BMJ Open

Risk factors for COVID-19 hospitalisations and deaths in Mexican children and adolescents: retrospective cross-sectional study

Libny Martínez-Valdez, Vesta Richardson López Collada,
Luis Enrique Castro-Ceronio, Ángela María Rodríguez Gutiérrez,
Aurora Bautista-Márquez [ORCID], Mauricio Hernandez-Avila

Coordinación del Servicio de Guardería, Instituto Mexicano del Seguro Social, Ciudad de Mexico, Mexico

Correspondence to
Vesta Richardson López Collada;
vesta.richardson@imss.gob.mx

ABSTRACT

Objective To describe the epidemiology and risk factors for hospitalisation and death in Mexican children under 18 years of age with COVID-19.

Design Retrospective, cross-sectional and analytical study.

Setting Mexican Ministry of Health open databases with COVID-19 cases occurred from 7 March 2020 to 30 September 2021.

Participants Mexican children under 18 years of age with COVID-19.

Main outcome measures COVID-19 hospitalisations and deaths were characterised by age group, sex, presence of pneumonia and comorbidities, intubation and intensive care unit admission, and institution that provided medical care. Cumulative incidence, mortality, case fatality rates and ORs for hospitalisation and death were estimated by age group.

Results 5.5% (204 641) of national COVID-19 cases were children under 18 years of age: 2.9% under 1 year, 12.5% from 1 to 5 years, 15% from 6 to 9 years and 69.4% from 10 to 17 years. 4.6% of all cases were hospitalised, from which 54.6% were male, 35.3% were children under 1 year old, 39.6% were adolescents and 34% had pneumonia. Pneumonia developed in 2.3% of cases, from which 50% were adolescents. Case fatality rate was higher in children less than 1 year old (4.2%). Risk analyses showed that male sex (OR 1.16–1.28), history of pneumonia (OR 29.7–65.4), immunosuppression (OR 5.3–42.9), cardiovascular disease (OR 4.4–14.6) and other comorbidities (OR 5.4–19.1), as well as age less than 1 year (OR 20.1, 95% CI 18.8 to 21.4), confer a greater risk of hospitalisation; in addition to comorbidities, age less than 1 year (OR 16.6, 95% CI 14.1 to 19.6), history of pneumonia (OR 14.1–135.1) and being an adolescent from an indigenous community (OR 2.6, 95% CI 1.23 to 5.54, p=0.012) increase the risk of death.

Conclusions In Mexico, children less than 1 year old with COVID-19 have higher risk of hospitalisation and death than older children. Adolescents with COVID-19 in association with comorbidities develop adverse outcomes more frequently.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ It is one the first publications that describes the epidemiology of COVID-19 in Mexican children and their risk of hospitalisation and death by age group.

⇒ The information comes from a database where representative medical units from all public institutions in the country register cases.

⇒ The analyses were limited to the variables contained in the database; access to medical reports was not possible.

⇒ No operational definition for comorbidities is included in the catalogues of the used database.

⇒ Since categorised as 'other comorbidities', most frequently comorbidities associated with hospitalisation and death were not known.

INTRODUCTION

After the WHO declared the disease caused by SARS-CoV-2 (COVID-19) a public health emergency of international concern in January 2020,[1 2] by 30 September 2021, a total of 233 136 147 confirmed cases and 4 771 408 deaths had been reported worldwide, with a global case fatality rate of 2%. In Mexico, as of the same date, 3 664 223 cases and 277 505 deaths due to COVID-19 had been confirmed.[3]

There is information available on the epidemiological and clinical characteristics of COVID-19 in vulnerable groups such as the elderly and people with chronic diseases; however, in children, the information is limited, particularly for the Latin American countries.[1 4–11] Children of all ages are susceptible to COVID-19,[1 2 12] and the American Academy of Pediatrics reported that, in the USA, cases in children represented 8.8% of all cases.[13] As of 29 November 2020, children still represented less than 13% of overall COVID-19 cases reported to the European Centre for Disease Prevention and Control

and deaths among cases under 18 years were extremely uncommon.[14] Children usually present an asymptomatic or less severe course,[1 2 5 6 15–20] with an estimated incidence of asymptomatic infection of 4.4%–21%.[1 7 14 21] However, 3.8% may develop a severe condition and even die,[1 2 8 10–12 16 17 22–24] with infants younger than 6 months being the most susceptible.[25 26]

The main route of transmission for COVID-19 in children has been family clustering, with percentages ranging from 56% to 82%.[2 8–10 21 27 28] Approximately one-quarter of children infected with SARS-CoV-2 may have associated diseases,[2 7 10 27] suggesting that these may lead to an increased risk of developing severe disease.[6 11 26] The objective of this study is to describe the epidemiological behaviour and risk factors for COVID-19 hospitalisation and death in Mexican children under 18 years of age.

METHODS

This is a retrospective, cross-sectional and analytical study of hospitalisations and deaths due to COVID-19 in Mexican children under 18 years of age, from 7 March 2020 to 30 September 2021, available in open access data of the Mexican Ministry of Health.[29] COVID-19-confirmed cases were those with a final classification determined by epidemiological association, by the committee of opinion and/or by a positive PCR or antigen test against SARS-CoV-2.

Analyses were carried out on all the registries within the database that were classified as confirmed cases as described above in the following age groups: less than 1 year, 1–5 years, 6–9 years and 10–17 years; therefore, there was no study sample. The studied variables were those included on the open database: age, sex, presence of comorbidities (immunosuppression, cardiovascular disease, obesity, high blood pressure, diabetes, chronic kidney disease, asthma, pulmonary chronic disease and other), health institution that provided care (public or private), type of attention (ambulatory or hospitalisation), presence of pneumonia, need of intensive care unit (ICU), intubation and death. No operational definition for comorbidities, including 'other comorbidities', was included in the catalogues of the used database; also, registry of comorbidities was based on patient report. Public health institutions included: Ministry of Health (SSA), Mexican Institute of Social Security (IMSS and IMSS-Bienestar), Institute of Social Security and Services for Workers (ISSSTE), State Health Services (State), Ministry of National Defense (SEDENA), Petróleos Mexicanos (PEMEX), National System for the Integral Development of the Family (DIF), Ministry of Marine (SEMAR), Municipal Health Services (Municipal) and university facilities. For population-related calculations, the National Population Council (CONAPO)[30] population projections for the year 2020 were used by age group.

