29 June 2020

Epidemiology, Spectrum, and Impact of COVID-19 on Children, Adolescents, and Pregnant Women

۲

Introduction and timeline of the pandemic

The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread from a local outbreak to a global pandemic within months. As of 29 June 2020, over 10 million confirmed cases of COVID-19 and 499,000 deaths have been reported in 216 countries, areas or territories across the world (1). Of all confirmed cases, the Americas (50.0%) and Europe (27.0%) represent the largest proportion of reported cases. This is followed by Eastern Mediterranean (10.0%), South-East Asia (8.0%), Africa (3.0%) and Western Pacific (2.0%) (2). Almost 75% of recent cases are reported from ten countries, United States of America (2496628), Brazil (1313667), Russian Federation (641156), India (548318), The United Kingdom (311155), Peru (275989), Chile (271982), Spain (248770), Italy (240310), Iran (Islamic Republic of) (222669). Many countries in all regions are still experiencing an increase in the number of cases (3).

What is known regarding COVID-19 in children and adolescents: experience to-date

Country reports to date show that children and adolescents comprise a very small proportion (1-5%) of the total reported COVID-19 cases (4-7), with an increasing trend across the 0-19 years continuum. This figure may be slightly higher in countries where children and adolescents constitute a higher proportion of the population. For example in Pakistan, 7% of all confirmed cases are children between 10-19 years old (8). Systematic collection and reporting of data on infections among children and pregnant women is urgently needed to better understand how COVID-19 impacts these groups, including from low- and middle-income countries where there are issues with testing capacity as well as a paucity of published reports. This section summarizes available data on the overall picture of COVID-19 in children, adolescents and pregnant women including the epidemiology, clinical course and outcomes, augmented by preliminary findings from an ongoing systematic reviews including the 61 case series (9).

Evidence to date suggests most cases in children result from household exposure. The US CDC Morbidity and Mortality Weekly Report (MMWR) reported among 184 cases in children



Acknowledgements:

This brief is part of a collaborative project between the International Pediatric Association (IPA) and UNICEF supported by a grant from UNICEF to the IPA. **Steering committee:** Jonathan Klein, Zulfiqar Bhutta, Gagan Gupta, Stefan Peterson. We thank Rajiv Bahl, Anshu Banerjee and Wilson Were for their contributions.

Primary Authors:

Omar Irfan¹, Kun Tang^{1,2}, Maya Arii⁴, Zulfiqar A Bhutta^{1,3} **Contributors:**

()

UNICEF: Gagan Gupta, Carlos Colorado, Stefan Peterson, Luwei Pearson, Robin Nandy,

Anne Detjen, Tedbabe

- Toronto, Canada 2. Vanke School of Public Health,
- Tsinghua University, Beijing, China 3. Institute for Global Health & Development, the Aga Khan
- University, South-Central Asia, East Africa & UK 4. UNICEF

Note: The recommendations in this brief are based on the best-available evidence as of June 29, 2020 and may evolve/ change with time.

Correspondence: Prof. Zulfiqar A Bhutta zulfiqar.bhutta@sickkids.ca





()

(�)

with known exposure information, 91% had exposure in the household or community, and 9% were associated with travel (5). Another case series of 171 pediatric cases from China reported 76.6% of the cases had history of contact with a family member with confirmed COVID-19 infection (10).

Data is also emerging regarding the role of children in transmission of COVID-19, with important implications for public health decision making including the safe reopening of schools. A recent report from Switzerland describing contract tracing of 40 children aged <16 years hospitalized with confirmed COVID-19 infection found a child was the suspected index case in only 8% of evaluable households (11). Another report from an Australian province, from March to mid-April 2020, identified a far lower infection rate in schools with 18 individuals (9 pupils and



9 staff) from 15 schools as confirmed COVID-19 cases; only two secondary infections were identified among 735 student contacts (one potentially from a staff member and the other potentially from two classmates) and no cases were identified among 128 staff contacts (12). In another study from France, no secondary cases of COVID-19 occurred among 112 school contacts who were exposed to a symptomatic nine-year-old child coinfected with COVID-19, influenza A, and picornavirus (13). Thus, accumulating evidence suggest that children are not the main drivers of COVID-19 transmission. However, the

reason for this, as well as why children are affected differently from adults from a pathophysiologic perspective are not yet clear. As restrictions measures are gradually eased and schools reopen, additional studies are needed to better understand the impact of COVID-19 infection in children. These risks of transmission are currently regarded as lower than that for adults (14).

