SRI LANKA COLLEGE OF PAEDIATRICIANS

Clinical Practice Guidelines on the Management of Children with Suspected or Confirmed COVID-19

Version 01 – 31st March 2020

Introduction

Coronaviruses are important human and animal pathogens. Towards the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China, followed by increasing numbers of cases in other countries throughout the world. On the 11th February 2020, the World Health Organization (WHO) designated the disease as **COVID-19**, which stands for *Coronavirus Disease 2019*[1]. The virus is an enveloped single-stranded RNA virus which belongs to the β-coronavirus genus that causes COVID-19. It is now designated as *Severe Acute Respiratory Syndrome Coronavirus 2* (**SARS-CoV-2**)[2].

The spread of this virus across the world was extensive and hence, a month after designating the COVID-19 disease, the WHO proclaimed it as a pandemic on 11th March 2020. On the same day the first confirmed Sri Lankan patient was identified and on 24th March 2020, the 100th case has been reported in Sri Lanka. There were 122 diagnosed cases with 2 adult deaths due to this illness by 30th March 2020. Importantly, there are some confirmed paediatric cases, including a 4 month old baby, who have been identified during the same time period in Sri Lanka. Although COVID-19 mainly impacts the adult population, many paediatric cases have been reported throughout the world. As much as adults, children of all ages, from one day of age, appear to be susceptible to COVID-19. There is no significant gender difference in children [2]. In contrast to infected adults, most infected children appear to have a milder clinical course. However, the determination of the transmission potential of these asymptomatic or mildly symptomatic patients is important for guiding the development of measures to control the ongoing pandemic.

Older adults and those with co-morbidities are at increased risk of severe disease. Similarly, children with chronic lung diseases or other co-morbidities and very young populations are particularly at risk. However, severe cases have been reported in all age groups of children throughout the world.

Considering all these facts, the Sri Lanka College of Paediatricians (SLCP) has formulated these Clinical Practice Guidelines to facilitate the management of children with suspected or confirmed COVID-19 illness. The literature regarding the paediatric cases of COVID-19 is scanty.

This guideline is based on the best available evidence as at 30th March 2020, together with consensus among members of the SLCP.

COVID-19: Adult Versus Paediatric disease

According to the available data, the total reported cases aged less than 18 years seems to be less than 5% of the total number of cases up to now[3]. Besides, the number of reported deaths among children due to COVID-19 is also remarkably low, only 2 being reported in China up to 30th March 2020, a 10 month old baby[4] and a 14 year old child[5]. In addition, a 17 year old boy with COVID-19 died in California, USA, but the case is under investigation to find out the exact cause of death[6,7]. Nevertheless, due to the rapid spread of the disease around the world and the locked-down status of most places for prolonged periods, the true picture about the paediatric morbidity and mortality of this disease is yet to be accurately ascertained.

Following are some proposed reasons or mechanisms for less numbers of paediatric cases due to COVID-19[8]

1. Fewer opportunities for exposure than adults due to various factors such as school vacation time and less exposure in some age groups like infants who naturally stay at home.
2. The relatively immature immune system which leads to less severe adverse inflammatory responses to the virus
3. Relatively less developed number, maturity and function of Angiotensin-Converting Enzyme 2 (ACE2) receptors in children. ACE2 is the receptor to which the virus gets attached to secure entry into the cells in the respiratory system.
4. Likely cross-reactivity of antibodies against other corona viruses with SARS-CoV-2 virus as children are likely to have more infections and hence, they have more antibodies against these other viruses which cause diseases in children more frequently.

Clinical symptoms also would vary in children in comparison to adults. Fever is one of the common presentations in adults. However, fever may be absent in more than half of children according to available data on paediatric cases of COVID-19[2-5] (Details are in the clinical features section). Hence, in contrast to adult disease, fever should not be an essential criterion to suspect a child to have COVID-19.

