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Short Communication

Decreased risk of COVID-19 pneumonia in children and adolescents during the Delta variant emergence

E. Murillo-Zamora [a, b], X. Trujillo [c], M. Huerta [c], M. Ríos-Silva [d], L.M. Baltazar-Rodríguez [b], J. Guzmán-Esquivel [b, e], V. Benites-Godínez [f], A.D. Ortega-Ramírez [g], O. Mendoza-Cano [h, *]

[a] Departamento de Epidemiología, Unidad de Medicina Familiar No. 19, Instituto Mexicano Del Seguro Social, Av. Javier Mina 301, Col. Centro, C.P. 28000, Colima, México
[b] Facultad de Medicina, Universidad de Colima, Av. Universidad 333, Col. Las Víboras, C.P. 28040, Colima, México
[c] Centro Universitario de Investigaciones Biomédicas, Universidad de Colima, Av. 25 de Julio 965, Col. Villas San Sebastián, C.P. 28045, Colima, México
[d] Universidad de Colima - CONACyT, Centro Universitario de Investigaciones Biomédicas, Av. 25 de Julio 965, Col. Villas San Sebastián, C.P. 28045, Colima, México
[e] Unidad de Investigación en Epidemiología Clínica, Instituto Mexicano Del Seguro Social, Av. de Los Maestros 149, Col. Centro, C.P. 28000, Colima, México
[f] Coordinación de Educación en Salud, Instituto Mexicano Del Seguro Social, Calzada Del Ejercito Nacional 14, Col. Fray Junípero Serra, C.P. 63160, Tepic, Nayarit, Mexico
[g] Programa de Posgrado en Ciencias Médicas, Facultad de Medicina, Universidad de Colima Av. Universidad 333, Col. Las Víboras, C.P. 28040, Colima, México
[h] Facultad de Ingeniería Civil, Universidad de Colima, Km. 9 Carretera Colima-Coquimatlán, Coquimatlán, C.P. 28400, Colima, México

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ABSTRACT

Objectives: This study aimed to evaluate factors associated with the risk of COVID-19 pneumonia in children (aged <10 years) and adolescents (aged 10–19 years) before (March 2020–April 2021) and during (May–July 2021) the Delta (B.1.617.2) variant emergence.
Study design: A retrospective and nationwide cohort study was conducted in Mexico.
Methods: Data from 26,961 laboratory-confirmed cases of COVID-19 were analyzed. Risk ratios (RRs) and 95% confidence intervals (CIs) were used to evaluate the association of the evaluated exposures with the risk of COVID-19 pneumonia.
Results: The overall incidence rate of pneumonia was 23.0 per 10,000 person-days, and it was lower during the Delta variant emergence (30.3 vs. 9.4 person-days, $p < 0.001$). In multiple analysis, a decreased risk of pneumonia was observed among those cases occurring in May 2021 or later (vs. March 2020–April 2021, RR = 0.98, 95% CI 0.97–0.99) and among older patients ($RR_{per\ year} = 0.998$, 95% CI 0.996–0.998). Other comorbidities (namely, obesity, chronic kidney disease, diabetes mellitus, immunosuppression, or malignant tumors) were associated with an increased risk of severe COVID-19 manifestations.
Conclusions: Our findings suggest that during the Delta variant emergence, children and adolescent patients were at reduced risk of COVID-19 pneumonia in Mexico. Further research is needed to identify factors determining the observed scenario.

Background

The severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) Delta variant (B.1.617.2), given its accelerated spread and reduced sensitivity to antibody neutralization, has become the dominant strain in many regions of the world including North America.[1,2] In Mexico, the Delta variant was first isolated in April 2021. Shortly after, persistently increasing trends symptomatic infections have been observed across the country.

The COVID-19 vaccination in Mexican younger adults (aged 18–29 years) started in the second half of July 2021, and by September 2021, the vaccine is not being offered for persons aged < 18 years. Therefore, concerns over rising coronavirus disease 2019 (COVID-19) cases related to the Delta variant in children and

* Corresponding author. Tel.: +52 (312) 3161167.
E-mail addresses: efren.murilloza@imss.gob.mx (E. Murillo-Zamora), pepeguzman_esquivel@hotmail.com (J. Guzmán-Esquivel), veronica.benites@imss.gob.mx (V. Benites-Godínez), aortega1@ucol.mx (A.D. Ortega-Ramírez), oliver@ucol.mx (O. Mendoza-Cano).

