**Diagnosis, treatment, and prevention of 2019NOVEL CORONAVIRUS INFECTION in children: Department of Pediatrics, Hayatabad Medical Complex, Peshawar**

**INTERIM PROTOCOL March 2020**

(This protocol is based on different studies and consensus statement developed/published from China and Iran in last 2 months.)

**Case Definition:**

**Suspected case:**

Fever with Cough OR Shortness of Breath And either of the following:

1. History of travel to or residence in the city or country where pandemic is going on, in the 14 days prior to symptom onset;

2. Has had close contact with a confirmed or probable patient with 2019-nCoV within 14 days of symptom onset.

**Probable case:**

A suspected case (as defined above) for whom testing for 2019-nCoV is inconclusive or tests have not been sent.

**Confirmed case:**

A child with laboratory confirmation of 2019-nCoV infection, irrespective of clinical signs and symptoms.

**Definition of Contact:**

A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

1. Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes.

2. Direct physical contact with a probable or confirmed case.

**Severity of the disease:**

**Mild disease:**

Upper respiratory symptoms (e.g. cough, sore throat, and fever) for a short duration or asymptomatic infection with normal respiratory rate, normal blood pressure, and SPO2 > 93% at room air.

**Moderate disease:**

Findings of mild disease with increased respiratory rate:

 (Birth - 2 months > 60 / min.

02 months -1 years >50/min.

 1year - 5 years >40/min.

More than 5 years >30/min).

**Severe disease:**

Moderate disease, plus any of the following manifestations:

1. Spo2 less than 93% at room air;

2. Altered menta lstatus, drowsiness, or convulsions;

3. Feeding difficulty.

4.Respiratory distress in the form of nasal flaring, sub costal/ intercostals recessions.

**ARDS (acute respiratory distress syndrome).**

Patient shall have all the features of severe disease plus unilateral / bilateral basal lung opacities which cannot be explained by cardiac failure or volume overload either clinically (clinical findings of peripheral edema or raised JVP) or echocardiographically, within seven days of onset of disease.

**Multiorgan failure:**

Any two of the following:

1. Systolic blood pressure less than lower limit of normal for age:

(Neonate:<60mm Hg.

Infant < 70 mm Hg.

Children 1-10 years, 70+Age in years x2).

Children more than 10 years <90mmhg.

2. Lactate level more than 2 mmol/l

3. Oliguria 0.5ml/kg/hr/ deranged RFTs (creatinine 2 times upper limit)

4 Coagulopathies , (INR >2)

5. Thrombocytopenia

6. Deranged LFTs ( ALT 2 times upper limit of normal)

7.refractory metabolic acidosis / Pao2 less than 60 mmHg

8. Evidence of myocardial injury in form of deranged cardiac enzymes

9. GCS of less than 11.

**Septic shock:**

Systemic inflammatory response syndrome (SIRS)\* plus evidence of infection plus cardiovascular dysfunction despite of adequate fluid resuscitation.

**\*SIRS criteria:**

 Two or more than two of the following one of which must be heart rate or temperature:

1. temperature >101.3F or , < 96.8 F;

2. tachycardia or bradycardia according to age;(above and below normal limit)

Normal values:

1-3 years 70-110/min:

4-6 years 65-110/min:

7-12 years 60-100/min

>12years 55-90/min

3. increased respiratory rate according to age;

4. abnormal leukocyte count < 4000 or >11000 , or more than 10 % band cells.

**Septic shock checklist:**

Vital signs; temperature , heart rate , respiratory rate ,blood pressure

Perfusion : capillary refil time more than 3 sec, skin mottling , Altered sensorium

**AT TRIAGE AREA:**

All pediatric patients will be assessed here for respiratory signs, symptoms, and fever. Children with no respiratory signs and symptoms or fever will be managed according to normal treatment protocols (and send to green zone-emergency unit/respective unit)

Children with respiratory signs and symptoms will be transferred to a specialized Team (Corona Combat Team) after giving surgical masks to the child and his/her parents to wear.

**Corona Combat Team:**

Member of this team will assess the child according to given protocol and divide the child’s condition in 3 categories:

1. Child having contact with a suspected/confirmed case of COVID-19 disease or came from abroad from a country with COVID-19 epidemics and with signs and symptoms suggestive of COVID-19 disease. (will go to RED ZONE);

2. Child having no contact with a suspected/confirmed case of COVID-19 disease or haven’t come from abroad from a country with COVID-19 epidemics but have signs and symptoms suggestive of COVID-19 disease. (will go to RED ZONE);

3. Child having contact with a suspected/confirmed case of COVID-19 disease or came from abroad from a country with COVID-19 epidemics with no signs and symptoms suggestive of COVID-19 disease presenting with some other medical or surgical problem. (will go to YELLOW ZONE).

