

# Effect of COVID-19 vaccination on influenza-associated respiratory infection (IARI): benefit or backfire

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**Abstract. – OBJECTIVE:** Undoubtedly, COVID-19 vaccine (C19V) has significantly changed the pandemic's trajectory positively. At the same time, reports of transient local and systemic post-vaccination reactions leave a concern about its unknown impact on common ailments. Its effect on IARI is unclear because the present IARI epidemic began immediately after C19V in the previous season.

**PATIENTS AND METHODS:** A retrospective observational cohort study among 250 Influenza-associated respiratory infection (IARI) patients by a structured interview questionnaire was conducted with the comparison between 3 groups with 1 dose, 2 doses and 2 doses plus booster dose of C19V. The  $p < 0.05$  was considered significant in this study.

**RESULTS:** Among samples 21.2% received one dose of the C19V, only 3.6% got Flu vaccination, 30% had  $\geq 2$  comorbidities such as diabetes (22.8%), hypertension (28.4%) and ionically, 77.2% were on chronic medications. Significant differences ( $p < 0.05$ ) were found between groups with duration of illness, cough, headache, fatigue, shortness of breath and hospital visits. The logistic regression analysis shows that the extended IARI symptoms and hospital visits were significantly high among Group 3 (OR=9.17, 95% CI=3.01-29.0) and the same trend remained significant after adjusting the incidence of comorbidities among samples, the chronic conditions (OR=5.13, 95% CI=1.37-14.91) and flu vaccination status (OR=4.96, 95% CI=1.41-16.2). Also, 66.4% of the patients were indecisive about getting vaccinated further.

**CONCLUSIONS:** It has been challenging to reach any definitive conclusions regarding the effects of C19V on IARI, conducting extensive, substantial population-based studies that integrate clinical and virological data from more than one season is absolutely required, despite the fact that the majority of the reported effects were mild and temporary.

*Key Words:*

COVID-19 vaccine, Influenza-associated respiratory infection, Flu, Side effect, Adverse event, Hesitance.

## Introduction

Influenza-associated respiratory infection (IARI) is one of the major public health issues worldwide as it is contagious. The influenza viruses that cause seasonal flu, are acute respiratory infections that can spread to anyone, anywhere in the world. It represents the annual burden of sickness with various degrees of severity, which can lead to hospitalization and death. It is estimated that 300,000-650,000 people die each year as a result of seasonal influenza-associated respiratory infections<sup>1</sup>. According to CDC estimates, there were 8,000,000-13,000,000 flu infections, 3,700,000-6,100,000 flu-related hospital visits, 82,000-170,000 flu-related hospitalizations, and 5,000-14,000 flu-related fatalities between October 1, 2021, and June 11, 2022<sup>2</sup>.

As the epidemic spreads, there is a documented rise in hospital admissions as well as respiratory or cardiovascular deaths. According to 2018 CDC study published in *Clinical Infectious Diseases*<sup>3</sup>, on average, 8% of the US population is infected with Flu in each season and it may go up to 11% depending upon the type of virus circulating with an even bigger impact in developing nations<sup>3-5</sup>. South-East Asia has the second-highest excess mortality rates (EMR), at 3.5-9.2 per 100,000 people, beside Sub-Saharan Africa (2.8-16.5 per 100,000)<sup>1</sup>. The projected global influenza mortality from respiratory infections shown in 2018 seems to be greater than a prior estimate of 148,000-249,000 in 2013<sup>6</sup>.

Pregnant women, children under the age of 59 months, the elderly, people with chronic medical conditions such as chronic cardiac, pulmonary, renal, metabolic, neurodevelopmental, liver, or hematologic diseases and people with immunosuppressive conditions (such as HIV/AIDS, receiving chemotherapy or steroids, or having cancer) are at higher risk of developing severe illness or complications when infected. It is very difficult for countries to deal with this key public health challenge since it has a major economic impact too in the form of healthcare costs and lost working hours.

Though it was evident that the relative impact of physical separation, restrictions on movement and travel, hand hygiene, and other COVID 19-related interventions considerably decreased the prevalence of influenza worldwide<sup>7</sup>, there is a resurgence of annual epidemics after international travel resumed. It is evinced by the recent spread of influenza A(H3N2) viruses in Cambodia and Bangladesh<sup>8</sup>. The Southern Hemisphere experienced an early and highly active influenza season in the last week of November 2022. In addition to increasing the danger of serious sickness and death for those who are already at risk due to the pandemic, the probable co-circulation of COVID-19 and seasonal influenza will likely place additional strain on hospitals and healthcare providers.

