Diagnostic Delay in Adolescents with Cancer During COVID-19 Pandemic: A New Price for Our Patients to Pay

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Worldwide, the coronavirus 19 disease pandemic caused a worse chance of a timely diagnosis for cancer patients. We conducted a retrospective analysis of new diagnoses registered in the national pediatric oncology database, comparing the first lockdown period (March–May 2020) with the same period of 2015–2019. The total number of cases (0–19 years) dropped by 20.8% (from 441 between 2015 and 2019 to 349 in 2020). A major reduction was observed for adolescents (15–19 years) (-32.9%) and for adolescents with solid tumors (-56.4%, p = 0.03). Our data suggest that the enforced lockdown reduced the possibility for these already vulnerable patients to access the referral centers.

Keywords: COVID-19, solid tumor, diagnostic delay

Introduction

Italy has been Western-world country massively hit by coronavirus 19 disease (COVID-19). In the world of pediatric oncology, the initial stages of the COVID-19 pandemic required a prompt and complex reorganization of all pediatric oncology centers affiliated to the national cooperative group Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP). Several measures have been implemented to minimize the risk of the virus spreading within hospitals, to adequately manage COVID-19–positive patients, and to ensure timely access to diagnostic and therapeutic services for new patients while continuing to develop oncological treatments.1,2

In Lombardy, the epicenter of the pandemic in Italy, a reduction in the number of newly diagnosed pediatric tumors was observed during the period of lockdown imposed by the government from March to May 2020.2,3

Similarly, a worse chance of a timely diagnosis for patients with pediatric tumors was reported in other countries.4,5

The aim of this report was to investigate the effect of COVID-19 pandemic and lockdown on the diagnosis of Italian pediatric cancer patients.

Methods and Results

We conducted a retrospective review of the number of new cancer diagnoses referred to all AIEOP Centers during the first lockdown period (from March to May 2020), and we compared them with the mean value of the diagnoses observed up to 5 years previously in the same period (March– May 2015–2019). To explore whether a drop in the number of cases might be followed by a rebound, we then analyzed the number of cases diagnosed in the subsequent 3 months (June–August 2020 vs. 2015–2019).

The number of cases was obtained from the web-based AIEOP national database (known as Mod.1.01 form) based on the AxMR (Advanced eXtended Multicentre Research) Information Technology solution and developed by the Italian Inter-University Consortium called CINECA. The AIEOP database records information on cancer patients and treated exclusively at AIEOP centers (49 U in total).6,7

In the analysis, we considered age at diagnosis (0–14 vs. 15–19 years), type of malignant tumors according to the International Classification of Childhood Cancer Third Edition, and region of provenance.

The overall number of new cases (age 0–19 years) was 349 patients in the March–May 2020 period and 441 patients (mean value) between 2015 and 2019 (-20.8%). The overall number of cases registered among children of 0–14 years of age was 298 in the period between March and May 2020 and 365 patients per year between 2015 and 2019 (-18.4%).

Considering patients aged 15–19 years, we observed 51 diagnoses in the March–May 2020 period and 76 diagnoses per year between 2015 and 2019 (-32.9%). Among these patients, we found a 56.4% reduction of solid tumor diagnoses during the lockdown period with respect to previous years (17 vs. 39 patients, $p = 0.03$).

In addition, when we analyzed patients of this age with any type of tumor referred to Northern Italian Centers, we observed a 42.9% reduction, that is, 24 cases in the March–May 2020 period versus 42 per year in 2015–2019 ($p = 0.02$).

In the trimester after the lockdown (June–August 2020), our analysis indicates that the number of new cases was back in line with expectations based on the previous year, except for central nervous system (CNS) tumors in adolescents, for which we observed a rebound with a higher incidence of new cases (+83.3%; 11 patients in the period between June and August 2020 vs. 6 patients per year in 2015–2019, $p = 0.07$; Table 1).

Discussion

Several publications have already reported inadequate access to care and consequent delay in the diagnosis of cancer (adults and children) during the first peak of the COVID-19 pandemic.4,5,8

In the Italian pediatric oncology scenario, we found a significant decrease in new diagnosis of cancer in adolescent patients in northern Italy (which was the Italian epicenter of the first COVID-19 wave) and a peculiar decrease of new solid tumor diagnosis in adolescents. It is generally recognized that this specific group of patients represents a ulnerable population with needs that are under-met and often overlooked by health care providers, with potential difficulties in the access to care.9

A feature often seen in adolescent patients with cancer is a lengthy symptom interval, especially in comparison with children.10,11 It has been suggested that inadequate awareness of cancer risk among adolescents may play an important role.

It is also likely that the pandemic-induced fear of contagion in hospitals together with the lack of parents' control may have further exacerbated this aspect. Diagnostic bias may also occur, since presenting signs of malignancy (fever, malaise) can initially be mistaken for COVID-19 symptoms.

Previous AIEOP studies reported a relevant migration of patients from central and southern Italian regions to the northern regions, and this phenomenon was more evident for patients with solid tumors (and especially CNS tumors).12

The ban on travel between Italian regions during the lockdown period could have contributed to a lack of patient referrals in northern Italy from other regions or from abroad.

Our data showed that the decrease in diagnosis during the height of the pandemic involved solid tumors other than acute leukemia or lymphoma. A possible explanation is that haematological

malignancies typically present acutely, making it harder to delay access to health care, whereas solid tumors present more indolently.13

Furthermore, as soon as the lockdown was lifted, we expected to see an overall rebound with a higher incidence of new cases. However, our analysis indicates that the number of new cases globally corresponds with expectations based on the previous year (Table 1). It is plausible that the transition from a context of ‘‘emergency management for a few weeks’’ to one of ‘‘risk management for an unspecified period of time’’ had an impact in the period after the first lockdown closer to a gradual increase rather than showing a sudden rebound peak.

This study has some limitations, the main one being the unavailability of overlapping epidemiological data according to period of diagnosis from population-based cancer registries and, to a lesser extent, from adult oncology centers as well as consequent lack of information on cancer patients who were not referred to pediatric centers.

A further limitation was the small sample size when we analyzed specific subcategories (e.g., 15–19 years old patients with solid tumors).

In conclusion, despite these limitations, our study suggests that the reduced likelihood of adolescents with solid tumors accessing referral centers and a consequent risk of delay in diagnosis were a consequence of the COVID-19 pandemic.

It remains to be seen what might be the impact of such collateral effect of the pandemic on the prognosis of our patients.14

Further efforts are necessary to provide adequate diagnostic procedures and to continue to ensure the best treatment for all pediatric oncological patients with a peculiar attention regarding the vulnerable group of adolescents with cancer.

This is particularly true as the pandemic is not over yet and the future trajectory of the COVID-19 spread remains uncertain while the epidemiology of pediatric and adolescent cancer diagnosis remains a certainty.

Authors’ Contributions

P.Q. and A.F. drafted the article and prepared the table. Ma.M. and M.Z. participated in the conception and design of the study. P.Q. and Mi.M. did the data analyses. G.M.M., A.T., M.B., M.S., M.P., and T.P. verified the data. F.F. and A.P. oversaw the research. All authors contributed

to the interpretation of the findings, editing of the article, and the approval of the final submitted version. All authors accept responsibility for the decision to submit for publication.

Author Disclosure Statement

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Table 1. Cases of Pediatric Tumor Newly Diagnosed During the Lockdown Period (March–May 2020) and the Subsequent Trimester (June–August 2020) in Comparison with the Previous Year

Age at diagnosis	*0–14 years*						
Period	*March–May 2015–2019*	*March–May 2020*	*Variation (%)*	*June–August 2015–2019*	*June–August 2020*	*Variation (%)*	p
Newly diagnosed cases	365	298	−18.4	346	347	0.3	*0.07*
Tumor type							
Leukemias and lymphomas	157	129	−17.8	153	145	−5.2	*0.38*
Solid tumors	208	169	−18.8	193	202	4.7	*0.09*
CNS tumors	90	57	−36.7	75	62	−17.3	*0.3*
Sarcomas	42	35	−16.7	41	33	−19.5	*0.9*
Region							
Northern Italy	165	127	−23.0	164	164	0.0	*0.1*
Central Italy	120	102	−15.0	120	107	−14.2	*0.86*
Southern Italy	80	69	−13.8	62	76	29.0	*0.09*
Age at diagnosis	*15–19 years*						
Period	*March–May 2015–2019*	*March–May 2020*	*Variation (%)*	*June–August 2015–2019*	*June–August 2020*	*Variation (%)*	p
Newly diagnosed cases	76	51	−32.9	71	80	12.7	*0.04*
Tumor type							
Leukemias and lymphomas	37	33	−10.8	34	45	32.4	*0.23*
Solid tumors	39	17	−56.4	37	35	−5.4	*0.03*
CNS tumors	11	4	−63.6	6	11	83.3	*0.07*
Sarcomas	14	8	−42.9	9	11	22.2	*0.22*
Region							
Northern Italy	42	24	−42.9	35	43	22.9	*0.02*
Central Italy	23	14	−39.1	25	25	0.0	*0.3*
Southern Italy	11	13	18.2	11	12	9.1	*0.88*