Children and COVID-19: Transmission and Clinical Presentation

COVID-19 em Crianças e Adolescentes: Transmissão e Apresentação Clínica

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Abstract

Children and adolescents have mostly milder or asymptomatic disease and are much less affected by severe coronavirus disease (COVID-19) than adults. Severe acute disease and paediatric multisystem inflammatory syndrome remains rare, and morbidity and mortality are extremely uncommon. However, mental health and social impact can be huge. School transmissions are not yet clearly understood but seem to reflect the level of the transmission in the community. As COVID-19 becomes a well-known condition and given the high vaccination rates, it is now important to rethink restrictions imposed on children and young people's education.

Keywords: Adolescent; Child; COVID-19

Resumo

As crianças e adolescentes são menos afetados pela infeção por SARS-CoV-2 do que os adultos e são frequentemente assintomáticos ou têm doença ligeira. A doença aguda grave e a síndrome inflamatória multissistémica pediátrica são raras, sendo a morbilidade e a mortalidade extremamente raras. No entanto, impacto na saúde mental e social podem ser enormes. A transmissão escolar não é ainda claramente compreendida, mas parece refletir o nível de transmissão da comunidade. À medida que a doença se conhece melhor e são alcançadas elevadas taxas de vacinação, é importante repensar as restrições impostas na educação das crianças e dos jovens.

Palavras-chave: Adolescente; COVID-19; Criança

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Introduction

If we had to choose a pandemic, probably we would choose one that affected children less …

Indeed, severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), the novel pathogen responsible for coronavirus disease 2019 (COVID-19), a global pandemic, has led to more than 220 million infections and 4 million deaths worldwide, nonetheless, children under 14 years old only represent 8% of the reported infections and 0.2% of the total deaths.[1] Children are largely asymptomatic or mildly symptomatic compared to adults.[2] As a result, children have lower intensive care unit (ICU) admissions,[3] accounting only for 1.5% of all COVID-19 admissions.[4] Moreover, COVID-19 case fatality rates in children have remained extremely low and restricted mainly to adolescents/children with severe life-limiting conditions, especially neurodisabilities.[5,6]

Despite the milder phenotype, the pandemic has had a detrimental effect on the global child and adolescent wellbeing, health, and education worldwide.[7-10] It is important to understand the quirks of paediatric COVID-19 to improve children´s transmission control, diagnosis, and management. Also, studying the apparent milder phenotype and significant survival advantage of children may shed some light on potentially modifiable risk factors in adults.

Do children have an important role in SARS-CoV-2 transmission?

The degree to which children and adolescents are infected by and transmit SARS-CoV-2 is unclear, and studies are contradictory.

Transmission by children is likely to depend on multiple factors, including symptom's severity, viral load and shedding duration, host factors (such as immunosuppression) and viral variants. Overall, evidence suggests that peak respiratory tract viral load in children infected with SARS-CoV-2 is identical to adults, but the duration of shedding is shorter in children when compared to adults, and even shorter in asymptomatic or milder infections.[11,12]

A systematic review published in September 2020, showed that children and adolescents have a lower susceptibility to SARS-CoV-2 infection, with an odds ratio of 0.56 for being an infected contact, when compared to adults.[13] A Norwegian study showed that with preventive measures implemented in schools, child-to-child (0.9%, 2/234) and child-to-adult (1.7%, 1/58) transmission was minimal.[14] Evidence from school-based studies demonstrates that schools are mostly safe for children (especially for children aged < 10 years); however, older children (10-19 years) might facilitate transmission.[13,15] Indeed, some studies point out adolescents in communities and high-schoolers as having a similar infection risk to adults.[15,16] National data from the UK after school reopening in September 2020, shows that secondary school-aged children are about eight times more likely to introduce the infection to a household than adults.[17]

Schools cannot be viewed/analysed alone and must be considered in the context of the epidemic and other interventions, such as masks, isolation practices and variants. Barcetllini *et al*[18] suggest schools do not amplify SARS-CoV-2 transmission, but rather reflect the level of the transmission in the community.

