

## INNOCENT COVID-19 CARRIERS, A SYSTEMATIC REVIEW

Seemi Tanvir, Ayesha Fazal, Mariam Babar, Shabbir Ahmed

Margalla Institute of Health Sciences, Rawalpindi Pakistan

### ABSTRACT

**Objective:** To assess symptomatology and spread of corona virus disease 2019 (COVID-19) in children.

**Study Design:** Literature review.

**Place and Duration of Study:** Online literature search was carried out from Jan 2020 to May 2020 using online search engines available including Google Scholar, Science Direct and Pub Med with the help of key words.

**Methodology:** This resulted in retrieval of 201 articles after removing duplicated ones. Following, which these articles were scrolled down, articles with incomplete information and covering comorbidities were not included. Case reports, case series, letters or editorials were also excluded. Articles related to clinical features and spread of corona virus disease 2019 (COVID-19) in children were included. Six articles were finally selected for the review.

**Result:** This review observed that although children are less affected by COVID-19 but they can play an important role in its spread especially to elderly population having comorbidities.

**Conclusion:** Children might be asymptomatic carriers of COVID-19.

**Keywords:** Children, Corona virus, COVID-19, SARS-CoV-2, Spread, Transmission.

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### INTRODUCTION

Second wave of COVID-19 in China this time in Beijing, says a press release on June 13, 2020 by World Health Organization, reporting 41 symptomatic and 46 asymptomatic patients to be COVID-19 positive<sup>1</sup>. It all started back in December 2019, when Wuhan (China) authorities informed the WHO about the pneumonia like illness sweeping across the country, which later became one of the lethal pandemics mankind has ever come across<sup>2</sup>.

By March 20, WHO classified the outbreak as pandemic. COVID-19 has claimed more than 4237,630 lives and infected more than 7.6 million, around 3.5 million people have recovered from the novel virus. As many as 188 countries have been effected. In our country Pakistan, 139230 COVID-19 cases and 2632 deaths have been recorded till June 13, 2020<sup>3</sup>.

COVID-19 is an RNA-enveloped virus, which on electron microscopy demonstrates club shaped spikes on its surface in the form of a

‘corona’ (halo). It has the ability to undergo mutations, making it highly pathogenic with high transmissible power, leading to quick spread from animals to humans. The virus has two variants namely SARS-COV and MERS-COV. Former (severe acute respiratory syndrome) caused an epidemic, in 2002, originating in China, while latter (Middle East respiratory syndrome) was first reported from Saudi Arabia in 2012<sup>4</sup>.

Symptoms of COVID-19 vary from mild to severe, including bronchitis, pneumonia, severe ARDS (acute respiratory distress syndrome), coagulopathy and multi-organ failure, with an incubation period of 5 to 6 days<sup>5</sup>.

COVID-19 targets everyone but children seem less likely to be effected by this virus as compared to adults. They exhibit mild symptoms or are often asymptomatic. Due to this reason, children may often be overlooked to carry out tests for this virus. There is not enough information regarding the proportion of asymptomatic children<sup>6-11</sup>. The purpose of the study is to learn about role of children in spread of coronavirus. It will help to allocate the necessary resources to tackle the emergency situation at hand.

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**Correspondence:** Dr Seemi Tanvir, House No. 21, Sector-A, DHA Phase-I, Rawalpindi Pakistan

Email: [dr.seemi.salman@gmail.com](mailto:dr.seemi.salman@gmail.com)

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The objective of this study was to assess symptomatology and spread of coronavirus disease 2019 (COVID-19) in children.

**METHODOLOGY**

A detailed literature review, from January 2020 May 2020, through online data bases like Google Scholar, Science Direct and PubMed was done. Key words like “COVID-19”, “SARS-CoV”, SARS-CoV2”, “children” and other corresponding terms were used for searching. After searching all the search engines and removing records that were duplicated, 201 articles were retrieved. All articles related to COVID-19 in children with study of diagnostic accuracy (STARD) were included. Exclusion criteria included case series, case reports, letters and editorials, and articles with comorbidities. Hence, 6 articles were selected for the review (fig-1).

**RESULTS**

Wie *et al*, assessed 20 pediatric patients infected with COVID-19 (age range of day 1 to 14 years), and then compared the clinical and CT

increased pro-calcitonin levels in 16/20 (80%) of the pediatric patients was seen, which showed an anomaly from adult patients. Moreover, unlike adults, consolidation with halo sign was also found in 10/20 (50%) patients (fig-2)<sup>12</sup>.

Yu *et al*, confirmed the transmission of SARS-COV-2 (Severe acute respiratory syndrome coronavirus 2) through asymptomatic carriers. Ten patients were being assessed who had epidemiological history to the exposure (that is being in contact with the person infected with COVID-19). No fever or cough was noted in these patients. Hence, clinical symptoms, travel history to any of the epidemic areas affected by COVID-19, or detection of virus through proper screening is important for the correct diagnosis of the disease, since asymptomatic patients (especially children) remain carriers for the remaining population<sup>13</sup>.

