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**Review Article** 

# Global viralepidemias! - truce is the future of global public health?

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### Abstract

**Background:** In premodern times, human diseases like Tuberculosis, Polio, Smallpox, and Diphtheria circulated widely, and caused substantial morbidity and mortality. The advent of antibiotics and vaccines in the past two decades, aided by medical advances, improved access to health care and improved sanitation have reduced the overall mortality and morbidity linked to infectious diseases, particularly of bacterial origins like lower respiratory tract infections and diarrhoeal diseases. Since 2020 entire world has been concerned with viral infections, with at least three out of- SARS-Cov-2, Dengue, Influenza, RSV, Hepatitis B, and Japanese encephalitis bothering every country. While in High-income countries three infectious diseases COVID-19, Influenza, and Dengue of viral origin are challenging public health in low and lower-middle-income countries in addition to three, Tuberculosis, enteric fevers, and other neglected tropical diseases add to public health challenges.

Materials and methods: Available data on the internet from various sources from key countries, clinical manifestations, and complications, the management practices and epidemiology, and learnings of many preventive strategies and control efforts. The data sources used are WHO disease-wise releases from headquarters and Regional Offices, COVID 19 Wordometer, CDC Atlanta reports for US outbreaks, Europe the ECDC Communicable Disease Threats Reports (CDTR bulletin), NHM India, NCDC India, The National Health Commission of the People's Republic of China notification to WHO, for search keywords used were burden, outbreaks total cases, deaths, Incidence, Prevalence, etc. by each disease

**Results:** The war against microbes started with the discovery of the antibiotic Penicillin in 1928, but their overuse has made many of them resistant to antibiotics. Since the beginning of the 20<sup>th</sup> century, Vaccines and antivirals have drastically reduced the number of cases of viral diseases such as polio, measles, chickenpox, the flu, hepatitis A, hepatitis B, Human Papillomavirus (HPV), and others. The treatment of viral infections has proved more challenging than that of bacterial infections, primarily because viruses are relatively tiny, reproduce inside cells, and do not succumb to antibiotics. However, antiviral medications have become available for herpes simplex virus, HIV/ AIDS, and influenza, their indiscriminate may lead to the development of drug-resistant viruses.

Conclusion: The swift development of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine speaks to the efficacy of modern science in rapidly countering threats from emerging pathogens. In such situations, People must learn and use as many preventive strategies as possible.

This article is a review of Viral diseases currently bothering all countries and reflecting the challenges of the decade to come.

### Abbreviations

RSV: Respiratory Syncytial Virus; BRICS: Flue- Influenza, Brazil, Russia, India, China, and South Africa; NHM: National Health Mission; KFD: Kyasanur Forest (Monkey) Disease; COVID 19: SARS-Cov-2

### Introduction

There are four main types of diseases of public health importance and challenging health systems differently in different countries. Infectious diseases, deficiency diseases mainly in developing countries, hereditary diseases, and physiological diseases across the world. Top common infectious diseases include the Common cold, The flu (influenza), COVID-19, Hepatitis, Gastroenteritis, enteric fevers, Tuberculosis, and Respiratory Syncytial Virus (RSV). Brazil, Russia, India, China, and South Africa (BRICS) contributed almost half of the global population and 32% of the global infectious disease deaths, in 2019 [1].

### Results

In 2023 Public health experts across the world are concerned about a "tripledemic" of viral diseases as, at least 3 viral diseases contributing to public health misery in each large country. In the USA it is of flu, respiratory syncytial virus (RSV), and COVID viral infections [2-4]. The United Kingdom is saddled with the outbreak of enterovirus, Echovirus 11 (E-11) infection in May 2023, and Autumn Flu in September 2023, apart from COVID-1919, 0.5% of the population with Hepatitis B infections. England has advanced its autumn flu and COVID-19 vaccination programs following the detection of the BA.2.86 variant in the country, which started on September 11 to the at-risk people and residents of care homes prioritization for the vaccines [5]. In Europe, the ECDC Communicable Disease Threats Reports (CDTR bulletin) of the 51st week covering 24 - 30 December 2023 included COVID-19, Hepatitis A, Seasonal & Zoonotic influenza, measles, Dengue, Crimean-Congo hemorrhagic fever, diphtheria, and meningococcal disease [6].

As per The National Health Commission of the People's Republic of China notification to WHO in December 2023, China is fighting Hepatitis (mainly Hep. B, C- 150,000), Influenzas (about 2 million), Respiratory Syncytial Virus (RSV), SARS-CoV-2, mycoplasma, HPAI, rabies, Japanese encephalitis, brucellosis, and schistosomiasis japonica as major emerging zoonoses and third case of human infection with an avian influenza A(H<sub>3</sub>N8) virus. The National Health Commission (NHC) is a cabinet-level executive department of the *State Council of* the *People's Republic of China* which is responsible for formulating national health policies since 2018 [7].

In 2023 India struggles to address Viral Hepatitis (A, B&C), Seasonal Influenza (Bird Flu), Novel Coronavirus (COVID-19), Dengue, Nipah Virus, Chikungunya, Mumps outbreaks, Measles, Chicken pox Congo haemorrhagic fevers, Monkey Pox (KFD), Zika Virus disease. On 30 January 2020, India reported its first case of COVID-19 in Thrissur, Kerala, which rose to three cases by 3 February 2020, all three were medical students who had returned from Wuhan, the epicenter of the pandemic. A year-wise cases count indicated that we had 10,303,409 cases in 2020, 24,585,723 in 2021, 9790281 cases in 2022 333,860 cases in 2023, and 15292 cases in the first 54 days until 23 February 2024 [8].

History reveals that millions of people died of diseases such as bubonic plague caused by Yersinia pestis bacteria, and smallpox, caused by the variola virus. In recent times, viral infections have been responsible for two major pandemics: the 1918 – 1919 "Spanish flu" epidemic that killed around 40 million people, and the HIV/AIDS epidemic that has killed almost 33 million people (as of 2019), and the COVID novel coronavirus pandemic, which has killed 7 million people as of end August 2023 [9].

In pre-modern times, human diseases like tuberculosis, polio, smallpox, and diphtheria circulated widely and caused substantial morbidity and mortality. With the advent of antibiotics and vaccines in the past two decades, medical advances, access to health care & improved sanitation have reduced the overall mortality and morbidity linked to infectious diseases, particularly for lower respiratory tract infections and diarrhoeal diseases [8]. Currently, infectious disease burden both mortality and morbidity remain substantial in countries with low and lower-middle incomes, with neglected tropical diseases, HIV infection, tuberculosis, and malaria. Deaths from emerging and re-emerging infections, and seasonal and endemic infections, have persisted throughout the twenty-first century, pointing to a new era of infectious disease, defined by outbreaks of emerging, re-emerging, and endemic pathogens that spread quickly, aided by global connectivity, and shifted ranges owing to climate change [10,11].

