Did Hospitalization Age Decrease in Children in the Omicron (B.1.1.529) Era?

To the Editors:

In mid-January 2022, it was announced by the Turkish Ministry of Health that the dominant variant in circulation is Omicron. A recent study from our center revealed that every variant reported before had different features, and the one before the Omicron variant, Delta variant (B.1.617.2), was associated with higher hospitalization rates.[1] We also compared the changing hospitalization trends of pediatric patients before and during the Omicron period in terms of age groups. Between March 2020 and January 2022, a total of 660 pediatric COVID-19 patients were reviewed retrospectively. The patients were classified into 4 age groups as <12 months, 12–71 months, 72–143 months, and ≥144 months. Of all patients, 576 were hospitalized before the Omicron era, and 84 were hospitalized during the Omicron era. The median age of the children hospitalized before the emergence of the Omicron variant was 71.5 months (min. 1 month to max. 17 years 10 months), and 23.3% of the patients were under 12 months. In the second group, the median age was 15 months (min. 1 month to max. 17 years), and 41.7% of the patients were under 12 months. The rates of the hospitalized patients 12 years and above before and during the Omicron era were 34% and 13.1%, respectively (Table 1). The average age of the patients hospitalized during the Omicron era is significantly lower compared with the previous period ($P < 0.001$). The share of patients under 12 months among all hospitalized patients has nearly doubled in the Omicron era; and it was found that the rate of patients 12 years of age and older has decreased to almost one-third.

Although reports from South Africa and England indicate that hospitalization rates are lower following Omicron infection compared with the Delta variant infection,[2,3] according to Scientific Advisory Group for Emergencies in the United Kingdom, hospital admissions of children under 1-year-old have risen significantly.[4] Centers for Disease Control and Prevention (CDC) reported that the rate of COVID-19-linked hospitalizations among children younger than 5 grew substantially between December 26, 2021, and January 1, 2022, whereas the same rate for children between the ages of 5 and 17 remained relatively stable.[5] However, it is controversial if it is due to the vulnerability of this age group to the Omicron variant. A possible reason for the increase in hospitalizations in this group may be that the overall number of cases has increased due to high transmissibility and the relative difficulty of eliminating the risk of serious bacterial infections in younger children.

TABLE 1. Rate of Hospitalized Patients Before and After the Emergence of the Omicron Variant

	Before Omicron (Other Variants) (%)	During Omicron Period (%)	*P*
<12 mo	23.3	41.7	0.0018
12–71 mo	26.7	35.7	>0.05
72–143 mo	16	9.5	>0.005
≥144 mo	34	13.1	0.0014

Immunization of children 12 years and above in Turkey started in September 2021. However, considering insufficient data on vaccination rates in this age group in Turkey, it is difficult to determine if the decrease in hospitalization in the age group 12 years and above is due to vaccination. Although the vaccination program in Turkey does not cover the age group of 5–11 years, there is no significant change in hospitalization rates in this age group.

In conclusion, this study emphasizes that the proportion of children younger than 1-year-old among hospitalized children with COVID-19 infection during the Omicron era is alarming for pediatricians.

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COVID-19 Disease in Children with Medical Complexity in a Pediatric Long-term Care Facility: *A Case Series*

To the Editors:

At the onset of the coronavirus disease 2019 (COVID-19) pandemic, nursing homes were hard-hit as epicenters of outbreaks with roughly one-fifth of cases linked to adult long-term care facilities (LTCF) by 2021.[1] This statistic caused concern among

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TABLE 1. Clinical and Laboratory Characteristics of 5 Medically Complex Children in Long-Term Care with COVID-19 Infection

	Case 1	Case 2	Case 3	Case 4	Case 5
Age	1 year	13 years	12 years	21 years	8 years
Gender	Male	Male	Male	Male	Male
Comorbidities/PMH	Cerebral palsy due to brain injury Severe neurologic impairment Tracheostomy Subglottic stenosis Chronic lung disease gastrostomy tube Epilepsy Autonomic instability	Cerebral palsy due to L1 syndrome Severe neurologic impairment Chronic lung disease Tracheostomy Chronic mechanical ventilation VP shunt aortic insufficiency gastrostomy tube Epilepsy	VARS2-related mitochondrial neurodegenerative disorder Severe neurologic impairment Gastrostomy tube Epilepsy History of stroke	Cerebral palsy Severe neurologic impairment Gastrostomy tube Epilepsy Chronic lung disease vesicostomy	Cerebral palsy due to septo-optic dysplasia Severe neurologic impairment Adrenal insufficiency Hypothyroidism G-tube Epilepsy
BMI (kg/m^2)	21.1	18	19.1	24.9	22.1
25-OH-Vitamin D level (ng/mL)	28.5	47.7	50.3	32.2	47.3
Melatonin use (mg/night)	0	6	10	0	6
Probiotic use	No	No	No	Florastor	No
COVID-19 symptoms	Hypoxia requiring supplemental oxygen. Increased secretions and respiratory rate. Has baseline waxing and waning of oxygen need and secretions.	None	Fever	Hypoxia requiring supplemental oxygen. Increased seizures.	Bradycardia
Relevant laboratories at presentation:					
WBC (4.5–13.5 10*3/uL)	7.94	N/A	7.68	5.89	N/A
Abs lymphocytes (1000–4800 cell/uL)	3,790	N/A	2,400	1,360	N/A
LDH (313–618 U/L)	N/A	N/A	N/A	436	N/A
Ferritin (17.9–464 ng/mL)	N/A	N/A	N/A	15.1	N/A
D-dimer (<500 ng/mL)	N/A	N/A	N/A	253	N/A
CRP (<1.0 mg/dL)	<0.5	0.7	0.9	4.8	N/A
Serology at diagnosis	N/A	IgM and IgG Ab negative.	N/A	IgM and IgG Ab negative.	N/A
Chest radiograph at initial COVID-19 presentation	Chronic lung disease, consistent with prior films. No acute disease.	Consistent with prior chest radiographs.	Peripheral airway infiltrates consistent with viral process.	Retrocardiac infiltrate versus atelectasis.	No acute disease.
COVID-19 treatment	Remdesivir, IV Steroids, Lovenox, Oxygen, Bronchodilators, and Chest physiotherapy	None	Chest physiotherapy (vest therapy)	Oxygen, Bronchodilator, Chest physiotherapy	None
Duration of symptoms	14 days	0 days	1 day	9 days	3 days
COVID-19 infection	9/16/2020	11/9/2020	11/12/2020	11/19/2020	3/8/2021
COVID-19 first vaccination	N/A	N/A	6/2/2021	1/11/2021	N/A
Date of COVID-19 second vaccination	N/A	N/A	6/23/2021	2/1/2021	N/A
Date of first study blood draw	6/1/2021	N/A	6/1/2021	6/1/2021	6/1/2021
Date of second study blood draw	N/A	N/A	7/13/2021	N/A	N/A

BMI indicates body mass index; COVID-19, coronavirus disease 2019; CRP, c-reactive protein; LDH, lactate dehydrogenase; PMH, past medical history; VARS2, valyl-tRNA synthetase 2; VP, ventriculoperitoneal; WBC, white blood cell.

pediatric LTCFs that children with medical complexity (CMC), who comprise the 7000 children living in the United States pediatric LTCFs, might suffer morbidity similar to geriatric LTCF residents.

CMC living in long-term care typically have physical disabilities, severe neurological impairment and medical technology dependence. Historically, CMC fares worse than typical children with common viral illnesses.[2] Nevertheless, reports on COVID-19 in children have demonstrated a milder clinical course and better hospital outcomes versus adults, regardless of risk factors.[3] Data on COVID-19 disease in CMC remains limited. We describe the clinical characteristics, outcomes and immunologic response following COVID-19 infection and vaccination of 5 CMC.