Clinical presentation and disease severity

Mothers and Newborns

()

The patterns of clinical presentation of COVID-19 infection during pregnancy have been broadly similar to the general population (15). Available data suggest that pregnant women have the same risk of acquiring COVID-19 infection as non-pregnant adults in general population. Pregnant women may have comorbidities that increase their risk for severe illness like the general population (e.g. diabetes, hypertension, cardiovascular disease, obesity, etc.). A systematic review of 33 studies reporting 385 pregnant women with COVID-19 infection concluded clinical presentation and severity of COVID-19 infection during pregnancy is similar to that in non-pregnant adults with 96.0% mild, 4.0% severe and less than 1.0% critical cases (16). Supporting the former statement with results from an ongoing preliminary analysis of 49 studies with 828 pregnant women (17), it was reported that 92.0% females experienced non-severe infection. More than half were asymptomatic (53.0%). Amongst symptomatic pregnant women fever (57.0%), and dry cough (49.0%) were most common symptoms. Two large case series from China of 116 (18) and 118 (19) pregnant women respectively, reported fever and cough as the most common presenting symptoms. Similar proportions were reported for severe disease (6.9% and 8%) as well as preterm births (21.0% and 21.2%). Frequency of spontaneous abortion does not appear to be increased based on currently available data, however data on first-trimester infections are limited. Existing evidence has not identified an increased risk of complications in babies born to mothers with COVID-19.

۲

()



The vertical transmission (intrauterine, via delivery, breast milk) of COVID-19 infection and neonatal disease are extremely rare. A recent systematic review of 49 studies including 666 neonates and 655 women concluded neonatal COVID-19 infection is uncommon, uncommonly symptomatic, and the rate of infection is no greater when a baby is delivered vaginally, breastfed, or allowed contact with the mother (18). Another systematic review reported out of 155 neonates born to women with laboratory confirmed or clinically diagnosed COVID-19 and who had throat swab nucleic-acid testing, all were negative for COVID-19 except for 3 cases (20). Most placentas studied to date had no evidence of infection, however viral RNA has been detected in a few cases. An experience from US reported a total of 11 placental or membrane swabs sent for testing immediately after delivery, out of which 3 swabs returned with positive results for SARS-CoV-2; none of the newborns tested positive or displayed symptoms (21). Another report from Italy described positive PCR results for SARS-CoV-2 in two mothers, their neonates, as well as the placental tissues; both neonates were asymptomatic (22). A recent review of 11 published neonatal cases of COVID-19 reported six newborns presenting within three days of life whereas the others presented between 5-28 days of life, with fever as the chief complaint (23). All neonates recovered without any complications.

Transmission of COVID-19 through breast milk causing infection has not been reported to date. There were 22 cases that had nucleic-acid testing in

breast milk samples and 6 cases with vaginal mucus samples, all were negative, although in a recent report, SARS-CoV-2 RNA was detected in milk for 4 consecutive days from a mother presenting with mild COVID-19 symptoms and testing positive for COVID-19 immediately after delivery (24). It is currently unknown whether newborns born to mothers with COVID-19 are protected from infection via antibodies passed through breast milk or via the placenta during pregnancy. The health benefits of breastfeeding are well established; breast milk provides protection against many illnesses and is the best source of nutrition for most infants. Reports of neonatal COVID-19 infections are still very limited. WHO and UNICEF recommend that mothers with suspected or confirmed COVID-19 should be encouraged to initiate and continue breastfeeding, while applying appropriate infection prevention and control (IPC) measures (25).

Caring for pregnant women and newborn care WHO and UNICEF underscore the importance of access to woman-centred, skilled care, including midwifery, obstetric and neonatal care, as well as mental health and psychosocial support for pregnant women with suspected, probable, or confirmed COVID-19 (25). Pregnant women with suspected or confirmed mild COVID-19 may not require acute care in hospital, unless there is concern for rapid deterioration or an inability to promptly return to the hospital (25).

- Induction of labour and caesarean section should be undertaken only when medically justified.
- Mothers should not be separated from their infants unless the mother is too sick to care for her baby.
- Mothers with suspected or confirmed COVID-19 should be encouraged to initiate and continue breastfeeding with precautions. The precautions include medical mask use, hand washing with soap and water or alcoholbased rub, and disinfection of surfaces with which the mother has been in contact.

Children & Adolescents

Studies have consistently shown a lower risk of children developing severe symptoms or critical illness from COVID-19 infection compared to adults. In a case series from China that included 728 children with laboratory-confirmed COVID-19 infection, approximately 55% were mild or asymptomatic, 40% were moderate (i.e. clinical or radiographic evidence of pneumonia without hypoxemia), 5% were severe (i.e. dyspnea, central cyanosis, hypoxemia), and <1% were critical (i.e. acute respiratory distress syndrome, respiratory failure, shock) (4). As of June 16th, 2020, 61 published case series have described clinical features in 784 paediatric cases (9), comparing the previous cohorts to the updated analysis as shown in Table 1. The proportion (12.1%-21.0%) of asymptomatic cases in the previously reported cohorts has been consistent with the results of the ongoing preliminary analysis shown in Table 1. To assess infectivity in children, a lab-team based in Germany analyzed viral loads observed during routine testing in both children and adults. Analysis of variance of viral loads in patients found no significant difference between any pair of age categories (26). However, viral load is not the only factor to determine infectivity. Equal viral load does not mean equal probability of transmission. Other limited evidence suggests that although infected children shed SARS-CoV-2 virus, transmission by children is uncommon, perhaps due to viral interference and/or milder symptoms (27).