According to Lee *et al*, case fatality rate of SARS-COV-2 in children range from 7-17%, while people with age >65 years or with comorbidities was found to be 50%. ACE 2 expression gene was found to decline with age. This gene was found

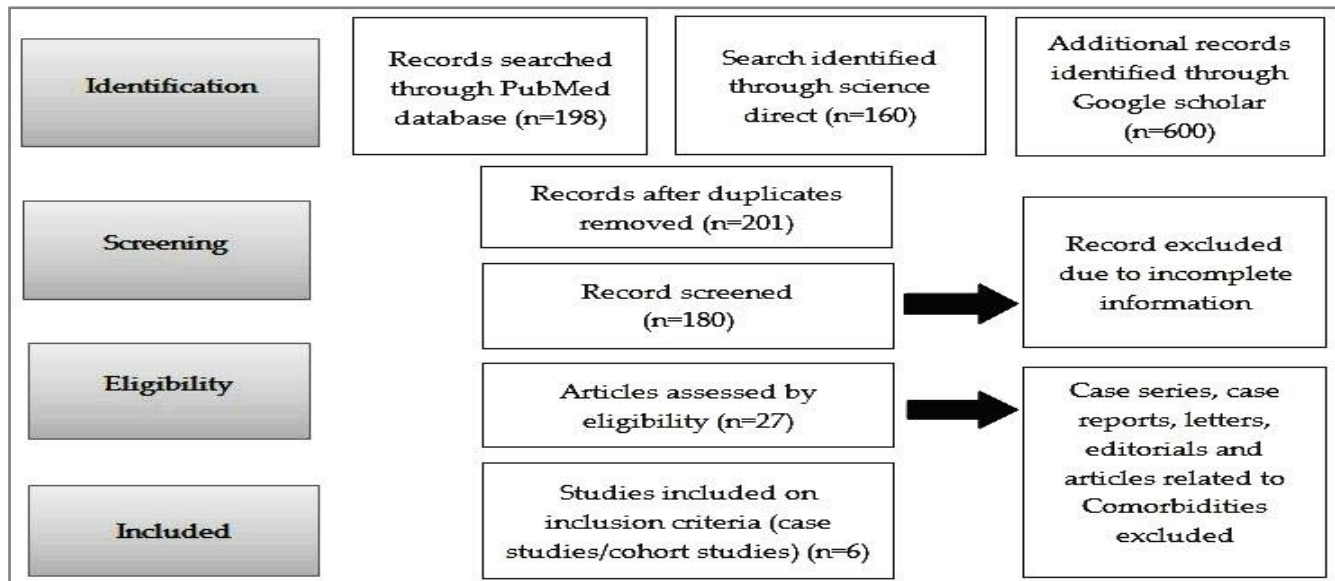


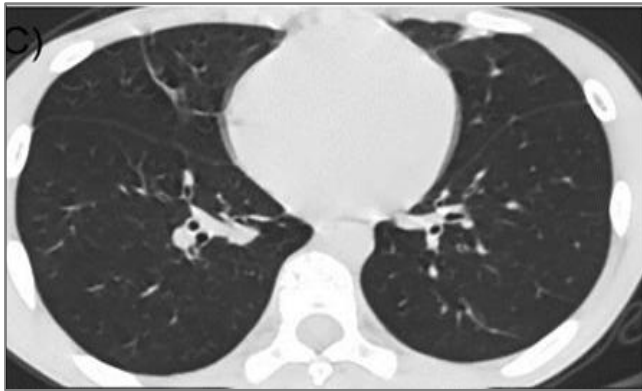
Figure-1: PRISMA 2009 flow diagram showing study characteristics.

findings with adult patients. Out of 20 patients, 13 (65%) had history of close contact with family members those infected with COVID-19. Fever was noted among 12 patients (60%), and 13/20 (65%) had cough. However, abnormally

to be used by SARS-COV-2 and human corona virus NL-63 (HCoV- NL63), which are responsible for COVID-19<sup>14</sup>.

Dong *et al*, followed more than 2000 children being the suspects or confirmed for COVID-19,

and found that 4% of the confirmed cases were asymptomatic. Among those who were symptomatic, 5% of the cases reported of shortness of breath, and 0.6% cases reported of deterioration of their respiratory conditions leading acute res-



**Figure-2: Chest CT of 14 year old male showing consolidation with halo sign in left lung and fibrous cords in both lungs.**

piratory distress syndromes or multi organ dysfunction. Moreover, viral transmission (through

COVID-19 infected children. It was noted that 32/36 (89%) children reported close contact with other family members, 12/36 (33%) had a travel history to the COVID-19 affected areas, 8/36 (22%) had been exposed to both. Out of 36, 19 (53%) infected children reported of moderate respiratory symptoms. Unlike adults, pro-calcitonin levels were found to be raised in 6/36 (17%) patients. All patients were treated with interferon alpha, antiviral drugs and oxygen inhalation. The success rate of the treatment was 100%<sup>15</sup>.

