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ORIGINAL ARTICLE

# COVID-19 IN CHILDREN IN THIRD WAVE : CLINICAL PRESENTATION, COMPLICATIONS AND EFFECT OF INFLUENZA VACCINATION

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## ABSTRACT

**Objective:**

1. To analyze the clinical presentation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in the paediatric population in the third wave.
2. To study the correlation between disease spectrum and epidemiological factors.
3. To follow up for 6 months after recovery, to identify any long-term post-Covid complications.
4. To study the effect of Influenza vaccination on the disease

**Method:** In a tertiary care institution, children who tested positive for COVID-19 between December 1, 2021, and March 31, 2022, were identified from the outpatient department, inpatient department, and swab testing facility and enrolled for the study. Demographic data, clinical details, and epidemiological factors, were collected from the parents of the patients through a structured interview. The data was then analyzed using statistical methods.

**Result:** Most children were symptomatic and respiratory symptoms were the commonest. The majority of the cases were within a nuclear family, with high rates of mother-to-child transmission. Children with co-morbidities had similar disease outcomes as others. Post-Covid complications seen in 5 children, who showed symptoms suggestive of MISC, 3 of these showed Kawasaki disease phenotype and were labelled as Incomplete/atypical Kawasaki disease. Out of the 162 children, 101 children had been vaccinated at least once against Influenza, only 4 of then required hospitalization.

**Conclusion:** Children were mostly symptomatic during third wave of COVID-19 and influenza vaccination seems to have a protective effect.

## ARTICLE HISTORY

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## KEYWORDS

COVID-19, Multisystem inflammatory syndrome in children (MIS-C), Post-Covid complications, Influenza vaccination

## Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 Virus. Coronaviruses (CoV) are a large family of viruses that cause illnesses ranging from the common cold to more severe diseases such as the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS-CoV). Common signs of infection include respiratory symptoms, fever, cough, shortness of breath, and breathing difficulties. In more severe cases, the infection can cause pneumonia, severe acute respiratory syndrome, kidney failure, and even death.[1]

While children are as likely to get COVID-19 as adults, they are less likely to get severely ill.[2,3] Certain medical conditions may increase a child's risk of serious illness with COVID-19, including Obesity, Diabetes, Asthma, Congenital Heart Disease, Genetic conditions, and conditions affecting the nervous system or metabolism.[4]

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There are limited number of studies that have been carried out in India regarding the effect of COVID-19 in children, especially in the third wave. Children affected during the third wave, when the Omicron variant was predominant had less severe health outcomes than children in the same age group affected with the Delta variant.[5]

Multisystem Inflammatory Syndrome in children (MIS-C) is a serious condition that appears to be linked to Coronavirus disease in 2019 (COVID-19). Most children who become infected with the COVID-19 virus only have mild illnesses, but in children who go on to develop MIS-C, some organs, and tissues such as the heart, lungs, kidneys, digestive system, brain, skin, or eyes may become severely inflamed. MIS-C was defined according to the WHO criteria.[6]

We present data, regarding the clinical presentation, characteristics, and outcome- both immediate and long-term and epidemiological factors significant for disease transmission in children who had tested positive for SARS Cov2, in a tertiary care center.

## Methodology

This study was conducted in a tertiary care center in a metropolitan city in Maharashtra. Data collection was

done after obtaining approval from the institutional ethics committee. Data of children (up to 18 years of age) were collected from

- Outpatient department: children who showed symptomatology of COVID-19
- Inpatient department: Children admitted to the ward/ICU showing signs and symptoms of Covid-19.
- The testing facility (swab collection center): children who presented for nasopharyngeal/oropharyngeal swab collection.

Out of this, children who had evidence of Severe acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection either through a positive Rapid Antigen Test or a positive Real-time reverse Transcription – Polymerase chain reaction (real time-PCR), between 1 December 2021 to 31 March 2022, were collected through a structured interview. Information was collected in the following manner:

Demographic details such as Age (Neonates, Infants, Toddlers, 5-10 years and >10 years), Sex, Height, and Weight.

Test done: Rapid antigen test or RT-PCR and date of the report.

Symptomatology: The first symptom to appear, duration and characteristic of each symptom, classification of symptoms in Respiratory and Gastrointestinal symptoms.