Occurrence of lymphocytopenia and elevated inflammatory laboratory markers was less common among children as compared to adults (7). A systematic review of 38 studies (29) reported abnormalities on chest computed tomography in 63.0% of the confirmed pediatric cases. The most prevalent abnormalities reported were ground glass opacities, patchy shadows and consolidations (10). An analysis of 61 adult and pediatric patients from China reported similar laboratory markers in the 2 age groups. However, pediatric patients had a lower rate of positive chest CT findings with lesser lobar involvement. Bronchial distribution was more common

Table 1: Summary of clinical symptoms from 4 previous cohorts (4, 5, 10, 28) and the ongoing preliminary analysisof 61 case series.

()

Characteristics	Lu 2020 (N= 171)	Dong 2020 (N=731)	CDC MMWR (N=2572)	Parri 2020 (N=100)	Other smaller Case Series (N=784)
Median age (range) – years	6.7 (1 day–15 years)	7 (2–13 years)	11 (0–17 years)	3.3 (0–17.5 years)	NR (30 h–17 years) Mean age 7.1 years
Symptoms – Number of cases/total (%)					
Asymptomatic No/total no (%)	27/171 (15.7)	94/731 (12.8)	NR	21/100 (21.0)	95/784 (12.1)
Fever	71/171 (41.5)	NR	163/291 (56.0)	54/100 (54.0)	473/784 (60.3)
Cough	83/171 (48.5)	NR	158/291 (54.3)	44/100 (44.0)	276/784 (35.2)
Dyspnea/ Tachypnea	49/171 (28.7)	NR	39/291 (13.4)	11/100 (11.0)	75/784 (9.6)
Fatigue/Lethargic/ decreased feeding	13/171 (7.6)	NR	NR	32/100 (32.0)	36/784 (4.6)
Rhinorrhea	NR	NR	21/291 (7.2)	22/100 (22.0)	76/784 (9.7)
GI Symptoms	15/171 (8.8)	NR	37/291 (12.7)	19/100 (19.0)	178/784 (22.7)
Headache	NR	NR	81/291 (27.8)	4/100 (4.0)	36/784 (4.6)
Sore throat	NR	NR	71/ 291 (24.4)	4/100 (4.0)	76/784 (9.7)
Hypoxia <92%	4/171 (2.3)	112/2143 (5.2) suspected	NR	1/100 (1.0)	Not analyzed

*NR=not reported

()

 (\bullet)

in the pediatric group. CT features did not differ across the two groups, except for bronchial wall thickening, which was more common in children (30).

 (\blacklozenge)

Robust evidence associating underlying comorbidities with severe disease in children is lacking. In case series, hospitalization and intensive care admission were more common among children with underlying conditions and infants <1 year of age, although hospitalization of infants may not reflect severity of illness. Most commonly reported underlying conditions include chronic lung disease (including asthma), cardiovascular disease, immunosuppression (5). In a recent study of 48 children with COVID-19 admitted to pediatric intensive care units in North America, 83% had pre-existing medical conditions, half of whom were children with special healthcare needs (e.g. long-term dependence on technological support associated with developmental delay and/or genetic anomalies), followed by immune suppression or malignancy, and obesity (31). There is scarce data on mortality among children with COVID-19. The preliminary analysis of 784 children reveals a case-fatality ratio of 0.9% (9), which is higher than the previously reported 0.1% from the two large Chinese and American cohorts (4, 5). Most recently, there is an increasing concern for the emerging multi-system inflammatory syndrome reported in children from North America and Europe, now also reported from South-East Asia (see below).

Management of COVID-19 in children

Similar to adults, the mainstay of treatment for children with COVID-19 is quality supportive care and monitoring for clinical deterioration, as well as prevention, detection and management of complications including infection prevention and control (IPC) (25). All areas in health facilities where children with severe COVID-19 may be cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal prongs and cannula, Venturi mask, and mask with reservoir bag), equipment for airway management (including pediatric sizes), and



staffed with trained multidisciplinary teams wherever possible, with appropriate provider-to-patient ratios. WHO and UNICEF recommend children with suspected or confirmed COVID-19 infection to be kept together with their caregivers wherever possible. Below are some key recommendations in the management of COVID-19 in children (25):

- For all suspect cases, it is recommended to collect upper respiratory tract (URT) specimens (nasopharyngeal and oropharyngeal) for testing by reverse transcription polymerase chain reaction (RT-PCR).
- It is recommended to formulate a differential diagnosis for suspect cases considering local areaspecific aetiologies (e.g. malaria, dengue and other arboviruses, etc.) combined with the clinical presentation, and investigate as appropriate.

For mild/moderate COVID-19 infection in children:

- A case-by-case basis assessment should be done to triage patients to outpatient or inpatient care. The assessment should consider the child's clinical presentation, requirement for supportive care including oxygen support, any risk factors for severe disease, and conditions at home, including capacity for the child to be well-cared for at home, as well as presence of vulnerable individuals at home.
- Caregivers of children with mild to moderate disease should be counseled to monitor for signs and symptoms of clinical deterioration requiring

urgent re-evaluation. These include difficulty breathing/fast or shallow breathing (for infants: grunting, inability to breastfeed), blue lips or face, chest pain or pressure, new confusion, inability to awaken/not interacting when awake, inability to drink or keep down any liquids.

 (\blacklozenge)

 Antibiotics may be administered when there is clinical suspicion of a bacterial infection or in children < 5 years with pneumonia.

For severe COVID-19 in children:

- Any child with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive emergency airway management and oxygen therapy. Those with an oxygen saturation SpO2 < 90% should receive immediate administration of supplemental oxygen therapy.
- Patients should closely be monitored for signs of clinical deterioration, such as rapidly progressive respiratory failure and shock, and should immediately receive appropriate supportive care interventions.
- Use cautious fluid management in patients with COVID-19 without tissue hypo-perfusion and fluid responsiveness. Continuously monitor for signs of volume overload and adjust fluid administration accordingly.
- In patients with progressive acute hypoxemic respiratory failure, when respiratory distress is failing to respond to standard oxygen therapy, adequate preparation should be made to provide advanced oxygen/ventilator support.

For critical disease in COVID-19: septic shock or acute respiratory distress syndrome (ARDS):

 Crystalloid fluid (10-20 mL/kg) as a bolus in the first 30–60 minutes is recommended for resuscitation of septic shock in children. Administer vasopressors if signs of shock persist after two fluid boluses. Epinephrine is considered the first-line treatment when pressor support is indicated (32).

- In patients who require ventilator support or with ARDS it is recommended that endotracheal intubation be performed by a trained and experienced provider using airborne and aerosol precautions.
- Mechanical ventilation should use lower tidal volumes (4–8 mL/kg predicted body weight [PBW]) and lower inspiratory pressures (plateau pressure < 30 cmH2O).

Other treatments in management of COVID-19:

- Dexamethasone, a common steroid, has recently been shown to have a beneficial effect on those patients severely ill with COVID-19. According to the early findings shared with WHO, for adult patients on oxygen alone the treatment was shown to reduce mortality by about one fifth while those requiring a ventilator, mortality was reduced by about one third. However, dexamethasone was shown to not have a beneficial effect for those with milder disease who did not need respiratory support (33, 34). Dexamethasone use in seriously ill children with COVID-19 needs further evidence.
- Preliminary analysis of 531 pediatric cases shows antivirals (37.7%), interferon-a (36.5%) and antibiotics (20.1%) as the most commonly used therapeutic trial modalities in addition to supportive care in hospitalized patients across all disease severity classifications (9). There is currently insufficient evidence to recommend any



7/6/20 2:11 PM

۲

specific therapies in adults or children. WHO recommends investigational therapeutics including antivirals, immunomodulators and other adjunctive therapies not be administered for COVID-19 outside the context of clinical trials.

Multi-system inflammatory syndrome (MIS-C) in children and adolescents in the context of COVID-19

Short history

On May 6th, 2020, Riphagen et al. in the UK reported 8 children presenting with a multi-system inflammatory phenotype, which overlaps the features of atypical Kawasaki disease (KD) and toxic shock syndrome (TSS) (35). According to the European CDC, 230 suspected cases of MIS-C associated with COVID-19 were reported till May 15th (36). In the US, after the first reports of 15 MIS-C cases associated with COVID-19 in New York, the New York State Department of Health identified 102 patients with similar presentations as of May 12th, many of whom have either RT-PCR or serologic evidence of recent or current infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (37). In middle and low income countries, there have been two published case reports of MIS-C from India (38, 39), as well as unpublished information on cases from Pakistan (Karachi and Lahore), Brazil, Ecuador and Mexico. While the true incidence of MIS-C is unknown, reports to date suggest it appears to be rare.

These cases generally present with a hyper-inflammatory state and share a number of clinical features with other pediatric inflammatory conditions, such as Kawasaki disease (KD), Toxic shock syndrome (TSS), sepsis and macrophage activation syndrome. However, the difference in clinical (age group, ethnicity) and lab findings of MIS-C and other multisystem inflammatory diseases, such as KD, may suggest a different mechanism. The pathophysiology of MIS-C is not yet well understood and is a priority area of research. Whittaker et al. studied the clinical and laboratory characteristics of 58 children

meeting published UK, US and WHO definition for pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection (PIMS-TS) and found a wide spectrum of presenting signs and symptoms including fever, gastrointestinal symptoms and rash, as well as disease severity, including myocardial injury, shock and development of coronary artery aneurysms. When comparing with children with KD, KD shock syndrome and TSS, the PIMS-TS case series showed differences in some features, including older age and greater elevation of inflammatory markers (40). Pulmonary involvement has not been a prominent feature in most cases to date; when respiratory symptoms (tachypnea, labored breathing) are present, they have mostly been due to severe shock.

Generally, the severity of MIS-C associated with COVID-19 may be classified based on clinical signs, vital signs (tachypnea, hyperthermia or hypothermia), oxygenation impairment; any hypotension, altered mental status, bradycardia or tachycardia, prolonged capillary refill or weak pulse, mottled or cool skin or petechial or purpuric rash; urine output; and lab results (e.g. high lactate) (37, 41-43).Patients diagnosed with MIS-C associated COVID-19 often require intensive care and aggressive treatment, but most patients have had favorable outcomes and very low mortality rate. However, the long-term outcomes of MIS-C, such as the sequelae of coronary artery aneurysm formation, remain unknown.

