GOVERNMENT OF KERALA

Abstract

Health & Family Welfare Department - Management of increasing Fever Cases - Kerala State Treatment Guidelines for ILI & SARI cases in the context of co-circulation of SARS-COV-2 and Influenza virus - Orders issued.

HEALTH & FAMILY WELFARE (F) DEPARTMENT

G.O.(Rt)No.1489/2023/H&FWD Dated,Thiruvananthapuram, 23-06-2023

Read Letter No. DHS/11700/2023-ADHS(PH) dated 20.06.2023 from the Director of Health Services

ORDER

In Kerala at present there is co-circulation of influenza and SARS-CoV-2 virus. In order to optimize targeted treatment for patients presentation with ILI symptoms, Government are pleased to issue the *'Kerala State Treatment Guidelines for influenza like illness [ILI] and severe acute respiratory infection [SARI] in the context of co-circulation of SARS-COV-2 and Influenza*' incorporating Clinical presentation of influenza vs Covid-19, Antiviral Treatment of Influenza, ABC guidelines for influenza, Kerala State ABC guidelines for Covid-19, Monitoring for red-flag signs in patients with ILI/ARI, Home Care of ILI Cat B1 and B2 patients etc; annexed to this order.

(By order of the Governor)
A P M MOHAMMED HANISH
PRINCIPAL SECRETARY

To:
The State Mission Director - National Health Mission, Thiruvananthapuram.
The Managing Director, Kerala Medical Services Corporation Ltd, Thiruvananthapuram.
The Director of Health Services, Thiruvananthapuram.
The Director of Medical Education, Thiruvananthapuram.
The Director, Public Health Lab, Thiruvananthapuram.

All District Medical Officers (Health)
All District Surveillance Officers
All District Programme Managers
Principal Accountant General (A&E/Audit) Kerala.
Information & Public Relations (Web & New Media) Department
Stock File/ Office Copy (to file F2/208/2023-HEALTH)

Forwarded /By order

Section Officer

Copy to:
Private Secretary to the Hon'ble Minister (H, W&CD)
PS to Principal Secretary (H&FWD)
PA to Secretary (H&FWD - ME)

ANNEXURE

KERALA STATE TREATMENT GUIDELINES FOR INFLUENZA LIKE ILLNESS [ILI] AND SEVERE ACUTE RESPIRATORY INFECTION [SARI] IN THE CONTEXT OF CO-CIRCULATION OF SARS-CoV-2 AND INFLUENZA

The WHO global influenza surveillance standards define the surveillance case definitions for influenza-like illness (ILI) and severe acute respiratory infections (SARI).

Key messages when using the case definitions:

- Influenza infection causes a clinical syndrome not easily distinguished from other respiratory infections.
- The case definitions for ILI and SARI are not necessarily intended to capture all cases but to describe trends over time.
- Using one common case definition globally will allow national health authorities to interpret their data in an international context.

ILI case definition

Acute respiratory infection with:

- measured fever of ≥38 °C
- and cough;
- with onset within the last 10 days.

SARI case definition

Acute respiratory infection with:

- history of fever or measured fever of ≥38 °C
- and cough;
- with onset within the last 10 days;
- and requires hospitalization

ARI

- *at least one of cough, sore throat, shortness of breath, runny nose with or without fever AND a clinician's judgement that the illness is due to an infection*

Table 2: Summary of performance characteristics of ILI, ARI and SARI case definitions for influenza and COVID-19

	Influenza		COVID-19 (2020 assessment)		COVID-19 (2021 assessment)	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
ILI	45 – 55%	85 – 95%	20 – 51%	60 – 90%	20 – 55%	38 – 90%
ARI	94%	27%	86%	23%	60 – 96%	10 – 45%
SARI	45 – 70%	45 – 70%	40 – 55%	33 – 60%	33 – 62%	31 – 77%

GISRS [Global Influenza Surveillance and Response system] uses existing WHO ILI and SARI case definitions in their sentinel surveillance for influenza and COVID-19. These case definitions are not intended to capture all cases of influenza or COVID-19. Regions with high testing capacities may continue to use the more sensitive but less specific ARI case definition.