Registries with missing data in one or more study variables were not included in the analyses. Simple frequencies of the studied variables were calculated to characterise COVID-19 hospitalisations and deaths by age group,

sex, presence of pneumonia and comorbidities, intubation and ICU admission, and institution that provided medical care. The cumulative incidence rate, mortality rate and case fatality rate for COVID-19 were calculated by age group. The case fatality rate was expressed as the percentage of deaths among the total COVID-19 cases for each age group. Using simple logistic regression, ORs were calculated by age group to estimate the risk of hospitalisation or death in relation to sex, presence of pneumonia and presence of comorbidities. Fisher's exact test was used to estimate statistical significance. To avoid erroneous conclusions, all rates were calculated separately for each age group.

RESULTS

Cumulative incidence

The open database of the Ministry of Health as of 30 September 2021 contains more than 11 million records, of which 3 664 223 corresponded to people with a positive result for SARS-CoV-2, and 204 641 were children less than 18 years (5.5%); of these, 6082 were children under 1 year of age (2.9%), 25 610 (12.5%) children aged 1–5 years, 30 858 (15%) children aged 6–9 years and 142 091 (69.4%) children aged 10–17 years. Considering the estimated population under 18 years of age, the cumulative incidence rate is 516.2 cases per 100 000 children under 18 years of age.

The states with the highest cumulative incidence rate for COVID-19 in children under 18 years of age were Mexico City (3956.09/100 000 children under 18 years of age), Tabasco (1413.24/100 000 children under 18 years of age) and Baja California (1327.63/100 000 children under 18 years of age). The area known as Megalopolis, made up of Mexico City, the State of Mexico, Hidalgo, Morelos, Puebla and Tlaxcala, had a cumulative incidence of 940 cases per 100 000 children under 18 years of age.

Hospitalisations

Of the 204 641 cases in children under 18 years of age, 9446 (4.6%) required hospitalisation. Of these, 22.7% (2148) were children less than 1 year and 25.4% (2402) were between 1 and 5 years old; that is, 48% of the hospitalised children were under 6 years of age. Also, 39% of hospitalised cases were adolescents (10–17 years old). From the 6082 COVID-19 cases in children under 1 year of age, 35.3% were hospitalised (table 1, figure 1).

Of the hospitalised minors, 53.6% were male, and this majority was consistent within all age groups except in the adolescents; 3229 (34.1%) hospitalised children had pneumonia, from which 1306 (40%) were adolescents; 1034 (10.9%) required attention in an ICU and 476 (46%) of them were children less than 1 year of age; 823 (8.7%) required intubation with mechanical ventilation, from which 33% (273/823) were children less than 1 year and 32% (265/823) were adolescents; 71.2% (586/823) of intubated children had pneumonia

Table 1 Contribution rate by condition for children younger than 18 years of age with COVID-19 from 7 March 2020 to 30 September 2021 in Mexico

Age group (year)	Cases n=204 641	Hospitalised n=9446	Pneumonia n=4854	ICU n=1034	Intubated n=823	Deaths n=934
<1	6082 (2.9%)	2148/6082 (35.3%)	888/6082 (14.6%)	476/2148 (22.1%)	273/2148 (12.7%)	257/6082 (4.2%)
1–5	25 610 (12.5%)	2402/25 610 (9.3%)	994/25 610 (3.8%)	193/2402 (8%)	207/2402 (8.6%)	225/25 610 (0.8%)
6–9	30 858 (15%)	1156/30 858 (3.7%)	555/30 858 (1.7%)	77/1156 (6.6%)	78/1156 (6.7%)	84/30 858 (0.2%)
10–17	142 091 (69.4%)	3740/142 091 (2.6%)	2417/142 091 (1.7%)	288/3740 (7.7%)	265/3740 (7%)	368/142 091 (0.2%)
Total	204 641 (100%)	9446/204 641 (4.6%)	4854/204 641 (2.3%)	1034/9446 (10.9%)	823/9446 (8.7%)	934/204 641 (0.4%)

Source: Mexican Ministry of Health.[29]
n=total number of cases in the category.
ICU, intensive care unit.

and 34% of them were 10–17 years old; 39% of children intubated without pneumonia were under 1 year of age (table 2).

Up to 10% of hospitalised children had some comorbidity classified as 'Other', followed by immunosuppression (6.8%) and obesity (5.3%). Obesity was more frequent in adolescents and cardiovascular disease was more frequent in children under 6 years of age. Regarding the institution providing care, 96.7% of the hospitalised children were treated in a public hospital and most of them had no social security (table 2).

Deaths

From the 204 641 children under 18 years of age diagnosed with COVID-19, a total of 934 deaths were recorded, equivalent to a case fatality rate of 0.46% and a mortality rate of 2.35 deaths per 100 000 children under 18 years of age. Of the total number of deaths, 257 (27.5%) occurred in children under 1 year of age, 225 (24%) in children aged 1–5 years, 84 (8.9%) in children aged 6–9 years and 368 (39.4%) in adolescents aged 10–17 years. 53.4% of deaths occurred in males. Of the patients who died, 94.7% were hospitalised; 66.9% were diagnosed with pneumonia, of them 40% (248/625) were adolescents; 27.3% required ICU, from which 38% (97/255) were children less than 1 year of age and 31% (80/255) were adolescents; up to 30% (114/377) and 35% (132/377) of children who were intubated and died had less than 1 year of age and were adolescents, respectively; most (37%, 112/299) of those who died and had a history of intubation and pneumonia were adolescents. Up to 18% of the deceased patients had some comorbidity classified as 'Other', followed by immunosuppression (8.9%) and obesity (8.9%). Sixty-two per cent and 40% of children who died and had a history of arterial hypertension or cardiovascular disease, respectively, had less than 1 year of age; other comorbidities were more prevalent in adolescents. 94.7% (885) of deaths occurred in a hospital and 48.6% of the deceased children were attended by the Ministry of Health (table 3).

