

Letters

RESEARCH LETTER

Frequency of Children vs Adults Carrying Severe Acute Respiratory Syndrome Coronavirus 2 Asymptotically

Children have been suggested as the facilitators of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission and amplification,¹ because many affected children might be asymptomatic.^{2,3} Accordingly, social and public health policies, such as school closure, have been implemented in many countries. However, the role of children in asymptotically carrying SARS-CoV-2 needs to be further explored. In this study, we investigated the frequency of individuals carrying SARS-CoV-2 among children admitted for noninfectious conditions and without any SARS-CoV-2-associated symptoms or signs and compare it with the frequency of individuals carrying SARS-CoV-2 among a similar adult population.

Methods | At the Fondazione Ca' Granda Ospedale Maggiore Policlinico in Milan, Italy, all patients who require hospitalization after accessing either the pediatric emergency department (for participants younger than 18 years) or the adult emergency department (for individuals 18 years and older) immediately undergo a nasopharyngeal swab for the detection of SARS-CoV-2, regardless of their symptoms. If the first sample has negative results, a second one is administered within 12 to 48 hours. For this study, eligible patients were those admitted for noninfectious conditions to this hospital from March 1 to April 30, 2020. We excluded individuals presenting with any signs or symptoms possibly associated with SARS-CoV-2 infection and those with a history of close and prolonged contact with individuals who had tested positive for SARS-CoV-2 or had a history of symptoms or signs consistent with COVID-19 in the previous 21 days. Individuals with only 1 nasopharyngeal swab available were also excluded. The Milano Area 2 ethics committee approved the study, which included a waiver of informed consent because of the retrospective nature of the investigation.

Data on age, sex, the reason for admission, and development of any SARS-CoV-2 signs of infection in the following 48 hours were retrospectively collected. A comparison of proportions between the pediatric and adult cohorts was made with the 2-tailed Fisher test. An odds ratio and its 95% CIs were calculated as a measure of risk of carrying SARS-CoV-2. Significance was assumed when $P < .05$. Statistical analysis was performed using the open-source statistical language R, version 3.5.3 (R Foundation for Statistical Computing).

Results | In the study period, 881 children presented to the pediatric emergency department, and 83 children (34 girls

and 49 boys; median [interquartile range] age, 5.3 [1.1-11.0] years) fulfilled the eligibility criteria. In the same period, among the 3610 adults presenting to the adult emergency department, 131 (51 women and 80 men; median [interquartile range] age, 77 [57-84] years) were included. The reasons for admission of the included individuals are given in the **Table**. Children were found to be less frequently positive than adults (1 in 83 children [1.2%] vs 12 in 131 adults [9.2%]; $P = .02$), with an odds ratio of 0.12 (95% CI, 0.02-0.95) compared with adults. Eleven of 12 adults were positive for SARS-CoV-2 at the first swab. None of the included individuals developed signs or symptoms of SARS-CoV-2 infection in the 48 hours after the admission.

Discussion | In this study conducted among individuals hospitalized in Milan, one of the cities with the highest SARS-CoV-2 burden in the world, about 1% of children and 9% of adults without any symptoms or signs of SARS-CoV-2 infection tested positive for the virus. It has been estimated that approximately 80% of adults with SARS-CoV-2 are asymptomatic.⁴ The few available reports⁵ on children are from China and suggest that children who are asymptomatic might be 15% of individuals positive for SARS-CoV-2. In this study, children without symptoms and signs of SARS-CoV-2 carried the virus less frequently than adults, suggesting that their role as facilitators of the spreading of SARS-CoV-2 infection could be reconsidered. Along with this potential important implication, some limitations should be acknowledged: first, we retrospectively analyzed only cases requiring hospitalization, and second, we report a single-center experience. However, these preliminary results can help understanding the epidemiology of SARS-CoV-2 infections. Particularly, these data do not support the hypothesis that children are at higher risk of carrying SARS-CoV-2 asymptotically than adults.