WHO Case definition

There is no internationally agreed case definition yet given the fact that there are still limited data. WHO has developed a preliminary case definition (42) and a case report form for "multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19." The WHO definition encompasses children of 0–19 years of age presenting with persistent fever with clinical features of any two or more systems (muco-cutaneous, circulatory, cardiac, hematological, gastrointestinal), elevated markers of inflammation, and no other obvious microbial cause of inflammation, and evidence of COVID-19 (RT-PCR, antigen test or serology

۲

positive), or likely contact with patients with COVID-19. Even if all criteria in the case definition are not met, all suspected cases should receive appropriate care and be reported, using the standardized WHO Case Report Form (44).

 (\blacklozenge)

Guidance on management

Currently, there are no established protocols or guidelines regarding the specific management of this condition. A suggestive investigation panel for such cases should include inflammatory markers, a complete blood count with differential, coagulation studies including D-dimer, Ferritin, cytokine panel, renal and liver function tests, and cardiac markers (such as troponin, BNP/NT-proBNP) where indicated along with serial echocardiography (35, 36, 39). If MIS-C is suspected or diagnosed, early multidisciplinary team care should be initiated, including pediatric infectious disease, immunology/rheumatology, and pediatric intensive care unit (PICU) team to guide treatment therapies. The majority of reported cases of MIS-C have been treated using the standard protocol for Kawasaki disease including being administered intravenous immunoglobulin (IVIG), both with and without aspirin. Some other used therapeutic agents include Steroids, Immunomodulatory agents including Infliximab (Anti TNF), Tocilizumab (IL-6 antagonist), and Anakinra (IL-1R antagonist). The choice of these agents has been based on preference of treating physicians and the availability (35, 36, 38, 40).

It is important for physicians and researchers to contribute to a better understanding of the epidemiology and pathophysiology of this disease, including through reporting cases using the WHO case report form – the results of which will help guide clinical management and public health response, with potentially significant implications for broader COVID-19 management and future COVID-19 vaccination strategies in adults and children.

Global COVID-19 Clinical Data Platform

WHO has an established platform for standardized, anonymized clinical data. Contributors can enter data into the web-based WHO COVID-19 Clinical Data Platform, which captures all COVID-19 variables listed in the case report form (CRF). Using the WHO platform facilitates aggregation, tabulation, and analysis across different settings globally and provides a secure, access-limited, password-protected, electronic database hosted in a secure server at WHO. WHO will maintain appropriate technical and organizational security measures to protect confidentiality and prevent the unauthorized disclosure of the anonymized COVID-19 data. To become a contributor: please email COVID_ClinPlatform@who.int and request log-in credentials.



Summary of indirect effects of COVID-19 on children and adolescents

The COVID-19 pandemic and its control measures have had significant indirect impacts on children worldwide (45):

- About 86 million children could fall into extreme poverty as a result of the pandemic this year, adding to the estimated 386 million children already in extreme poverty in 2019 (46).
- 188 countries have imposed countrywide school closures, affecting more than 1.5 billion children and youth (47). The national distance learning platforms introduced in more than two-thirds of countries have reached less than half of the students in low-income countries.

 Moreover, the 368.5 million children across 143 countries who normally rely on school meals for a source of daily nutrition must now have alternative sources (48). However, the emerging modelling studies of COVID-19 extrapolate that school transmission is minimal, as children are not the main driver of transmission (49).

 (\blacklozenge)

 The current relationship between economies and mortality could result in hundreds of thousands of additional child deaths in 2020, with economic hardships experienced by families as a result of the global economic downturn.



- A recent analysis of 118 low-middle income countries modelled three hypothetical scenarios in which the coverage of essential maternal and child health interventions is reduced by 9.8–51.9% and the prevalence of wasting is increased by 10–50%, reflecting real-world situations. Analysis showed additional deaths representing an increase of 9.8–44.7% in under-5 child deaths per month, and an 8.3–38.6% increase in maternal deaths per month. The analysis shows that with healthcare disruption and decrease in access to food, the increase in child and maternal deaths will be substantial (50).
- Data collected in April 2020 by the WHO, UNICEF, Gavi and the Sabin Vaccine Institute shows substantial hindrance in at least 68 countries in the provision of routine immunization services, likely affecting approximately 80 million children under

the age of one living in these countries (51) and increasing the risk of vaccine preventable diseases. Longer the disruption in immunization services, greater will be the risk of outbreak. UNICEF's earlier estimates indicate that given the stoppage of campaigns, some 117 million children worldwide are at risk of missing measles immunizations (52). Countries have shown a variable impact on routine services during this pandemic, with disruptions in some countries, while in others services have continued to be delivered. Disruptions are largely due to capacity gaps and the diversion of attention and resources to the immediate COVID response. On the other hand, even when services are delivered, people have either been unable to access services (due to transport disruptions and lockdowns) or unwilling to access them (due to fear of being exposed to Covid-19 infected individuals. In addition, health workers themselves are concerned about their own health particularly in the context of PPE shortages.

 Lockdowns also heighten the risk of children witnessing or suffering violence and abuse. There is increased risk to child safety and wellbeing including in conflict settings, as well as for those living in unsanitary and crowded conditions such as refugee camps and informal settlements.

Conclusions and call for action

Children are at a lower risk of severe COVID-19 outcomes compared to adults; however, they run the risk of being its biggest victims due to collateral effects of the pandemic and its control measures. It is crucial that decisions about prevention and control measures be continuously informed by an assessment of its associated risks and benefits, in order to limit the spread of COVID-19 infection, and to prevent and minimize collateral impacts including secondary morbidity and mortality. International Pediatric Association (53) has provided recommendations for child health and healthcare during this crisis, providing guidance for paediatricians and paediatric

۲

societies in managing children's health needs with a focus on equity of access during current times of school and daycare closures, and physical distancing. International Paediatric Association and UNICEF call on paediatricians and physicians caring for children and adolescents in the context of COVID-19 to take action as below:

 $(\blacklozenge$

- Healthcare providers should promote no separation of mothers from their infants unless the mother is too sick and encourage mothers to initiate and continue breastfeeding irrespective of the COVID-19 status. Decisions on the need for C-section should be determined by the medical condition of the mother, and not her COVID status (25).
- Physicians should encourage families to enhance respiratory and hand hygiene, physical distancing, and seeking early medical advice for COVID-19 symptoms, and Infection Prevention Control measures in line with WHO recommendations should strictly be followed in all clinical settings.
- Healthcare providers are encouraged to collect data on COVID-19 infection among children and pregnant women to better inform public health and clinical response, including on MIS-C via the WHO clinical data platform, which allows for analysis of aggregated data to address gaps in knowledge.



- Physicians engaged in school health are encouraged to work with local public health and education authorities in the planning of school reopening based on local transmission dynamics and other factors, ensuring appropriate hand and respiratory hygiene practices and adapted physical distancing in schools, as prerequisites for safe reopening of schools. WHO and interagency guidance on reopening of schools and interim guidance from the Interagency Standing Committee for COVID-19 prevention and control in schools are available to help plan and prepare for reopening schools and safe school operations (54-56).
- Healthcare providers should work with public health authorities in finding ways to maintain nutrition for children who rely on school lunches and provide online mental health services for stress management for families whose routines might be disrupted.
- It is crucial to reach children in vulnerable settings with COVID-19 prevention and essential health services including in low-income and middleincome countries, as well as in fragile settings. It is important to emphasize risk-informed decision making on public health measures, according to the local context, with special emphasis on community engagement.
- Provide practical support to parents and caregivers to address the importance of responsive and nurturing care in promoting the mental health and wellbeing of children.
- Pediatric societies should advocate and work with their public health authorities to mitigate delays in access and reduction in demand for routine healthcare services and immunizations due to lockdowns and fear of infection in health facilities. They also should prioritize continuation of routine vaccination, including catch up of missed vaccine doses after the lifting of restrictions whenever feasible, supported by adapted communication campaigns.

()

7/6/20 2:11 PM

- Pediatric societies should work in tandem with public health authorities in dispensing accurate information to healthcare providers and the general public about prevention and treatment strategies, and mitigating collateral impact on the health and wellbeing of children, and guidance on parenting by providing links to reputable resources to address any misconceptions and build trust in the health system.
- Child health providers should work with WHO, UNICEF, National Immunization Technical Advisory

Groups (NITAGs), and Governments in monitoring delayed and interrupted vaccination, any disruption in routine health care services, any inaccessibility of special needs of children with disabilities during COVID-19 and suggest plans for achieving targets depending on their local and national situation.

 Healthcare providers are encouraged to work with public health authorities to develop policies and programmes on digital platforms to encourage and facilitate the shift of some clinical encounters to telemedicine service delivery when appropriate.

References

 WHO. Coronavirus disease (COVID-19) outbreak situation. https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
World Health Organization. WHO Coronavirus Disease (COVID-

19) Dashboard 2020 [Available from: https://covid19.who.int/.

3. World Health Organization. Coronavirus disease (COVID-19) Situation Report -162 2020 [cited 2020 29 June]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200629-covid-19-sitrep-161.pdf?sfvrsn=74fde64e_2.

4. Dong Y MX, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics. 2020; doi: 10.1542/peds.2020-0702.

5. CC-R T. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(14):422-6. Epub 2020/04/10.

6. European Centre for Disease Prevention and Control. COVID-19 cases 2020 [Available from: https://qap.ecdc.europa.eu/public/ extensions/COVID-19/COVID-19.html.

7. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatrica. 2020 Jun;109(6):1088-95.

8. World Health Organization. Key Messages and Actions for COVID-19 Prevention and Control in Schools 2020 [cited 2020 25 June]. Available from: https://www.who.int/docs/default-source/coronaviruse/key-messages-and-actions-for-covid-19-prevention-and-control-in-schools-march-2020.pdf?sfvrsn=baf81d52_4.

9. Irfan O, Tang K, Lassi Z, Bhutta Z. Systematic review of clinical characteristics, treatment modalities and outcomes of SARS-Cov-2 infection in newborns, infants, children and adolescents as per the infection severity. Systematic Review in progress. PROSPERO 2020 CRD42020183134 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020183134. 2020.

10. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. N Engl J Med 2020; 382: 1663-5.

11. Posfay Barbe C WN, Gauthey M, Moussaoui D, Loevy N, Diana A, L'Huillier A. . COVID-19 in Children and the Dynamics of Infection in Families. Pediatrics. 2020:e20201576.

12. National Centre for Immunisation Research and Surveillance (NCIRS). COVID-19 in schools – the experience in NSW. 2020. http://ncirs. org.au/sites/default/files/2020-04/NCIRS% 20NSW % 20Schools % 20 COVID_Summary_FINAL% 20public_26% 20April% 202020.pdf.

13. Danis K, Epaulard O, Bénet T, Gaymard A, Campoy S,

Bothelo-Nevers E, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. Clin Infect Dis. 2020:ciaa424.

14. Davies NG KP, Liu Y, et al. Age-dependent effects in the transmission and control of COVID-19 epidemics [published online ahead of print, 2020 Jun 16]. Nat Med. 2020;10.1038/s41591-020-0962-9. doi:10.1038/s41591-020-0962-9. 2020.

15. Monteleone PA, Nakano M, Lazar V, Gomes AP, de Martin H, Bonetti TC. A review of initial data on pregnancy during the COVID-19 outbreak: implications for assisted reproductive treatments. JBRA Assisted Reproduction. 2020 Apr;24(2):219.

16. Elshafeey F MR, Hindi N, et al. A systematic scoping review of COVID-19 during pregnancy and childbirth. Int J Gynaecol Obstet. 2020;150(1):47-52. doi:10.1002/ijgo.13182.

17. Lassi Z, Ali A, Das J, Salam R, Irfan O, Bhutta Z. A systematic analysis of pregnant women with COVID-19: clinical presentation, and pregnancy and neonatal outcomes as per COVID-19 severity. Systematic Review in progress. PROSPERO 2020 CRD42020182048 Available from: https://www.crd.york.ac.uk/prospero/display_record. php?ID=CRD42020182048.

18. Yan J, Guo J, Fan C, Juan J, Yu X, Li J, et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. Am J Obstet Gynecol. 2020;223(1):111.e1-.e14.

19. Chen L LQ, Zheng D, et al. Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China. N Engl J Med. 2020;382(25):e100. doi:10.1056/NEJMc2009226. 2020.

20. Juan J GM, Rong Z, Zhang Y, Yang H, Poon LC. Effects of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcomes: a systematic review [published online ahead of print, 2020 May 19]. Ultrasound Obstet Gynecol. 2020;10.1002/uog.22088. doi:10.1002/uog.22088.

21. Penfield C BS, Limaye M et al. . Detection of severe acute respiratory syndromecoronavirus 2 in placental and fetal membranesamples. Am J Obstet Gynecol MFM 2020 May 8;100133. doi: 10.1016/j. ajogmf.2020.100133.

22. Patanè L, Morotti D, Giunta MR, Sigismondi C, Piccoli MG, Frigerio L, et al. Vertical transmission of coronavirus disease 2019: severe acute respiratory syndrome coronavirus 2 RNA on the fetal side of the placenta in pregnancies with coronavirus disease 2019–positive mothers and neonates at birth. American Journal of Obstetrics & Gynecology MFM. 2020:100145.

23. Dumpa V, Kamity R, Vinci AN, Noyola E, Noor A. Neonatal Coronavirus 2019 (COVID-19) Infection: A Case Report and Review

۲

(�)

of Literature. Cureus. 2020;12(5):e8165. Published 2020 May 17. doi:10.7759/cureus.8165.

 $(\blacklozenge$

24. Groß R CC, Müller JA, et al. Detection of SARS-CoV-2 in human breastmilk. Lancet. 2020;395(10239):1757-1758. doi:10.1016/S0140-6736(20)31181-8.

25. World Health Organization. Clinical management of COVID-19: interim guidance, 27 May 2020. World Health Organization; 2020.

26. Jones TC MB, Veith T, Zuchowski M, Hofmann J, Stein A, Edelmann A, Corman VM, Drosten C. An analysis of SARS-CoV-2 viral load by patient age. German Research network Zoonotic Infectious Diseases website. 2020. doi: https://doi.org/10.1101/202 0.06.08.20125484.

27. Lu Y LY, Deng W, Liu M, He Y, Huang L, Lv M, Li J, Du H. . Symptomatic infection is associated with prolonged duration of viral shedding in mild coronavirus disease 2019: a retrospective study of 110 children in Wuhan. The Pediatric Infectious Disease Journal. 2020 Jul 1;39(7):e95-9.

28. Parri N LM, Buonsenso D. Coronavirus Infection in Pediatric Emergency Departments (CONFIDENCE) Research Group. Children with Covid-19 in Pediatric Emergency Departments in Italy [published online ahead of print, 2020 May 1]. N Engl J Med. 2020;NEJMc2007617. doi:10.1056/NEJMc2007617.

29. de Souza TH, Nadal JA, Nogueira RJ, Pereira RM, Brandao MB. Clinical Manifestations of Children with COVID-19: a Systematic Review. Pediatric Pulmonology. 2020 June 3. https://doi.org/10.1002/ ppul.24885.