**RED ZONE:**

Member of this zone will assess the child for vital parameters (pulse, temperature, respiratory rate, blood pressure, capillary refill time, and oxygen saturation) to classify the severity of the illness and will either send the patient home with proper instructions for home isolation or send the patient to Isolation unit for admission and investigations.

**INVESTIGATIONS:**

1. Nasopharyngeal and oropharyngeal swab;

2.Baseline investigations;

Full blood count,

LFTs, RFTs, RBS , PT/ APTT,

Serum lactate, ECG , G6PD, ABGs,

Serum procalcitonin, D-Dimers, CRP, ESR,

Chest X ray(In the early stages, the CXR may be normal and does not show ground glass lesions, but in severe cases bilateral lmultifocal consolidation and even progression to the white lung can be seen),

CT Chest (CT scan findings of COVID-19 pneumonia manifested as multifocal unilateral or bilateral ground glass opacity (GGO) to mixed GGO and consolidation mostly peripherally located, and crazy pavement appearance).

3.If there is strong clinical suspicion for COVID-19 but the first PCR is negative, continue isolation precautions and repeat nasopharyngeal PCR in 3 days.

**MANAGEMENT:**

**Management of mild/ moderate disease:**

**OUTPATIENT MANGEMENT:**

Home Care Recommendation for a child with Suspected or Confirmed 2019 novel Coronavirus (2019-nCoV):

**For a child:**

✓ keep him/her in a well-ventilated single room

✓ Limit him/her movement within the house

✓ Avoid shared spaces

✓ Use surgical mask at all times. If the mask gets wet or dirty with secretions, it must be changed immediately (older child)

✓ Cover him/her mouth with a tissue when coughing or sneezing and immediately throw the tissue (younger child)

✓ Keep him/her hands clean by using soap and water or an alcohol disinfectant

**What precautions do people should take who are caring a child with suspected or confirmed 2019 novel Coronavirus (2019-nCoV):**

✓only healthy people with no other health issues should take care of such child

✓ The caregiver should wear a surgical mask when in the same room with the child

✓ The masks should not be touched or handled during use

✓ Throw the mask away after use.

✓ Clean their hands using soap and water or an alcohol disinfectant after taking the mask off

**What precautions do the people take who live with a child with suspected or confirmed 2019 novel Coronavirus (2019-nCoV):**

✓ Avoid visitors while you have symptoms

✓ Household members should stay in a different room or if that is not possible, maintain a distance of at least 1 meter

✓Hand must be cleaned before and after preparing food, before eating, after using the toilet, and whenever hands look dirty.

**SYMPTOMATIC TREATMENT:**

1.Give antibiotics, if indicated

2.Suggest steam, antihistamines, plenty of fluids.

3.Acetaminophen may be used to reduce fever

4.Ask parents to bring the child if the child develops shortness of breath or worsening symptoms.

**INPATIENT MANAGEMENT**:

**TRANSPORTING & ALLOCATION OF ROOMS FOR COVID-19 PATIENTS:**

• Patients must NOT be transported to other departments unless absolutely necessary (e.g. for emergent, life-saving procedures or ICU)

• In the event of transfer, do the following:

a. Inform the receiving department over the phone with details of isolation precautions required;

 b. The patient must wear a surgical mask during transfer;

 c. Post appropriate isolation signs outside the patient’s room;

d. Healthcare staff do not need to wear PPE while transporting patients;

Once transferred, the patient should be moved directly to the intended room/procedure room etc.- patients must NOT be seated in the waiting area, Single rooms must be allocated while patients are under investigation for COVID-19.

 Patients with confirmed COVID-19 may be cohorted i.e. placed in the same room depending upon resources with 1 m distance between suspected patients;

**IMMEDIATE IMPLEMENTATION OF APPROPRIATE INFECTION PREVENTION AND CONTROL (IPC) MEASURES:**

• Standard precautions should always be applied in all areas of health care facilities

• Standard precautions include hand hygiene and the use of personal protective equipment (PPE) when in indirect and direct contact with patients’ blood, body fluids, secretions (including respiratory secretions) and non-intact skin. Standard precautions also include prevention of needle-stick or sharps injury; safe

•Waste management; cleaning and disinfection of equipment; and cleaning of the environment.

**Apply droplet precautions:**

Droplet precautions prevent large droplet transmission of respiratory viruses. Use a medical mask if working within 1 m of the patient.

When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use eye protection (face mask & goggles), because sprays of secretions may occur.

Limit patient movement within the institution and ensure that patients wear medical masks when outside their rooms.