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adolescent patients have emerged. This study aimed to evaluate factors associated with the risk of COVID-19 pneumonia in children and adolescents before and during the Delta variant emergence.

Methods

We performed a nationwide cohort study in Mexico, and a broader description of research methods was previously published.[3] Children (aged <10 years) and adolescents (aged 10–19 years) with laboratory-positive (reverse transcription-polymerase chain reaction or rapid antigen-based test) COVID-19, from March 2020 to July 2021, were eligible. Asymptomatic cases were excluded. The medical units where the patients received care are public facilities and belong to the Mexican Institute of Social Security (IMSS, the Spanish acronym).

Pneumonia was the main binary outcome, and it was defined by clinical (fever or chills, cough, shortness of breath, and tachypnea) and radiographic findings (ground glass patterns in X-ray or computed tomography scanning)[4] that required hospital admission. Clinical and epidemiological data of interest were collected from clinical files and death certificates, if applicable. Enrolled patients were classified according to the date of symptoms onset since those occurring during May 2021 or later were more likely to be related to the Delta strain.

We used risk ratios (RRs) and 95% confidence intervals (CIs), computed through generalized linear regression models, to evaluate the association of the evaluated expositions with the risk of COVID-19 pneumonia in children and adolescents. This study was approved by the Local Health Research Committee of the IMSS (approval R-601-2020-015).

Results

Data from 26,961 COVID-19 patients were analyzed for a total follow-up of 297,099 person-days. The overall incidence rate of pneumonia was 23.0 per 10,000 person-days, and it was lower during the Delta variant emergence (30.3 vs. 9.4 per 10,000 person-days, $p < 0.001$). The number of analyzed cases according to the date of symptoms onset and the proportion of pneumonia cases are presented as Supplementary data 1. None of the enrolled subjects had received any dose of any COVID-19 vaccine.

The characteristics of analyzed patients for selected variables are presented as Supplementary data 2. Children and adolescents with pneumonia, and when compared with those with non-severe manifestations, were younger and were more likely to have occurred before May 2021 and to present any comorbidity (namely obesity, diabetes mellitus, arterial hypertension, immunosuppression (due to any cause excepting diabetes), chronic kidney diseases, and malignant tumors at any site).

In multiple regression analysis (Table 1), we observed a decreased risk of pneumonia among older patients (reference: <1 year old; 1–4, RR = 0.95, 95% CI 0.94–0.97; 5–9 years old, RR = 0.94, 95% CI 0.93–0.95; 10–19 years old, RR = 0.93, 95% CI 0.92–0.94), in patients with symptoms onset from May to July 2021 (RR = 0.98, 95% CI 0.97–0.99) and among patients with personal history of arterial hypertension (RR = 0.97, 95% CI 0.94–0.99).

Table 1
Predictors of COVID-19 pneumonia in children and teenagers, Mexico 2020–2021.

Characteristic	RR (95% CI), *p*					
	Bivariate analysis			Multiple analysis		
Gender						
Female	1.00			1.00		
Male	1.01	(0.99–1.02)	0.213	1.01	(0.99–1.02)	0.369
Age (years)						
<1	1.00			1.00		
1–4	0.95	(0.94–0.96)	<0.001	0.95	(0.94–0.97)	<0.001
5–9	0.95	(0.94–0.96)	<0.001	0.94	(0.93–0.95)	<0.001
10–19	0.93	(0.92–0.94)	<0.001	0.93	(0.92–0.94)	<0.001
Date of symptoms onset						
March 2020 to April 2021	1.00			1.00		
May 2021 to July 2021	0.98	(0.97–0.98)	<0.001	0.98	(0.97–0.99)	<0.001
Personal history of:						
Obesity						
No	1.00			1.00		
Yes	1.03	(1.02–1.04)	<0.001	1.03	(1.02–1.04)	<0.001
Diabetes mellitus						
No	1.00			1.00		
Yes	1.10	(1.06–1.14)	<0.001	1.09	(1.06–1.13)	<0.001
Arterial hypertension						
No	1.00			1.00		
Yes	1.03	(1.01–1.06)	0.033	0.97	(0.94–0.99)	0.027
Immunosuppression						
No	1.00			1.00		
Yes	1.22	(1.17–1.26)	<0.001	1.16	(1.12–1.21)	<0.001
CKD						
No	1.00			1.00		
Yes	1.27	(1.23–1.31)	<0.001	1.27	(1.23–1.31)	<0.001
Asthma						
No	1.00			1.00		
Yes	1.02	(0.99–1.04)	0.060	1.01	(0.99–1.03)	0.114
Malignant tumor						
No	1.00			1.00		
Yes	1.13	(1.09–1.17)	<0.001	1.07	(1.03–1.11)	<0.001