Clinical case definitions of COVID-19 in children[9,10]
Based on the guidelines issued by the WHO and the Sri Lankan Ministry of Health, together with the available data on childhood COVID-19, clinically suspected and confirmed cases are defined as follows:-

Clinically Suspected Case
A child with features of acute respiratory illness (with cough, shortness of breath, sore throat) with or without[2,11] a history of fever***, at any point of time during this illness, returning to Sri Lanka from any country within the last 14 days.
(****Fever should not be considered to be an essential criterion in children if other clinical features are compatible because fever may be absent in up to half of affected children*)

OR

A child with an acute respiratory illness, as mentioned above, who has been in close-contact (*staying in an enclosed environment like the same household, educational place, social gathering or travelling in the same vehicle for over 15 minutes*) with a confirmed or suspected COVID-19 case during the last 14 days before the onset of symptoms.

OR

A child with severe acute pneumonia, who is critically ill and the disease being not explainable by any other aetiology, regardless of travel or contact history, and as decided by the treating Consultant Paediatrician.

Confirmed case
A child with laboratory confirmation of SARS-CoV-2 infection, irrespective of a contact history, travel history, symptoms or clinical signs.

Transmission of COVID-19
The SARS-CoV-2 virus is transmitted primarily by respiratory droplets. If a person with the disease coughs, sneezes or talks, the virus could be released with the respiratory secretions and can infect another person if it makes direct contact with the mucous membranes of the recipient[2,12,13]. In addition, this virus could remain viable on objects or surfaces. Hence, transmission happens if a person

touches an infected object or surface and then touches his or her eyes, nose, or mouth. According to a study done in controlled laboratory conditions, it was found that the virus is viable for 3-6 hours depending on the surface[14]. It stays viable for longer periods on stainless steel and plastic.

Droplets typically do not travel more than six feet (about two metres) and do not linger in the air. However, SARS-CoV-2 remained viable in aerosols under experimental conditions for at least three hours. Nevertheless, there is no concrete evidence which supports pure air-borne transmission[15]. Viral shedding has been demonstrated in the stools[16, 17] of patients with COVID-19 but definite evidence for faeco-oral transmission is lacking. Hence, faeco-oral transmission does not appear to be a significant factor in the transmission[18].

There is no strong evidence to support the vertical transmission of this virus from a pregnant mother to her foetus[19,20]. Available limited evidence shows that this virus has not been found in amniotic fluid and vaginal secretions. Therefore, it is unlikely that the baby is exposed during the antenatal period or during birth. In addition, there is no evidence to support viral transmission through breast milk as well[21].

However, a case report which was published on 26th March 2020, revealed positive IgM antibodies against SARS-CoV-2 at 2 hours of age in a baby born to a mother with COVID-19 in China[22]. This indicates possible antenatal transmission but RT-PCRs for the virus in baby's nasopharyngeal swabs were repeatedly negative till the time of discharge from the hospital. Besides, the mother's vaginal secretions at the delivery and breast milk were also negative for the virus[21]. Unfortunately, no PCR testing of amniotic fluid or placenta were performed. Hence, more evidence is needed to establish possible vertical transmission of COVID-19.

Patients with more symptoms seem to be more contagious. Nevertheless, transmission from totally asymptomatic persons or during the incubation period is also possible in this disease[23, 24, 25]. Asymptomatic or mildly symptomatic children with the disease would be a potential source of spread of the infection to the rest of the family members due to the very close contacts with children in a family.

Clinical presentation

The incubation period ranges from 1-14 days. According to the available data in adults, the average incubation period is 5-6 days and 97% of infected people develop symptoms by 11.5 days[26]. Therefore, most of the infected people show symptoms on day 5 or 6 after exposure and all, possibly with rare exceptions, show symptoms by 14 days[26].

The symptoms of COVID-19 are similar in children and adults[27, 28, 29]. However, children generally present with mild symptoms. Yet for all that, severe cases too have been reported among children. Most children present with non-specific symptoms of a viral respiratory infection such as *fever, fatigue, cough, and sore throat*. As indicated previously, fever may not be present in a significant proportion of cases. *Nasal congestion* and *rhinorrhoea* are less commonly seen. Some have reported gastrointestinal symptoms like *abdominal pain, vomiting and diarrhoea*[30].

Fever is usually mild to moderate. However, as stated above, it may even be absent in children. One retrospective study done at the Wuhan Children's hospital with a participation of 171 children with confirmed COVID-19 revealed that fever was present only in 41.5% at any time during the illness[4]. Also, in the same study, 15.8% had an asymptomatic infection. Perhaps, the asymptomatic infected proportion could be higher because investigations are not routinely done on asymptomatic children.