The twenty-first century has witnessed a wave of severe infectious disease outbreaks, the 2003 saw severe acute respiratory syndrome coronavirus outbreak, the 2009 swine flu pandemic, the 2012 Middle East respiratory syndrome coronavirus outbreak, the 2013 – 2016 Ebola virus disease epidemic in West Africa and the 2015 Zika virus disease epidemic all resulted in substantial morbidity and mortality while spreading across borders to infect people in multiple countries. 2019 saw the COVID-19 pandemic, which has had a devastating impact on lives and livelihoods around the globe [11].

First ever, global comprehensive estimates of the burden of bacterial infections published indicate that in 2019, of the estimated 13.7 million infection-related deaths that occurred 7.7 million were associated with the 33 bacterial pathogens studied, making bacterial infections the second largest cause of death globally, after ischemic heart disease only. Bacterial infections have long been an underestimated cause of global health burden, calling for urgent strengthening of mitigation strategies [1].

Bacterial and viral infections have many things in common. Both are caused by microbes' bacteria and viruses, respectively, and spread by droplets of coughing and sneezing, contact with infected people, especially through kissing and sex, contact with contaminated surfaces, food, and water, contact with infected creatures, including pets, livestock, and insects such as fleas and ticks [9]. Most bacterial and viral infections cause mild, moderate, and severe diseases. Bacterial and viral infections can cause similar symptoms such as coughing and sneezing, fever, inflammation, vomiting, diarrhea, fatigue, and cramping due to the human immune system's ways of getting rid of the body of infectious organisms [10].

Global Burden of Disease Study Classification System for Diseases 2019

A. Infectious and parasitic diseases: 1. <u>Tuberculosis</u>, 2. <u>Sexually transmitted</u> <u>diseases</u>, excluding HIV- a. <u>Syphilis</u>, b. <u>Chlamydia</u>, c. <u>Gonorrhoea</u>, 3. *HIV/AIDS*, 4. <u>Diarrheal diseases</u>. 5. Childhood cluster diseases a. <u>Pertussis</u>, b. <u>Poliomyelitis</u>, c. <u>Diphtheria</u>, d. <u>Measles</u>, e. <u>Tetanus</u>. 6. <u>Bacterial meningitis and meningococcaemia</u>, 7. <u>Hepatitis A, B and hepatitis C</u>, 8. Malaria. 9. Tropical-cluster causes- a. **Trypanosomiasis**, b. Chagas' disease, c. Schistosomiasis, d. Leishmaniasis, e. Lymphatic filariasis, f. Onchocerciasis. 10. <u>Leprosy</u>, 11. <u>Dengue</u>, 12. Japanese encephalitis, 13. Trachoma, 14. Intestinal nematode infections- a Ascariasis, b. **Trichiniasis**, c. Ancylostomiasis and necatoriasis

B. Respiratory infections- 1. Lower respiratory infections, 2. Upper respiratory infections, 3. Otitis Media

Index: Underline- Bacterial, Underlined & Italics- Viral diseases, Bold- Parasitic diseases, Underlined, Italic and bold =Bacterial and Viral (both)

While Bacteria are relatively complex, single-celled creatures, many with a rigid wall, and a thin, rubbery membrane surrounding the fluid inside the cell. They can reproduce on their own, and survive in extreme heat and cold, radioactive waste, and the human body. Most help in digesting food, destroying disease-causing microbes, fighting cancer cells, and providing essential nutrients. Less than 1% of bacteria like Staphylococcus aureus, Escherichia coli, Streptococcus & Klebsiella pneumoniae, Pseudomonas aeruginosa, and, Mycobacterium tuberculosis cause diseases in people [9,10]. The war against microbes started with the discovery of the antibiotic Penicillin on September 28, 1928, by Alexander Flemming. But bacteria are very adaptable, and the overuse of antibiotics has made many of them resistant to antibiotics. This has created serious problems, especially in hospital settings.

On the other hand, Viruses are tinier (the largest of them are smaller than the smallest bacteria), and all have a protein coat and a core of genetic material, either RNA or DNA. Viruses can't survive without a host and can only reproduce by attaching themselves to cells. In most cases, they reprogram the cells to make new viruses until the cells burst and die. In a few cases, they turn normal cells into malignant or cancerous cells. Most viruses cause disease, attacking specific cells like, cells in the liver, respiratory system, or blood. In some cases, viruses target bacteria [9,10]. Antibiotics are not effective against viruses and are not to be used unless there is clear evidence of a secondary bacterial infection.

The treatment of viral infections has proved more challenging, primarily because viruses are relatively tiny and reproduce inside cells. However, Since the beginning of the 20<sup>th</sup> century, vaccines have been developed, that have helped in reducing the number of new cases of polio, measles, the flu, chickenpox, hepatitis A, hepatitis B, human papillomavirus (HPV), and others. For diseases, like herpes simplex virus infections, HIV/AIDS, and influenza, antiviral medications have become available, and the indiscriminate use of antiviral medications has led to the development of drug-resistant viruses but their widespread use in larger countries need to be ensured. [12].

### **Discussion**

## A brief account of common viral diseases across the world is:

- i) Marburg virus: This is the most dangerous hemorrhagic fever virus, causes convulsions and bleeding of mucous membranes, skin, and organs and has a fatality rate of 90%.
- ii) Ebola virus: There are five strains of the Ebola virus, named Zaire, Sudan, Tai Forest, Bundibugyo, and Reston. The Zaire Ebola virus is the deadliest, with a mortality rate of 90%, currently spreading in Guinea, Sierra Leone, and Liberia.
- **iii) Hanta virus:** The Hantavirus describes several types of viruses, that cause lung disease, fever, and kidney failure.
- iv) Influenza (Seasonal): The various strains of bird flu regularly cause epidemics and panic due to a high mortality rate of around 70%. The risk of contracting the H5N1 strain, one of the best known is low and currently, H3N2 is common. Humans can only be infected through direct contact with poultry, therefore, most cases are seen in Asia, where people often live close to chickens, currently circulating in humans are subtype A(H1N1) and A(H3N2) influenza viruses. The new virus A (H1N1), called swine flu, is transmitted from person to person, and not through contact with pigs or pork products. In week 33 of this year ending on 19 August 2023 of the 1442 samples tested 37 specimens were found positive. Of the 37, 28 were type A, and 9 were type B variety. Among the Type A majority 16 were subjected to subtyping yielding 11 (69%) were H1N1 and 5 (31%) were H3N2. Among the type B, only 4 were subtyped and all of them turned out to be Victoria Lineage.
- v) Lassa virus: The Lassa virus is transmitted by rodents (15% carry the virus) in Nigeria and reoccur there at any time.
- vi) Junín virus: The Junín virus is associated with Argentine hemorrhagic fever, which exhibits tissue inflammation, sepsis, and skin bleeding, and diagnosis is rarely made in the early days.
- vii) The crimea-Congo fever: The Crimea-Congo fever virus is a hemorrhagic fever transmitted by ticks. In the first few days of infection, sufferers present with pinsized bleeding in the face, mouth, and pharynx.
- viii) The Machupo virus: The Machupo virus is associated

with Bolivian hemorrhagic fever or black typhus. The infection causes high fever, accompanied by heavy bleeding. The virus can be transmitted from human to human, and rodents often carry it. Its prognosis is poor with more than 80% case fatality.