Any co-morbidities and details of the same.

Duration of illness.

Details of hospitalization for Covid if any

Status of influenza vaccination in the child.

Status of COVID-19 vaccination in the family members.

Details of treatment received for Covid (Symptomatic, Nutritional supplementation, oxygen therapy, antibiotics)

Epidemiological details such as

- Number of family members
- Index case
- Travel history if any
- Isolation history
- Housing details (Number of bedrooms, bathrooms) to assess overcrowding if any.
- Occupation of earning members
- Socioeconomic status of the family.

Precautionary measures being taken against COVID-19.

**Follow-up details:** Clinical and psychological condition of the child 6 months post the infectivity period, any illness post-Covid, any reason for hospitalization post-COVID-19 infection.

Details of hospitalization of the few children who were admitted after testing positive for COVID-19 were extracted, and reports of their laboratory investigations which included Complete blood count, C-reactive protein, Liver function tests, Renal function tests, Coagulation profile, Ferritin, Lactate dehydrogenase, Interleukin-6, and D-dimer were compiled. Follow-up of all the patients enrolled in the study was carried out over 6 months. Detailed examination of the children who fit into the MIS-C criteria of WHO and were admitted to the hospital was done, and bedside 2D Echocardiography of such patients was also carried out. A few children presented with features of typical Kawasaki disease a few months after testing COVID-19 positive.

The treatment for children with MIS-C was noted, which was mainly in the form of respiratory support, intravenous Immunoglobulin, steroids, Aspirin, and Low Molecular Weight Heparin.

Children who required only home care were compared for their clinical characteristics and outcome.

Statistical Analysis of the data collected was done and represented via bar diagrams, histograms, and pie charts. A two-sided p-value <0.05 was considered significant. An association between the disease spectrum of COVID-19 and Influenza vaccination was noted using Odd's ratio.

Results

**Table 1.** Age distribution.

| Age Group | Number of Childrens |
|---|---|
| 0-1 month | 6 |
| 1 month-1 year | 9 |
| 1 year-5 years | 36 |
| 5 years-10 years | 48 |
| >10 years | 63 |

Among the 162 that were enrolled in the study, the maximum children were more than 10 years of age (38.8%), and minimum to the Neonatal age group (3.7%). However, the disease spectrum and severity showed no significant correlation to age.

SEX - There were 85 males and 77 females enrolled in the study. Both genders were equally affected and the COVID-19 virus didn't seem to have any gender predilection.

**Table 2.** Gender distribution.

| Gender | Number of Childrens |
|---|---|
| Males | 85 |
| Females | 77 |

**Table 3.** Test Undertaken

| Test Done | Number of Childrens |
|---|---|
| Rapid Antigen Test | 21 (13%) |
| RTPCR | 107 (66%) |
| Both | 34 (21%) |

**SYMPTOMATOLOGY**

The majority of the children who tested positive for COVID-19 were symptomatic

and fever was the most prevalent symptom amongst the symptomatic children.

Fever was also the first symptom to appear in most children. Respiratory symptoms such as sore throat, rhinorrhoea, dry cough, productive cough, and breathlessness were more common than gastrointestinal symptoms such as diarrhoea, nausea, and vomiting.

**Table 4.** Symptomatology.

| Symptom | Number of Childrens |
|---|---|
| Symptomatic Children | 118 (72.8%) |
| Asymptomatic Children | 44 (27.2%) |

**Symptomatology in different age groups:** Maximum symptoms were seen in the 5 years to 10 year age group that is the school going age group.

**Table 5.** Symptomatology in different age groups.

| Age Group | Symptomatic | Asymptomatic |
|---|---|---|
| 0-1 month (Neonates) | 4 | 0 |
| 1 month - 1 year (Infant) | 12 | 2 |
| 1 year – 5 years | 23 | 9 |
| 5 years – 10 years | 41 | 15 |
| >10 years | 38 | 18 |