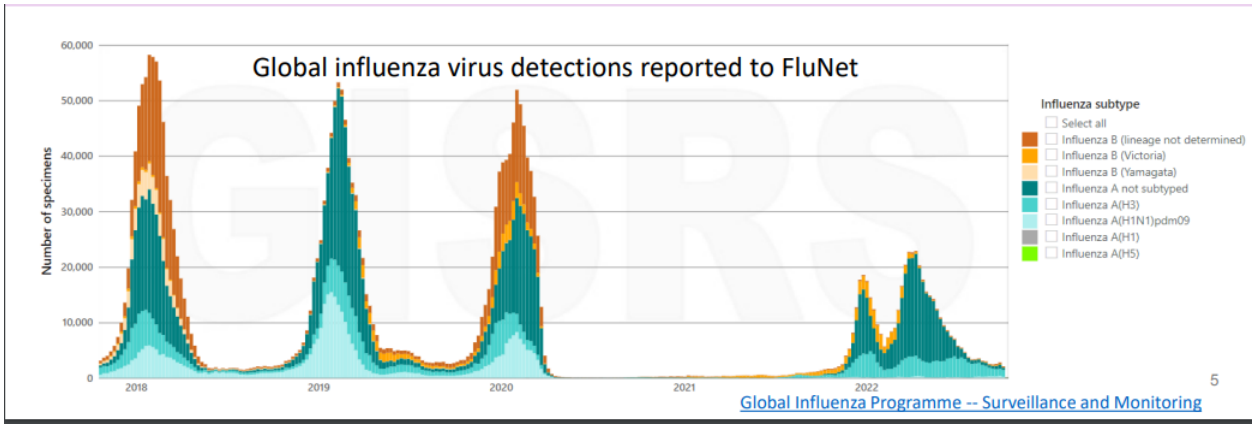
GLOBAL SCENARIO

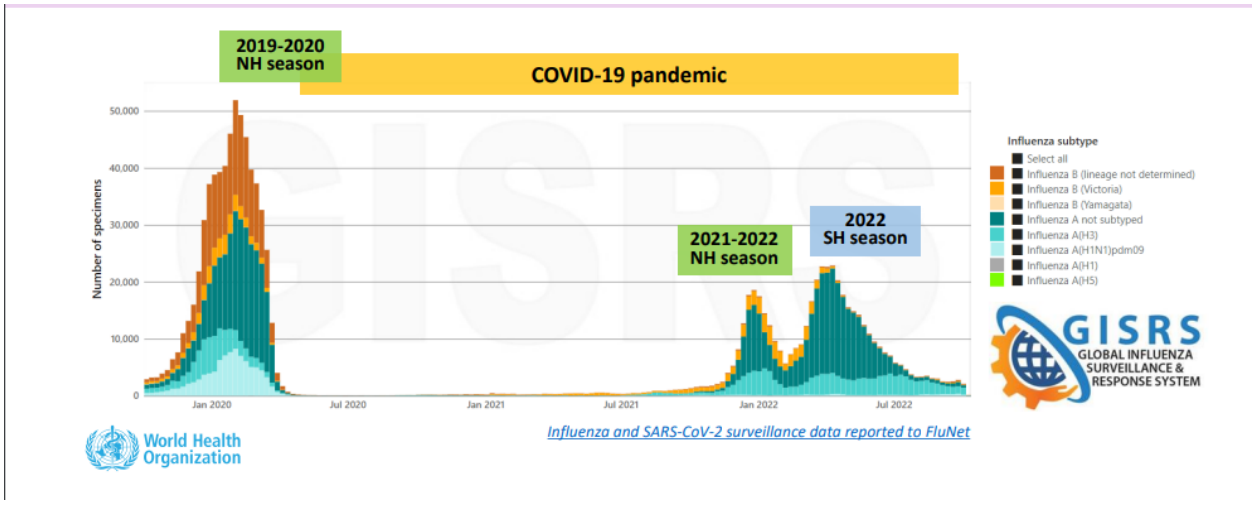
In the past decade, seasonal influenza has caused severe illness and death

• Before the current COVID 19 pandemic, seasonal influenza was estimated to have infected 1 billion people a year globally, caused severe disease in 3-5 million people, and 290,000- 650,000 influenza related respiratory deaths

• It burdens health systems in low and middle income countries which can least afford them