In some children, if the disease becomes progressive, extra-pulmonary systemic toxic symptoms like poor feeding, loss of appetite, malaise, less activity or restlessness could develop. Also, when pneumonia is progressive, usually during the second week of the illness, they might have breathing difficulties.

Clinical classification of severity[(2,11,26,30,31,32)]

1. Asymptomatic infection

Children who show a test positive for SARS-CoV-2 without manifestations of clinical symptoms or abnormal chest imaging findings.

However, even children with asymptomatic infection may have objective radiological abnormalities. As an example, in a study of 24 adult patients with asymptomatic infection who underwent chest CT, 50 per cent had typical ground-glass opacities or patchy shadowing, and another 20 per cent had atypical imaging abnormalities.

Diagnostic testing for COVID-19 is not done for asymptomatic children in Sri Lanka at the moment. Hence, this group cannot be identified. **However, they could act as a potential source for spread of the infection and hence, it may be necessary to consider screening for asymptomatic children who have very close household contacts with those who are positive**.

2. Acute upper respiratory tract infection

Children with fever, cough, pharyngeal pain, nasal congestion, fatigue, headache, myalgia etc., and without signs of pneumonia (clinically and radiologically) or sepsis. On current evidence, fever is not a mandatory criterion.

Some patients who have mild symptoms initially may progress over a week or so to pneumonia or more severe disease. In a study of 138 adult patients hospitalized in Wuhan due to COVID-19, dyspnoea developed after a median of five days since the onset of symptoms.

3. Mild pneumonia:

Children with or without fever, who exhibit respiratory symptoms such as cough, with chest imaging abnormalities indicating pneumonia but not fulfilling the criteria of severe pneumonia.

4. Severe pneumonia: (one or more of the following criteria is/are present with features of pneumonia)
- Tachypnoea
- Oxygen saturation less than 92%
- Increased work of breathing (recessions, nasal flaring, use of accessory muscles etc.) cyanosis or intermittent apnoea (especially in neonates and infants)
- Disturbance of consciousness, somnolence, coma, or convulsions
- Food refusal or feeding difficulty, with signs of dehydration

5. Critical cases: Those who meet **any** of the following criteria
- Respiratory failure requiring mechanical ventilation
- Septic shock
- Acute cardiac injury, cardiac arrhythmias
- Failure of other organs (Multi-organ dysfunction).

Vulnerable groups of children for severe or complicated disease

1. Those with an underlying significant chronic respiratory condition
- Conditions such as chronic lung disease of prematurity, cystic fibrosis, primary ciliary dyskinesia, bronchiolitis obliterans/obliterative bronchiolitis, non-cystic fibrosis bronchiectasis,

childhood interstitial lung disease and having significant respiratory compromise or those with long-term oxygen dependency.
- Severe or uncontrolled asthma
- Respiratory complications due to extra-pulmonary causes such as neurological or neuromuscular disorders

2. Immuno-compromised states (due to disease or some form of treatment)
- Primary immuno-deficiencies
- On treatment for a malignancy
- Immunosuppressive medication including the long-term (*more than 28 consecutive days*) usage of daily systemic steroids (*not alternate day low dose steroids or hydrocortisone maintenance treatment for adrenal or pituitary disorders*)
- Post-transplant patients (*solid organ or stem cell transplants*)
- Asplenia (*functional or surgical*)

3. Haemodynamically significant acyanotic or cyanotic heart disease

4. Chronic Kidney Disease stages IV, V or those on dialysis

5. Severe malnutrition

Predictors of possible severe complicated disease
1. Dyspnoea
2. Persistent high fever for 3–5 days
3. Poor mental response, lethargy, disturbance of consciousness, and other changes of consciousness
4. Abnormally increased enzymatic indices and inflammatory markers such as myocardial enzymes, liver enzymes, lactate dehydrogenase, C-reactive proteins and procalcitonin
5. Unexplained metabolic acidosis
6. Chest imaging findings indicating bilateral or multi-lobe infiltrations, pleural effusion, or rapid progression during a very short period of time
7. Infants younger than 3 months
8. Extra-pulmonary complications
9. Evidence of co-infection with other viruses and/or bacteria

Severity according to age groups
According to a case series of 2143 paediatric patients (confirmed 731 and suspected 1412) in China[5], the median age of patients was 7 years and the age range was one day to 18 years. The proportions of severe and critical cases in this cohort are as follows:-

<1y: 10.6%, 1-5y: 7.3%, 6-10y: 4.2%, 11-15y: 4.1%, 15-18y: 3.0%

These results suggest that all ages of children from one day onwards are susceptible to the COVID-19 disease while, young children, particularly infants, are vulnerable to severe disease.