The states with the highest mortality from COVID-19 were Aguascalientes (5.13/100 000 children under 18 years of age), Baja California (4.48/100 000 children under 18 years of age) and Oaxaca (3.58/100 000 children under 18 years of age). The area known as Megalopolis (Mexico City, State of Mexico, Hidalgo, Morelos, Puebla and Tlaxcala) had a mortality rate of 2.85 cases per 100 000 children under 18 years of age and a case fatality rate of 0.30%. The states of Baja California, Aguascalientes and Puebla had the highest case fatality rates (2.70%, 2.12% and 1.65%, respectively), and Mexico City had the lowest case fatality rate (0.09%). Although the overall case fatality rate in children under 18 years of age was 0.4%, by age group it was 0.2% in children 10–17 and 6–9 years old, 0.8% in children 1–5 years old and 4.2% in children under 1 year old (table 1).
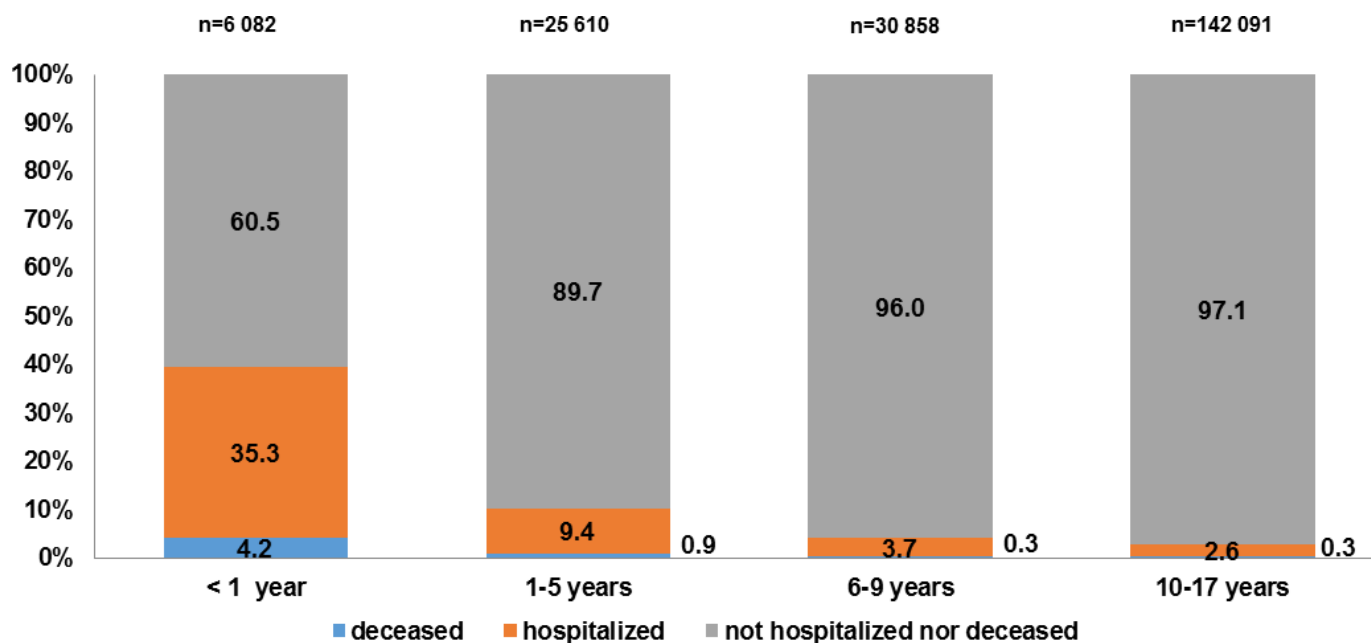
Figure 1 Percentage of distribution of hospitalisations and deaths for children under 18 years of age with COVID-19 from March 2020 to September 2021 in Mexico. n=total number of cases in the category. Categories are not exclusive, they reflect a percentage over the total children in each category. Source: Mexican Ministry of Health.[29]

Risks

It was identified that children under 1 year of age are more likely to be hospitalised (OR 20.1; 95% CI 18.8 to 21.4, p=0.000) and to die (OR 16.6; 95% CI 14.13454 to 19.6617, p=0.020), compared with older children. Major probability of hospitalisation was observed in males under 10 years of age (OR 1.16; 95% CI 1.04 to 1.3 in children under 1 year, OR 1.28; 95% CI 1.17 to 1.39 in children 1–5 years old, OR 1.25; 95% CI 1.1 to 1.41 in children 6–9 years). Also, major probability of hospitalisation was observed in children with pneumonia; this probability increased with age (OR 29.7; 95% CI 23.1 to 38.1 in children under 1 year, OR 51.1; 95% CI 43.3 to 60.2 in children 1–5 years old, OR 51.8; 95% CI 42.9 to 62.5 in children 6–9 years old, OR 65.45; 95% CI 59.6 to 71.7 in children 10–17 years old).

Considering comorbidities as risk factors, it stands out that other comorbidities, immunosuppression and cardiovascular disease increase the probability of hospitalisation in all age groups; being from an indigenous community, high blood pressure and diabetes increase the probability of hospitalisation in children older than 1 year of age; and obesity and chronic renal disease increase the probability of hospitalisation in children older than 5 years. Having more than one comorbidity increases the chances of being hospitalised in all age groups.