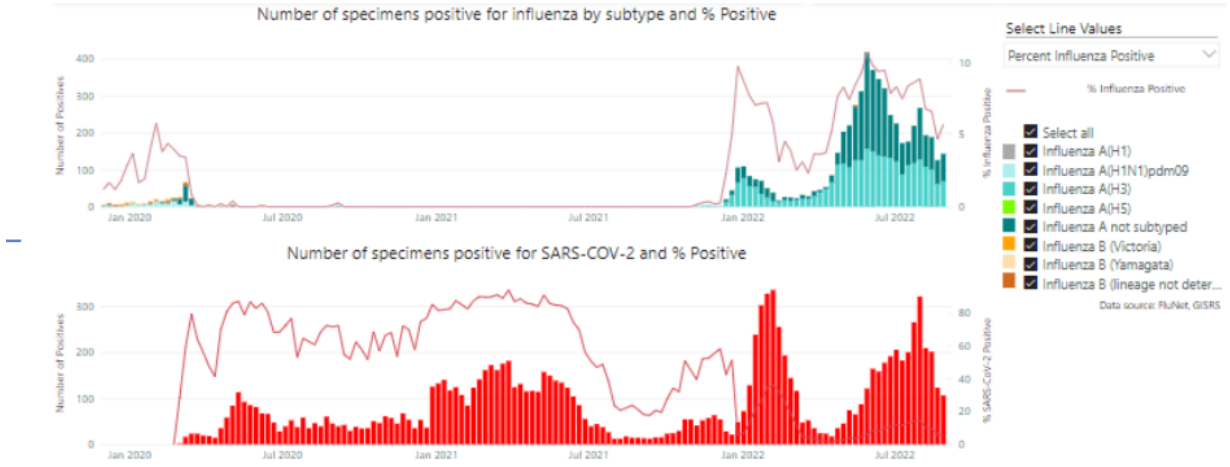
• Seasonal influenza also leads to high economic burden, due to direct and indirect medical costs, and loss of income and productivity due to illness

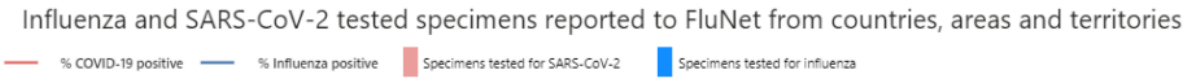




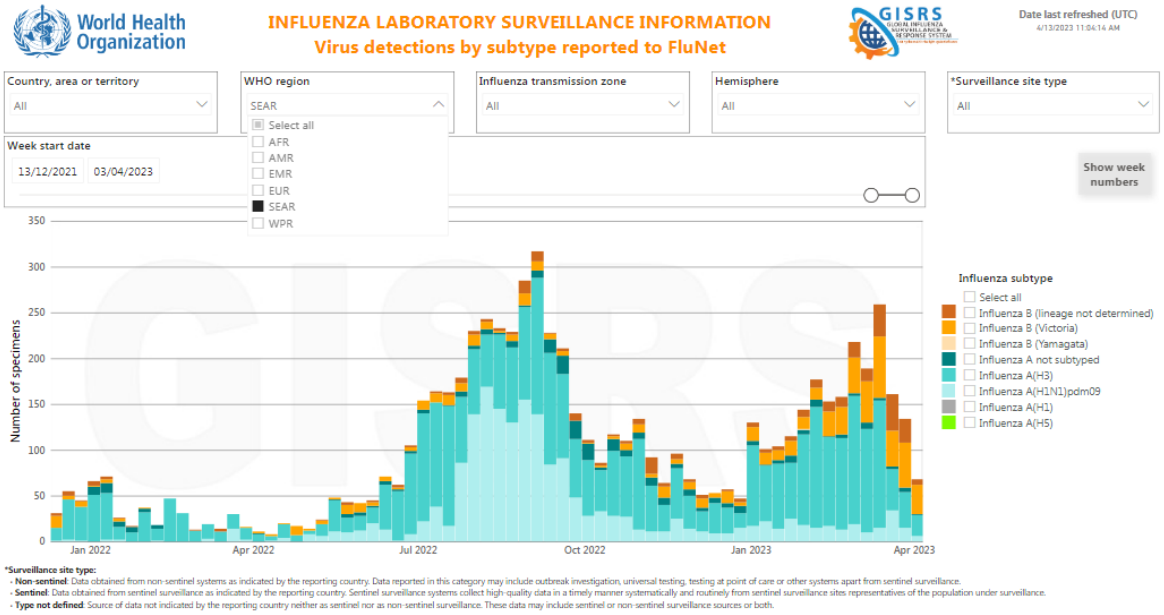
The above graphs clearly depicts the success of non-pharmacological interventions [NPI] like physical distancing, universal masking, hand hygiene, school closures and lockdowns in preventing respiratory infections like seasonal influenza during from middle of 2020 to 2021.However once NPI were lifted a surge in respiratory viral infections like seasonal influenza , RSV [respiratory synctitial virus] ,Adeno virus etc have been witnessed across the world during 2022.Influenza activity globally has reached pre-

COVID-19 levels or even higher and is now co-circulating with SARS-CoV-2 as depicted in the graph below. Based on clinical features alone it is very difficult to distinguish between Influenza and COVID-19.