Approach to a child who is a potential suspected case
It is recommended to use a checklist at the triage station to screen all children who present to an Out-patient Department, Preliminary Care Unit or an Emergency Treatment Unit, to identify children with potential contacts which are mentioned above. **There were some instances in which the contact history had not been divulged properly or wilfully camouflaged or irresponsibly withheld, thereby exposing medical teams to the virus unnecessarily. Hence, the need for a very high**

degree of suspicion, together with intensive direct questioning are emphasized during this pandemic.

There should be a separate place away from the patient waiting area in the out-patient departments to arrange the initial management of children with acute respiratory symptoms and a potential contact history. However, if there is evidence of community spread of COVID-19 in the future, all children who are presenting with unexplained acute respiratory infections, despite a negative contact history, should be attended to, while taking all precautions to prevent the spread of the disease to the health care workers as well as to other non-COVID-19 patients. It is necessary to inform the general public that, if they have any respiratory symptoms, to wear any kind of face mask which is available, when they attend for medical care.

If there is a child who fulfils the criteria for a suspected case, he/she and parents/guardian should be offered face masks if they are not already wearing them. Then they should be moved to the specific isolation area to arrange an initial assessment. **The healthcare workers who are attending to the child should wear a complete set of personal protective equipment (PPE).**

Sore throat is a common symptom in children as well as in those with COVID-19. However, routine assessment of the throat of a **suspected** COVID-19 child, without protective equipment, including a face shield, is not recommended due to the high risk of spread to medical personnel. If there is evidence of community spread of COVID-19, ENT assessment of children who are presenting with respiratory symptoms should be done while taking necessary precautions. However, the intensity of these precautions will be decided according to the severity of the community spread, if it happens in the future, the clinical symptoms of the child, the absolute necessity for the ENT examination and available resources, including PPEs.

If the child is clinically stable, he/she can be transferred to the closest designated hospital for COVID-19 patients by an ambulance or to the designated isolation unit of the same hospital if it is already a designated COVID-19 care hospital, to arrange for confirmatory testing. **If the child is clinically ill, initial management should be arranged at the OPD according to the requirements while taking all the precautions and transferred later to a designated hospital when stable.**

Diagnosis
Testing criteria for children are the same as for adults at the moment. Depending on the presence of symptoms, travel history, contact history with a confirmed COVID-19 patient, if the criteria for a suspected case is fulfilled, or if there is a need to rule out unexplained pneumonia without a positive contact history, a diagnostic test is indicated[9]. **It is recommended that the final decision should be made by the Specialist Consultant Paediatrician in charge of the case.**

All those in whom a diagnostic test is indicated should be admitted and isolated until the test result is available. The recommended test is a real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) for the detection of SARS-CoV-2 viral RNA[33] in respiratory samples of a suspected case. This is a confirmatory test and it is the test being used in Sri Lanka at the moment.

Studies to assess the rates of detection of the virus in different respiratory samples are severely limited and there are no exclusive paediatric studies up to the publication of this guideline. One study done in China with participation of 205 patients (age range 5-67y, mean 44y) and 1070 specimens from different sites revealed positive rates of 32%, 63% and 72% from pharyngeal swabs, nasal swab and saliva respectively[18]. Another study done in China revealed 42.9% and 61.1% positive rates in sputum

and nasal swabs[34]. Lower respiratory samples like broncho-alveolar lavage showed higher yield. More good quality studies are required to determine the best upper respiratory sample for testing. However, taking two or more specimens from different sites at the same time and mixing them in the same viral transport medium or mixing before doing the PCR is recommended to obtain a better yield.