Major probability of death was observed in children with pneumonia; this probability increased with age (OR 99.7; 95% CI 69.6 to 142.8, p=0.000 in children under 1 year, OR 227.8; 95% CI 164.7 to 314.9, p=0.000 in children 1–5 years old, OR 228.7; 95% CI 142.2 to 368.1, p=0.000 in children 6–9 years old, OR 280.4; 95% CI 220.4 to 356.7 in children 10–17 years old). Also, major chances of death were observed in adolescents from indigenous communities (OR 2.52; 95% CI 1.12 to 5.6, p=0.025). Immunosuppression, other comorbidities, cardiovascular disease, high blood pressure and chronic renal disease were related with a major probability of death in all age groups; obesity was related to a major chance of death in children older than 1 year of age; chronic respiratory disease increases the probability of death in adolescents, and diabetes also increases the chances to die in all age groups with the exception of the 6–9 years age group. Table 4 shows the risks of death and hospitalisation by age group and comorbidity.

DISCUSSION

The first series of cases reported in China included 2135 children under 18 years of age with COVID-19,[1 17] of whom 870 (40%) were less than 6 years old; of these, 379 (43.5%) were under 1 year of age. In our study, 204 641 children under 18 years of age were registered with COVID-19 (cumulative incidence of 516.2 per 100 000 children under 18 years of age), of whom only 2.9% were under 1 year of age, with the highest percentage of cases falling in the 10–17 years age group. The number of SARS-CoV-2-positive children under 18 years of age in Mexico increased substantially during December 2020 and January 2021, and during July and August 2021, which can be explained by an increased circulation and transmission of the virus, as has been seen in other countries. In the database used for this study, 51.8% of children under 18 years of age had a history of contact with another SARS-CoV-2-positive case, which contrasts with a study in Switzerland,[31] where in 79% of households, one or more adults in the family had suspected or confirmed COVID-19 before the onset of symptoms in children. This

Table 2 Characteristics of hospitalised children under 18 years of age with COVID-19 from 7 March 2020 to 30 September 2021 in Mexico

Characteristics	<1 year n=2148	1–5 years n=2402	6–9 years n=1156	10–17 years n=3740	Total <18 years old n=9446
Male	1232 (57.3)	1385 (57.6)	658 (56.9)	1790 (47.8)	5065 (53.6)
Female	916 (42.6)	1017 (42.3)	498 (43)	1950 (52.1)	4381 (46.3)
ICU	476 (22.1)	193 (8)	77 (6.6)	288 (7.7)	1034 (10.9)
Pneumonia	812 (37.8)	786 (32.7)	325 (28.1)	1306 (34.9)	3229 (34.1)
Intubated	273 (12.7)	207 (8.6)	78 (6.7)	265 (7)	823 (8.7)
With pneumonia	181/273 (66.3)	150/207 (72.4)	53/78 (67.9)	202/265 (76.2)	586/823 (71.2)
Without pneumonia	92/273 (33.7)	57/207 (27.5)	25/78 (32)	63/265 (23.7)	237/823 (28.8)
Comorbidities					
Other	150 (6.9)	302 (12.5)	131 (11.3)	362 (9.6)	945 (10)
Immunosuppression	66 (3)	166 (6.9)	129 (11.1)	285 (7.6)	646 (6.8)
Obesity	50 (2.3)	21 (0.8)	44 (3.8)	388 (10.3)	503 (5.3)
Asthma	4 (0.1)	56 (2.3)	57 (4.9)	144 (3.8)	261 (2.7)
Cardiovascular disease	75 (3.4)	99 (4.1)	14 (1.2)	69 (1.8)	257 (2.7)
Diabetes	56 (2.6)	22 (0.9)	8 (0.6)	133 (3.5)	219 (2.3)
High blood pressure	66 (3)	25 (1)	5 (0.4)	78 (2)	174 (1.8)
Chronic kidney disease	10 (0.4)	18 (0.7)	9 (0.7)	112 (2.9)	149 (1.5)
Smoking	NA	NA	2 (0.1)	38 (1)	40 (0.4)
COPD	12 (0.5)	6 (0.2)	–	4 (0.1)	22 (0.2)
Healthcare institution					
Social security	2090 (97.2)	2297 (95.6)	1121 (96.9)	3624 (96.8)	9132 (96.7)
Private	58 (2.7)	105 (4.3)	35 (3)	116 (3.1)	314 (3.3)

Source: Mexican Ministry of Health.[29]
n=total number of cases in the category.
COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; NA, not applicable.

difference may be attributable to the lack of an intentional case finding and contact study.

COVID-19 in children usually starts with mild respiratory symptoms, the main ones being fever, cough and irritability, followed by sneezing, rhinorrhoea, nasal congestion or even gastrointestinal symptoms[7 9–12 20 21 24 26 28 32] for 2 or 3 days,[6] and it has been reported that most children are in the early stages of the disease when they are hospitalised.[16] According to data from the US Centers for Disease Control and Prevention (CDC), between 0.6% and 8.9% of COVID-19 cases in children under 18 years of age[13] are hospitalised[13] and only 1.5% (310 out of 20 133) of patients under 18 years of age in a report from the UK were hospitalised.[14] When comparing these data with ours, we found a similar percentage (4.6%) as in the USA, contrary to that reported in a study in Madrid, where 60% of children with COVID-19 were hospitalised.[33] According to a study in China in which more than 2000 children with COVID-19 were analysed, more than 90% of them were asymptomatic or had very mild symptoms; however, the youngest children were those who mainly required hospitalisation.[1 17] In the case of Mexico, the percentage of children with COVID-19 under 1 year of age requiring

hospitalisation was 35.3% and only 2.6% of those older than 10 years (table 1); even more, almost half of hospitalised children with COVID-19 were less than 6 years old. Also, as has been observed during the pandemic, males are hospitalised more frequently.

A systematic review and meta-analysis of 31 studies including 1181 children under 5 years reported that 49% of children who required hospitalisation (moderate/severe disease) required oxygen therapy (not inclusive of mechanical ventilation).[34] In our study, one-third of hospitalised children had pneumonia and most of them (40%) were children aged 10–17 years; despite this, the proportion of children with pneumonia who required intubation and mechanical ventilation was very similar in children under 1 year of age and adolescents (table 2). This study also found that pneumonia substantially increases the probability of hospitalisation, and that it increases even more with age.

Other causes of hospitalisation related to COVID-19, such as multisystem inflammatory syndrome (MIS-C), have been identified in other studies; no cases of MIS-C were identified in the data source consulted for this analysis.

