic. *Acta Paediatr.* 2020;109(8):1672-1676. [CrossRef]
- Patt D, Gordan L, Diaz M, et al. Impact of COVID-19 on cancer care: how the pandemic is delaying cancer diagnosis and treatment for American seniors. *JCO Clin Cancer Inform.* 2020;4:1059-1071. [CrossRef]
- London JW, Fazio-Eynullayeva E, Palchuk MB, Sankey P, McNair C. Effects of the COVID-19 pandemic on cancer-related patient encounters. *JCO Clin Cancer Inform.* 2020;4:657-665. [CrossRef]
- Miller MJ, Xu L, Qin J, et al. Impact of COVID-19 on cervical cancer screening rates among women aged 21-65 years in a large integrated health care system-Southern California, January 1-September 30, 2019, and January 1-September 30, 2020. *MMWR Morb Mortal Wkly Rep.* 2021;70(4):109-113. [CrossRef]
- Chiaravalli S, Ferrari A, Sironi G, et al. A collateral effect of the COVID-19 pandemic: delayed diagnosis in pediatric solid tumors. *Pediatr Blood Cancer.* 2020;67(10):e28640. [CrossRef]

19. Offenbacher R, Knoll MA, Loeb DM. Delayed presentations of pediatric solid tumors at a tertiary care hospital in the Bronx due to COVID-19. *Pediatr Blood Cancer*. 2021;68(2):e28615. [\[CrossRef\]](#)
20. Dinmohamed AG, Visser O, Verhoeven RHA, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. *Lancet Oncol*. 2020;21(6):750-751. [\[CrossRef\]](#)
21. Pelland-Marcotte MC, Xie L, Barber R, et al. Incidence of childhood cancer in Canada during the COVID-19 pandemic. *CMAJ*. 2021;193(47):E1798-E1806. [\[CrossRef\]](#)
22. Sullivan M, Bouffet E, Rodriguez-Galindo C, et al. The COVID-19 pandemic: A rapid global response for children with cancer from SIOP, COG, SIOP-E, SIOP-PODC, IPSO, PROS, CCI, and St Jude Global. *Pediatr Blood Cancer*. 2020;67(7):e28409. [\[CrossRef\]](#)
23. Kebudi R, Kurucu N, Tuğcu D, et al. COVID-19 infection in children with cancer and stem cell transplant recipients in Turkey: a nationwide study. *Pediatr Blood Cancer*. 2021;68(6):e28915. [\[CrossRef\]](#)
24. Kebudi R, Chantada G, Kurucu N, Tuğcu D, Mukkada S, C Moreira D. COVID-19: Consequences for children with cancer in Turkey and globally. *Turk Arch Peditr*. 2021;56(4):295-299. [\[CrossRef\]](#)