On the current evidence and at the time of writing of this version of the guideline, both *naso-pharyngeal and oro-pharyngeal swabs* (taken at the same time) are the recommended respiratory specimens for the diagnosis of COVID-19. Sampling both sites, oropharynx and also the naso-pharynx together, is recommended to optimise the chances of virus detection. For oro-pharyngeal (throat) swabs, it is recommended to swab the tonsillar beds and the back of the throat, avoiding the tongue. For nasopharyngeal swabs, the right or left naso-pharynx should be swabbed by gently inserting the swab along the floor of the nasal cavity until resistance is encountered, and rotating the swab gently for 10-15 seconds followed by withdrawal and repetition of the same with the same swab in the other nostril. To conserve swabs, the same swab that has been used to sample the oropharynx may also be utilised for naso-pharynx sampling.

Nasopharyngeal aspirate into a mucous extractor bottle is an alternative method for swabs. Depending on the severity of the disease endotracheal aspirates or broncho-alveolar lavage may be indicated.

The virus has been detected in posterior oro-pharyngeal saliva samples taken in adults. However, due to practical issues with children and risk of increased infectivity, salivary samples are not undertaken in children at the present time. Sputum is **NOT** recommended as a specimen in paediatric patients.

Specimen collection should be done in an adequately ventilated, designated and isolated place. **The health care worker should wear a full set of standard personal protective equipment and should strictly follow the guidelines issued by the Ministry of Health.**

All the specimen should be put in viral transport media, labelled properly and transported to the designated lab as soon as possible with ice (4^0C) in a triple package.

If there is any delay in transport, specimens can be stored in a refrigerator ($4°$C) up to 48 hours. However, it should not be frozen.

Although, the accuracy is of the best available level, the cost and relative time for the analysis are higher in the real time RT-PCR method. Therefore, the possibility of using the assessment of specific IgG and IgM antibodies in blood samples is being evaluated. The relative cost of this assessment is less and results will be available in a shorter time, and hence, there might be a place for this as a screening tool if the number of suspected cases go up higher or if a policy decision is taken to expand the screening to detect more patients early by the Ministry of Health.

Differential diagnosis
If the RT-PCR for SARS-CoV-2 virus is negative, other possible causes for the clinical symptoms should be considered and explored.
Re-testing for suspected cases that got a negative test result is not indicated at the moment due to limited resources (In that context, please follow the updated guidelines by the Ministry of Health on re-testing, if available).

The possible differential diagnoses for the aetiology are influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, SARS coronavirus or other coronaviruses, other known viral infections, any bacterial infection, Mycoplasma pneumoniae and Chlamydia pneumoniae.

Chest imaging:

Data on the findings of chest imaging in children with COVID-19 are significantly limited. According to the available evidence, CXR and chest CT findings are non-specific[35,36]. They may be completely normal in the initial phase of the disease.

The commonest CXR features are lobar or multi-lobar or bilateral, patchy consolidations.
The commonest chest CT findings are patchy bilateral ground-glass opacities or consolidations.
These changes may be progressive in severe cases.

Laboratory findings[2, 3, 11, 26]

WBC:
Common findings are leucopenia and lymphocytopenia. Progressive lymphocytopenia was noted in severe disease. Nevertheless, leucocytosis is seen in some cases.

Platelets:
Thrombocytopenia in severe cases and considered as a poor prognostic sign in adult patients.

CRP:
Normal or elevated.

Procalcitonin:
Elevated.

Liver function tests:
Elevated transaminases are seen in some cases

Other investigations:
Elevated levels of D-dimer are seen in severe cases. It has been identified as a marker of poor prognosis in adult patients. Cardiac enzymes need to be done if there are clinical features of myocarditis.

Clinical management:

Isolation
All children with suspected or confirmed COVID-19 infection should be managed as in-patients. No community management is recommended for any suspected or confirmed child, even for very mild cases.
According to the current recommendations by the Ministry of Health, all confirmed children with COVID-19 should be transferred to the National Institute of Infectious Diseases, Angoda or nearest designated hospital for children with COVID-19, after initial stabilization. If any child requires critical care he/she will be transferred to the Lady Ridgeway Hospital for further management. **(Please refer to the updated guidelines by the Ministry of Health, if available, regarding this as these institutions and instructions may vary over time).**

All suspected or confirmed children should be managed within a designated standard isolation facility. A suspected case should be isolated in a single room, while confirmed cases can be arranged in the same cubicle if single rooms are not available.