- ix) Kyasanur Forest Virus (KFD): Kyasanur Forest Virus (KFD) virus in woodlands on the southwestern coast of India Shimoga district in Karnataka in 1955. It is transmitted by ticks, Rats, birds, and boars are suspected to be hosts. People infected with the virus suffer from high fever, strong headaches, and muscle pain which can cause bleeding,
- x) Dengue fever: Dengue fever transmitted by mosquitoes, affects between 50 and 100 million people a year mostly in Thailand and India, where more than 2 billion people are at risk of dengue fever.
- xi) Respiratory Syncytial Virus (RSV): RSV is a common cause of lower respiratory tract infections in all age groups. Common symptoms include a runny nose, decreased appetite, coughing, sneezing, fever, and wheezing. It is extremely common as most children get infected by the age of two and get reinfected many times during their lives. RSV infections resolve themselves within a week or two, but occasionally the virus can make children seriously ill [4].

The entire world and India have witnessed outbreaks, epidemics, or pandemics all but Marburg, Lassa, and Junín virus infections, in the last decade. However, in terms of major morbidity and mortality, SARS-CoV-2, Influenza and Dengue Viruses have panicked populations and health Systems worldwide since 2020.

WHO urges countries to prepare for the autumn and winter season and step up efforts to develop or strengthen their integrated surveillance and response to COVID-19, influenza, and RSV.

On January 30, 2023, the World Health Organization (WHO) declared that the COVID-19 pandemic continues to constitute a public health emergency of international concern, Infectious diseases, have unpredictable and far-reaching consequences, and to control the spread worldwide, and protect people's lives and safety, regular analysis of global infectious disease cases is attempted by World Health Organization. In January 2023, their latest report indicates that the cases of COVID-19 and monkeypox (Mpox) have significantly decreased. the United States is having its worst influenza season since the COVID-19 pandemic. Dengue, measles, and cholera remain public health concerns worldwide. The report recommended giving attention to Low-incidence Infectious Diseases (LIDs) and Sporadic Infectious Diseases (SIDs), like Chikungunya fever, legionellosis, avian influenza, and scarlet fever, to avoid global pandemics (Figure 1).



Figure 1: Global distribution of infectious diseases from 24 July 2023 to 23 August 2023. Source: Global Infectious Diseases in January 2023, https://www.scienceopen.com, Jan 2024 (12).

### Current situation of key Viral diseases across the world

1. COVID-19: As of 22 February 2024, the COVID-19 pandemic has caused 774,493,392 cases and 7,026,534 confirmed deaths [11]. The top 3 countries contributing to these numbers are 1) the United States of America = 103.4 m, China = 99.3 m, and India = 45 m. India has reported 4,50,28,732 cases and 5,33,476 confirmed deaths due to the disease as of 22 February 2024. About 1.5 million new COVID-19 cases an increase of 80% and over 2500 COVID 19 deaths a decrease of 57%, were reported in the last 4 weeks (10 July to 6 August 2023), 28th weekend in comparison to the 4 weeks of 12 June -9 July. However, only the Western Pacific Region has reported an increase in cases and a decrease in deaths. As of 31 August 2023, over 695 million confirmed cases and over 6.9 million deaths have been reported globally. Currently, reported cases do not accurately represent infection rates due to the reduction in testing and reporting. The daily case count was 52065 on 25 March 2020, reached a peak of 3,846,402 on 20 January 2022, and was 46770 on 14 February 2024 [10,13,14].

While the United States leads with 111,401,806 cases and 1,199,333 deaths, in North America 915, India with 45,028,565 cases and 533,476 deaths in Asia, France with 40,138,560, cases and 167,642 deaths, and Germany with 38,819,650 cases 182,470 deaths in Europe and Brazil 38,407,327cases and 709,765 deaths in South America, South Korea- cases-34,571,873 deaths- 35,934 and Japan (+Diamond Princess) with 33,803,572 cases and 74,694 deaths in Asia recorded more than 30 million cases each so far since 2019. The least number of cases of less than 1000 were reported Niue- C = 883- D = 0, Tokelau-C = 80 D = 0 in Australia/Oceania, Holy See- C = 29, D = 0 in Europe, Western Sahara in Africa -C = 10, D = 1 and MS Zaandam-C = 9, D = 2. On 27 August 44,500 cases and 279 deaths were reported [9]. There were 1532 active cases in the country, as per the latest data. The total cases to date are 4,49,95,856, total deaths are 531,918. The recovery rate is 98.81% and the case fatality rate is 1.18%.

As of December 30, 2023, approximately 23,000 hospitalizations per week were reported among patients with COVID-19, with the highest rates among persons aged  $\geq$  65 years. Currently, healthcare providers are positioned to mitigate COVID-19 morbidity and mortality with safe and effective vaccines and early diagnosis and treatment. About 70% of hospitalizations are among those who are 65 and older. SARS-CoV-2 rebound, the recurrence of signs or symptoms, or a new positive viral test result after initial recovery from COVID-19 known as Long COVID-19 are concerning [1-3]. The evidence suggests that SARS-CoV-2 rebound occurs initially as a mild illness, 3-7 days after resolution of the initial acute illness, and occurs in both treated and untreated patients. Two new variants -- Omicron variant EG.5 (Eris) designated as a Variant of Interest (VOI), dominant in the US, and BA.2.86 have started to spread [11,15].

### Epidemiology of COVID-19 as understood by the end of 2023

Globally, as of 22 February 2024, the COVID 19 pandemic

has caused 774,493,392 cases and 7,026,534 confirmed deaths globally. The number of new cases increased by 4% during the 28-day period of 11 December 2023 to 7 January 2024 as compared to the previous 28-day period, with over 1.1 million new cases. The number of new deaths decreased by 26% as compared to the previous 28-day period, with 8700 new fatalities reported.

During the period from 11 December 2023 to 7 January 2024, COVID-19 new hospitalizations and admissions to an Intensive Care Unit (ICU) both recorded an overall increase of 40% and 13% with over 173,000 and 1900 admissions, respectively.