**Figure 1.** Symptoms.

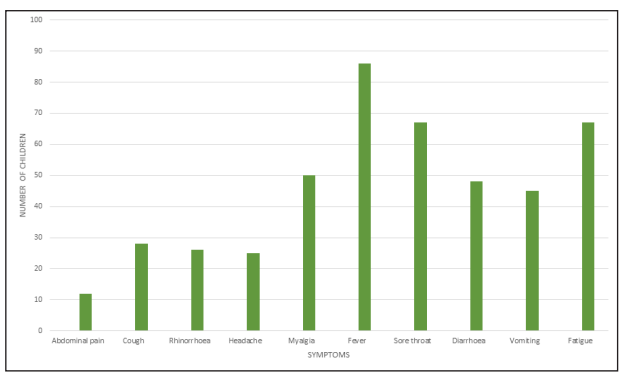


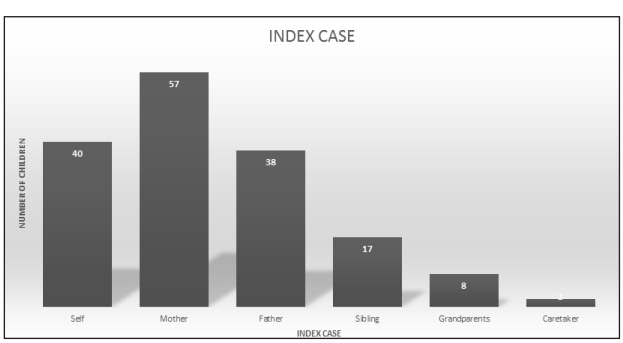

**Table 6.** Types of symptoms.

| Types of Symptoms | Number of Childrens |
|---|---|
| Respiratory | 66 (41%) |
| Gastrointestinal | 15 (9%) |
| Both | 23 (14%) |
| Other | 24 (15%) |

**INDEX CASE**

Index case is defined as the first identified and documented case/patient in a group of related cases of a particular disease, included in an epidemiological study. In this study, in the majority of the families, the mother of the child was the index case. This could have been a leading factor in propagating the disease through mother-to-child transmission.

**Figure 2.** Index case.




**CO-MORBIDITIES :**

Out of the 162 children who were enrolled for the study, only 8 children had significant co-morbidities which were: Cerebral palsy, Down syndrome, Obesity, Chronic Kidney Disease, Apert syndrome, febrile seizures, Prematurity, and Low Birth Weight. The child who is a known case of febrile seizures had a repeat episode of febrile convulsion and had to be admitted for the same, while the child with Downs Syndrome had severe breathlessness and had to be given oxygen supplementation. The disease spectrum in the other children with co-morbidities was no different from the ones without any co-morbidities.

**INFLUENZA VACCINATION**

The majority of the children, i.e. 62% received the Influenza vaccine at least once, while 38% of the children had never received the influenza vaccination.

**Table 7.** Influenza Vaccination Coverage.

| Received Influenza Vaccination | Number of Childrens |
|---|---|
| Yes | 101 (62%) |
| No | 61 (38%) |

15 out of 162 Children had to be hospitalized for COVID-19 infection. 101 children out of 162 children had received the Influenza vaccination, out of these only 4 children required hospitalization. $p \leq 0.05$, was considered to denote a significant difference by using the chi-square test.

**Table 8.** Influenza vaccination & need for hospitalization

| Received Influenza Vaccine | Hospital admission for covid | | P-value |
|---|---|---|---|
| | Yes n(%) | No n(%) | |
| Yes | 4 (4%) | 97 (96%) | <0.00001 |

The p-value as seen above, is 0.00001 i.e. <0.05, which is statistically significant. Thus, the Influenza vaccine can be considered to have a protective effect and reduce the disease severity of those children affected with COVID-19, thus reducing their need of hospital admission. The Influenza vaccination didn't seem to have an effect on the duration of illness in those children affected with COVID-19.

**Table 9.** Influenza vaccination & duration of illness.

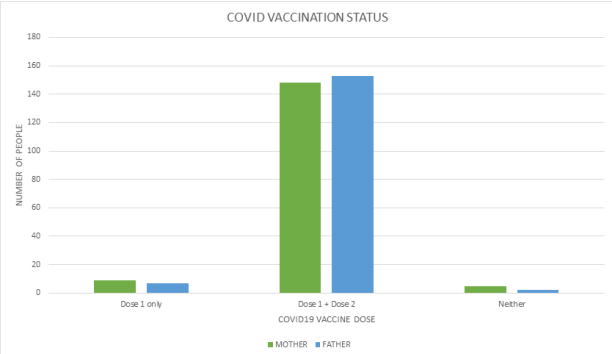
| Duration of illness (days) | Received influenza vaccine | | P-value |
|---|---|---|---|
| | Yes Mean ± std.dev | No Mean ± std.dev | |
| | 4.68 ± 1.44 | 4.84 ± 2.03 | 0.632 |

Here, as seen above the p-value is 0.632 which shows a lack of association between Influenza vaccination and the duration of illness.

