

**LETTER TO THE EDITOR****Obesity and immunodeficiencies are the main pre-existing conditions associated with mild to moderate COVID-19 in children**

To the Editor,

As the COVID-19 pandemic spreads, it has become a public health need to identify the most common risk factors and pre-existing conditions associated with all the stages of COVID-19. Currently, there is insufficient data on the paediatric population to clearly identify which conditions are associated with SARS-CoV-2 infection and its clinical progression.<sup>1</sup>

The Mexican Open Registry<sup>2</sup> of patients with COVID-19 suspicion collects the nationwide data of SARS-CoV-2 RT-PCR assays taken to every patient with respiratory distress or severe respiratory infections and a tenth of patients with mild outpatient respiratory infections. To be considered under clinical suspicion, a patient must have had symptoms associated with COVID-19 at least a week before presentation to a healthcare centre. To date, this dataset records the individual anonymized data of 21 161 patients younger than 18 years old regarding sex, pre-existing conditions, whether the patient is

infected with SARS-CoV-2, its clinical progression to COVID-19 pneumonia, the need of regular or Intensive Care Unit Admission or death. Multiple robust Poisson regressions were applied to obtain adjusted prevalence ratios (aPRs) using age and sex for each outcome. For inpatient diagnosis, both MIS-C and COVID-19 pneumonia are included in 'SARS-CoV-2 admission'. Post estimation marginal analysis was used to obtain the adjusted prevalence ratio of each disease with each outcome. Because the dataset does not include enough information to standardize the stage of the disease, a 'mild' case is defined as the SARS-CoV-2-positive or COVID-19 pneumonia patient who did not require hospitalization, a 'moderate' case stood for those who required hospitalization but did not require ICU admission and 'severe' as those who did require ICU admission.

The three most common pre-existing conditions in this population were immunodeficiencies (3.8%), asthma (3.8%) and obesity (3.1%). The main finding of this study was that immunodeficiencies (aPR: 0.773, 95% CI 0.66-0.88) were associated with 23% less SARS-CoV-2

**TABLE 1** aPR by age, sex and altitude of residence to consider the cluster effect of data on certain locations

Pre-existing condition	n Prevalence	SARS-CoV-2 infection aPr/95% CI	COVID-19 pneumonia aPr/95% CI	Admission aPr/95% CI	ICU admission aPr/95% CI	Fatalities aPr/95% CI
Immunodeficiencies	808 3.80%	<b>0.773</b> <b>0.664 to 0.882</b>	<b>3.919</b> <b>1.14 to 6.69</b>	<b>8.774</b> <b>6.01 to 11.49</b>	0.913 -0.3 to 2.13	14.436 -0.99 to 29.86
Asthma	806 3.80%	0.904 0.793 to 1.015	1.048 -0.16 to 2.11	0.642 0.02 to 1.27	1.998 -1.7 to 5.7	— —
Obesity	655 3.10%	<b>1.390</b> <b>1.25 to 1.53</b>	<b>4.504</b> <b>2.17 to 6.84</b>	<b>2.467</b> <b>1.46 to 3.46</b>	0.802 -0.37 to 1.98	2.644 -0.7 to 5.9
CV diseases	357 1.70%	0.892 0.707 to 1.08	3.969 -1.48 to 9.42	4.131 0.72 to 7.54	— —	0.000 -0.000011 to 0.0000226
CKD	167 0.80%	0.800 0.571 to 1.03	4.528 0.12 to 8.93	<b>5.860</b> <b>2.4 to 9.3</b>	3.842 -0.16 to 7.84	6.424 -7.1 to 19.9
HTA	152 0.70%	1.108 0.827 to 1.389	3.948 -0.47 to 8.4	<b>7.746</b> <b>4.12 to 11.36</b>	— —	0.000 -0.0000106 to 0.0000223
DBM	132 0.60%	1.209 0.894 to 1.524	5.265 -0.49 to 11.02	3.954 0.25 to 7.65	0.000 -1.13e-06 to 6.18e-06	0.000 -0.0000101 to 0.0000204

Note: aPR presented along 95% confidence intervals. Bold: Statistically significant results,  $P < .05$ .

Abbreviations: aPR, adjusted prevalence ratio; CKD, chronic kidney disease; CV, cardiovascular; DBM, diabetes; HTA, hypertension.

infections but obesity increased the probability to 39% (aPR: 1.390, 95%CI 1.25-1.53) (Table 1). Immunodeficiencies were subsequently associated with 4-fold (aPR: 3.9, 95%CI: 1.14-6.69) rates of COVID-19 pneumonia and an 8-fold probability of admission with SARS-CoV-2/MIS-C (aPR: 8.774, 95%CI: 6.01-11.49). Additionally, children and adolescents with hypertension had a 7-fold probability of admission once SARS-CoV-2 positive (aPR: 7.746; 95%CI: 4.12-11.36), and patients with chronic kidney disease displayed a 5-fold probability of admission (aPR: 5.8; 95% CI 2.4-9.3.). Other less prevalent diseases such as cardiovascular diseases (1.7%), asthma, and type 1 diabetes (0.6%) were not associated with COVID-19 progression.

Obesity is a problem that affects millions of children worldwide generating a considerable amount of morbidity in nearly 14% to 20% of children in the United States. In our study, it presented consistently as one of the two main risk factors associated with higher cases of SARS-CoV-2 infection, development of COVID-19 pneumonia, and hospitalization. The chronic pro-inflammatory status seen in kids with obesity may play in synergy with the acute state of systemic inflammation, as some consider these children at risk of severe COVID-19 outcomes. However, recent studies have found that, although the 'cytokine storm' seen in adult patients is not present, children with obesity hospitalized with COVID-19 display a dysregulation on their immune response, with increased titers of Interleukin-10 and low counts of neutrophil levels.<sup>3</sup> Moreover, researchers have found that for those who are not hospitalized, current lockdowns worsen childhood obesity.<sup>4</sup>

Immunodeficiencies stood consistently as the other main condition associated with all stages of COVID-19 in this paediatric population. This spectrum includes the four most commonly diagnosed primary immunodeficiency diseases (PID), transient hypogammaglobulinemia, IgG subclass deficiency, impaired polysaccharide responsiveness, and IgA deficiency; illnesses characterized by recurrent bacterial respiratory infections. Paediatricians have raised the concern that children who are immunocompromised may be more susceptible to COVID-19, despite reports showing that even children with underlying conditions usually display only mild symptoms of the disease. This could be due to the relatively low frequency of presentation of such diseases, as primary immunodeficiencies are reported to occur in 1 in 2000 children,<sup>5</sup> or the atypical presentation in patients under chemotherapy or immune suppressant therapy.

In conclusion, obesity and immunodeficiencies are the main associated pre-existing conditions seen in children and adolescents in mild and moderate forms of COVID-19 disease. Focus on the prevention

of infection and early awareness of possible inpatient complications of this vulnerable population might reduce the rate of infection and thus avoid severe COVID-19 outcomes.

#### CONFLICT OF INTEREST

The author declares no conflicts of interest.

#### DATA AVAILABILITY STATEMENT

Processed data files used in the present study are available at request. The author follows the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement for data collection, analysis and reporting.

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