Moreover, household remains an important–place of SARS-CoV-2 transmission,[19] and children and adolescents were found to have more than the 2-fold greater risk of infection in household and community settings than in schools.[15,20]

Remarkably, in closed camps, the transmission seems to be higher, as reflected in an outbreak in an overnight camp youth in Georgia with an attack rate of 56% (351 of 627 among all attendees).[21]

The emergence of variants raised concerns about transmission among children.[22] SARS-CoV-2 variant B.1.617.2, named as 'Delta' variant,[23] was initially detected in India in December 2020. Since July 2021, after Delta had become the predominant circulating variant in the USA, the rate of new COVID-19 cases, COVID-19-related Emergency Department visits and hospital admissions significantly increased in patients under 17 years.[24] In a Scottish demographic distribution of cases analysis from April to June 2021, patients aged 5-9 years had already shown a greater proportion of Delta variant positivity.[25] In England, a national matched case-control study concluded that the odds ratio of household transmission was 1.64 among Delta variant cases (95% CI 1.26-2.13, $p < 0.001$) compared to Alpha cases. Moreover, the adjusted odds ratio of household transmission among those with an index case aged < 10 years old were 1.46 times (95% CI 1.23-1.75, $p < 0.001$) those aged 30 to 39 years.[26] In this study, more than 70% of patients were not vaccinated.

As adults are vaccinated and as schools reopen, the longer-term effect of schools on community transmission is still to be evaluated.[27] Some modelling studies suggest that school re-opening might have a small effect on community transmission when prevention strategies are in place, however, the risk increases as community rates are higher[28-30] and more transmissible variants propagate, although this is not completely understood. It may be anticipated that as adults are vaccinated, a greater proportion of SARS-CoV-2 cases will be in children.[12]

Most children have milder disease, but there are some exceptions

Most children remain asymptomatic or develop mild symptoms that commonly last only a few days.[31-34] In hospital admitted patients, three main clusters of symptoms have been described: respiratory (fever, cough, shortness of breath, nausea, and vomiting), systemic mucocutaneous-enteric (headache, myalgia, sore throat, vomiting, abdominal pain, diarrhoea, fatigue, rash, lymphadenopathy, and conjunctivitis) and neurologic (seizures and confusion). Respiratory mild symptoms are the most reported, but pediatric ARDS is exceptional and neurological symptoms are also rare.[35] In a Portuguese cohort of COVID-19 hospitalized children, the most frequent symptoms were cough, fever, and respiratory distress.[36]

Paediatric multisystem inflammatory syndrome (PIMS-TS), also known as multisystem inflammatory syndrome in children (MIS-C) is a rare syndrome, that usually appears one month after COVID-19 acute infection and has similar features with Kawasaki disease (KD), and toxic shock syndrome (TSS).[37,38] The definitions differ but have in common fever, multiorgan dysfunction, laboratory evidence of hyperinflammation, and infection by SARS-CoV-2. WHO definition is more detailed than CDC and UK definitions and emphasises the mucocutaneous involvement and hypotension (Table 1).[39-41]

The temporal pattern (one month after SARS-CoV-2 peak) together with positive serology (84%) or previous contact, suggests an immune aetiology probably in a genetically predisposed patient. The incidence varies between 2/100 000 in the USA[42] to 5/10 000 infected children in the UK.[40] Affected children are often healthy, with a median age of 8-9 years,[37,43] frequently from South Asian and Latin American origin.[37,43-45]

All MIS-C patients have fever, and about half have a polymorphic rash, bilateral conjunctivitis, and mucosal involvement, like in KD. Myocarditis is frequent and can be associated with cardiogenic-vasoplegic shock. Coronary artery inflammation is present in 4%-24% of the patients and is more often transient.[46] Multiple organ dysfunction is usual, with more than four organs involvement in 70% of cases.[44] Gastrointestinal symptoms are common (80%),[47] varying from intense abdominal pain, mild ascites and gallbladder and bowel wall thickening.[48,49] Neurological symptoms, such as meningitis-like symptoms or encephalitis, are also more frequently observed in MISC than in classic KD.[50] Patients usually have lymphopenia, thrombocytopenia, and higher ferritin levels.[37,38,50]