Zimmermann *et al*, concluded that children may not develop symptoms similar to adults, but may report positive for COVID-19. They compared different forms of novel corona virus (including circulating human corona virus (HCoV), SARS-COV, MERS-COV, and SARS-COV-2. SARS-COV-1 and SARS-COV-2 had zoonotic origin (mainly bats) and reported fever among 91-100% and 44-50% of the total cases respectively. Cough in pediatric patients 43-80%



**Figure-3: World Map showing COVID-19 Peak Cases.**

close contact and less care) and viral shedding (through oro-fecal route) is more common in children than adults<sup>6</sup>.

Haiyan *et al*, in their retrospective study, from January 17, 2020 March 2020, assessed clinical and epidemiological characteristics in 36

and 38% respectively. Lab findings indicated decrease in neutrophil count, with an increased D-dimers in severe cases. On chest radiography, ground glass appearance with consolidations were seen. Case fatality rates in children affected by SARS-COV-1 and SARS-COV-2 were found



to be 0% in both, unlike adults (6-17% and 2.3-3% in SARS-COV-1 and SARS-COV-2 cases respectively)<sup>16</sup>.

## DISCUSSION

“COVID-19 Pandemic” the whole world has been facing for the last five months, has reached peaks in many countries (fig-3). Because of its novelty, COVID-19 is still under study. This infectious disease has many faces various clinical manifestations reflecting its potential to affect multiple organ systems in the humans. Most of the research targets adult population<sup>17-20</sup>. Fact that children comprise 27% of the world’s population and prevalence of such a communicable disease among them is a serious matter that cannot be ignored<sup>21</sup>.

In our systematic review, we studied research publications regarding COVID-19 transmission and manifestations in children. We found out that children are equally exposed as well as prone to SARS-COV-2 infections as adults. Clinical picture of COVID-19 in children resemble that of adults. Among COVID-19 diagnostic investigations, CT Chest has been found to be more reliable, showing lung consolidation in children, apart from ground glass opacities that are commonly seen in adults<sup>22</sup>. But the difference lies in disease severity and prognosis<sup>23</sup>.

Children are still one of the least effected groups by this virus, it may be due to their minimum contact to the outside world, with less international travel or outdoor activities<sup>24</sup>. They are more effected by upper respiratory tract infections as compared to lower respiratory tract infections. Children have ACE-2 receptors which are believed to protect them from potential lung injury<sup>25</sup>.

Similar findings were observed by Jonas F. Ludvigsson who reviewed research material published till March 20. After analyzing 45 papers and editorials, he concluded that children have same presentations and laboratory findings of COVID-19 but magnitude of problem is lesser in adults<sup>8</sup>.

Streng *et al*, included 12 case series up till March 31, 2020 in their systematic review on COVID-19 in hospitalized children and adults. They also observed mild upper respiratory system even in hospitalized children coinciding with our observations<sup>26</sup>. Mehta *et al*, pointed out similar incidence rate in children as in adults in their review of 24 studies, March 9, 2020<sup>10</sup>.

However systematic review by Souza *et al*, observed some differences. They analyzed 38 studies from Dec 1 to April 6, 2020 and observed clinical presentations, outcomes and investigations of PCR-confirmed COVID-19 patients under 18 years of age. They concluded fever and respiratory symptoms not be considered as indicative of COVID-19 in children<sup>7</sup>. At national level, most of the research has been done on adults. Research data related to children with COVID-19 is limited. However same clinical picture and transmission pattern has been reported<sup>27,28</sup>.

As coronavirus infection is still an emerging and developing disease, fluctuations are expected in every dimension predominantly in clinical presentations. For diagnosis, RT-PCR is mostly used as screening test. There are multiple issues in this regard like reporting bias may be there, since many cases being asymptomatic would never have been tested. Secondly, unavailability of sufficient kits as per population is a harsh fact faced by different countries<sup>29</sup>. To early screening in terms of development of sign and symptoms might also be one of the reasons of false negative results<sup>30</sup>. Detection in SARS-CoV-2 infected individual with no sign or symptoms has also given positive findings on CTchest<sup>31</sup>. But CT chest is less specific as its ground glass appearance of both lungs along consolidation fig-2, resembling lung diseases like viral pneumonia<sup>32,33</sup>. CT chest also aids non-pulmonary findings in COVID-19 patients<sup>34,35</sup>. Possibility of rare presentations in children cannot be ruled out as it occurs in other conditions<sup>36</sup>.

Children may become silent “spreaders”<sup>24</sup>. This can have a negative impact on the economy, increasing the burden of disease. Additionally

appropriate public health measures will become impossible to put into practice, contact tracing will become difficult. Asymptomatic children have still the ability to transmit the infection to others.

### LIMITATION OF STUDY

Limited number of studies were included. Vertical transmission in children was not assessed.

### CONCLUSION

Children have been mildly affected by COVID-19 but they can be potential carriers. Children overcome this infectious state more amicably resulting in fewer serious cases and casualties. Children might be the culprits rather an easy target of household disease contact.

### CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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