However, influenza epidemics are yearly events with established seasonality in temperate locations, they can happen all year long with unpredictable peaks in tropical region<sup>9</sup>. With influenza A(H1N1) pdm09 viruses predominating, influenza A(H3N2) and influenza B (Victoria lineage when determined) detections were reported in Southern Asia, among which India had the majority of A(H1N1) pdm09 virus detections<sup>6</sup>. This increase in the reported IARI cases in India as well as worldwide made WHO call for regionwide Influenza pan-

demically preparedness planning. Further, the current IARI epidemic is an immediate season following post COVID-19 vaccination (C19V). The impact of this unique C19V on the future flu season is a significant area of uncertainty as the C19V is known to produce certain localized and systemic side effects. Hence, any possible correlation of post C19V effect on IARI cannot be ignored.

In fact, the COVID-19 pandemic prompted the quick development and approval for emergency usage of the vaccine<sup>10</sup>. The vaccines were quickly reviewed before being made available to the public in order to help contain the pandemic. Due to the newer form of vaccines and the urgency, the examination of the side effect profiles was conducted according to protocol but was less thorough than for earlier vaccines<sup>11</sup>. Although the C19V has significantly changed the pandemic's trajectory and saved tens of millions of lives worldwide, it causes transient local and systemic post-vaccination reactions<sup>12-17</sup>. Overall, among healthcare workers (HCWs) and the general population in the USA, the C19V campaign has given rise to a lot of worries, doubts, and disagreements about the safety of both the new vaccines and their administration<sup>18</sup>. In this scenario, it is vital to research the impact of C19Vs on IARI to educate healthcare professionals as well as the general public. There are only few studies in literature about the side effects of the C19V that concentrate exclusively on IARI like the frequency, severity of symptoms and related hospitalizations occurring after receiving this vaccine. Hence, this study's goal was to examine the C19V's impact in individuals with IARI symptoms and their attitude towards C19V.

## Patients and Methods

### *Design*

The aim of the study was to determine the effect of C19V on patients with IARI. We conducted a retrospective observational cohort study among patients with the symptoms of IARI. Every day during the 10-week period between August to October 2022 from 7 am to 8 pm, trained nurses collected the data from the patients. Those eligible were enrolled and consent to participate in the study was obtained.

### *Population and Setting*

Patients presented with IARI symptoms were the study population. This study included patients

who visited the outpatient clinics of selected hospitals at Chennai, India during data collection period. The study had received ethical approval from the local institutional review board.

### **Sample Size and Sampling Process**

By the non-probability convenient sampling technique, 250 individuals who presented with IARI symptoms were included in this study from the 541 IARI patients who enrolled in the clinics during the data collection period. The minimum suggested sample size was 239, according to the Raosoft online sample size calculator<sup>19</sup>, with an overall population of 541 patients, 99% confidence with a margin of error of 5% and the response distribution of 80%. Patients with a minimum of 3 days of IARI symptoms, aged >18 years, able to communicate verbally, and with no other psychological issues such as mood and anxiety disorders were included in the study. In order to gather clinical data, outpatients and patients who had been discharged from the hospital were contacted 7 days after the onset of their symptoms. If their symptoms persisted, they were then contacted once again 7 days later until they were asymptomatic.

### **Data Collection Tools/Instruments**

The tool consisted of 3 sections. Section A: The socio-demographic characteristics of the participants. Section B: Clinical data including duration of IARI, clinical features, comorbidities, smoking history, Flu vaccination history, subsequent outpatient visits and hospitalization were collected using a structured questionnaire. Section C: Checklist to assess attitude of the IARI patients on C19V. To assess the attitude, only patients in Group 1 and 2 were included. The content validity of the tool was obtained from five experts in nurses and one general physician. The reliability of the tool was assessed after the pilot study by Cronbach's Alpha test (internal consistency), which was highly reliable. Clinical data such as comorbidities were verified from each patient's current electronic health records.

### **Ethical Consideration**

Ethical permission was obtained from the Institutional Ethical Committee with IEC/LCN/2022-09 and consent from the participants were collected before starting the study by explaining the aim of the study, their role, confidentiality of the information and their right to leave from the study

at any point of data collection.

### **Statistical Analysis**

Statistical analysis was performed using IBM SPSS 22.0 (IBM Corp., Armonk, NY, USA). The sample population was divided into three groups: Group 1 (1 dose of C19V), Group 2 (2 doses of C19V) and Group 3 (2 doses plus 1 Booster dose C19V), to allow for direct comparisons with IARI symptoms and COVID-19 vaccination status (C19V status). The independent Student's *t*-test, Mann-Whitney U, Chi-squared and Fisher's exact tests were used where appropriate for group comparisons in socio-demographics, number of comorbidities, clinical characteristics across different groups with C19V status. Logistic regression analyses were then conducted to determine the influence of C19V status on severity IARI symptoms using a composite variable of extended duration of illness, after separate adjustments for potential confounders, such as number of comorbidities, presence of chronic conditions, and the absence of flu vaccine. In this analysis, Group 1 was considered the reference category, and comparisons were made between Group 1 and Group 2, as well as Group 1 and Group 3. The  $p < 0.05$  was considered significant in this study.

## **Results**

### **Demographic and Clinical Status**

Out of 250 study samples with IARI, 53 (21.2%) received one dose of the C19V and 56.4% received 2 doses. Only 3.6% of the samples got Flu vaccination and among this 2.8% was by the patients who received 2 doses plus booster vaccination. One hundred and eight were female and 121 (48.4%) were aged 51- 65 years. Regarding the age, majority of the participants (48.4%) were in the age of 51-65 years and among this group, 61.7% got 2 doses of C19V. Thirty percentage of the samples had 2 or more than 2 comorbidities. Around 50% of the samples had diabetes (22.8%), hypertension (28.4%) and 12% of them had respiratory illness such as asthma (9.2%) and chronic obstructive pulmonary disease (COPD) (2.4%). Ironically, 77.2% of them were using chronic medications (Table I).

### **Clinical Features of IARI and C19V status**

The Clinical features and C19V status of the study samples are presented in Table II. Only 20.4% of the participants had symptoms for less than 7 days and 86% of them had symptoms for

**Table I.** Demographic and clinical status of the samples.

Variables	COVID-19 vaccination Status (C19V)			
	All	Group 1	Group 2	Group 3
<b>Number of patients (%)</b>	250	53 (21.2)	141 (56.4)	56 (22.4)
<b>Number of flu vaccination</b>	9 (3.6)	0	2 (0.8)	7 (2.8)
<b>Gender</b>				
Male	142 (56.8)	14 (26.4)	89 (63.1)	39 (69.6)
Female	108 (43.2)	39 (73.6)	52 (36.9)	17 (30.4)
<b>Age</b>				
20-35 years	19 (7.6)	11 (20.8)	7 (5)	1 (1.8)
36-50 years	46 (18.4)	9 (17)	11 (7.8)	26 (46.4)
51-65 years	121 (48.4)	13 (24.5)	87 (61.7)	21 (37.5)
>65 Years	64 (25.6)	20 (37.7)	36 (25.5)	8 (14.3)
<b>Number of comorbidities</b>				
None	124 (49.6)	42 (79.2)	72 (51.1)	10 (17.9)
1	51 (20.4)	3 (5.7)	26 (18.4)	22 (39.3)
≥2	75 (30)	8 (15.1)	43 (30.5)	24 (42.9)
<b>Chronic conditions</b>				
Diabetes mellitus (DM)	57 (22.8)	13 (24.5)	30 (21.3)	14 (25)
Hypertension (HT)	71 (28.4)	18 (34)	39 (27.7)	14 (25)
Asthma	23 (9.2)	7 (13.2)	14 (9.9)	2 (3.6)
COPD	6 (2.4)	2 (3.8)	4 (2.8)	0
Neuromuscular disease	0	0	0	0
cognitive dysfunction	0	0	0	0
cardiovascular disease (CVD)	16 (6.4)	3 (5.7)	8 (5.7)	5 (8.9)
Chronic kidney disease	4 (1.6)	0	4 (2.8)	0
Chronic liver disease	1 (0.4)	0	1 (0.7)	0
Heavy alcohol use	4 (1.6)	1 (1.9)	3 (2.1)	1 (1.8)
Obesity	17 (6.8)	2 (3.8)	6 (4.3)	2 (3.6)
Any cancer	3 (1.2)	1 (1.9)	2 (1.4)	0
<b>Use of any chronic medication</b>				
Yes	193 (77.2)	42 (79.2)	118 (83.7)	33 (58.9)
No	57 (22.8)	11 (20.8)	23 (16.3)	23 (41.1)

more than 7 days. Significant differences found between the groups with C19V status and clinical variables, such as duration of illness, cough, headache, fatigue, shortness of breath and shortness of breath on exertion which was significant  $p<0.05$ . The above symptoms were moderate to severe among Group 2 and 3. Differences in the number of patients with cough was around 60% in Group 2 and 3 compared to only 32% among Group 1 patients ( $p<0.04$ ). Headache was reported to have high significance comparatively among the Group 3 patients ( $p<0.05$ ) and similar trend was noticed with fatigue as well. Around 14% of the patients had shortness of breath and 17.2% had shortness of breath on exertion ( $p<0.05$ ).