Treatment consists of IVIG 2 g/kg associated with methylprednisolone in more advanced disease.[39] The fatality rate of MISC has been estimated at 1%-2%, higher than that reported for KD (< 0.1% in Japan),[42,51] with 64%-80% needing intensive care support.[44]

In a Portuguese multicentre study (unpublished data) covering the period from March 2020 to June 2021, the analysis of hospitalization data from most Portuguese pediatric services revealed 57 admissions due to PIMS-TS. The outcome was good in all cases.

Among other rare clinical features reported in children and adolescents, there are infectious myocarditis, subacute post-infectious inflammatory myocarditis,[52] encephalitis and other syndromes.[53,54]

Whilst significantly less common in adolescents and young children than in adults, the condition commonly termed 'long COVID', 'long hauliers' or 'post-acute COVID syndrome' has yet to have a consensus case definition, making the risk, burden and outcomes difficult to define in any age-group.[55] Data from children in the UK shows that prolonged illness can occur but is infrequent (4.4% at 28 days and 1.8% at 56 days) and lower than for adults (13.3% at 28 days and 4.5% at 56 days). The most common reported pediatric symptoms were headache (62.2%), fatigue (55.0%) and anosmia (39.6%).[56]

COVID-19 and mental health

Schools closure was one of the most impacting measures implemented during the COVID-19 pandemic. It had adverse social, educational, health and economic impacts. The World Bank estimated that globally, school closure in 2020, made learning losses that have an estimated value of $10 trillion.[57] The world probably will lose as much as 16% of the investments that governments make in this cohort of students' basic education.

The potential negative impacts of school closure on mental health are likely to remain for a long time after reopening, especially in vulnerable children and children with disabilities.[58] The NHS recently reported data from the Mental Health and Young People Survey from 2017 to 2021.[59] The rates of mental disorders have increased from 11.6% to 17.4% in six to 16-year-olds, eating problems increased from 6.7% to 13.0% in 11 to 16-year-olds, and problems with sleep affected over a third (38.4%) of 11 to 16-year-olds.

Who are at increased risk?

A recent report on child mortality following SARS-CoV2, during the first year of pandemics in England, concluded that 99.9% of the patients survived.[57] The 25 deaths, equate to a mortality rate of 0.2/100 000 and represent 0.8% of the pediatric mortality by other causes. Patients with multiple comorbidities represented 76% of all COVID-19 associated deaths and those with complex neurodisability and life-limiting conditions were at the highest risk.[60,61] Those who died of SARS-CoV-2 were older than those who died from other causes.[61]

Table 1. Paediatric multisystem inflammatory syndrome (PIMS-TS) or multisystem inflammatory syndrome in children (MIS-C) definitions.

	World health organization (WHO)	Centers for disease control and prevention (CDC)	Royal college of pediatrics and Child health (UK)
Age	< 20 years	< 21 years	Children
Fever	≥ 3 days	Lasting ≥ 24 h	Persistent
Multisystemic involvement	Two of the following: 1. Rash or bilateral nonpurulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet) 2. Hypotension or shock 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echo findings or elevated troponin/NT- pro BNP) 4. Evidence of coagulopathy (by PT, APTT, elevated D-dimers) 5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain)	Both of the following: - clinically severe illness requiring hospitalization - Multisystem (>2) organ involvement: cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurologic	Evidence of single or multiorgan dysfunction: shock, cardiac, respiratory, kidney, gastrointestinal or neurologic disorder
Laboratory evidence of inflammation	One or more of the following: ESR, CRP, Procalcitonin	One or more of the following: CRP, ESR, fibrinogen, ferritin, LDH, IL-6, elevated neutrophils low lymphocytes and albumin	Neutrophilia, elevated CRP and lymphopenia
Exclusion of other diagnoses	No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes	No alternative plausible diagnoses	Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus
SARS-COV-2 infection	One of the following: - Evidence of COVID-19 (RT-PCR, antigen test or serology positive) - Likely contact with patients with COVID-19	One of the following: - Positive for current or recent SARS-CoV-2 infection by RTPCR, serology, or antigen test - COVID-19 exposure within the 4 weeks before the onset of symptoms	One of the following: Positive or negative SARS-CoV-2 PCR testing