Table 3 Characteristics of deceased children under 18 years of age with COVID-19 from 7 March 2020 to 30 September 2021 in Mexico

Characteristics	<1 year n=257	1–5 years n=225	6–9 years n=84	10–17 years n=368	Total <18 years old n=934
Male	145 (56.4)	119 (52.8)	48 (57.1)	187 (50.8)	499 (53.4)
Female	112 (43.5)	106 (47.1)	36 (42.8)	181 (49.1)	435 (46.5)
Outpatient	15 (5.8)	9 (4)	3 (3.5)	22 (5.9)	49 (5.2)
Hospitalised	242 (94.1)	216 (96)	81 (96.4)	346 (94)	885 (94.7)
ICU	97 (37.7)	62 (27.5)	16 (19)	80 (21.7)	255 (27.3)
Pneumonia	171 (66.5)	153 (68)	53 (63.1)	248 (67.3)	625 (66.9)
Intubated	114 (44.3)	103 (45.7)	28 (33.3)	132 (35.8)	377 (40.3)
With pneumonia	82 (71.9)	84 (81.5)	21 (75)	112 (84.8)	299 (79.3)
Without pneumonia	32 (28)	19 (18.4)	7 (25)	20 (15.1)	78 (20.6)
Comorbidities					
Other	27 (10.5)	53 (23.5)	24 (28.5)	65 (17.6)	169 (18)
Immunosuppression	10 (3.8)	16 (7.1)	15 (17.8)	43 (11.6)	84 (8.9)
Obesity	10 (3.8)	5 (2.2)	7 (8.3)	62 (16.8)	84 (8.9)
Cardiovascular disease	25 (9.7)	18 (8)	2 (2.3)	17 (4.6)	62 (6.6)
High blood pressure	31 (12)	6 (2.6)	2 (2.3)	11 (2.9)	50 (5.3)
Diabetes	21 (8.1)	3 (1.3)	1 (1.1)	23 (6.2)	48 (5.1)
Chronic kidney disease	5 (1.9)	3 (1.3)	2 (2.3)	29 (7.8)	39 (4.1)
Asthma	1 (0.3)	1 (0.4)	1 (1.1)	12 (3.2)	15 (1.6)
COPD	1 (0.3)	–	–	2 (0.5)	3 (0.3)
Smoking	NA	NA	–	1 (0.2)	1 (0.1)
Healthcare institution					
Social security	254 (98.8)	223 (99.1)	84 (100)	362 (98.3)	923 (98.8)
Private	3 (1.1)	2 (0.8)	–	6 (1.6)	11 (1.2)

Source: Mexican Ministry of Health.[29]
n=total number of cases in the category.
COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; NA, not applicable.

Regarding the need for intensive care, the US CDC Morbidity and Mortality Report (January 2021) reported that of 1 222 023 confirmed cases of COVID-19 in children under 18 years of age, 2.3% were hospitalised, 0.8% required ICU care and the case fatality was less than 0.1%.[35] A systematic review of 31 studies reported that 7% of cases in children under 5 years were severe cases requiring ICU[34]; a European multicentre study reports that 8% of SARS-CoV-2-positive children required ICU admission and 4% required mechanical ventilation.[10] By contrast, a study of paediatric ICUs in the USA and Canada reports that 38% of patients admitted to the ICU required invasive ventilation.[36] In this analysis, we found that 8.4% (1034) of hospitalised children required ICU care, from which 64.7% were under 6 years of age. If only patients admitted to an ICU are considered, 79.5% (823/1034) were intubated; of them, one-third were children under 1 year and one-third were adolescents (table 2); also relevant is the finding that 39% of children intubated for a disease different from pneumonia were less than 1 year old, which could be related with the

prevalence of respiratory and cardiovascular diseases in this age group.

The severity of COVID-19 depends on several factors. A multicentre study in Europe found that being male, being less than 1 month old, a pre-existing medical condition, as well as signs of lower respiratory infection were associated with ICU admission.[10] It has been reported that approximately one-quarter of infected children may have associated diseases[7 10 27 32] such as congenital heart disease, blood disorders, immunosuppression, chronic kidney, liver or lung disease,[2 11 15 32] suggesting that these conditions lead to an increased risk of developing a severe form of the disease.[2 11 26 37 38] In a systematic review, among 9353 paediatric patients with SARS-CoV-2 infection and underlying comorbidities, 481 (5.1%) had severe COVID-19 and/or were admitted to an ICU. In contrast, only 579 of the 275 661 (0.21%) pooled paediatric patients without comorbidities had a severe manifestation of COVID-19.[39] However, a study of 260 children hospitalised in Wuhan in March 2020 reports that the likelihood of comorbidities was not different between the severe and non-severe

Table 4 Risk of death or hospitalisation according to age group and health condition for children younger than 18 years of age with COVID-19 from 7 March 2020 to 30 September 2021 in Mexico

Age group	OR	Fisher's exact test P value	95% CI
Risk of death by age group			
<1 year (n: 5703)	16.67	0.000	14.13 to 19.66
1–5 years (n: 24 067)	3.34	0.000	2.82 to 3.96
6–9 years (n: 28 764)	1.07	0.055	0.84 to 1.36
10–17 years (n: 132 195)	1	–	–
Risk of hospitalisation by age			
<1 year (n: 5703)	20.11	0.000	18.87 to 21.43
1–5 years (n: 24 067)	3.77	0.000	3.57 to 3.98
6–9 years (n: 28 764)	1.43	0.000	1.34 to 1.54
10–17 years (n: 132 195)	1	–	–