STATUS OF COVID VACCINATION AMONG PARENTS:

The majority of the parents of the children affected with COVID-19 in the third wave had received the first 2 doses of the Covid vaccine.

**Figure 3.** Covid vaccination status among parents.




This shows rising awareness regarding the necessity of vaccination and preventive methods taken.

**DETAILS OF TREATMENT:** The COVID-19 affected children have taken combined treatment measures, however symptomatic management was the most common mode while oxygen supplementation was required by very few children.

**Figure 4.** Details of treatment.

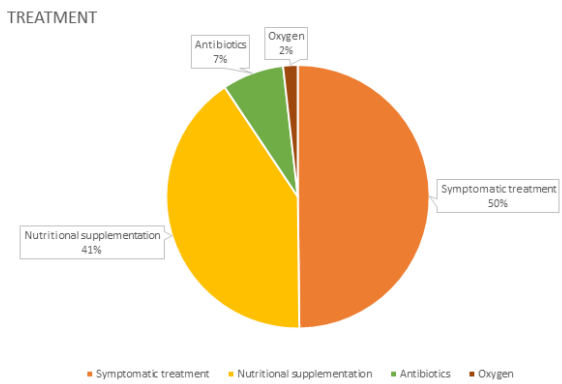
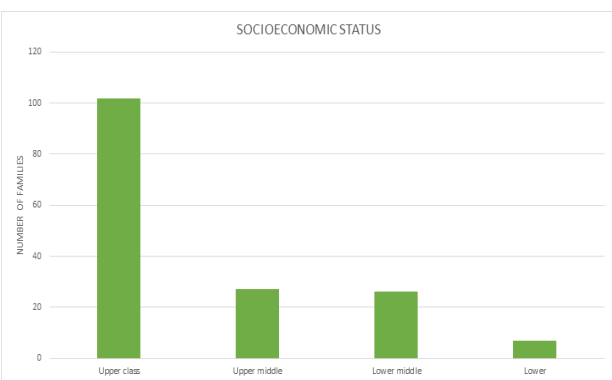



**Figure 5.** Socioeconomic Status.




The majority of the children, who tested positive in our tertiary care center, belonged to a higher socioeconomic class.

FOLLOW UP:

**Table 10.** Post COVID status.

| Status | Number of Childrens |
|---|---|
| Full Recovery Post COVID | 153 |
| Post COVID Health Problems | 9 |

Post-Covid 9 illness, 9 children from our study, faced certain health problems, not all of which were related to Covid. 2 children had typical symptoms of Kawasaki disease along with Coronary artery changes. 3 children had features of Post Covid Multisystem Inflammatory syndrome in children (MIS-C) with Kawasaki disease phenotype. These children could also be classified into Incomplete Kawasaki disease. There was 1 case of Post Covid Depressive symptoms and 1 case of newly diagnosed Systemic Lupus Erythematous (SLE). 2 children presented with viral bronchiolitis and required Intensive care treatment. There was one child who was a known case of advanced Chronic Kidney Disease; he had recovered completely from Covid. He presented 2 months later, received intensive care, but passed away, the cause of death being severe metabolic acidosis in a known case of Chronic Kidney Disease.

## Discussion

Following the subsidence of the first wave of COVID-19 in September 2020 and the beginning of the second wave in mid-February 2021, there had been speculations about the increased possibility of a third wave increasing the burden on the healthcare system.[7] Hence we planned our study around the third wave of COVID-19 in children.

In India, previous studies state that COVID-19 has a lower incidence and causes milder disease with a lower need for intensive care admission and a lower mortality rate in children compared with adults (8), same data is reported from China[9] and UK.[10]

MIS-C is a rare but severe complication in children. We studied the clinical characteristics and course of children presenting with COVID-19 symptoms in the third wave and follow up with those children to observe post-Covid complications if any, including MIS-C. We did not carry out genome sequencing to confirm the presence of the omicron variant in the patients.