National Influenza Centres (NICs) and other national influenza laboratories from 115 countries, areas or territories reported data to FluNet [WHO-GISRS] for the time period from 06 March 2023 to 19 March 2023* . The WHO GISRS laboratories tested more than 349 552 specimens during that time period. 46 911 were positive for influenza viruses, of which 34 346 (73.22%) were typed as influenza A and 12 565 (26.78%) as influenza B. Of the sub-typed influenza A viruses, 20 264 (70.30%) were influenza A(H1N1)pdm09 and 8560 (29.70%) were influenza A(H3N2). Of the characterized B viruses, 100% (1479) belonged to the B/Victoria lineage. But during the same time period in South East Asia Region,H3N2 is more prevalent than H1N1.



NATIONAL SCENARIO

Influenza data from ICMR network of laboratories

In India, an integrated surveillance of Influenza like Illness (ILI) and Severe Acute Respiratory Illness (SARI) for the detection of human influenza virus and SARS-COV-2 virus is ongoing through structured ILI/SARI surveillance network of 28 sites. The surveillance network is comprised of 27 DHR-ICMR's Virus Research & Diagnostic Laboratories and country's National Influenza Centre (WHO-NIC) housed at ICMR-National Institute of Virology Pune, also a WHO Collaborating Centre for Global Influenza Surveillance & Response System (GISRS).

During the period of first 9 weeks (January 2nd to March 5th) of 2023, the surveillance network has monitored the human influenza virus and SARS-CoV-2 infection in SARI and ILI cases. The influenza typing results are summarized below:

Week	Week 1	Week 2	Week 3	Week 4	Week 5	W
Influenza A H1N1pdm09	8	8	4	6	5	
Influenza A H3N2	46	57	44	42	47	
Influenza B Victoria	4	11	6	4	12	

It can be seen that Influenza H3N2 is the predominant sub-type among the samples testing positive for influenza, since the beginning of this year. Currently there is a surge in COVID 19 cases across the country driven by recombinant variant XBB.1.16.

THE KERALA SCENARIO

Just like in rest of India, in Kerala also at present there is co-circulation of Influenza virus and SARS-CoV-2 virus. Among Influenza infections, majority of cases are due to Influenza A especially H1N1 and H3N2. As the symptomatology of both Influenza and COVID 19 are the same, a practical algorithmic approach to differentiate between the two is essential at primary and secondary care level so as to optimize targeted treatment for patients presenting with ILI symptoms.

Clinical Presentation of Influenza Versus COVID-19

The signs and symptoms of uncomplicated, clinically mild influenza overlap with those of mild COVID-19. Ageusia and anosmia can occur with both diseases, but these symptoms are more common with COVID-19 than with influenza. Fever is not always present in patients with either disease, particularly in young infants, adults of advanced age, and patients who are immunosuppressed. Complications of influenza and COVID-19 can be similar, but the onset of influenza complications and severe disease typically occurs within a week of illness onset, whereas the onset of severe COVID-19 usually occurs in the second week of illness.

Because of the overlap in signs and symptoms, when SARS-CoV-2 and influenza viruses are co-circulating, diagnostic testing for both viruses is needed to distinguish between SARS-CoV-2 and influenza virus and to identify co-infection in people with an acute respiratory illness. Co-infection with influenza virus and SARS-CoV-2 has been described in case reports and case series, but it is uncommon. Observational studies have reported greater disease severity in patients with influenza virus and SARS-CoV-2 co-infection than in patients with SARS-CoV-2 infection alone

Diagnosis of Influenza and COVID-19 When Influenza Viruses and SARS-CoV-2 Are Co-circulating

- Only testing can distinguish between SARS-CoV-2 and influenza virus infections and identify SARS-CoV-2 and influenza virus co-infection.
- Influenza testing in addition to SARS-CoV-2 testing in outpatients with acute respiratory illness should be considered if the results will change the clinical management strategy for the patient .As per current ABC criteria for Influenza, testing is recommended only in cases of ILI with unusual clinical presentations, failure to respond to oseltamivir therapy and as part of cluster/outbreak investigation. So in patients with ILI, if COVID testing is

negative oseltamivir should be initiated if patients are categorized as B1/B2 or C based on clinical risk stratification.