Pediatric patients who develop severe disease and were admitted to the ICU had significantly higher markers of inflammation (CRP, pro-brain natriuretic peptide, procalcitonin) compared with patients in the medical unit.[62] Respiratory COVID-19 severity was associated with older age (17.3 years in critically ill patient's versus 3.6 years in noncritical; $p = 0.04$).[63] Obesity was an independent risk factor for critical illness (adjusted risk ratio [ARR] 2.02, 95% CI 1.17 to 3.48), related to a greater risk for critical illness in adolescents ([ARR 3.09, 95% CI 1.48 to 6.47]), but not in children.[61,64] However, no risk factors were associated with PIMS-TS.[65] Patients with neurological involvement developed life-threatening complications in 12%, with 40% having new neurologic deficits at hospital discharge.[54]

What should be done in schools?

All measures should be adapted to the level of community SARS-CoV-2 transmission and be balanced by the need to prevent transmission and the need to enable learning and social interactions.[12]

The 2021/2022 school reference guide for SARS-CoV-2 of the Portuguese General Directorate of Health,[66] recommends that schools must follow hygiene-related measures (such as promotion of 'stay at home when sick', ensuring appropriate cleaning and ventilation) and physical distance, as cohorting of classes and groups, increasing spaces between desks and staggering arrival times, measures also proposed by the ECDC. The guide also suggests the implementation of face masks for children over 10 years and if feasible, between 6 and 9 years, which has been a matter of controversy.

We all agree that closing schools should be avoided and remain the last choice. Also, for the well-being of children, all procedures drawn up by schools and not included in the official national guidance should be eliminated (as shortening breaks between classes, not letting parents in, or not allowing children to enter with a toy). School breaks must be respected and promoted by educators and children should always leave the classroom to play, chat and socialize.

Regarding face masks, it is not clear what the right answer is. Children over 12 seem to be capable of wearing face masks as adults.[67,68] The CDC, ECDC, WHO, Spanish, French and other European countries authorities, with regional differences, still recommend face masks in children 12 (six in Spain) and over, when indoors. The United Kingdom withdrew face masks in all grades, including high schoolers. In Portugal, with 85% vaccinated population, including children over 12, it is possible that soon, masks can be slowly reduced, depending on the epidemiologic situation.

Conclusion

Children and adolescents, including those previously considered to be at higher risk, have mostly milder or asymptomatic disease and are much less affected by severe COVID-19 than adults. Severe acute COVID-19 and MIS-C/ PIMS-TS remain rare, and morbidity and mortality are extremely uncommon. However, mental health and social impact can be huge. School transmission and the impact of variants are not yet clearly understood, but it is expected that as adults are vaccinated a greater proportion of SARS-CoV-2 cases will be children. In the meantime, in this controversial area, children and adolescents at school should not be differentiated by vaccine uptake.

As COVID-19 becomes a well-known condition and given the high vaccination rates, it is now important to decrease restrictions imposed on children and young people's education. Bubbles and tactless procedures, such as limited schools' breaks, should be revised. Parents should be allowed to participate in school activities and enter previously common spaces. Schools' prevention strategies, such as ventilation, masks and hygiene measures remain important, however, the use of masks can probably be adapted to the rate of community COVID-19 spread. In Portugal, the USA and most European countries school masks remain mandatory/highly recommended. In the UK, masks have been removed from schools last May. The future will tell us what the best strategy is.

In SARS-CoV-2 infection, children are not little adults. Pediatric COVID-19 has its singularities and decisions extrapolated from adult data will probably have limited value in this population.

Responsabilidades Éticas

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