RR, risk ratio; CI, confidence interval; CKD, chronic kidney disease.
Notes: (1) Generalized linear regression models were used to obtain RR and 95% CI; (2) Multiple regression coefficients were adjusted by variables listed in the table; (3) Immunosuppression referred to any cause of the related deficiency except for diabetes mellitus or renal impairment; (4) Malignant tumor referred to any cancer at any site.

The COVID-19 patients with a previous diagnosis of chronic kidney disease had a 27% increase in the risk of pneumonia (RR = 1.27, 95% CI 1.23–1.31). Other factors associated with a slightly increased risk of severe disease were obesity, diabetes mellitus, immunosuppression, and malignant tumors.

Discussion

Our study characterized factors associated with the risk of COVID-19 pneumonia in children and adolescents before and during the Delta variant emergence in Mexico, where the related economic and social burden of the disease has been high. The presented results suggest that even when an increased incidence of symptomatic infections was observed during the Delta emergence, the COVID-19 cases in children and teenagers were more likely to be non-severe, and a reduced risk of pneumonia was documented.

We also observed a reduced risk of pneumonia in older patients ($RR_{per\ year} = 0.998$, 95% CI 0.996–0.998), and infants (aged <1 year) were at higher risk of developing severe manifestations. Similar findings had been previously published.[5] Despite this later, no significant differences ($p = 0.563$) were observed in our study in the age-stratified risk of a fatal outcome among patients with COVID-19 pneumonia (<1 year, 20.6%; 1–4 years, 23.3%; 5–9 years, 14.9%; and 10–19 years, 19.0%).

Children and teenagers with a personal history of arterial hypertension seemed to have a reduced risk of pneumonia (RR = 0.97, 95% CI 0.94–0.99). Unfortunately, we were unable to determine if they were receiving any specific antihypertensive drugs such as calcium channel blockers that have been associated with a reduction of fatal outcomes among COVID-19 patients.[6]

Renal impairment was related to the highest increase in the risk of severe manifestations in the study sample. Pediatric patients with chronic kidney disease also had a 2-fold increase in the risk of dying (9.2% vs. 4.6%, $p = 0.079$).

Children and teenagers with obesity also were at greater risk of pneumonia. This was observed despite the low prevalence of obesity in the study sample (4.7%) when compared with the national mean (35.6%).[6] According to normative standards of Mexico, the World Health Organization body mass index-for-age charts must be used in pediatric patients to assess their nutritional status. However, the obesity variable was collected as a binary exposure (yes/no), and we were unable to verify if the standards were strictly followed.

The limitation of our study must be discussed. First, the observed reduced risk of COVID-19 pneumonia in the analyzed children and adolescents may not be fully attributed to the prevalent Delta variant, and other determinants may be involved. However, all the analyzed subjects were unvaccinated for COVID-19, and no major changes in the available treatments were observed during the study period. Besides and in a real-world scenario, none of the available treatments for COVID-19 pneumonia has shown to be effective in reducing the all-cause mortality in Mexico.[7]

Second, the prevalence of arterial hypertension in the study sample was low (0.4%), and, even when a reduced risk of pneumonia was documented among them, we are unable to conclude that these patients were at reduced risk of severe COVID-19 because of its cardiovascular condition. Third, data regarding the comorbidities of the participants were collected from medical records as dichotomous variables (yes/no). Additional information such as elapsed time since diagnosis and current treatment would have enriched our study. And fourth, we did not analyze other relevant outcomes (i.e. pediatric inflammatory multisystem syndrome temporally associated with COVID-19 or PIMS-TS)[8] that might have occurred in the participants.

Conclusions

Our findings suggest that during the Delta variant emergence in Mexico, children and adolescents were at reduced risk of COVID-19 pneumonia. However, non-adult patients play a major role in the spread of respiratory pathogens, and efforts focusing on the prevention of infections in these patients may have a favorable impact on other age groups.

Author statements

Ethical approval

This study was approved by the Local Health Research Committee 601 of the Mexican Institute of Social Security (approval R-601-2020-015).

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None declared.

Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2021.12.017.

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