Globally, JN.1 is currently the most circulating virus of Interest (VOI) and is now reported by 71 countries, accounting for around 66% of the sequences in week 52 of 2023. Its parent lineage, BA.2.86, is stable and accounts for 7.8% of sequences. The overall status of low public health risk at the global level.

Initially, in 2020 the entire world felt as if the COVID-19 Pandemic was a war, and controlling it was like fighting a war, mostly because it affected more western world, free of many infectious diseases. It had disrupted their productivity, and economics, in addition to being a public health challenge. In war, we need to worry about winning and about paying for it, but the COVID 19 pandemic led to a sharper reduction in the per capita income of richer countries and India. This led to intercountry and inter-state income equality. By the metrics of the population of India, both cases & deaths per million remained among the lowest in the world [16].

What was initially understood as mainly a respiratory illness leading to Pneumonic consolidation of the lungs, the world is still in a learning curve of things about it. The initial list of symptoms consisted of throaty pain, cough, fever, and breathlessness, but now includes loss of smell, Anosmia and ageusia are common, and skin rashes, eye infection, diarrhea, happy hypoxia, and even viral carditis are also being reported. Severe backache, abdominal pain, rashes, or aching calves could also be the calling card of the virus. More recently neurological signs like Encephalopathy, Encephalitis, and Guillain-Barré syndrome are being associated and acute cerebrovascular disease is also emerging as an important complication. The mode of transmission was initially assumed as droplet infections that could be controlled by frequent handwashing, avoiding touching the face, and eyes, cough etiquette, physical distancing, and wearing a mask. Current evidence suggests that the virus spreads mainly between people who are in close contact with each other, for example at a conversational distance. The virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing, or breathe. When infectious particles pass through the air are inhaled at short range (short-range aerosol or airborne transmission) or (long-range aerosol or long-range airborne transmission), and if infectious particles come into direct contact with the eyes, nose, or mouth (droplet transmission) [17].

While all the countries had focused their attention acutely on the higher fatality rate the virus has caused among the elderly and launched a scientific inquiry into why children have emerged relatively unaffected. As the Global tally of cases crossed 28 million cases and nearly a million deaths on 10th September 2020, it was estimated that children under 14 years contributed less than 0.5% and therefore the Children were not the face of this pandemic. The sub-national data in states reporting desegregated data in the USA and India indicate that the children contributed between 0.1% to 10% in 2020. The pandemic caused only a mild illness in children and immediate health impact, or mortality rates were not alarming. A few weeks following the peak of the COVID-19 epidemic in the US and the European Union, a novel systemic illness called Multisystem inflammatory syndrome in children (MIS-C) was reported with devastating effects. In developing countries including India, the pandemic caused disruption in health services, broken medical supplies, interrupted access to nutritious food, immunization services, informal learning, emotional bonding among peers, Anganwadi worker's affectionate care especially when the parents were facing income loss due to loss of jobs or reduction in pay packages and low opportunities of alternatives of earning livelihood [16,18].

SARS-CoV-2 infection in young children is often mild or asymptomatic; however, some children are at risk for severe disease. Among vaccine-eligible children aged < 5 years hospitalized or seeking care in emergency departments for acute respiratory illness from July 2022 to September 2023, 86% had not received any COVID-19 vaccine. Despite low vaccination coverage, only 5% of children received a positive SARS-CoV-2 test result. Receipt of  $\geq$  2 COVID-19 mRNA vaccine doses was 40% effective in preventing emergency department visits and hospitalization. In June 2022, original monovalent COVID-19 mRNA vaccines were recommended for infants and children aged 6 months - 4 years [18].

The swift development of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine speaks to the efficacy of modern science in rapidly countering threats from emerging pathogens [16].

**2. Dengue fever:** In 2023, over six million dengue cases and over 6000 dengue-related deaths were reported from 92 countries/territories (Figure 2).

In January 2024, over half a million dengue cases and over 100 dengue-related deaths were reported globally. Most cases were reported in the WHO PAHO region, with a cumulative number of 550 277 suspected cases reported in the first four weeks of 2024, showing an increase of 189% compared to the same period in 2023, according to the epidemiological bulletin of 8 February 2024. An upsurge of cases has been reported in Brazil, where all four dengue serotypes are circulating. The Region of the Americas has seen over 4.2 million new cases of dengue fever reported in 2023, including more than 6,500 severe dengue cases and 2,050 deaths. This surpasses the previous record seen in 2019 (3.1 million cases), by over a million new cases. Between EW 1 and EW 49, there have been 4,192,479 reported cases, with an incidence rate of 421 cases per 100,000 population. Of the reported cases, 1,898,640 were lab-confirmed, and 6,766 were classified as severe dengue. The highest number of cases were reported in Brazil with 2,909,404 cases, Peru with 271,279 cases, and Mexico with 244,511 cases. While South America has reported more than 100 cases per 100,000 population, India reported less than 10 cases per 100, 000 population [17,19].



#### Figure 2: Countries/territories reporting Dengue cases since February 2023 and as of January 2024.

The year 2019 marked an unprecedented peak, with reported instances of 5.2 million cases spreading across 129 countries. After a slight decline in cases between the years 2020–2022 due to the COVID-19 pandemic and lower reporting rate, in 2023, an upsurge in dengue cases has been observed globally, characterized by a significant increase in the number, scale, and simultaneous occurrence of multiple outbreaks, spreading into regions previously unaffected by dengue. Warming temperatures have become a leading driver in the increase of dengue transmission, particularly in tropical and sub-tropical climates but also extending at times to more temperate zones.

Dengue is a self-limiting viral febrile illness transmitted by Aedes aegypti. The infection is transmitted from mosquitoes to humans through the Aedes mosquito – the primary vector. Its symptoms are characterized by biphasic fever, myalgia/ arthralgia, rash, leukopenia & Thrombocytopenia. If untreated, the condition can lead to fatal complications like shock, bleeding, and multiple organ failure.

Dengue Hemorrhagic Fever (DHF) is characterized by abnormalities in hemostasis and leakage of fluid and protein from capillaries, leading to hemodynamic compromise and shock. Molecular and gene studies show that NS-1 antigen and antibody-dependent enhancement act to render increased vascular permeability in dengue [19].

**Epidemiology:** Dengue virus (DENV) is transmitted to humans through the bite of infected mosquitoes mostly in urban and semi-urban areas in tropical and sub-tropical climates. The primary vectors that transmit the disease are Aedes aegypti, & albopictus mosquitoes.

DENV has four serotypes (DENV-1, DENV-2, DENV-3, DENV-4). Infection with one serotype provides long-term immunity to the same serotype and only transient immunity to the other serotypes, after which secondary infections with a different serotype increase the risk for severe dengue. While most Dengue cases have mild febrile illness, some cases will develop Haemorrhagic fever which involves shock, severe bleeding, or severe organ impairment, a stage after the fever subsided and is preceded by warning signs such as intense abdominal pain, persistent vomiting, bleeding gums, fluid accumulation, lethargy or restlessness, and liver enlargement. There is no specific treatment for dengue, but timely diagnosis and appropriate clinical management are key elements of care. Dengue is largely underreported.