All health care workers attending to the needs of these children should wear standard PPEs and follow the standard universal precautions.

Bystanders - mother, father or a suitable guardian should be allowed to stay with the child, as done with other paediatric patients. However, strict precautions should be taken to prevent transmission of the infection to the bystander. The same bystander should stay with the child as much as possible and multiple bystanders at a time and visitors should not be allowed.

General measures:

As this is a viral infection and complications are less common in children, most children could be managed with bed rest and supportive measures only.

- **Adequate hydration and nutrition** - These are key elements in supportive management. However, a restrictive fluid management strategy is recommended to reduce extravascular lung water in severe cases due to the possible syndrome of inappropriate antidiuretic hormone (SIADH) secretion. Wherever possible, avoid 'maintenance' intravenous fluids, high volume enteral nutrition and fluid boluses for hypotension.

- **Breastfeeding -** If a baby is already on breast feeding, the mother may continue breast feeding. However, maximum precaution should be taken to prevent the transmission of the disease to the mother and caregivers. If mother decides not to breast feed temporarily till the baby recovers, the treating team should respect the mother's decision.

- **Antipyretics** - Paracetamol 10-15mg/kg per dose could be used when the child is febrile (maximum 4 times a day). *NSAIDs are not recommended as antipyretic agents and should be avoided as much as possible*.

- **Monitoring** - Monitor the vital signs regularly and any evidence of respiratory distress, hypoxia or systemic involvement should be detected early.

- **Investigations** - Repeat blood counts, CRPs, liver function tests according to the clinical severity of the disease and serial chest imaging is indicated if the child shows worsening respiratory symptoms. The frequency of these investigations depends on the progression of the disease and the level of abnormal results.

- **Bronchodilators** - Not indicated routinely. If required, metered dose inhalers are preferred and nebulization should be avoided as much as possible because it may cause significant aerosol generation and may increase the infectivity. If the nebulizer systems are reused, strict sterilization practices should be followed.

- **Supportive Oxygen therapy** - Early identification of hypoxia and prompt supply of oxygen via nasal cannulae or a non-rebreathable face mask. The ordinary face mask should be best avoided as it may increase the spread of droplets.

- **The child should be monitored closely and may need transfer to a designated high dependency or paediatric intensive care unit electively whenever necessary and as far as possible, before further clinical deterioration.**

- **Further respiratory support** - Heated humidified high flow nasal cannula oxygen (HFNCO) and non-invasive ventilation (NIV) are the options for severe respiratory distress before considering invasive ventilation. However, both these methods are associated with increased aerosol generation and hence, might accelerate the infectivity.

  HFNCO is the initial recommended therapy for hypoxia associated with COVID-19 disease. But the staff should wear optimal airborne controlling PPEs. The risk of airborne transmission to staff is low with well fitted newer HFNCO systems when optimal PPEs and other infection

control precautions are being used. Negative pressure rooms are preferable if available for patients receiving HFNCO therapy.

NIV: Routine use of non-invasive ventilation (NIV) is not recommended.

Current experience with adult patients suggests that NIV for COVID-19 hypoxic respiratory failure is associated with a high failure rate, delayed intubation, and possibly increased risk of aerosolization with poorly fitting masks.

Deteriorating patients should be considered for early endotracheal intubation and invasive mechanical ventilation. Even if used, all patients receiving NIV should have a clear plan for treatment failure.

- Patients with worsening hypercapnia, acidaemia, respiratory fatigue, haemodynamic instability or those with altered mental status should be considered for early invasive mechanical ventilation if appropriate and hence, elective intubation is recommended.

- **Early transfer** to a designated hospital with adequate facilities to manage critically ill children with COVID-19 is recommended. LRH is the identified hospital at the moment.

- **Intubation** should be done by the most experienced member of the team to minimize the chance of failure[37]. Repeated attempts at intubation and non-elective intubations would increase the risk of exposure to the medical team. All standard precautions should be followed because intubation necessitates very close contact with the patient.

- **Mechanical ventilation (MV) -** Lung protective mechanical ventilation is recommended for management of acute respiratory failure.

  MV should be employed with the use of a low tidal volume strategy (4-8ml/kg for predicted body weight) and limiting plateau pressures to less than 30cm H_2O. Permissive hypercapnia is usually well-tolerated and may reduce volutrauma. Higher levels of Positive End-Expiratory Pressure (PEEP) may be required.

  Alternate modes of ventilation such as airway pressure release ventilation (APRV) may be considered based on clinician preferences and local experience. Viral filters, rather than HME filters, should be utilized if available, and circuits should be maintained for as long as allowable, as opposed to routine changes.

- **Strict infection control methods** - It is emphasized again that strict precautions should be followed while providing any form of respiratory support like high flow oxygen, NIV or mechanical ventilation, interventions like nebulizations and when taking respiratory samples if required, because all these are associated with significantly increased aerosol generation and hence, increased risk of infectivity.

- **Children who are on ACE inhibitors or ACE receptor blockers** - There is a potential risk of severe disease in children who are on long term ACE inhibitors due to possible up regulation of the number of ACE receptors in these children as the virus binds and gains access to the cells via ACE2 receptors[38, 39]. However, there is no evidence or justification to recommend discontinuation of these drugs during this pandemic[40,41].

The place for other medications and therapies:

Antibiotics – They are not recommended routinely. If evidence of pneumonia is present, azithromycin may be considered because some limited evidence in adult patients shows a potential antiviral role in combination with HCQ[42]. However, broad-spectrum antibiotics should be avoided as much as possible.

Nevertheless, appropriate empirical antibiotics should still be administered within one hour of the identification of sepsis or septic shock. Some patients with COVID-19 infection may present with a secondary bacterial lower respiratory tract infection.

All final decisions regarding the use of these drugs should be taken by the Specialist Consultant Paediatrician in-charge of the patient.

Antivirals - No specific antiviral therapy is available for the SARS-CoV-2 virus[43]. Alpha-interferon, Lopinavir/litonavir, Remdesivir, Ribavirin, oseltamivir have been used individually or in combinations in some adult patients but the efficacy is not proven. Hence, these are not recommended in children at the present time.

> Remdesivir – There are some randomized trials that are underway to evaluate the efficacy of remdesivir for moderate or severe COVID-19 in adults[44]. Remdesivir is a novel nucleotide analogue that has some activity against SARS-CoV-2 *in vitro* and related coronaviruses (including SARS and MERS-CoV), both *in vitro* and in animal studies. However, there is no concrete evidence to recommend its use in children with COVID-19 as yet.

Hydroxychloroquine (HCQ)[45-48] - It can interfere with the function of ACE2 and reduce the binding of the coronavirus because the coronaviruses gain entry to the cells of the respiratory system *via* the ACE2 receptor. Hence, it hampers cell invasion by the virus. Besides, HCQ interferes with the inflammatory response and attenuates the possibility of a cytokine storm. Therefore, it has been used in adult patients and limited evidence including an RCT suggests that it could reduce the viral load in patients with COVID-19.

However, due to potential adverse effects including arrhythmias and lack of evidence in the paediatric population, it is not recommended as a first-line treatment modality in children with COVID-19. Nevertheless, for severe cases, the treating Specialist Consultant Paediatrician in-charge of the patient may consider HCQ on an individual basis if there are no other options and benefits significantly outweigh the risks. ECG monitoring is recommended while on HCQ.

There is no established paediatric dose of HCQ in COVID-19. As data and experience in paediatric patients continue to rapidly evolve, dosing will be updated as appropriate. Some experts have recommended interim paediatric dosing as follows as a treatment for symptomatic and confirmed cases of COVID-19.

6.5mg/kg/dose orally 12 hourly the first day (maximum dose 400mg), followed by 3.25mg/kg/dose orally 12 hourly for 4 days (maximum dose 200mg).

HCQ is not recommended as prophylaxis for COVID-19 in children at present.

Corticosteroids – Routine use of corticosteroids is not recommended in COVID-19, unless a child has a specific indication like associated exacerbation of asthma. However, although there is no supportive evidence, corticosteroids may be considered, based on the severity of systemic inflammatory response, degree of dyspnoea, with or without ARDS and the progress status of chest imaging findings. This is to be considered on an individual basis by the treating Specialist Consultant Paediatrician. It may be used for a short period (3-5 days). Recommended dose is prednisolone 1-2 mg/kg/day or the equi-potent dose of any other corticosteroid.