- Testing for both viruses should be performed in all patients hospitalized following acute respiratory illness .
- Clinicians should consider testing patients for other pathogens based on the specific clinical circumstances. Additional testing for bacterial pathogens is important for patients with influenza and clinical signs that suggest bacterial superinfections, especially for patients who are immunocompromised or intubated.
- In all RAT negative ILI/SARI cases who require hospitalization, molecular diagnosis [PCR] for both SARS-CoV-2 and Influenza should be performed either simultaneously or sequentially.

Antiviral Treatment of Influenza When Influenza Viruses and SARS-CoV-2 Are Co-circulating

- Hospitalized patients who are suspected of having either influenza or COVID-19 should be started on empiric treatment for influenza with **oseltamivir** as soon as possible and without waiting for influenza test results .Oseltamivir has no activity against SARS-CoV-2.
- All pregnant ladies with ILI/ARI symptoms should be initiated on oseltamivir.
- Antiviral treatment for influenza can be stopped when influenza has been ruled out by the results of a nucleic acid detection assay. The assay should be performed on upper respiratory tract specimens for nonintubated patients and on both upper and lower respiratory tract specimens for intubated patients.
- When the result of an influenza nucleic acid detection assay from an upper respiratory tract specimen is negative in a patient who is receiving antiviral treatment for influenza:

In a patient who is not intubated*:* Antiviral treatment for influenza can be stopped.

In a patient who is intubated*:* Antiviral treatment for influenza should be continued, and if a lower respiratory tract specimen (e.g., endotracheal aspirate) can be safely obtained, it should be tested using an influenza nucleic acid detection assay. If the lower respiratory tract specimen is also negative, antiviral treatment for influenza can be stopped.

ABC Guidelines for Influenza

CATEGORIZATION OF PATIENTS				
Sr	**Category**	**Chief Symptoms**	**Swab collection**	**Treatment**
1	A	Mild fever(<38C), Cough, sore throat ,myalgia, headache, diarrhea / vomiting	Not recommended	No Oseltamivir, Symptomatic treatment, Review after 24 hours, Home isolation
2	B1	In addition to above symptoms Fever > 38C, severe sore throat.	Not recommended	Oseltamivir needed
	B2	CAT A Symptoms in those with comorbidities	Not recommended	Oseltamivir needed
3	C	In addition to above symptoms breathlessness, chest pain, haemoptysis, hypotension, bluish discoloration of nails and in children irritation and drowsiness	Recommended	Oseltamivir and hospitalization

KERALA STATE ABC GUIDELINES FOR COVID 19

A	Mild sore throat / cough / rhinitis /diarrhea/anosmia
B	Fever and/or severe sore throat / cough /diarrhea/anosmia OR Category-A with any one of • Lung/ heart / liver/ kidney / neurological disease/ Hypertension / haematological disorders/ uncontrolled diabetes/ cancer /HIV-AIDS/ Cardiovascular disease • On long term steroids /immunosuppressive drugs. • Pregnant woman • Age –more than 60 years
C	• Breathlessness, chest pain, drowsiness, fall in blood pressure, haemoptysis, cyanosis [red flag signs] • Children with ILI (influenza like illness) with *red flag signs* (Somnolence, high/persistent fever, inability to feed well, convulsions, dyspnoea /respiratory distress, etc) • Worsening of underlying chronic conditions

***Categorization should be reassessed every 24-48 hours for Category A & B**

COMBINED ABC APPROACH TO ILI/ARI AND SARI IN CONTEXT OF CO-CIRCULATION OF SARS-CoV-2 AND COVID 19

When SARS-CoV-2 and influenza are co-circulating, an algorithmic approach is needed to optimize the testing and treatment strategies .This can be achieved by fusing the existing ABC guidelines for Influenza and COVID 19.