**Apply contact precautions:**

 Contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces).

Use PPE (medical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving and practice hand hygiene following PPE removal.

If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs, pulse oximeters and thermometers).

 If equipment needs to be shared among patients, clean and disinfect between each patient use.

 Ensure that health care workers refrain from touching their eyes, nose and mouth with potentially contaminated gloved or ungloved hands. Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). Avoid medically unnecessary movement of patients or transport. Perform hand hygiene.

**Apply airborne precautions:**

When performing an aerosol generating procedure ensure that health care workers performing aerosol-generating procedures (e.g. open suctioning of respiratory tract, intubation, bronchoscopy, cardiopulmonary resuscitation) use the appropriate PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection).

Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures. Avoid the presence of unnecessary individuals.

Observe STRICT hand hygiene.

Avoid touching eyes or the mask.

**MANAGEMENT OF SEVERE DISEASE:**

**BASIC STEPS:**

Start patient on vital monitoring on arrival;

**O2 inhalation** through nasal prongs or face masks targeting Spo2 of 93%;

**Fluid management:**

Use conservative fluid management (2/3rd of maintenance in patients with severe acute respiratory infection) when there is no evidence of shock.

**Antibiotics:**

All severe pneumonia patient shall be started on Meropenem (i.v 40mg/kg/dose TDS ) and Vancomycin ( i.v 20mg/kg/dose TDS ) The decision to continue these antibiotics has to be reviewed on the availability of procalcitonin level after 48 hours.

**Fever:**

Paracetamol shall be used. Avoid NSAIDs. (If someone is already on aspirin / NSAIDs for compelling indications, they shall continue and to be discussed with the consultant).

**Wheeze:**

Use Salbutamol inhaler via spacer as far as possible

**Systemic Corticosteroids:**

Do not routinely give systemic corticosteroids for treatment of viral pneumonia or severe acute respiratory infection outside of clinical trials, unless they are indicated for another reason.

**SUPPORTIVE CARE** will include:

Bed rest and ensuring sufficient caloric and water intake;

Monitoring vital signs and oxygen saturation every 2hourly;

Keeping respiratory tract unobstructed and inhaling oxygen when necessary;

**SPECIFIC THERAPY:**

It should be noted that due to insufficient evidence for COVID-19 treatment in children, recommended treatment protocol is not based on strong clinical evidence, and treatment may be changed if further studies are undertaken. The following specific therapies have been adapted from **‘An Algorithmic Approach to Diagnosis and Treatment of Coronavirus Disease 2019 (COVID-19) in Children: Iranian Expert’s Consensus Statement’ and published in Arch Pediatr Infect Dis. 2020 April; 8(2):e102400.**

Treatment for patients who admitted in intensive care unit is included combined antiviral agents and immunomodulators **[oseltamivir + hydroxychloroquine +Kaletra (lopinavir + ritonavir)] ± ribavirin** and if necessary antibiotics according to the patient’s condition.

Recommended drug dosages are as follow:

1**. Oseltamivir**

- Preterm infants consult with a Pediatric Infectious Diseases Specialist.

- Term infants 0 - 12 month, 3 mg/kg/dose, twice daily

- Children\_ 12 month by body weight

≤15 kg: 30 mg, twice daily

> 15 - 23 kg: 45 mg, twice daily

> 23 - 40 kg: 60 mg, twice daily

> 40 kg: 75 mg, twice daily

Adults 75 mg, twice daily

For at least 5 days.

2. **Hydroxychloroquine**

Infants and children: IV, hydroxychloroquine sulfate: 3- 5 mg/kg/day (max dose 400 mg), BID For 5 days.

But look for QT interval prolongation, torsade’s de pointes, and ventricular arrhythmias reported with Chloroquine specially in concurrent use with Kaletra; risk is greater if chloroquine is administered at high doses; use with caution in patients with cardiac disease, a history of ventricular arrhythmias, uncorrected hypokalemia and/or hypomagnesemia, or bradycardia (< 50 bpm), and it can also be used as a single dose in high risk patients.

ECG prior to starting chloroquine and after onset of drug, cardiac monitoring is recommended.

3**. Kaletra (Lopinavir + Ritonavir)**

Based on surface area:

14 days to 12 months: 16 mg/kg/dose or 300mg/m2/dose (lopinavir component) orally twice a day

12 months to 18 years: Based on BSA: 230 mg/m2/dose (lopinavir component) orally twice a day (maximum dose: lopinavir 400 mg), ritonavir 100 mg/dose, orally twice a day.

Based on weight:

Less than 15 kg: 12 mg/kg/dose (lopinavir component) orally twice a day

15 to 40 kg: 10 mg/kg/dose (lopinavir component) orally twice a day

Greater than 40 kg/ dose: Lopinavir/ ritonavir2x200/50 mg tablet, orally twice a day

For 5 - 14 days, depends on physician’s judgment.

Notice: Kaletra should not be administered to neonates before gestational age of 42 weeks and postnatal age of at least 14 days.

4. **Ribavirin (Oral)**

For children over 3 years old:

< 47 kg: 15 mg/kg/day-BID

47 - 59: 400 mg-BID

60 - 73: 400 mg- in the morning, 600 mg- in the evening

> 73: 600 mg-BID

For up to 14 days, depends on patient’s response.

Closely monitor patients with severe acute respiratory infection for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis. Apply supportive care interventions immediately.

Understand the child’s co-morbid condition(s) to tailor the management of critical illness and appreciate the prognosis.

**MANAGEMENT OF SEPTIC SHOCK**

**MONITOR VITALS**

Do vital monitoring 1 hourly

**FLUID RESUSCITATION**

Guidelines recommend a 20 ml/kg to 60ml/kg intravenous bolus of a crystalloid solution (either 0.9% normal saline or Lactated Ringer’s (LR)) over 30min in above 1 year old and over 1 hour in patient below 1 year old.

 If intravenous access cannot be established, intraosseous access should be considered if appropriate expertise to obtain central venous access is not immediately available.

**Norepinephrine** is considered first-line ionotropic support.

Dose: infusion 0.01-3.3mcg/kg/min;

Because of the risk of tachyarrhythmia, reserve **Dopamine** for selected patients with low risk of tachyarrhythmia or those with bradycardia.

Dose infusion 5-20 mcg/kg/min.

**Monitoring**

 After each fluid bolus check heart rate, CRT, Peripheral pulses, Skin Temperature, mental status, GCS, urine output.

**Fluid Overload**

Resuscitation may lead to volume overload, including respiratory failure, particularly with ARDS.

If there is no response to fluid loading or signs of volume overload appear (e.g. jugular venous distension, crackles on lung auscultation, hepatomegaly, worsening respiratory distress, pulmonary edema on imaging), then reduce or discontinue fluid administration.

**PREVENTION OF COMPLICATIONS**

Prevent bed sores by changing position of child and using air mattress;

Give early enteral nutrition;

Administer H2 blockers or PPI for prevention of GI bleeding.

**Management of ARDS:**

**O2inhalation:**

Give O2 inhalation through wide bore nasal prongs or face mask to attain SpO2 of 92%.

Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy and prepare to provide advanced oxygen/ventilatory support.

The decision to intubate and ventilate will be individualized on case to case basis, depending upon the co-morbidities, patient age, prior functional status and availability of resources.

Mechanical Ventilation will be considered if SpO2 remains < 92% in spite of 6-8 L/min supplemental O2 via nasal prongs or face mask.

**MECHANICAL VENTILATION:**

**LUNG PROTECTIVE VENTILATION:**

**Low tidal volume**3-6ml/kg if poor compliance; 5-8ml/kg if preserved compliance;

**Peak plateau** less than or equal to 28cm H2O;

**PEEP** more than 10 cm H2O;

**Permissive hypercapnia**; PaCO2 should not exceed 60mmHg;

**Ph** should be maintained in the range of 7.15 – 7.30.

**Fluid management:**

Conservative fluid management is recommended in patient of ARDS .

**Sedation:**

Sedation is given to ensure patient safety from ventilator equipment induced trauma.

Providing analgesia and anxiolysis help to maintain the child in a calm but responsive state.

**Infusion midazolam:**

 Dose: iv maintenance 20-100 mcg/kg/hour with loading dose of 10-50 mcg/kg stat.

**Prone Position**

Prone position help in improving oxygenation and outcome in patients of ARDS, recommended time is maximum 16 hours in 24 hours.

**Neuromuscular Blockade**

Consider NMB (cistricurium ) to achieve peak plateau of above mentioned range.

Dose of **cistricurium** .0005- 0.01mg/kg/min iv in 24 hours.

**DECISION OF END OF LIFE CARE**

These decisions shall be individualized on case to case basis, keeping in view the advice of hospital ethical committee on recommendations of multidisciplinary team taking care of these patients

**DISCHARGE CRITERIA**

The patient may be discharged if he/she meets the following criteria:

 At least 3 days (72 hours) have passed since recovery defined as resolution of fever

without the use of fever-reducing medications;

Improvement in respiratory symptoms (e.g., cough, shortness of breath);

 At least 7 days have passed since symptoms first appeared; AND

negative nasopharyngeal swabs 24 hours apart.