Intravenous immunoglobulins – There is no supportive data on efficacy. It may be used in critically ill patients according to the decision by the treating Specialist Consultant Paediatrician on an individual basis.

Convalescent plasma - Transfusion of compatible plasma of patients who have recovered from COVID-19, which contains antibodies against the SARS-CoV-2 virus might provide some passive immunity and has been practiced in some adult patients[49-51]. FDA approval has been given for its use in serious or immediately life threatening COVID-19 infections[52]. However, there is no published recommendation or evidence to support its use in paediatric practice.

Discharge criteria:
Prolonged viral shedding is a recognized feature of this condition despite the clinical improvement of patients. A study done among adult patients at Wuhan, China revealed the median duration of viral shedding to be 20 days among survivors (IQR 17-24), while in one patient it went up to 37 days [28]. Although, paediatric data on viral shedding is not available at the moment prolonged viral shedding could be expected in children as well. Hence, although clinically improved, it is essential to make sure that they are not infectious before discharge.
All of the following criteria should be fulfilled for discharge.

1. Afebrile for at least 3 days,
2. Significant improvement in respiratory symptoms,
3. Progressive improvement of chest imaging findings which suggest resorption of the inflammation
4. Two consecutively negative RT-PCR tests of respiratory samples which have been done at least 24 hours apart.

Recovered children should be home quarantined for another 2-3 weeks following discharge from the hospital.

Special situations:
Infants born to mothers with COVID-19[19-21,53-56]
If a pregnant mother is a suspected case of COVID-19 disease, she should be transferred to a designated hospital to arrange sampling for confirmatory testing.
If the test for SARS-CoV-2 is positive, the pregnant mother should be transferred to the National Centre for the management of pregnant mothers with confirmed COVID-19 or other similar recognized hospital **(Please refer to the guidelines by the Ministry of Health regarding the designated maternity hospitals for confirmed COVID-19)**

The mode of delivery is to be decided by the treating VOG depending on the mother's clinical and obstetric condition because there is no evidence of transmission of the infection via blood or vaginal secretions and no strong evidence to favour elective LSCS.

All staff attending the delivery should follow the guidelines issued by the Ministry of Health and every effort should be made to prevent exposure to the virus. This includes paediatric staff, who may be called upon to care for the baby.

There is no strong evidence to support the transmission of SARS-CoV-2 virus ante-natally or through breastfeeding up to the publication of this guideline. However, if a mother is positive, the baby can get the disease post-partum due to direct close contact with the mother. A 36-hour old baby has been diagnosed to have COVID-19 in China[5].

There are three options available for the management of a newborn baby if the mother is a confirmed COVID-19 patient or till ruling out the disease if the mother is a suspected case.

1. Keep the baby with the mother if the mother is clinically well and continue breast feeding while the mother is taking maximum precautions to prevent transmission of the infection to the baby. However, due to the very close contact of the newborn baby with the mother, and the highly infectious nature of the SARS-CoV-2 virus, the risk of the baby getting the infection would be very high.

2. Temporarily separating the baby from the mother just after birth and providing expressed breast milk. However, COVID-19 positive mother should wear a proper face mask, wash her hands thoroughly and disinfect the pump and bottles while following recommendations for proper pump cleaning after each use. Someone healthy and well experienced should feed and take care of the baby.

3. Temporarily separate the baby from the mother just after birth and provide formula feeds to prevent any form of contact with the mother and hence, completely abolishing the risk of infection to the baby from the mother. A well experienced person should take care of the baby.

All these options have their own pros and cons and there is no strong evidence to recommend the most suitable method. Therefore, while acknowledging the policy of giving priority to breast feeding due to its all benefits, it is recommended that the final decision is taken by the in-charge Specialist Consultant Paediatrician of the treating team after considering the mother's wish and her clinical condition while carefully assessing all of the medical and practical circumstances during this epidemic.

Routine testing for the newborn baby is not recommended unless the baby is symptomatic. Baby can be discharged with the mother when the mother meets the discharge criteria and if the baby doesn't have any symptoms of the disease.

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*******************THE END*******************