Risk of death or hospitalisation by age group according to health condition

Condition	<1 year Hospitalised	<1 year Deceased	1–5 years Hospitalised	1–5 years Deceased	6–9 years Hospitalised	6–9 years Deceased	10–17 years Hospitalised	10–17 years Deceased
Male	1.16 (1.0–1.3)	–	1.28 (1.1–1.3)	–	1.25 (1.1–1.4)	–	–	–
Pneumonia	29.70 (23.1–38.1)	99.72 (69.6–142.8)	51.12 (43.3–60.2)	227.81 (164.7–314.9)	51.84 (42.9–62.5)	228.79 (142.2–368.1)	65.45 (59.6–71.7)	280.40 (220.4–356.7)
Indigenous	–	–	3.84 (2.8–5.1)	–	2.61 (1.6–4.2)	–	3.49 (2.8–4.3)	2.52 (1.12–5.67)
Immunosuppression	5.34 (3.2–8.7)	7.02 (3.1–15.5)	25.15 (18.5–34.0)	28.43 (15.8–50.9)	42.25 (31.7–56.2)	77.61 (42.5–141.6)	42.99 (35.9–51.4)	72.23 (50.5–103.2)
Other comorbidity	5.41 (3.9–7.4)	8.20 (4.95–13.6)	16.04 (13.3–19.3)	35.51 (25.1–50.1)	19.13 (15.1–24.1)	55.73 (33.4–92.9)	16.01 (14.0–18.2)	32.90 (24.7–43.6)
Chronic kidney disease	–	4.80 (1.31–17.5)	4.99 (2.5–9.7)	12.86 (3.8–42.9)	6.31 (2.9–13.7)	22.13 (5.2–93.9)	21.60 (16.9–27.4)	63.87 (42.2–96.5)
Cardiovascular disease	4.44 (2.87–6.88)	13.85 (7.8–24.3)	14.60 (10.5–20.1)	32.4 (18.8–55.8)	5.38 (3.0–9.6)	10.72 (2.5–44.5)	7.33 (5.6–9.5)	19.26 (11.5–32.2)
High blood pressure	–	4.81 (3.1–7.3)	5.27 (3.1–8.7)	11.57 (4.9–27.1)	2.73 (1.0–6.8)	14.42 (3.4–60.3)	7.83 (6.0–10.0)	10.10 (5.5–18.5)
Obesity	–	–	–	–	2.11 (1.5–2.9)	5.39 (2.4–11.7)	3.24 (2.9–3.6)	5.18 (3.8–6.9)
Diabetes	–	4.41 (2.6–7.3)	4.92 (2.9–8.2)	7.47 (2.2–24.2)	3.42 (1.6–7.1)	–	9.40 (7.6–11.4)	16.75 (10.5–26.5)

Continued

Table 4 Continued

Risk of death or hospitalisation by age group according to health condition

Condition	<1year		1–5 years		6–9 years		10–17 years	
	Hospitalised	Deceased	Hospitalised	Deceased	Hospitalised	Deceased	Hospitalised	Deceased
COPD	3.60 (1.35–9.61)	–	11.97 (3.2–44.6)	–	–	–	–	8.32 (2.0–33.9)
Asthma	–	–	1.99 (1.4–2.6)	–	1.92 (1.4–2.5)	–	1.42 (1.1–1.6)	–
1–2 comorbidities	5.34 (4.6–6.0)	41.30 (22.3–76.4)	16.17 (14.5–17.9)	74.39 (51.71–107.0)	11.41 (10.0–12.9)	40.48 (23.3–70.0)	10.66 (9.9–11.4)	51.28 (37.2–70.5)
3–4 comorbidities	5.73 (3.7–8.7)	41.30 (22.3–76.4)	59.15 (36.5–95.6)	354.47 (168.5–745.6)	58.14 (33.9–99.7)	628.92 (261.4–1512.7)	99.40 (79.2–124.6)	848.1 (543.0–1324.6)

Source: Mexican Ministry of Health.[29]

n=total number of cases in the category.

Includes risks with statistical significance.

COPD, chronic obstructive pulmonary disease.;

COVID-19 groups,[40] and even children with comorbidities who tested positive for SARS-CoV-2 had a good prognosis.[41] According to US CDC data from January 2021, up to 27.6% of children aged 0–17 years with SARS-CoV-2 infection had a concomitant illness; the most prevalent were chronic lung disease (6%), other (2%) and disability (1.1%).[35] An analysis of nationwide data from paediatric cases in Mexico reported that obese children were 39% more likely to have SARS-CoV-2 infection, and surprisingly, an Italian study reported a much lower prevalence of asthma in their paediatric COVID-19 cohort than in the general population (2% vs 11%).[42] It has been reported that obesity was the most common comorbidity among hospitalised COVID-19-positive children, with a significant association between obesity and severe cases requiring mechanical ventilation in children 2 years and older.[42] In addition, the number of comorbidities (one, two, or three or more vs none) increased the risk of death (0.60 (0.42–0.85)), as did all the main specific pre-existing medical conditions.[43]

In this study, we found that a pre-existing medical condition increases the probabilities of hospitalisation; pre-existing medical conditions and increased probability of being hospitalised varied with age group. In general, we can say that older children, who have higher prevalence of chronic diseases, have more probabilities to be hospitalised due to COVID-19. The lack of information regarding 'other comorbidities' and that these increase the risk of hospitalisation is worth noting.

It has been reported that paediatric deaths from COVID-19 are extremely rare,[19 36 44] as shown in a report as of February 2021 with data in children aged 0–19 years from France, Germany, Italy, Korea, Spain, England and the USA, where 259 deaths occurred, for a mortality rate of 0.19 per 100 000.[23] In our country, 934 deaths were recorded in children under 18 years of age in approximately 18 months' follow-up period, which is equivalent to a mortality rate of 2.35 per 100 000 children under 18 years of age, a rate 12 times higher than the above-mentioned report. By contrast, the overall mortality rate for COVID-19 in Mexico for the same period was 234.4 per 100 000 people.[45] Six hundred and twenty-five children who died were diagnosed with pneumonia, which represent 12.8% of total pneumonia cases due to COVID-19 in this age group for the study period; it also represents 66.9% of all deaths. For the same study period, it is recorded that 73% of deaths due to COVID-19 in adults in Mexico involved pneumonia, and up to 42% of all cases of COVID-19 pneumonia died.[29]

Regarding risk of death, age per se is identified as conferring a higher risk of death in children under 1 year of age (OR 10.59), which agrees with a study that mentions that age under 1 year and the presence of underlying conditions represent serious risk factors.[46] The overall case fatality rate for COVID-19 has been reported to be 3% (0%–29%); however, it varies among countries and among different age groups.[47] In children under 18 years of age, rates of 0%–0.03% have been reported, and

in populations aged 85 years and older, rates of up to 30.5% have been reported.[48] In a recent study in patients younger than 20 years with COVID-19 in Brazil, the estimated probability of death was 4.8% during the first 10 days after hospital admission, 6.7% during the first 20 days and 8.1% at the end of follow-up. Risk of death was increased in infants younger than 2 years (HR 2.36; 95% CI 1.94 to 2.88) and adolescents aged 12–19 years (HR 2.23; 95% CI 1.84 to 2.71) relative to children aged 2–11 years.[43]

The present study shows that, nationally, the COVID-19 case fatality in children under 18 years of age is 0.4%, and varies significantly by age, being 4.2% in children under 1 year, 0.8% in children 1–5 years and 0.2% in children 6–9 and 11–17 years (table 1). Age less than 1 year old, presence of pneumonia, being adolescent from an indigenous community, other comorbidities, immunosuppression, cardiovascular disease, high blood pressure, diabetes, obesity and chronic renal disease increase the probability of death in the studied population. Interestingly, we also found that the probability of death due to pneumonia increases with age. Another study that includes only Mexico City reported the relative risk attributable to the presence of comorbidities was highest among children and adolescents, comorbidities being accountable for 80%–98% of the age-specific mortality. In children under 10 years of age, comorbid conditions associated with increased mortality were mainly those coded as 'other comorbidities'. In those between 11 and 20 years old, diabetes, obesity, immunosuppression and chronic renal disease were the most significant associated factors.[49]

In our country, the age group with the highest number of hospitalisations and deaths due to COVID-19 was children under 1 year of age. It is noteworthy that the higher the age, the lower the proportion of hospitalisations and deaths (table 1, figure 1).

The most important limitation of this study is the impossibility to verify the correct and complete registry of comorbidities, so it is possible that its prevalence is underestimated or overestimated, which can modify the real influence of a disease in the probability of hospitalisation and death.

CONCLUSIONS

In general, Mexico has higher fatality rates and mortality rates than those reported in other countries in children and adolescents. This analysis suggests that in our country, among those under 18 years of age, children under 1 year of age are the most vulnerable population to develop serious illness and death from COVID-19, so measures to prevent the transmission of SARS-CoV-2 should be strengthened in this age group, carry out a complete study of contacts, know the suspicious signs and symptoms of the disease in children, make early diagnosis, intentionally look for complications and provide timely hospital care to improve prognosis. Special attention deserves the adolescent population who develop pneumonia and have a comorbidity, since their risk of hospitalisation and death increases.

These epidemiological characteristics of COVID-19 in children under 18 years of age could be comparable to other Latin American countries.

ORCID iD
Aurora Bautista-Márquez http://orcid.org/0000-0002-2604-8446

REFERENCES

1 Dong Y, Mo X, Hu Y, *et al*. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;145:e20200702.
2 Khan EA. COVID-19 in children: epidemiology, presentation, diagnosis and management. *J Pak Med Assoc* 2020;70:1–12.
3 Secretary of Health, Government of Mexico. Coronavirus COVID19 daily technical releases September 2021 [online], 2021. Available: https://www.gob.mx/salud/documentos/coronavirus-covid19-comunicados-tecnicos-diarios-septiembre-2021 [Accessed 12 Dec 2021].
4 Medeiros GCBSde, Nunes ACdeF, Azevedo KPMde, *et al*. The control and prevention of COVID-19 transmission in children: a protocol for systematic review and meta-analysis. *Medicine* 2020;99:e21393.
5 Chan KJ, Beck C, Chauvin-Kimoff L, *et al*. The acute management of COVID-19 in paediatrics (spring 2021 update) [online], 2021. Canadian paediatric Society. Available: https://cps.ca/en/documents/position/the-acute-management-of-paediatric-coronavirus-disease-2019covid-19 [Accessed 06/13/2022].
6 Huang X, Wei F, Hu L, *et al*. Epidemiology and clinical characteristics of COVID-19. *Arch Iran Med* 2020;23:268–71.
7 Patel NA. Pediatric COVID-19: systematic review of the literature. *Am J Otolaryngol* 2020;41:102573.
8 Guo C-X, He L, Yin J-Y, *et al*. Epidemiological and clinical features of pediatric COVID-19. *BMC Med* 2020;18:250.
9 She J, Liu L, Liu W. COVID-19 epidemic: disease characteristics in children. *J Med Virol* 2020;92:747–54.
10 Götzinger F, Santiago-García B, Noguera-Julián A, *et al*. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. *Lancet Child Adolesc Health* 2020;4:653–61.
11 Ranabothu S, Onteddu S, Nalleballe K, *et al*. Spectrum of COVID-19 in children. *Acta Paediatr* 2020;109:1899–900.
12 Montaño-Luna VE*et al*. Clinical management of COVID-19 in children. *Rev Med Inst Mex Seguro Soc* 2020.
13 American Academy of Pediatrics CHA. Children and COVID-19: state data report. Summary of publicly reported data from 49

states, NYC, DC, PR, and GU Version: 7/30/20 [online], 2020. Available: https://downloads.aap.org/AAP/PDF/AAP%20and%20CHA%20-%20Children%20and%20COVID- [Accessed 14 Aug 2020].

14 Gaythorpe KAM, Bhatia S, Mangal T. Children's role in the COVID-19 pandemic: a systematic review of early surveillance data on susceptibility, severity, and transmissibility [published correction appears in Sci Rep. 2021 Sep 16;11(1):18814]. *Sci Rep* 2021;11:13903.

15 Zhou Z-W, Xie X-L, Peng Y-G, *et al*. From SARS to COVID-19: what we have learned about children infected with COVID-19. *Int J Infect Dis* 2020;96:710–4.

16 Ma H, Hu J, Tian J, *et al*. A single-center, retrospective study of COVID-19 features in children: a descriptive investigation. *BMC Med* 2020;18:123.

17 Ludvigsson JF. Children are unlikely to be the main drivers of the COVID-19 pandemic - A systematic review. *Acta Paediatr* 2020;109:1525–30.

18 Leung C. Clinical characteristics of COVID-19 in children: are they similar to those of SARS? *Pediatr Pulmonol* 2020;55:1592–7.

19 Rasmussen SA, Thompson LA. Coronavirus disease 2019 and children: what pediatric health care clinicians need to know. *JAMA Pediatr* 2020;174:743–4.

20 Yasuhara J, Kuno T, Takagi H, *et al*. Clinical characteristics of COVID-19 in children: a systematic review. *Pediatr Pulmonol* 2020;55:2565–75.

21 Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. *Pediatr Infect Dis J* 2020;39:355–68.

22 Radia T, Williams N, Agrawal P, *et al*. Multi-system inflammatory syndrome in children & adolescents (MIS-C): A systematic review of clinical features and presentation. *Paediatr Respir Rev* 2021;38:51–8.

23 Bhopal SS, Bagaria J, Bhopal R. Risks to children during the covid-19 pandemic: some essential epidemiology. *BMJ* 2020;369:m2290.

24 Kim L, Whitaker M, O'Halloran A, *et al*. Hospitalization rates and characteristics of children aged <18 years hospitalized with laboratory-confirmed COVID-19 - COVID-NET, 14 States, March 1-July 25, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1081–8.

25 Parri N, Magistà AM, Marchetti F, *et al*. Characteristic of COVID-19 infection in pediatric patients: early findings from two Italian pediatric research networks. *Eur J Pediatr* 2020;179:1315–23.

26 Shen K-L, Yang Y-H, Jiang R-M, *et al*. Updated diagnosis, treatment and prevention of COVID-19 in children: experts' consensus statement (condensed version of the second edition). *World J Pediatr* 2020;16:232–9.

27 Ciofi Degli Atti ML, Campana A, Muda AO, *et al*. Facing SARS-CoV-2 pandemic at a COVID-19 regional children's hospital in Italy. *Pediatr Infect Dis J* 2020;39:e221–5.

28 Lu X, Zhang L, Du H. Chinese pediatric novel coronavirus study team. SARS-CoV-2 infection in children. *N Engl J Med* 2020;382:1663–5.

29 General Directorate of Epidemiology. Datos abiertos bases históricas [online]. Secretary of Health, Government of Mexico, 2021. Available: https://www.gob.mx/salud/documentos/datos-abiertos-bases-historicas-direccion-general-de-epidemiologia [Accessed 31 Oct 2021].

30 National Population Council. Population projections of Mexico's municipalities, 2015-2030, 2019. Available: https://www.gob.

mx/conapo/documentos/proyecciones-de-la-poblacion-de-los-municipios-de-mexico-2015-2030 [Accessed 6 Mar 2021].

31 Posfay-Barbe KM, Wagner N, Gauthey M, *et al*. COVID-19 in children and the dynamics of infection in families. *Pediatrics* 2020;146:e20201576.

32 CDC COVID-19 Response Team. Coronavirus disease 2019 in children - United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:422–6.

33 Tagarro A, Epalza C, Santos M. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. *JAMA Pediatr* 2020:1346.

34 Bhuiyan MU, Stiboy E, Hassan MZ, *et al*. Epidemiology of COVID-19 infection in young children under five years: a systematic review and meta-analysis. *Vaccine* 2021;39:667–77.

35 Leidman E, Duca LM, Omura JD, *et al*. COVID-19 trends among persons aged 0-24 years - United States, March 1-December 12, 2020. *MMWR Morb Mortal Wkly Rep* 2021;70:88–94.

36 Devrim İlker, Bayram N. Infection control practices in children during COVID-19 pandemic: differences from adults. *Am J Infect Control* 2020;48:933–9.

37 Bixler D, Miller AD, Mattison CP, *et al*. SARS-CoV-2-associated deaths among persons aged <21 years - United States, February 12-July 31, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1324–9.

38 Shekerdemian LS, Mahmood NR, Wolfe KK, *et al*. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr* 2020;174:868–73.

39 Tsankov BK, Allaire JM, Irvine MA, *et al*. Severe COVID-19 infection and pediatric comorbidities: a systematic review and meta-analysis. *Int J Infect Dis* 2021;103:246–56.

40 Wang Y, Zhu F, Wang C, *et al*. Children hospitalized with severe COVID-19 in Wuhan. *Pediatr Infect Dis J* 2020;39:e91–4.

41 Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020;109:1088–95.

42 Siebach MK, Piedimonte G, Ley SH. COVID-19 in childhood: transmission, clinical presentation, complications and risk factors. *Pediatr Pulmonol* 2021;56:1342–56.

43 Oliveira EA, Colosimo EA, Simões E Silva AC, *et al*. Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database. *Lancet Child Adolesc Health* 2021;5:559–68.

44 COVID-19 National Incident Room Surveillance Team. COVID-19, Australia: epidemiology report 16 (reporting week to 23:59 AEST 17 may 2020). *Commun Dis Intell* 2018.

45 National Institute of Public Health, Indicators. Interactive dashboard on COVID 19. Available: https://www.insp.mx/informacion-institucional-covid-19.html [Accessed 13 Dec 2021].

46 Bellino S, Punzo O, Rota MC, COVID-19 Working Group. COVID-19 disease severity risk factors for pediatric.

47 Worldometer. COVID-19 coronavirus pandemic [online], 2020. Available: https://www.worldometers.info/coronavirus/ [Accessed 6 Dec 2020].

48 Wiersinga WJ, Rhodes A, Cheng AC, *et al*. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020;324:782–93.

49 González-García N, Castilla-Peón MF, Solórzano Santos F, *et al*. Covid-19 incidence and mortality by age strata and comorbidities in Mexico City: a focus in the pediatric population. *Front Public Health* 2021;9:738423.