Table. Characteristics of the Included Children and Adults (N = 214)

Characteristic	Patients, No. (%)	
	Children	Adults
No.	83	131
Female	34 (41)	51 (39)
Age, median (interquartile range), y	5.3 (1.1-11.0)	77 (57-84)
Positive for SARS-CoV-2	1 (1.2)	12 (9.2)
Reason for hospital admission		
Surgical intervention	22 (27)	28 (21)
Neurologic disease	18 (22)	32 (24)
Trauma	10 (12)	11 (8)
Cardiac disease	1 (1)	13 (10)
Psychiatric disorder	3 (4)	8 (6)
Intoxication	3 (4)	1 (1)
Other conditions	26 (31)	38 (29)

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Polysubstance Involvement in Opioid Overdose Deaths in Adolescents and Young Adults, 1999-2018

From 1999 to 2016, opioid-related mortality among adolescents and young adults aged 13 to 25 years (referred to as *youth*) increased 3-fold.¹ Opioid overdose deaths in adult populations often involve other substances, particularly benzodiazepines and, increasingly, stimulants.^{2,3} Little is known about polysubstance involvement in opioid overdose deaths among youth. In this cross-sectional study, we examined national trends in polysubstance-involved opioid overdose deaths among youth in the US.

Methods | We used serial cross-sectional data from the US Centers for Disease Control and Prevention (CDC) Wide-

Ranging Online Data for Epidemiologic Research (WONDER) Multiple Cause of Death file from January 1999 to December 2018.⁴ We identified deaths that involved opioids among youth with complete demographic information using *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)*, codes X40-45, X60-65, X85, and Y10-15. Opioids were classified as synthetic opioids, including fentanyl (T40.4); heroin (T40.1); prescription opioids (T40.2-40.3); and other opioids, including opium (T40.0) and other/unspecified narcotics (T40.6). Methadone was classified as a prescription opioid.^{1,5} This research was not considered human subjects research by the Boston University Medical Campus Institutional Review Board and did not require ethical review and informed consent procedures.

We extracted total opioid overdose deaths and those involving other substances, including benzodiazepines (T42.2), alcohol (T51.0-51.9), antidepressants (T43.0-T43.2), cannabis (T40.7), antipsychotics/neuroleptics (T43.3-T43.5), barbiturates (T42.3), cocaine (T40.5), and psychostimulants other than cocaine (T43.6). We created a category for any stimulant combining cocaine and other psychostimulants. We calculated overdose deaths involving only opioids as total opioid overdose deaths minus opioid overdose deaths involving 1 or more other substance.

We used descriptive statistics with 2-tailed χ^2 tests to characterize deaths by age, sex, race/ethnicity, substances involved, and census region. Significance was set at $P < .05$. Analyses were performed using Stata version 15.1 (StataCorp).

Results | Between 1999 and 2018, opioid-only and polysubstance-involved overdose deaths among youth increased by 384% and 760%, respectively. In 2018, polysubstance-involved opioid overdose deaths became more prevalent than those involving only opioids (polysubstance: 0.22 deaths per 100 000 individuals; 95% CI, 0.21-0.23; opioids only: 0.19 deaths per 100 000 individuals; 95% CI, 0.18-0.20) (Figure, A). From 2010 to 2018, opioid overdose deaths involving stimulants increased 351%, surpassing those involving benzodiazepines (stimulants: 0.14 deaths per 100 000 individuals; 95% CI, 0.13-0.15; benzodiazepines: 0.09 deaths per 100 000 individuals; 95% CI, 0.08-0.09) (Figure, B). Overall overdose deaths declined between 2017 and 2018 (2017: 0.46 deaths per 100 000 individuals; 95% CI, 0.45-0.48; 2018: 0.41 deaths per 100 000 individuals; 95% CI, 0.40-0.43).

In 2018, there were 4623 opioid overdose deaths among youth (Table). Synthetic opioids were most commonly involved (3387 [73.3%]). More than half of all deaths (2476 [53.6%]) involved 1 or more other substance. Stimulants were involved in 1541 of 2476 polysubstance-involved opioid overdose deaths (62.2%) and 1541 of 4623 total opioid overdose deaths (33.3%). By 2018, cocaine was the substance most commonly involved in overdose deaths involving other substances (989 of 2476 [39.9%]).

Discussion | To our knowledge, this is the first study characterizing polysubstance involvement in opioid overdose deaths among youth. For the first time, in 2018, polysubstance-involved opioid overdose deaths became more prevalent