Out of the 162 children that we studied, the maximum numbers of children, i.e. 38.8% children were above 10 years of age. 118 children (72.8%) were symptomatic, out of which the majority of the symptomatic children 34.7% were in the 5-10 year age group. Fever was the most predominant symptom (53%), followed by respiratory symptoms, and very few gastrointestinal and non-specific symptoms.

The index case, i.e. the first confirmed case of COVID-19 in most families was the mother. (35 %) A study carried out by the University of Birmingham[11] states that fewer than two per cent of babies born to mothers with SARS-CoV-2 infection also test positive for the virus, but they are more likely to test positive when the women have severe COVID-19 or were diagnosed after childbirth. In our study, we observe increased mother-to-child transmission which can be attributed to the fact that in most Indian families the mother is the primary caregiver and it is difficult to isolate the child from the mother at all times.

In terms of treatment for COVID-19 in children, only 7% children in our study required antibiotics and only 2% children required supportive oxygenation. The rest of the children were given symptomatic treatment and nutritional supplementation.

Our study shows that 62.9% of children who had

tested positive for COVID-19 to be belonging to a higher socioeconomic status, which could be attributed to the fact that the testing centre is a tertiary care centre, and testing volumes might be less in the lower socioeconomic strata.

We followed up all the children who tested positive for 6 months after complete recovery.

A multisystem inflammatory syndrome in children (MIS-C) is a rare but serious complication associated with COVID-19, initiated by an overactive immune response in kids that usually hits weeks after exposure to COVID-19. MIS-C is a disorder in which inflammation could occur in different parts of the body. The disease puts pressure on the heart, as blood vessels leading towards the heart get inflamed and incapable of carrying adequate blood, hence producing cardiac complications in children hospitalised with MIS-C.[12]

9 out of 162 children had post-Covid complications. 2 children were diagnosed with typical Kawasaki disease, with coronary artery involvement and 3 children had MIS-C like features with Kawasaki phenotype. No study till date is available in the literature about the prevalence of MIS-C in children.

We did not find any non-MIS-C complications.

In our study we observed a significant relation between the Influenza vaccination status and the need for hospitalization in the paediatric population. Influenza vaccine appears to have a protective effect against SARS-Cov2 in terms of hospitalization. A study, which was not restricted to the paediatric population, demonstrated a significant lower risk for mechanical ventilation in the Influenza vaccinated COVID-19 patients over the non-vaccinated ones.[13]

However there were no statistical differences between Influenza vaccinated and non-vaccinated COVID-19 patients, in any of the mortality rates, hospital admission, hospitalisation time, ICU admission, ICU time, and appearance of symptoms.

Fink et al[14] discussed an explanation of the association between the influenza vaccine and the lower risk of Covid-19 related outcomes. This included the possibility that live vaccines can trigger the trained innate immunity and result in a recognized "off target" protection against various pathogens besides those directly targeted by the given vaccine. They reported that recently Influenza vaccinated cases had an average of 7% lower odds, 17% lower odds, and 16% lower odds of ICU treatment, invasive respiratory support requirement, and death, respectively.

Another study which included paediatric patients[15] concluded that seasonal influenza and pneumococcal vaccination might be protective in symptomatic COVID-19 diseases. Also in children, influenza infection without vaccination can increase the susceptibility to other serious illnesses and also make them increasingly vulnerable to COVID-19.

**Conclusion**

During the third wave of the pandemic, most of the children who tested positive for COVID-19 were symptomatic at our hospital. Only 9% of the children who tested positive for COVID-19 had to be hospitalized and the recovery rate was good among them.

In the follow-up period of 6 months, six children required hospitalization, which included 1 case of viral bronchiolitis, 5 cases of MIS-C, and 3 cases of MISC with Kawasaki disease phenotype. Epidemiological factors such as the type of housing play an important role as overcrowding has been shown to increase the risk of disease transmission. Also, the inability to isolate children, especially neonates, infants and toddlers from mothers, increases the risk of mother-to-child transmission. The majority of the parents are well aware of the modes of transmission of the Coronavirus and precautions that are to be taken.