The natural disease course is as follows: Incubation -1 - 5 days, Fever -5 days, Capillary leaks -5 - 15 days, Thrombocytopenia -5 - 15 days; hence, monitor for hypovolemia up to 17 days. Stages of dengue include - febrile illness, critical illness, and recovery phase. In children, clinical manifestations of both, primary and secondary infection are Leukopenia, Maculopapular rash, Petechia, Facial flush, Cold extremities & Liver enlargement.

Types 1 and 3 often cause mild febrile illness in children, while types 2 and 4 cause asymptomatic infection. Laboratory investigations for diagnosing dengue are RT-PCR, NS-1 protein detection, and ELISA. The sensitivity of the NS-1 test is lower in secondary infection. Seroconversion IgM provides confirmatory diagnosis and can be detected as early as 4 days.

Management of dengue depends on the stage at diagnosis and the severity of the symptoms. Supportive therapy with adequate fluids and food intake. Inability to take food or pass urine, and severe symptoms prompt hospitalization. Infants and those with co-morbid conditions who acquire dengue infection require hospitalization. Management strategies include – fluid infusion, platelet and fresh frozen plasma resuscitation, supportive care, and symptomatic management. The cornerstone of management for in-patients is titrated isotonic, non-dextrose-containing crystalloid fluid administration, based on the physiological parameters. Fluid management in dengue is challenging and continuous fluid and vital sign monitoring is warranted in these patients. Resorptive phase; monitor for fluid overload [17,19].

**3.** Seasonal influenza: Influenza virus (H3N2) : Seasonal influenza is an acute respiratory infection caused by influenza viruses that circulate in all parts of the world. There are 4 types of influenza viruses, types A, B, C, and D. Influenza A and B viruses circulate and cause seasonal epidemics of disease. Influenza A viruses are further classified into subtypes according to the combinations of the hemagglutinin (HA) and the neuraminidase (NA), the proteins on the surface of the virus. Currently circulating in humans are subtype A(H1N1) and A(H3N2) influenza viruses. Only influenza-type A viruses are known to have caused pandemics [3].

Based on more than 208 169 specimens (by the WHO GISRS laboratories tested) between 24 July and 06 August 2023, 5261 were positive for influenza viruses, of which 3827 (72.74%) were typed as influenza A and 1434 (27.26%) as influenza B. Of the sub-typed influenza, A viruses, 1015 (37.58%) were influenza A(H1N1) pdm09 and 1686 (62.42%) were influenza A(H3N2). Of the type B viruses for which lineage was determined, all (480) belonged to the B/Victoria lineage [20].

Virus variants and mutations: Viruses are constantly evolving and changing. Every time a virus replicates (makes copies of itself), changes in its structure may appear. Each of these changes is a "mutation." A virus with one or more mutations is called a "variant" of the original virus. Some mutations can lead to changes in important characteristics of the virus, including characteristics that affect its ability to spread and/or its ability to cause more severe illness and death.

Seasonal influenza is an acute respiratory infection caused by influenza viruses that circulate in all parts of the world, and the cases are seen to increase during certain months globally. India every year witnesses two peaks of seasonal influenza: one from Jan to March and the other in the monsoon season. The cases arising from seasonal influenza are expected to decline from March end. There are around a billion cases of seasonal influenza annually, including 3 – 5 million cases of severe illness. It causes 290,000 to 650,000 respiratory deaths annually. Ninety-nine percent of deaths in children under 5 years of age with influenza-related lower respiratory tract infections are in developing countries. Symptoms begin 1 - 4 days after infection and usually last around a week [20,21].

As per the Centers for Disease Control and Prevention, and The World Health Organization (WHO) reports in January 2024 H<sub>3</sub>N<sub>2</sub> is responsible for most influenza-related hospitalizations and deaths globally. However, the current outbreak in India is of particular concern as it has already claimed several lives and is spreading at an alarming rate. Most people recover from H<sub>3</sub>N<sub>2</sub> infection within a week, but in some cases, it leads to pneumonia, bronchitis, and even death. As per the ICMR statement in the 2023 outbreak of H<sub>3</sub>N<sub>2</sub> about 10% of the patients suffering from SARI required oxygen support and 7% required ICU care.

There are 4 types of influenza viruses, types A, B, C, and D. Influenza A and B viruses circulate and cause seasonal epidemics of disease. Influenza A viruses are further classified into subtypes according to the combinations of the proteins on the surface of the virus. Currently circulating in humans are subtype A(H1N1) and A(H3N2) influenza viruses. The A(H1N1) also caused the pandemic in 2009 and replaced the previous A(H1N1) virus which had circulated prior to 2009. Only influenza-type A viruses are known to have caused pandemics. Influenza B viruses are not classified into subtypes but can be broken down into lineages. Influenza type B viruses belong to either the B/Yamagata or B/Victoria lineage. Influenza C virus is detected less frequently and usually causes mild infections, thus does not present public health importance. Influenza D viruses primarily affect cattle and are not known to infect or cause illness in people.

**Signs and symptoms:** Symptoms of influenza usually begin around 2 days after being infected by someone who has the virus. The common symptoms include sudden onset of fever, cough (usually dry), headache, muscle and joint pain, severe malaise, sore throat, and runny nose. The cough can be severe and can last 2 weeks or more [22].

Most people recover from fever and other symptoms within a week without requiring medical attention. However, influenza can cause severe illness or death, especially in people at high risk. Influenza can worsen symptoms of other chronic diseases. In severe cases, influenza can lead to pneumonia and sepsis. People with other medical issues or who have severe symptoms should seek medical care. Hospitalization and death due to influenza occur mainly among high-risk groups. Most deaths associated with influenza occur among people aged 65 years or older.

**Seasonal influenza in India:** Near real-time surveillance of cases of Influenza Illness (ILI) and Severe Acute Respiratory Infections (SARI) presenting in OPDs and IPDs of health facilities is undertaken by Integrated Disease Surveillance Programme (IDSP), National Centre for Disease Control (NCDC).

• Looking at the trends of seasonal Flue (H1N1) there appears to be a cyclical trend, showing a large number of cases every 3 years. Starting from 2018 when we had 15266cases and 1128 deaths, in 2019 the country had

28798 cases and 1218 deaths, following 2 years cases and death was very few in 2020- cases= of 2752 deaths= 44, 2021- 778 cases and 12 deaths. In 2022 there were 13202 cases and 410 deaths and in the current year 2023, there are 8097 cases and 129 deaths as of 31/12/2023.

- Latest data are available on IDSP-IHIP (integrated health Information Platform), a total of 3038 laboratory-confirmed cases of various subtypes of Influenza including H3N2 have been reported till 9<sup>th</sup> March 2023-including 1245 cases in January 1307 in February, and 486 cases in March (till 9<sup>th</sup> March) by the States. IDSP-IHIP data from health facilities indicate that during the month of January 2023, a total of 397,814 cases of Acute Respiratory Illness/Influenza Like Illness (ARI/ILI) were reported in the country which increased slightly to 436,523 during February 2023. In the first 9 days of March 2023, this number stands at 133,412 cases.
- The corresponding data for admitted cases of severe acute respiratory illness (SARI) is 7041 cases in January 2023, 6919 during February 2023, and 1866 during the first 9 days of March 2023.

Despite India claiming real-time data through IDSP-IHIP, no updates have been available since November 2023 for nearly 3 months. However, most of the information is from local print media, {All- 1353, Articles-1315, Videos-24, Photos-14} outbreaks across the country.

## Influenza data from the ICMR network of laboratories in India

In India, integrated surveillance of Influenza Illness (ILI) and Severe Acute Respiratory Illness (SARI) for the detection of the human influenza virus and SARS-COV-2 virus is ongoing through a structured ILI/SARI surveillance network of 28 sites. The surveillance network is comprised of 27 DHR-ICMR Virus Research & Diagnostic Laboratories and countries.

In 2023 Influenza H3N2 is the predominant sub-type among the samples testing positive for influenza, since the beginning of this year [22,23].

The H<sub>3</sub>N<sub>2</sub> virus is a subtype of the influenza A virus that has been associated with more severe illness and higher mortality rates, particularly among young children, older adults, and those with underlying health conditions. H<sub>3</sub>N<sub>2</sub> variety flu is responsible for most influenza-related hospitalizations and deaths globally [15].

The 2023 outbreaks in India are of particular concern as they have already claimed several lives and spreading at an alarming rate [12], over the past few months. Influenza surveillance data from the ICMR shows that the H3N2 virus has been the predominant strain circulating in India during the current flu season, with a high level of activity reported in several states. ICMR reports that out of all the patient admissions in the hospital with SARI, 50% were found to have H3N2. In the current outbreak of H3N2, about 10% of the patients suffering from SARI caused by the virus required oxygen support and 7% required ICU care [12].

The WHO has also highlighted the potential impact of the H3N2 virus on public health, particularly in regions with high population density and limited healthcare resources. The organization has stressed the need for increased surveillance, timely diagnosis, and appropriate treatment to prevent the further spread of the virus and reduce its impact on vulnerable populations [20,23].

Antiviral medications, such as zanamivir and oseltamivir can be used to treat the flu, including H3N2, work best when started within 48 h of symptom onset and can help to reduce the severity and duration of the illness. Over-the-counter medications, such as acetaminophen (Tylenol) and ibuprofen (Advil), are routinely used to reduce fever and alleviate headache and body aches. Resting and staying hydrated can also help the body fight off the virus and recover more quickly.

## Indian guidelines for antiviral treatment of seasonal flue cases

While the IDSP or ICMR data up to 2023 is in the public domain, the print media reports of outbreaks across the country are flooding till now [13,14,16].

Phylogenetic analysis of the HA gene of A(H1N1) pdm09, A(H3N2), and Type B Victoria lineage stains from India showed the global prevalence clades are in circulation, and they match with the WHO recommended Vaccine component of Southern Hemisphere 2024.

The surveillance data for antiviral resistance among the tested Influenza viruses indicates, complete sensitivity to neuraminidase inhibitors. Suggesting that the current neuraminidase inhibitors remain effective for the treatment of Influenza infections. On this background, it will be prudent to use the Southern Hemisphere 2024 quadrivalent vaccine in the coming influenza season. However, if the SH 2024 recommended component influenza vaccine is not available



then it is recommended to procure the latest available quadrivalent influenza vaccine [21,24].

**Flu vaccination:** One of the best ways to prevent the flu, including H3N2, is to get vaccinated. The flu vaccine is safe, effective, and widely available. It is recommended that everyone over the age of 6 months gets vaccinated, especially those at higher risk of severe illness, such as young children, older adults, and individuals with underlying health conditions. Good hygiene can help to prevent the spread of the virus. This includes frequent hand washing with soap and water (hand sanitizer may be used when soap and water are not available), covering your mouth when you cough or sneeze, and avoiding close contact with sick individuals. Further, it is important to stay home to avoid spreading the virus to others if you have flu-like symptoms [24].

In addition to these measures, individuals can also take steps to boost their immune systems, such as eating a healthy diet, getting enough sleep, and exercising regularly. These lifestyle choices can help strengthen the body's natural defense against viral infections and reduce the risk of getting sick.

4. Respiratory Syncytial Virus (RSV) : RSV is a leading cause of acute respiratory tract infections in young children, with an estimated 30 million cases, 3.6 million hospital admissions, and 100,000 deaths each year, worldwide. However, the coronavirus disease 2019 (COVID-19) pandemic has drastically changed the epidemiology of Respiratory Syncytial Virus (RSV) respiratory tract infections. Infants younger than six months are at higher risk of severe disease, particularly those born prematurely, with chronic lung or congenital heart disease, and children with neurological conditions or immunodeficiency. In 2020, the first year of the COVID-19 pandemic, when community actions of respiratory etiquettes, handwashing, surface cleaning, and use of masks were aggressively implemented, RSV cases plummeted worldwide [25]. Later in 2021, as these measures were gradually relaxed, many countries of the world experienced different degrees of off-season resurgence of cases. The prolonged lack of viral exposure and decrease in social contacts might have increased the pool of vulnerable children and adults. Modifications in health-seeking behaviors, as well as the health system's focus on the pandemic.

In the United States, respiratory syncytial virus (RSV) infections caused an estimated 58,000-80,000 hospitalizations among children aged <5 years and 60,000-160,000 hospitalizations among adults aged  $\geq 65$  years each year. The share of RSV, SARS-CoV-2, and influenza among hospitalized children with acute lower respiratory infections (ALRI) were 27%, 16.5%, and 4.1%, respectively in 2023. The RSV subgroup A was dominant over subgroup B with more severe clinical symptoms [26].

RSV mainly peaks in winter in North India and some correlation with low temperature has been observed. Prevalence of RSV-associated ARTI in India is 28% in children < 5 years. RSV-B was the dominant subtype detected with a prevalence of 72.14%. In general, it causes severe respiratory disease leading to hypoxemia. RSV-A infection had more symptoms

leading to hypoxemia than RSV-B. The common clinical and socio-demographic characteristics were age <1year, fever for >4 days, cough, conjunctivitis, stuffiness, fatigue, six or more people at home, and families having pets at home. and inhaling toxic fumes. Climatic factors like increases in temperature (°C), wind speed (Km/h), wind gust (Km/h), rainfall (mm), and atmospheric pressure (mb) like in north India showed a strong correlation with the RSV infection [27].