30. Chen A, Huang J, Liao Y, Liu Z, Chen D, Yang C, et al. Differences in clinical and imaging presentation of pediatric patients with COVID-19 in comparison with adults. Radiology: Cardiothoracic Imaging. 2020;2(2):e200117.

31. Shekerdemian LS MN, Wolfe KK, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units [published online ahead of print, 2020 May 11]. JAMA Pediatr. 2020. doi:10.1001/jamapediatrics.2020.1948.

32. Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-associated Organ Dysfunction in Children. Intensive Care Med. 2020;46(Suppl 1):10-67. Epub 2020/02/08.

33. Ledford H. Coronavirus breakthrough: dexamethasone is first drug shown to save lives. Nature. 2020;582(7813):469.

34. WHO. News release: WHO welcomes preliminary results about dexamethasone use in treating critically ill COVID-19 patients 2020 [Available from: https://www.who.int/news-room/detail/16-06-2020-who-welcomes-preliminary-results-about-dexamethasone-use-in-treating-critically-ill-covid-19-patients

35. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020. Epub 2020/05/11.

36. European Centre for Disease Prevention and Control. Paediatric inflammatory multisystem syndrome and SARS-CoV-2 infection in children – 15 May 2020. ECDC: Stockholm; 2020.

37. CDC U. Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C). https://www.cdc.gov/mis-c/hcp/.

38. Rauf A VA, John ST, Krishnan R, Latheef A. Multisystem Inflammatory Syndrome with Features of Atypical Kawasaki Disease during COVID-19 Pandemic [published online ahead of print, 2020 May 28]. Indian J Pediatr. 2020;10.1007/s12098-020-03357-1. doi:10.1007/s12098-020-03357-1.

39. Balasubramanian S NT, Ramachandran B, Ramanan AV. Hyper-inflammatory Syndrome in a Child With COVID-19 Treated Successfully With Intravenous Immunoglobulin and Tocilizumab [published online ahead of print, 2020 May 10]. Indian Pediatr. 2020;S097475591600180.

40. Whittaker E BA, Kenny J, et al. Clinical Characteristics of 58 Children with a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. JAMA. Published online June 08, 2020. doi:10.1001/jama.2020.1036.

41. CDC U. Severe outcomes among patients with COVID-19— United States, Feb 12-March 16, 2020. MMWR.

42. "Multisystem inflammatory syndrome in children and adolescents with COVID-19: Scientific brief" www.who.int. World Health Organization. Archived from the original on 15 May 2020.

43. Health RCoPaC. Guidance: paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS). 2020 [Available from: https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf.

44. WHO. Global COVID-19 clinical platform: case report form for suspected cases of multisystem inflammatory syndrome (MIS) in children and adolescents temporally related to COVID-19. World Health Organization, 2020.

45. UN Policy Brief: The Impact of COVID-19 on children. April 15, 2020. https://unsdg.un.org/sites/default/files/2020-04/160420_Covid_Children_Policy_Brief.pdf.

46. UNICEF. https://www.unicef.org/press-releases/covid-19-number-children-living-household-poverty-soar-86-million-end-year. 27 May 2020.

47. UNESCO. Education: From disruption to recovery https:// en.unesco.org/covid19/educationresponse.

48. Programme WF. 2020 – Global Report on Food Crises.

49. Viner RM, Russell SJ, Croker H, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. Lancet Child Adolesc Health. 2020;4(5):397-404. doi:10.1016/S2352-4642(20)30095-X.

50. Roberton T CE, Chou VB, Stegmuller AR, Jackson BD, Tam Y, Sawadogo-Lewis T, Walker N. . Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. The Lancet Global Health. 2020 May 12.

51. WHO. News release 22 May 2020. https://www.who.int/ news-room/detail/22-05-2020-at-least-80-million-children-under-oneat-risk-of-diseases-such-as-diphtheria-measles-and-polio-as-covid-19-disrupts-routine-vaccination-efforts-warn-gavi-who-and-unicef.

52. Statement by the Measles & Rubella Initiative: American Red Cross, U.S. CDC, UNICEF, UN Foundation and WHO 13 April 2020. https://www.unicef.org/press-releases/more-117-million-children-risk-missing-out-measles-vaccines-covid-19-surges.

53. Klein JD, Koletzko B, El-Shabrawi MH, Hadjipanayis A, Thacker N, Bhutta Z. Promoting and supporting children's health and healthcare during COVID-19 – International Paediatric Association Position Statement. Arch Dis Child. 2020;105(7):620-624. doi:10.1136/ archdischild-2020-319370.

54. WHO. Considerations for school-related public health measures in the context of COVID-19 2020 [Available from: https://www. who.int/publications/i/item/considerations-for-school-related-publichealth-measures-in-the-context-of-covid-19.

55. UNICEF W, IFRC. Interim Guidance for COVID-19 Prevention and Control in Schools 2020 [Available from: https://interagencystandingcommittee.org/other/interim-guidance-covid-19-prevention-and-control-schools-jointly-developed-ifrc-unicef-and.

56. UNESCO U, the World Bank, the World Food Programme and UNHCR. Framework for Reopening Schools 2020 [Available from: https://www.unicef.org/documents/framework-reopening-schools.

UNICEF-IPA_COVID_brief_FINAL_29June.indd 12

 (\bullet)