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Editorial

Paedíatric aspects of COVID-19: An update

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1. Introduction

Since December 2019, coronavirus disease 2019 (COVID-19) has become a worldwide health problem threating the life of people. On 11 March 2020, the World Health Organization (WHO) classified the outbreak as a pandemic. As of April 29, 2020, the COVID-19 has been responsible for more than 3052,370 infections and 216,563 deaths worldwide [1]. Adults represent the population with the highest infection rate; however, babies, children, and old aged patients can also be contaminated by the SARS-CoV-2. Intriguing findings worldwide has shown that children are less susceptible to COVID-19. Data from China's analysis has shown that children aged less than 10 years account for only 1% of COVID-19 patients [2]. Otherwise, the Korean Center for Disease Control and Prevention has reported that up to 20th of March, 6.3% of subjects with COVID-19 were children aged less than 19 years old [3]. Findings from Italian research, has reported that up to 18th March, only 1.2% of 22,512 Italian patients were children [4]. By March 16, 2020, 0.8% of confirmed patients in Madrid, the capital of Spain were aged less than 18 years old [5]. Besides, the United States US has reported that up to 16th March 5% of patients with COVID-19 cases were children [6] while this proportion was reduced to 1.7% on the 2 April [7]. Available statistic data support the evidence that children are less infected elsewhere in the world but clinical characteristics details and countries' difference of paediatric COVID-19 aspects are rarely reported. Such ambiguity may present a dangerous situation that lead paradoxically to a less protection and a neglect of children from the part of their parents and countries.

The aim of this manuscript is to focus on COVID-19 paediatric aspects explaining why parents and doctors should be more vigilant when dealing with children during the period of COVID-19.

1.1. Clinical presentation of children with COVID-19

According to a Chinese paediatric case study including 2143 infants the median age is about 7 years old [8]. By contrast, the median age is higher in the US approximately 11 years (range 0–17 years) [7] and lower in Spain respectively 1 year old with a range of 0–15 years [5]. Nearly one third among 2,572 COVID-19 American confirmed children, were aged between 15 and 17 years [7].

Whereas signs and symptoms seemed the same, the percentage of paediatric hospitalization and critical cases differed from country to another [7].

Most frequently, children with COVID-19 may present with mild respiratory symptoms like dry cough associated or not to fever, fatigue or nasal congestion [9,10,11]. In the US, fever, cough and shorten of breath has been reported respectively in 56%, 54% and 13%of paediatric patients [7]. Relatively similar, 41.5% of Chinese children had presented fever and 48.5% had cough [12].

Others signs have been reported like gastrointestinal presentations: abdominal discomfort and pain, vomiting and nausea [5,9].

Children might present with less symptoms or be asymptomatic [9].

Consistent with this, 68% of 78 paediatric American confirmed cases had presented no fever nor cough nor shorten of breath but they weren't classified as asymptomatic due to the incomplete symptoms information [7].

Such mild to moderate clinical presentations may suggest a lower viral circulation in children than in adults. In support with this hypothesis, a Spanish study has shown that only 11.2% of children among 365 with a clinical presentation compatible of COVID-19 had positive SARS-CoV-2 nucleic acid test [5].

Overall, the prognosis is good and recovery occurs almost at 1 to 2 weeks [9].

Whereas most COVID-19 paediatric cases were not severe, data from published studies has shown, additionally severe clinical presentations in children with COVID-19, even rare in different countries [5,7].

The first critically ill infant has been reported in one-year-old boy in Wuhan China [13]. The gastrointestinal presentation was dominating at the first and he had reported intermittent diarrhea, vomiting for 6 days, and fever with shortness of breathe. Paradoxically, his pharyngeal swab SARS-CoV-2 nucleic acid test on the second and the seventh days of hospitalization were negative to be positive on the eighth day. He has pneumonia in the right lung in his chest radiographs. The child was immediately intubated on the intensive care unit. He was successfully weaned off from the ventilator on the 10th day of admission.

According to a larger Chinese study including 2143 children [8], 5.8% of children has reported severe to critical manifestations and has presented at least one of these symptoms: dyspnoea, reduced oxygen saturation, acute respiratory distress syndrome, shock, encephalopathy, heart failure, abnormal coagulation and

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acute renal failure. Severely affected children have remained at the intensive care unit over 20 days [14].

Relatively, fewer paediatric cases had been hospitalized in the US about 5.7% among 2572 COVID-19 American children while only 0.58% has been admitted to the intensive unit care [7]. Children aged less than 1 year had presented the highest percentage of the hospitalization in the US and accounted about 15%.

In the others setting, the percentage of hospitalization of children were higher in Spain [5]. About 60% of confirmed children had been admitted to the hospital and 10% of them had required intensive care and respiratory support [5].

1.2. How clinicians explain the lowest percentage of children infection with COVID-19?

The reason of the lowest percentage of COVID-19 in children despite of the immaturity of their immune system has been explained by numerous arguments [15]. First, the reduced number and the immaturity of ACE2 receptors in children comparing to adults is one of these hypothesis. Indeed, the SARS-CoV-2 use the ACE2 receptor and the cellular protease TMPRSS2 [16]. Second, the innate immune response, the first line of defense, seems to be more active in children. The thymus is present and the CD8 T cells are more efficient participating in the virus lysis [17]. Finally, children have little comorbidity and are also less exposed to smoking comparing to adults [18].

1.3. Why parents and communities should be more careful?

Well known, Infants and young children are typically at high risk for severe respiratory tract infection because of the immaturity of their immune system but also of their respiratory tract. For longer, the viral respiratory infection were the most common condition threatening the life of many children and causes admission in paediatric Intensive Care Unit requiring mechanical ventilation [19]. The respiratory syncytial virus subtype A [RSV-A] was the most frequent [19] before the SARS-CoV-2. Among 117 Spanish children with viral respiratory infection, 91% of them required mechanical ventilation [19].

Currently, almost 6% of Chinese children and 10% of Spanish infants with COVID-19 have developed severe to critical presentation and required intensive cares [8]. Although the mortality is extremely rare, there were two cases of Chinese children death who have been reported: one of child aged 14 years old and other aged 10 months [20] and three children in the US [7].

Besides, although the clinical presentation of COVID-19 in children seemed to be mild to moderate in almost the case, the prevalence of pneumonia with COVID-19 was 53% higher than with H1N1 influenza (11%] [21].

The limited number of paediatric Chinese patients with COVID-19 has been explained by numerous arguments. Probably there is a regulating mechanism between the immune system and the respiratory tract contributing to milder disease [22]. But this hypothesis and the others ones weren't justified by scientific proof [22]. Nevertheless, a systematic review has suggested that COVID-19 is either rare in children or it has not been diagnosed because the predominant asymptomatic forms [20]. Consistent with this, a Chinese observational study including 36 children, has shown that 28% of these children had no symptoms although they had a positive SARS-CoV-2 nucleic test [21]. This study has also suggested that the percentage of the asymptomatic forms in children might attempt the half of the infected children in China. However, such conclusions are based on observational results with very low evidence and should be taken with caution. In fact, contracting to the Chinese study, only 1.3% of paediatric cases in the US were asymptomatic [7]. The asymptomatic form is defined by testing positive for SARS-CoV-2, but without clinical symptoms or abnormal chest imaging findings [6].

More investigations are necessary and serological data may be helpful to confirm or to infirm this hypothesis.

If really this asymptomatic form is predominant in children, this may present a dangerous situation in the community. Because these children may therefore contribute to the human-to-human transmission in the community and accelerate the pandemic [23].

Meanwhile, children aged less than 3 years old accounts for majority of cases about 40% in a multi center Chinese study [24]. This population of children demand more attentions during home caring and hospitalization.

1.4. Why doctors should be more careful when dealing with children with COVID-19?

Whereas the clinical presentations detailed above were the most reported in children, the paediatric clinical spectrum continue to evolve and others manifestation can be appear [25]. Clinicians should be therefore more vigilant and do not forget to screen for SARS-CoV-2 when children come to hospital for ocular or cardiac or others doubtful conditions. COVID-19 can be presented in children just only by ocular abnormalities. In fact, recently, a case of a child aged 2 years and 10 months who was admitted to the hospital for conjunctivitis and eyelid dermatitis without any other symptom, has been reported [26]. The final diagnostic was therefore COVID-19 [26]. More severe potential association in paediatric patients has been suggested this last time. Paediatrics has noted the rising of the presenting cases with multi-system hyperinflammatory state, toxic shock syndrome and atypical Kawasaki disease (KD) during this critical period, seen in both children with positive and negative SARS-CoV-2 nucleic acid test [27]. The association wasn't confirmed due to the lack of serological data. However, there are some arguments that support this observation. The KD is an acute vasculitis in childhood that can occur after viral infection in childhood. Although that the real cause of KD remains until today unclear, several studies has reported that this condition may be attributable to enterovirus, rhinovirus, parainfluenza and others viruses [28]. The SARS-CoV-2 belongs to the coronavirus and its implication in KD can't be rejected. Besides, Venaa G and al has published since the 7 April a case of a baby aged six months who presented a classic KD and in whom the diagnostic of COVID-19 has been confirmed [25]. This author has pointed toward this association and suggested that KD might be one of the complication or manifestation of paediatric COVID-19 [25]. Although there is actually no scientific proof confirming this association (between KD and COVID-19), doctors should take it into consideration. This is because the KD may alter the quality of life of children and is the most common cause leading to paediatric heart disease [29]. Echocardiogram is necessary at the baseline and at the six week. This disease often occurs in children aged less than 5 years old but an early treatment by intravenous immunoglobulin can reduce the mortality and morbidity [29]. The diagnostic of the KD requires the presence of persistent fever at least five days, in combination with four of five features belonging to this following list: conjunctivitis, lymphadenopathy,rash, erythema and hyperaemia of lip and oral mucosa and finally hyperaemia and desquamation in extremities [29]. Doctors should be vigilant and evoke KD in children with fever, rash and severe inflammation in patients with or without confirmed COVID-19 but should also screen for SARS-CoV-2 in patients with KD. Further studies are necessary to infirm or confirm this association. This novel virus may be severe in children and lead to hospitalization.

Interestingly, the American study has shown that children with one or more underlying conditions were more susceptible to mod-

erate and severe COVID-19 clinical aspect requiring hospitalization [7].

77% of hospitalized children had at least one underlying condition against 12% of those with underlying conditions were not hospitalized [7]. Most commonly, these conditions were chronic lung and cardiovascular diseases and immunosuppression. Therefore, doctors should be more vigilant when examining children presenting underlying conditions.

In addition, data of Chinese reports has shown that a more attention should be given to the results of SARS-CoV-2 nucleic acid test in children. Su and al. has reported that five of six discharged children with two successive negative SARS-CoV-2 nucleic acid test at 2–3 weeks after symptoms returned to the hospital because of positive test in their stool [15]. Probably, the virus SARS-CoV-2 spread more time in children than in adults [15].

However, Atkinson and al advised clinicians to use the results of SARS-CoV-2 nucleic acid test with caution [30]. This is because that viral RNA can persist longer after the disappearance of infectious virus. Assessing the SARS-CoV-2 nucleic acid in distance to the acute infectious period, can't distinguish accurately between infectious virus and non-infectious nucleic acid [30].

Besides, another point that doctors should take into consideration that SARS-CoV-2 can persist in faeces long after it disappear from nasopharyngeal secretions.

In the other hand, there are no clear recommendations for the management of children with COVID-19. Recently, Brazilian paediatric experts have proposed a protocol for a better diagnostic and management with children with COVID-19 [31]. Nevertheless, experts do not recommend the use of aggressive treatments like antiviral agents, or empirical antibiotics, for the management of non-severe cases due to lack of evidences [32,33].

2. Conclusion

The most reported paediatric studies from the different countries agree that children are probably less susceptible to COVID-19. Whereas, the most reported clinical presentation are mild to moderate, severe cases can occur in children and death may happen. Paediatric patients might not have fever or cough or shorten of breath. This may present a dangerous situation in the community and accelerate human-to-human transmission. Social distancing and preventive measures: hand hygiene and home isolation remain important for all age. Doctors should take into considerations these particularities of COVID-19 in children for a better management and be more vigilant in particular when dealing with children presenting at least one underlying condition.

Disclosure of interest

The authors declare that they have no competing interest.

Author's contribution

Rim kammoun and Kaouthar Masmoudi participate to the writing and the elaboration of this manuscript

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