**5. Monkeypox (MPOX)** : As of August 2023, the number of new cases of Mpox has continued to climb, with the total number of cases to 7565 in Spain, 4150 in France, and 3694 in Germany. All cases have been associated with international travel or imported animals from central and western Africa. The USA had seen the first two cases of Mpox virus infection in humans returning to the United States from Nigeria in 2021. The number of cases in the rest of the developing world included 557 in Ecuador, 10 in Taiwan, China, and 3 in Hong Kong, China.

The Mpox virus is transmitted by the exchange of body fluids in the oral cavity and nasopharynx or by intradermal injection, followed by rapid replication at the site of inoculation and spread to nearby lymph nodes. Skin lesions begin in the oropharynx and can spread throughout the body. Antibodies to the Mpox virus can be detected in serum approximately 2 weeks after exposure [28]. Case fatality rates of the disease range from 1% – 10% [29]. Mpox virus infection is usually mild, and most patients recover without treatment. For patients with severe symptoms of Mpox, treatment with cidofovir (Vistide) is recommended. The smallpox vaccine has the potential to provide some protection against Mpox infection due to the genetic similarity.

### Newer insights of trip epidemic viruses and the diseases [30]

- 1. SARS COV-2 (COVID 19):
- a) Nirmatrelvir and Ritonavir: The National Institutes of Health (NIH) is conducting phase 2 trials to examine treatments for patients with long-term COVID-19 as a part of the Researching COVID-19 to Enhance Recovery (RECOVER) Initiative. It examined drugs like Paxlovid (nirmatrelvir and ritonavir) to examine brain fog and memory problems and a device, that enables brain activity and blood flow by home-based transcranial direct current stimulation in the RECOVER-NEURO trial, yielding encouraging results. (Source: NIH, July 31, 2023).
- **b)** Metformin may control elevated blood glucose levels in COVID patients: A new study from Brazil has found that SARS-CoV-2 increases the production of glucose by infecting the hepatocytes and may cause hyperglycemia in hospitalized patients with COVID-19 irrespective of the baseline blood glucose levels. Metformin was more effective than insulin in reducing the elevated blood glucose levels in these patients (Source: Pharmacy Times, August 1, 2023).

- c) Japan's first indigenous mRNA COVID-19 vaccine: Japan has developed its first indigenous mRNA COVID-19 vaccine, known as DS-5670. The Japanese health ministry panel has recommended approval for the vaccine, which is intended to serve as a booster in persons who have completed the primary immunization. The vaccine would be available by the name of Daichi Rona (Medscape, August 1, 2023).
- d) Rapid worsening of kidney function in CKD patients with COVID-19: Deterioration in renal function was observed in 76% of patients with chronic kidney disease (CKD) during the pandemic. COVID-19 enhanced the risk for rapid worsening of kidney function in 2.5% of patients with stages 3-4 CKD compared to their status before the pandemic. Other factors that increased the risk for impaired kidney function during the pandemic were Asian race, higher Charlson Comorbidity Index, advancing CKD stage, and pre-pandemic rapid kidney function decline. (Source-Kidney Medicine, July 25, 2023).
- e) Simnotrelvir-ritonavir for mild to moderate COVID-19 (January 2024): Although nirmatrelvir-ritonavir reduces hospitalization and death from COVID-19, the many drug interactions make it difficult to use in some patients. Simnotrelvir-ritonavir is a similar protease inhibitor combination that inhibits viral replication but does not have as many drug interactions. In a randomized, double-blinded study of over 1000 patients with mild to moderate COVID-19 (majority fully vaccinated), 5 days of simnotrelvir-ritonavir reduced time to symptom resolution by 1.5 days. Since no participant progressed to severe disease or died by day 29, it is unknown whether the drug prevents hospitalizations or death from COVID-19. Simnotrelvirritonavir has emergency use approval in China but is not yet approved for use in other countries. (Source-"COVID-19: Management of adults with acute illness in the outpatient setting", section on 'Therapies of limited or uncertain benefit').
- f) Convalescent plasma in mechanically ventilated patients with COVID-19 (November 2023): Most randomized trials have not demonstrated a benefit for convalescent plasma in hospitalized patients with COVID-19. However, an open-label trial of 475 patients who were mechanically ventilated for severe COVID-19 did report a reduction in 28-day mortality with high-titer convalescent plasma compared with standard care (35 versus 45%). This inconsistency compared with the lack of effect in most other trials decreases confidence in the mortality benefit. The value of convalescent plasma against Omicron variants is uncertain. (Source "COVID-19: Management in hospitalized adults", WHO, section on 'Limited role for antibody-based therapiesmonoclonal antibodies & convalescent plasma).
- g) Adjunctive immunomodulators for severe COVID-19 (August 2023): For patients hospitalized for COVID-19

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who require high-flow oxygen or ventilatory support, adding baricitinib or tocilizumab to dexamethasone further reduces mortality. In a randomized trial of patients with severe COVID-19, most of whom were on remdesivir and glucocorticoids, infliximab and abatacept each reduced 28-day mortality compared with placebo (10 and 11 versus 15%) but did not improve time to clinical improvement. There are no clear advantages over baricitinib or tocilizumab, with established benefits. The United States has approved this indication. (See "COVID-19: Management in hospitalized adults", the section on 'Limited roles for alternative immunomodulators').

- h) Thrombocytopenia and thrombosis syndrome with adenovirus infection (August 2023): Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT) is a rare, autoantibody-mediated syndrome of thrombocytopenia and thrombosis (central venous thrombosis is common) that can occur after vaccination with an adenoviralvectored COVID-19 vaccine. This finding suggests that a component of the adenoviral sequence may provide the source of the neoantigen. (See "COVID-19: Vaccineinduced Immune Thrombotic Thrombocytopenia (VITT)", the section on 'Mechanisms/triggers of antibody formation'.
- i) Turning to be a very weird virus: The first was the pulmonologists, who noticed the striking levels of hypoxemia, and the rapidity with which stable patients crashed in the intensive care unit. The second, was the nephrologists as the dialysis machines stopped working right, seeing clots forming on the dialysis filters. Some patients could barely get in a full treatment because the filters would clog so quickly. We knew it was worse than the flu because of the mortality rates, but these oddities made us realize that it was different too not just a particularly nasty respiratory virus but one that had effects on the body that we hadn't seen before. A study in Japan appearing in the Annals of Internal Medicine staggering cohort of more than 20 million individuals living in those countries from 2020 to 2021, indicates that compared with those infected with flu, those infected with COVID were more likely to be diagnosed with any autoimmune condition, connective tissue disease, and inflammatory arthritis, after statistical balancing, the authors looked at the risk for a variety of autoimmune diseases. This risk seemed to be highest in the 6 months following the COVID infection, proving that COVID 19 is somehow screwing up the immune system. The mechanism of protection is not prevention of infection; Perhaps vaccination helps to get the immune system in a state to respond to COVID infection more, appropriately [30-32].

#### 2. Dengue fever & vaccines:

Although dengue primed individuals can already benefit from vaccination with the first licensed dengue vaccine CYD-TDV, the public health need for the dengue-naive population has not yet been met. Currently used vaccine has an efficacy of 60%. The efficacy of the vaccines is further reduced, and the severity risk increased among those who did not have prior dengue exposure. The biggest hurdle is the immunological interaction between the four antigenically distinct dengue serotypes. The advantages of second-generation dengue vaccines are the inclusion of non-structural proteins of the dengue backbone and more convenient dosing with reduced numbers of doses needed. All second-generation dengue vaccines still need to go through full phase 3 trials. The 5-year efficacy and safety data for both second-generation dengue vaccines are imminent. Only one dengue vaccine is currently available for use- A tetravalent, live-attenuated dengue vaccine (Dengvaxia<sup>®</sup>). Dengvaxia is used in children 9 through 16 years old who have laboratory-confirmed previous dengue virus infection and are living in an area where dengue is endemic (occurs frequently or continuously). - for example, in the U.S. territories of American Samoa, Puerto Rico, and the U.S. Virgin Islands, and freely associated states [19b].

#### 3. Seasonal influenza and flu vaccination :

Vaccination is the best way to prevent influenza. Safe and effective vaccines have been used for more than 60 years. Immunity from vaccination goes away over time so annual vaccination is recommended to protect against influenza especially high-risk individuals namely pregnant women, children aged 6 months to 5 years, people over age 65, or with chronic medical conditions, and health workers. The vaccine is less effective in older people, but it will make the illness less severe and reduce the chance of complications and death. Influvac Tetra 2023/2024 Vaccine helps protect you from influenza (flu). It works by exposing you to a small dose of the flu virus which helps your body to develop immunity against the disease. Vaccination will not treat an existing flu virus infection. Efficacy of recombinant influenza vaccine in adults < 65 years of age (January 2024).

Data suggest that the recombinant influenza vaccine is more effective than the standard-dose inactivated influenza vaccine in preventing influenza among adults  $\geq$  65 years of age; the relative efficacy of the recombinant vaccine in adults < 65 years is uncertain. In a study during the 2018 - 2020 influenza seasons, clinical facilities of a large healthcare system were randomly assigned to administer either the recombinant vaccine or a standard-dose inactivated influenza vaccine and alternated the vaccine administered each week. Among adults aged 50 to 64 years, receipt of the recombinant vaccine was associated with a lower rate of influenza (2.00 versus 2.34 cases per 1000); the relative vaccine effectiveness was 15.3 percent. Pending further data, administering any inactivated influenza vaccine for adults aged 50 to 64 years is advised. (Source: WHO "Seasonal influenza vaccination in adults", the section on 'Alternatives to egg-based inactivated influenza vaccines').

## 4. Respiratory syncytial virus vaccination in pregnancy (Modified in October 2023):

Respiratory Syncytial Virus (RSV) is a major cause of morbidity and mortality in infants. In October 2023, the United

States Centres for Disease Control and Prevention, along with guidelines from other expert groups, endorsed RSV vaccination of pregnant individuals to reduce severe RSV infections in their infants.

Nirsevimab, a monoclonal antibody that can be given to infants postnatally to reduce the risk of severe RSV, has also been recently approved and endorsed by expert guidance panels. In settings where Nirsevimab is not available, vaccination of pregnant individuals between 32 and 36 weeks of gestation in September 2023 through January 2024 in the northern hemisphere, with inactivated nonadjuvanted recombinant RSV vaccine (RSVPreF; Abrysvo). (Source: WHO "Immunizations during pregnancy", – 'Choosing the optimal strategy').

### Viral infections, Non-HIV

Testing for hepatitis C virus infection in infants with perinatal exposure (November 2023). New guidance from the Centres for Disease Control and Prevention recommends early testing for infants with perinatal exposure to HCV: • Test for HCV RNA during early infancy after two months of age, and ideally before six months of age. • After 18 months of age, test any infant who has not previously been tested by measuring anti-HCV antibodies, with reflexive testing for HCV RNA. A negative HCV RNA result at any time point after two months of age virtually excludes HCV infection and further testing is not required. Children with a positive HCV RNA test before three years of age should have repeat testing for HCV RNA before initiating antiviral therapy to determine whether they have spontaneously cleared the infection. (Source: WHO "Hepatitis C virus infection in children", – 'How to test').

### Valacyclovir for prevention of congenital cytomegalovirus infection (October 2023)

In a 2023 individual patient data meta-analysis maternal valacyclovir administration upon diagnosis of periconception or first-trimester primary CMV infection was associated with a 66% reduction in congenital CMV (11 versus 25%). This evidence suggests that maternal administration of valacyclovir for primary cytomegalovirus (CMV) infection substantially reduces the risk of congenital CMV infection, especially if begun prior to 14 weeks of gestation and within 8 weeks of the maternal infection. A high-dose oral valacyclovir (8 g per day) for patients with a primary CMV infection in early pregnancy. Source: WHO ("Cytomegalovirus infection in pregnancy", a section on 'Antiviral medication').

### Conclusion

In 2023 the COVID 19, Dengue, RSV and H3N2 outbreaks rocked advanced and developing countries. In India too they are a significant concern requiring immediate attention and action from both the government and individuals.

Surveillance of viral outbreaks even in developed countries is the need of the time, including possible importing from travel to endemic countries of various viruses.

In an informal survey of more than 100 doctors conducted in Karnataka less than half of the doctors are now working with full energy due to overworking fatigue compared to before they had COVID-19, 18% were unable to work, while nearly 50% reported some loss of earnings.

Viral disease mostly is self-restricted with mild symptoms, therefore can be managed symptomatically, and anti-viral drugs be used in only severe cases.

As the title of the article suggests neither we can, nor we need to fight or WAR with but make TRUCE with VIRUSES and try to live harmoniously.

People must learn and use as many preventive strategies as possible like practicing hand hygiene, consistently and correctly wearing a high-quality mask, using vaccines (by high-risk individuals), ventilation, and keeping distance, from sick or those who tested positive.

The states must try to improve the environment, especially in urban areas, clean & disinfect commonly used surfaces where people congregate, arrange diagnostic testing, and appropriate management for all cases irrespective of their paying capacities.

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