Between September 2020 and March 2021 5 residents of a 76-bed pediatric LTCF tested positive for COVID-19 infection during weekly facility-wide surveillance testing and were enrolled in our descriptive study. Following institutional review board approval (IRB#21.0789) we performed a

TABLE 2. Virus Neutralization, B cell, and CD4+ and CD8+ T cell Responses to COVID-19 Infection and Vaccination

	Microneutralization Assay		Serology					AIM Assay Marker				Fold Change (+ Pep/No Pep)		
								$CD4^+$ T		$CD8^+$ T				
Patients	WA	Delta	Spike IgG	Spike IgA	RBD IgG	RBD IgA	Nucleo-capsid IgG	+ Pep	No Pep	+ Pep	No Pep	CD4	CD8	T Cell Re-activity
Case 1 9 months post-COVID	1:1024	<1:128	<1:100	<1:100	<1:100	<1:100	<1:100	2.6	1.56	3.12	0.33	1.67	9.45	Activation (CD8 only)
Case 2 7 months post-COVID	1:2048	<1:128	<1:100	<1:100	<1:100	<1:100	<1:100	2.73	1.71	5.06	3.03	1.6	1.67	-
Case 3 7 months post-COVID	1:2580	<1:128	<1:100	<1:100	<1:100	<1:100	<1:100	0.87	0.56	0.63	0.3	1.55	2.1	-
Case 3 7 months post-COVID 1 month post vaccination	1:10,321	1:1024	1:81,000	1:900	1:2700	1:100	<1:100	6.3	0.59	1.13	0.12	10.68	9.42	Activation (CD4 & CD8)
Case 4 7 months post-COVID 5 months post vaccination	1:1290	1:2048	1:8100	1:1559	1:900	1:900	<1:100	2.06	0.47	4.31	0.7	4.38	6.16	Activation (CD4 & CD8)
Case 5 3 months post-COVID	1:1625	<1:128	<1:100	<1:100	<1:100	<1:100	<1:100	6.11	0.55	0.45	1.14	11.11	0.39	Activation (CD4 only)

AIM indicates activation-induced marker.

retrospective review of hospital and facility records to evaluate the disease course 2 weeks post-COVID diagnosis. Blood samples were collected for serologic testing following COVID-19 infection and vaccination. Serologic tests performed include enzyme-linked immunosorbent assays (ELISA), microneutralization assays and activation-induced marker assay to evaluate T cell responses. Signed informed consent was obtained from participant guardians.

Despite underlying comorbidities, participants did not suffer significant morbidity from their COVID-19 infection (Table 1). One patient (case 1) was treated with remdesivir and steroids for a mild oxygen requirement, but on review of his records, intermittent oxygen use is consistent with his baseline. One participant (case 4) had increased seizure activity and mild daytime hypoxia (oxygen use at night is his baseline). Three participants remained asymptomatic.

None of our patients had measurable IgG or IgA titers to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigens 3–9 months after infection, but vaccination induced a robust antibody response (Table 2, ELISA). Neutralization assays were performed to detect functional systemic antibodies. All participants were able to neutralize the SARS-CoV-2 Washington strain following illness. Only vaccinated patients were able to neutralize the Delta variant, which correlates with the presence of high antibody titers in these participants following vaccination. T cell data indicate variable (weak to none) activation of SARS-CoV-2-specific CD4+ and CD8+ T cells following infection, but vaccination induced strong activation of SARS-CoV-2-specific CD4+ T cells.

CMC in our LTCF experienced mild illness with SARS-CoV-2 infection despite comorbidities. This may be because factors hypothesized to explain age-related differences in severity of COVID-19 infection, such as changes in immune function, antibody cross-protection or differences in intensity of initial viral exposure are unrelated to being a CMC.[4] In our small sample, asymptomatic or mild illness did not confer immunity but the immunologic response to vaccination was robust with lasting antibody formation, high virus neutralization titers against the Delta COVID-19 variant and T cell activity. The authors advocate for vaccination for CMC regardless of past COVID-19 illness history.

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