COMBINED ABC APPROACH TO ILI IN THE CONTEXT OF CO-CIRCULATION OF SARS-CoV-2 AND INFLUENZA

Sr No	Category	Chief Symptoms	Swab Collection	Treatment
1	A	Mild Fever(<38 C), Cough, Throat irritation, bodyache, headache, rhinitis,diarrhoea / vomiting	Test for COVID 19	Monitor for red flag signs and reclassify every 24-48 hrs based on symptoms.Supportive treatment.
2	B B1	In addition to above symptoms Fever >38 C, severe sore throat, , cough.	Test for COVID 19	Monitor for red flag signs+ Oseltamivir if COVID test is negative.
	B2	Cat A in those with co-morbidities .	Test for COVID 19	.Monitor for red flag signs+ Oseltamivir if COVID test is negative. For highest risk category like cancer chemotherapy with B1 symptoms, early remdesivir may be considered if COVID positive.
3	**C**	In addition to above symptoms-breathlessness, Chest pain, hemoptysis, hypotension, bluish discoloration of nails, and in children irritation & drowsiness.	Test for COVID 19 and influenza.	Hospitalization.+oseltamivir.If COVID positive, treatment as per Kerala State COVID 19 treatment Guidelines.

MONITORING FOR REDFLAG SIGNS IN PATIENTS WITH ILI/ARI

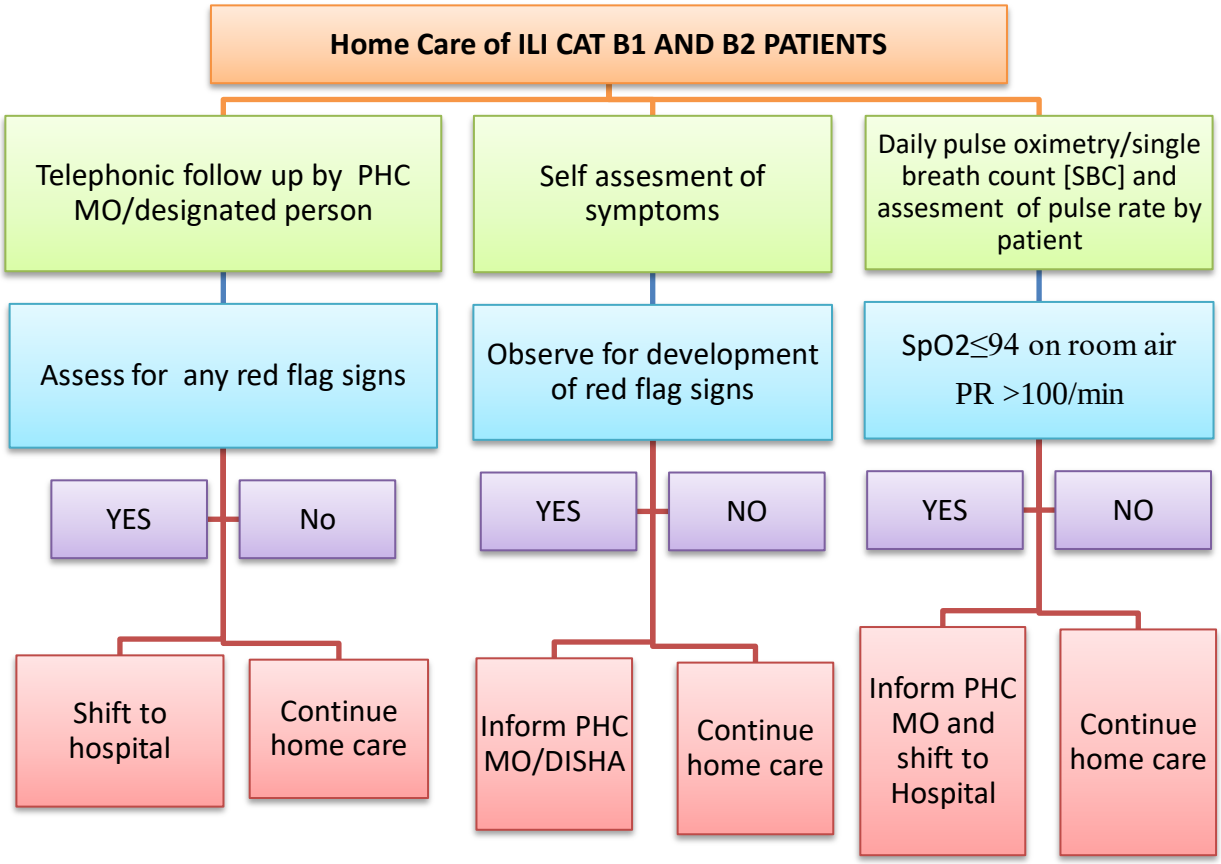
Redflag signs which indicate organ involvement and necessitate hospital admission are the same for all ILIs including COVID-19, Influenza, Respiratory synctitial virus, adenovirus etc. So any patient with ILI or fever should daily monitor for development of red flag signs and should contact health authorities in case of development of the same. In patients with co-morbidities, elderly and children below 5 yrs, monitoring for redflag signs is extremely important as they may rapidly deteriorate to severe disease.