Influenza vaccination seems to have a protective effect as it reduces the rate of hospital admission. Only 4% of the Influenza vaccinated children who were COVID-19 positive required hospital admission. The duration of hospitalization or disease outcome did not have a strong association with the Influenza vaccination status in our study. Further studies in a larger paediatric population are required to understand better the significance of Influenza vaccination in the course of Covid-19 in children, including viral interference if any.

**WHAT THIS STUDY ADDS:**

Clinical presentation, epidemiological correlation, complications of COVID-19 third wave and protective effect of influenza vaccination in children.

Ethics Clearance: RHC/BIOPMRFIEC/2022122

**Compliance with Ethical Standards**

Funding: None

Conflict of Interest: None

**References:**

1. World Health Organization (https://www.who.int/health-topics/coronavirus) WHO/2019-nCoV/Surveillance_Case_Definition/2022.1
2. Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in the severity of SARS-CoV-2 infections. Arch Dis Child 2021;106:429-439. doi:10.1136/archdischild-2020-320338.
3. Florian Götzinger, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. Lancet Child Adolescent Health 2020; 4: 653-61.
4. Tsabouri S, Makis A, Kosmeri C, Siomou E. Risk Factors for Severity in Children with Coronavirus Disease 2019: A Comprehensive Literature Review. Pediatr Clin North Am. 2021 Feb;68(1):321-338. doi: 10.1016/j.pcl.2020.07.014. Epub 2020 Jul 30. PMID: 33228941; PMCID: PMC7392074.
5. Lindsey Wang, et al. Incidence rates and Clinical Outcomes of SARS-CoV-2 Infection with the Omicron and Delta variants in children younger than 5 years in the United States - JAMA Paediatrics August 2022 Volume 176, Number 8.
6. Multisystem Inflammatory syndrome in children and adolescents with Covid-19 - Scientific brief. (WHO/2019-nCoV/Sci Brief/Multisystem_Syndrome_Children/2020.1)
7. Plausibility of the third wave of Covid-19 in India: A mathematical modelling based analysis by Sandip Mandal, Nimalan Arinaminpathy, Balram Bhargava, Samiran Panda.
8. The Pandemic and India's children (Indian Association of Paediatrics- (https://www.indianpediatrics.net/july2021/july-607-608.htm)

9. Yuanyuan Dong, et, al. Epidemiology of COVID-19 among Children in China. PEDIATRICS Volume 145, number 6, June 2020:e20200702.
10. Olivia V Swann, Karl A Holden et al. Clinical characteristics of children and young people admitted to the hospital with Covid 19 in the United Kingdom: prospective multicentre observational cohort study. BMJ 2020;370:m3249 | doi: 10.1136/bmj.m3249.
11. Mother to Child transmission, the University of Birmingham (https://www.birmingham.ac.uk/research/who-collaborating-centre/pregcov/about/mother-to-child-transmission.)
12. Multisystem Inflammatory Syndrome in Children (MISC) Associated with Coronavirus Disease 2019. Centers for Disease Control and Prevention. Emergency preparedness and response: Health alert network. May 14, 2020. Available from: https://emergency.cdc.gov/han/2020/han00432.asp. Accessed July 15, 2020.
13. Almadhoon HW et al. The effect of influenza vaccine in reducing the severity of clinical outcomes in patients with COVID-19: a systematic review and meta-analysis. Sci Rep. 2022 Aug 22;12(1):14266. doi: 10.1038/s41598-022-18618-6. PMID: 35995930; PMCID: PMC9395333.
14. Fink G et al. Inactivated trivalent influenza vaccination is associated with lower mortality among patients with COVID-19 in Brazil. BMJ Evid Based Med. 2020 Dec 11:bmjebm-2020-111549. doi: 10.1136/bmjebm-2020-111549. Epub ahead of print. PMID: 33310766; PMCID: PMC7735072.
15. Patwardhan A, Ohler A. The Flu Vaccination May Have a Protective Effect on the Course of COVID-19 in the Pediatric Population: When Does Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Meet Influenza? Cureus. 2021 Jan 6; 13(1):e12533. doi: 10.7759/cureus.12533. PMID: 33425565; PMCID: