

Clinical Management Protocol for Seasonal Influenza

1. Epidemiology

1.1 The agent

Influenza viruses belong to Orthomyxoviridae family of viruses. Its nucleic acid consists of single stranded RNA. There are 3 Influenza virus types, namely Types A, B, C. Types A and B are important for humans. Type A viruses cause greatest morbidity and mortality. Seasonal Influenza is caused by a number of circulating Influenza viruses such as Influenza A HI N 1, H3N2, H2N2, Influenza B etc. The Pandemic Influenza A (H1N1) pdm 2009 virus that caused Pandemic [2009-2010] continues to circulate causing outbreaks of Seasonal Influenza in various parts of the country.

1.2 Host factors

Seasonal Influenza may affect all age groups; globally incidence is higher in young children and those above 65 years. Health workers and persons with co-morbid conditions (such as lung disease, heart disease, liver disease, kidney disease, blood disorders, Diabetes) and immuno-compromised persons are at higher risk. Influenza may have an aggressive course in extremes of age and in co-morbid conditions.

1.3 Environmental Factors

Monsoon is the usual seasonality for large parts of India. In north, north-west and Central India, the surge in cases usually occurs in winter months (January to March)

1.4 Mode of Transmission

The transmission is air borne from person-to-person, through large droplets generated by the act coughing and sneezing. These droplets when inhaled are highly contagious to susceptible persons.

There are other modes of transmission, including indirect contact by touching a contaminated object or surface (fomite transmission), close contact (including hand shaking)

1.5 Incubation period

Incubation period is 1- 4 days (typically 2-3 days). Viral shedding can begin before symptom onset and peaks on day 1 of the symptoms. Adults may continue to shed virus for 4-6 days, Children and Immuno suppressed/immune-compromised patients affected with influenza can shed for months.

1.6 Period of Communicability

From 1 day before to 7 days after the onset of symptoms. If illness persist for more than 7 days, chances of communicability may persist till resolution of illness. Children may spread the virus for a longer period.

2. Clinical features

2.1 Symptoms

The hallmark of influenza is the sudden, rapid onset of symptoms. Influenza symptoms may include fever, chills, body aches, sore throat, non-productive cough, runny nose and headache. Gastrointestinal symptoms and muscle inflammation occur more often in young children, and infants can present with a sepsis-like syndrome.

2.2 Physical findings

- Fever: rapid onset, peaking at 38.40⁰C (up to 41 ⁰C, especially in children), typically lasting 3 days (up to 4-8 days), gradually diminishing
- Face: flushed
- Skin: hot and moist
- Eyes: watery, reddened
- Nose: nasal discharge
- Ear: otitis
- Mucous membranes: hyperemic
- Cervical lymph nodes enlargement: (especially in children)

2.3 Course of Illness

Severity varies from afebrile symptoms mimicking common cold to severe prostration without major respiratory signs and symptoms, especially in the elderly. Fever and systemic symptoms typically last 3 days, occasionally 5-8 days, and gradually diminish. Cough and malaise may persist more than 2 weeks. Full recovery may take 1-2 weeks or longer, especially in the elderly.

2.4 Complications

In infants and children complications include sinus or ear infections, viral and bacterial pneumonia, bronchiolitis, croup, dehydration (with or without diarrhoea) febrile seizures, and worsening underlying chronic conditions. Immediate hospitalization, assessment and management may be required for exacerbation of chronic disease, severe dehydration, sepsis-like syndrome, respiratory complications (Bronchiolitis, Croup, Reactive airway disease, Pneumonia), Rhabdomyolysis, encephalopathy /encephalitis and cardiac complications such as Myocarditis and Pericarditis. Reye syndrome (with aspirin use), Toxic shock syndrome and Sudden death (may be due to cytokine dysregulation) have also been reported.

In adults and elderly, exacerbation of chronic illness [Cardiac (congestive cardiac failure, coronary artery disease); Chronic pulmonary disease (COPD), Metabolic disease (diabetes) etc] is the most common reason for hospitalization due to complications from influenza. Respiratory complications include Bronchitis, Sinusitis, Reactive airway disease and Pneumonia. There may be invasive bacterial co-infection (sepsis, pneumonia), mainly from Staphylococcus aureus [MRSA, MSSA], Streptococcus pneumoniae, Group A Streptococcus and Hemophilous influenza. In geriatric age group, viral pneumonia is common.

3. High Risk Groups

Infants, young children, pregnant women and elderly above the age of 65 are at higher risk of acquiring influenza.

Persons of any age with the following chronic conditions are at higher risk

- Chronic pulmonary or cardiovascular conditions
- Chronic neurological conditions that impair breathing or clearance of respiratory secretions
- Chronic metabolic diseases
- Renal dysfunction

- Hemoglobinopathies
- Immunosuppressed, immunocompromised
- Children 6 months -18 years on chronic aspirin therapy

4. Investigations

Routine investigations required for evaluation and management of a patient with symptoms as described above will be required. These may include haematological, biochemical, radiological and microbiological tests as necessary. Confirmation of seasonal influenza (including HI N 1) infection is through:

- Real time RTPCR or
- Isolation of the virus in culture or
- Four-fold rise in virus specific neutralizing antibodies.

For confirmation of diagnosis, clinical specimens such as nasopharyngeal swab, throat swab, nasal swab, wash or aspirate, and tracheal aspirate (for intubated patients) are to be obtained. The sample should be collected by a trained physician/microbiologist/technical or nursing staff, preferably before administration of the anti-viral drug. Keep specimens at 4⁰C in viral transport media until transported for testing. The samples should be transported to designated laboratories within 24 hours. If they cannot be transported then it needs to be stored at -70⁰ C. Paired blood samples at an interval of 14 days for serological testing may also be collected, if required.

5. Treatment

The guiding principles are:

- Early implementation of infection control precautions to minimize nosocomial/ household spread of disease
- Prompt treatment to prevent severe illness & death.
- Early identification and follow up of persons at risk.

5.1. Infrastructure / manpower / material support

- Isolation facilities: if dedicated isolation room is not available then patients can be cohorted in a well ventilated isolation ward with beds kept one metre apart.
- Manpower: Dedicated doctors, nurses and paramedical workers.
- Equipment: Portable X Ray machine, ventilators, large oxygen cylinders, pulse oxymeter and other supportive equipments
- Supplies: Adequate quantities of PPE, disinfectants and medications (Oseltamivir, antibiotics and other medicines)

5.2. Standard Operating Procedures

- Reinforce standard infection control precautions i.e. all those entering the room must use hand washing practices, high efficiency masks, gowns, goggles, gloves, cap and shoe cover.
- Restrict number of visitors and provide them with PPE.
- Provide antiviral prophylaxis to unprotected / unvaccinated / accidentally exposed health care personnel managing a case and ask them to monitor their own health twice a day.
- Dispose waste properly by placing it in sealed impermeable bags labelled as Bio-Hazard.

5.3 Oseltamivir Medication

- Oseltamivir is the recommended drug for treatment.
- Dose for treatment is as follows -

By Weight:

- For weight <15kg 30 mg BD for 5 days
- 15-23kg 45 mg BD for 5 days
- 24-<40kg 60 mg BD for 5 days
- >40kg 75 mg BD for 5 days

For infants:

- < 3 months 12 mg BD for 5 days
- 3-5 months 20 mg BD for 5 days
- 6-11 months 25 mg BD for 5 days

It is also available as syrup (12mg per ml)

If needed dose & duration can be modified as per clinical condition

5.3.1. Adverse reactions:

Oseltamivir is generally well tolerated, gastrointestinal side effects (transient nausea, vomiting) may increase with increasing doses, particularly above 300 mg/day. Occasionally it may cause bronchitis, insomnia and vertigo. Less commonly angina, pseudo membranous colitis and peritonsillar abscess have also been reported. There have been rare reports of anaphylaxis and skin rashes. In children, most frequently reported side effect is vomiting. Infrequently, abdominal pain, epistaxis, bronchitis, otitis media, dermatitis and conjunctivitis have also been observed. There is no recommendation for dose reduction in patients with hepatic disease. Though rare reporting of fatal neuro-psychiatric illness in children and adolescents has been linked to oseltamivir, there is no scientific evidence of a causal relationship.

5.4 Supportive therapy

- IV Fluids.
- Parenteral nutrition.
- Oxygen therapy/ ventilatory support.
- Antibiotics for secondary infection.
- Vasopressors for shock.
- Paracetamol or ibuprofen is prescribed for fever, myalgia and headache. Patient is advised to drink plenty of fluids. Smokers should avoid smoking. For sore throat, short course of topical decongestants, saline nasal drops, throat lozenges and steam inhalation may be beneficial.
- Salicylate / aspirin is strictly contra-indicated in any influenza patient due to its potential to cause Reye's syndrome.
- The suspected cases would be constantly monitored for clinical / radiological evidence of lower respiratory tract infection and for hypoxia (respiratory rate, oxygen saturation, level of consciousness).
- Patients with signs of tachypnea, dyspnea, respiratory distress and oxygen saturation less than 90 per cent should be supplemented with oxygen therapy. Types of oxygen devices depending on the severity of hypoxic conditions, can be started from oxygen cannula, simple mask, partial re-breathing mask (mask with reservoir bag) and non re-breathing mask. In children, oxygen hood or head boxes can be used.
- Patients with severe pneumonia and acute respiratory failure ($SpO_2 < 90\%$ and $PaO_2 < 60$ mmHg with oxygen therapy) must be supported with mechanical ventilation. Invasive mechanical ventilation is preferred choice. Non invasive ventilation is an option when mechanical ventilation is not available. To reduce spread of infectious aerosols, use of HEPA filters on expiratory ports of the ventilator circuit / high flow oxygen masks is recommended.
- Maintain airway, breathing and circulation (ABC);
- Maintain hydration, electrolyte balance and nutrition.
- If the laboratory reports are negative, the patient would be discharged after giving full course of oseltamivir. Even if the test results are negative, all cases with strong epidemiological criteria need to be followed up.
- Immunomodulating drugs have not been found to be beneficial in treatment of ARDS or sepsis associated multi organ failure. High dose corticosteroids in particular have no evidence of benefit and there is potential for harm. Low dose corticosteroids (Hydrocortisone 200-400 mg/ day) may be useful in persisting septic shock ($SBP < 90$).

- Suspected case not having pneumonia do not require antibiotic therapy. Antibacterial agents should be administered, if required, as per locally accepted clinical practice guidelines. Patient on mechanical ventilation should be administered antibiotics prophylactically to prevent hospital associated infections.

5.5 Protocol for the ventilator management of patient with ALI/ARDS following Seasonal Influenza:

Indications for Mechanical Ventilation:

- Severe Respiratory Failure
- Failure to achieve oxygen saturation of $>$ or equal to 90% (or pO_2 of $>$ or equal to 60 mm Hg) on an $FIO_2 < 0.6$.

Ventilator Settings:

- Pressure pre-set (controlled)
- Low tidal volume ventilator support
- Tidal volume — 6 ml/kg ideal body weight (Respiratory rate to a maximum of 30-35 per minute).
- Open lung strategy of ventilation with PEEP titration to keep the lung recruited to achieve an FIO_2 of < 0.5 and a saturation of $> 90\%$ or a PaO_2 of > 60 mmHg
- Plateau (Pause) pressure not to exceed of $> 30-35$ mmHg.
- Alternative modes of ventilation APRV (Airway Pressure Release Ventilation), IRV (Inverse Ratio Ventilation) in patients with persistent Hypoxemia (SpO_2 of $< 88-90\%$ with high PEEP & $FIO_2 > 0.8$).
- Rescue therapy — recruitment manoeuvres, Sedation, Neuromuscular Blockage & Prone Ventilations can be considered if above oxygen goals are not met.

6. Discharge Policy

- Adult patients should be discharged 7 days after symptoms have subsided.
- Children should be discharged 14 days after symptoms have subsided.