- Breathlessness, chest pain, drowsiness, fall in blood pressure, haemoptysis, cyanosis [red flag signs]
- Children with ILI (influenza like illness) with *red flag signs* (Somnolence, high/persistent fever, inability to feed well, convulsions, dyspnoea /respiratory distress, etc)
- Worsening of underlying chronic conditions

Highest-risk individuals at risk of disease progression

- Body mass index (BMI) ≥35
- Chronic kidney disease stage with eGFR<60ml/min especially in those on MHD.
- Diabetes mellitus [HBA1C >10] or diabetes with end organ damage.
- Chronic liver disease
- Immunocompromising conditions.
- Currently receiving immunosuppressive treatment
- Age ≥65 years
- Cardiovascular disease
- Chronic respiratory diseases.
- Malignancies on chemotherapy
- Sickle cell disease
- Congenital or acquired heart disease
- Neurodevelopmental disorders [eg cerebral palsy]
- Unvaccinated with any co-morbidity

Those with high risk factors should wear masks always [mandatory] and should try to avoid 3C settings like closed spaces , congested spaces and close contact settings. Other family members of those with high risk factors also should wear masks always to minimize risk of transmission to vulnerable family members. Maintaining optimal glycemic status, controlling hypertension and body weight will help in preventing complications even if infected. Pre-cautionary dose of COVID19 vaccine and annual influenza vaccine can help prevent progression to severe disease in high risk groups.



- If pulse oximeter is not available, a single breath holding test [SBC] may be done. [Patient has to take a full but not too deep breath and hold it as long as possible].Based on duration of breath holding, patients are categorized into
  >25 seconds -Normal cardiopulmonary reserve
  15 to 25 seconds-Limited cardiopulmonary reserve
  <15 seconds –Very poor cardiopulmonary reserve

CHECKLIST FOR SELF REPORTING FOR CAT A ILI PATIENTS

High Fever	Yes	No
Altered sensorium	Yes	No
Breathlessness	Yes	No
Chest pain	Yes	No
Drowsiness	Yes	No
Haemoptysis	Yes	No
Excessive fatiguability	Yes	No
Syncope	Yes	No
Palpitation	Yes	No

Pulse rate > 100/Min	Yes	No
SpO2 ≤ 94%	Yes	No
SBC< 25 sec	Yes	No

CHECK LIST FOR TELEPHONIC MONITORING AND SELF MONITORING OF CAT B1 AND B2 ILI PATIENTS

Fever	Yes	No
Altered sensorium	Yes	No
Breathlessness	Yes	No
Chest pain	Yes	No
Drowsiness	Yes	No
Haemoptysis	Yes	No
Excessive fatiguability	Yes	No
Syncope	Yes	No
Palpitation	Yes	No
Pulse rate > 100/Min	Yes	No
SpO2 ≤ 94%	Yes	No
SBC<25 sec	Yes	No

GUIDELINES TO PREVENT DEVELOPMENT OF COVID-19 /INFLUENZA CLUSTERS INSIDE HOSPITALS

- All hospitalised patients with ILI/ARI/SARI symptoms should be tested for both COVID19 and Influenza. If RAT is negative, PCR must be performed.
- All COVID-19/Influenza positive patients must be isolated in designated areas.
- All patients, bystanders and health care workers must wear mask at all points of time. Health care workers should preferably use N95 masks.
- Bystander traffic should be minimised.
- Symptomatic bystanders should be tested .
- Health care workers with ILI/ARI/SARI should be tested.

References.

1. End-to –end integration of SARS-CoV-2 and Influenza sentinel surveillance-GISRS-Revised interim Guidance Jan 31,2022.
2. FluNet Summary-Global Influenza Programme WHO.
3. Influenza-COVID 19 Treatment Guidelines: NIH sep 30,2022