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Journal Pre-proof



The curious case of COVID-19 in children

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PII: S0022-3476(20)30566-7

DOI: <https://doi.org/10.1016/j.jpeds.2020.04.062>

Reference: YMPD 11462

To appear in: *The Journal of Pediatrics*

Received Date: 13 April 2020

Revised Date: 24 April 2020

Accepted Date: 24 April 2020

Please cite this article as: Gupta S, Malhotra N, Gupta N, Agrawal S, Ish P, The curious case of COVID-19 in children, *The Journal of Pediatrics* (2020), doi: <https://doi.org/10.1016/j.jpeds.2020.04.062>.

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TITLE- The curious case of COVID-19 in children

TYPE- LETTER TO EDITOR

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The authors declare no conflicts of interest.

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To the Editor:

The pediatric population has classically been viewed to be highly vulnerable to infectious diseases. Consequently, this cohort deserves diligent watchfulness during an infectious outbreak. The Centers for Disease Control and Prevention (CDC, USA) considers children, especially those under 5 years of age, as a high-risk category for influenza-related disease.^[1]

During the last influenza-A pandemic (H1N1-2009), 13% of the infected individuals were younger than 5 years.^[2]

The age distribution of patients in the COVID-19 pandemic is incongruent with that of the H1N1 pandemic of 2009. At our tertiary care center, 215 individuals been evaluated for COVID-19 through April 10, 2020. Of those tested, all 22 individuals under the age of 18 years were negative for SARS-CoV-2. In a systematic review of 45 datasets, Ludvigsson found that <5% of COVID-19 cases occurred in children under 18 years of age.^[3] Two other novel coronavirus diseases, SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome), also show similarly low rates of infection in the pediatric population.^[4] Further, retrospective studies to date suggest that children infected with SARS-CoV-2 generally have mild or no symptoms. In a study of 2143 COVID-19 cases in children, disease manifestations were found to be highest in age under 1 year, with a falling trend in severity with increasing age up to 18 years.^[5]

A number of hypotheses have been proposed for the relative sparing of children in the COVID-19 pandemic: a more likely stimulus-naïve immune system, immaturity of ACE2 receptors, and underdeveloped humoral and cellular immune responses resulting in milder inflammation.^[5,6] It also is hypothesized that recurrent viral infections that typify childhood

may induce higher or more frequent innate and adaptive responses, such as to lead to higher total immunoglobulin levels that might be protective against a novel virus.^[5]

We present the epidemiological differences among 3 coronavirus diseases (SARS, MERS, and COVID-19) and the influenza pandemic (H1N1-2009) disease in the Table. Although we present data about the H1N1 pandemic that were amassed during the decade that has passed since, the landscape of SARS-CoV-2 infection and COVID-19, especially in children, is evolving, and a more mature analysis may unearth a different trend. Although the current figures are encouraging, the true burden of COVID-19 pandemic on children is yet unknown.

Table 1. – Epidemiological differences in three coronavirus diseases (SARS, MERS and COVID-19) and H1N1-influenza pandemic (2009).

| | SARS [4,7,8] | MERS ^[4] | H1N1 pandemic 2009 [2, 9-14] | COVID-19 ^[3,6,15-17] |
|--|-----------------|---------------------|------------------------------------|--|
| Percentage of positive cases that were children (0-18 years age) | <5% | 0.1-4% | 73% (0-24 years age) | PRC: 2.4% ITA: 1.2% USA: 5% |
| Percentage of positive cases that were children (0-9 years age) | SDN | SDN | 13% (0-4 years age) | PRC: 1% ITA: 0.5% USA: SDN |
| Percentage of patients with severe or critical illness children | 5% | SDN | SDN | PRC: 2.7% ITA: SDN USA: 2% |
| Percentage of children requiring mechanical ventilation | <1% | <1% | SDN | PRC: <1% ITA: <1% USA: <1% |
| Percentage children among hospitalized individuals | SDN | SDN | 40% | PRC: 10% ITA: <0.1% USA: <1% |
| Mortality rate in children | <1% | 6% | 0.002-0.013% | PRC: <0.1% ITA: <0.1% USA: <0.1% |

| | | | | |
|---|-----|-----|-----------|-------------------------------------|
| Mortality rate in ICU admissions children | SDN | SDN | 6.3-11.6% | PRC:<0.1% ITA: <1% USA: <0.1% |
|---|-----|-----|-----------|-------------------------------------|

SDN – Sufficient data is not available. PRC: China, ITA: Italy, USA: United States of America. SARS: Severe Acute Respiratory Syndrome, MERS: Middle East Respiratory Syndrome