#### **Hospital Visits and Admission by C19V status**

In Table III, the number of hospital visits and admission status of the participants was presented. Among the 250 samples, 133 visited the

hospitals for one or more times and there was significant difference among groups at  $p<0.05$ . Among the samples, 22.8% of the patients visited the hospitals for 4 times for the treatment of IARI symptoms, 10.6% and 73.2%, respectively, from group 2 and 3. Thirteen patients were admitted in the hospital for flu treatment, of which 7.1% were group 3 patients (i.e., who had 2 doses and the one booster dose) which is high among the groups though it was not significant.

#### **Logistic Regression**

As mentioned in the methods, logistic regression analyses were conducted to determine the influence of C19V status on severity of IARI symptoms using a composite variable of extended duration of illness with or without hospital admission, after separate adjustments for potential confounders (Table IV). The odds ratio (OD) and 95% confidence intervals (CI) between the extended IARI symptoms according to C19V

status shows that there is significant difference between the groups at  $p < 0.05$ . Association between unadjusted model and model 1 (Adjusted for potential confounders: number of comorbidities, chronic conditions such as diabetes Mellitus, Hypertension, cardio-vascular diseases, asthma and chronic obstructive pulmonary disease was presented. Similarly, the association between model 1 and 2 (Adjusted for all factors in Model 1 and Flu Vaccination Status) was also shown in table IV. The extended IARI symptoms and hospital visits was significantly high among Group 3 samples i.e., those who had 2 doses plus booster dose (OR=9.17, 95% CI=3.01-29.0). The same trend remained significant after the adjustment of number of comorbidities, chronic conditions such as DM, HT, CVS, asthma, COPD (OR=5.13, 95% CI=1.37-14.91) and additional adjustment of flu vaccination status (OR=4.96, 95% CI=1.41-16.2).

#### Attitude on COVID-19 Vaccination

Figure 1 shows the attitude of the patients with IARI symptoms towards C19V. It shows that among the Group 1 and 2, considerable percentage of patients said that they will not get vaccinated further. The reasons for avoiding further vaccination mentioned were as losing trust on C19V, lack of adequate testing to monitor side effects

and using different vaccines. Overall, 66.4% of the patients was unsure about getting vaccinated further.

### Discussion

Because influenza is a disease that is constantly changing, attempts at prevention, readiness, and response must be continuously modified. This is due to the fact that an influenza outbreak would probably have a significant impact on how well a country's health system works generally and would cost a lot of money and medical staff. A flu pandemic is expected to cost the United States \$60 billion annually. As winter 2022 is the immediate season post-COVID pandemic and its rapid vaccination drive, it is critical to investigate the C19V on IARI, although there is numerous COVID-19 vaccine-related side effects that are widespread or have clinical significance, including rare side effects such as myocarditis, costochondritis, hematuria, menstruation problem, stroke, etc<sup>21</sup>. In this study, we assessed the influence of C19V status on clinical features and outcomes of IARI related symptoms and the attitude of patients on C19V.

This study described the IARI clinical features of 250 samples between August to October

**Table II.** Clinical features of IARI by C19VS.

Variables	COVID-19 vaccination Status (C19V)				p-value
	All	Group 1	Group 2	Group 3	
<b>Duration of illness</b>					
<7	51 (20.4)	33 (62.3)	13 (9.2)	5 (8.9)	0.021*
7 to 14	127 (50.8)	14 (26.4)	81 (57.5)	32 (57.1)	
>14	72 (28.8)	6 (11.3)	47 (33.3)	19 (33.9)	
<b>Clinical symptoms</b>					
Fever	203 (81.2)	49 (92.5)	127 (90.1)	51 (91.1)	0.32
Chill or rigor	30 (12)	24 (45.3)	71 (50.4)	27 (48.2)	0.74
Cough	228 (91.2)	17 (32.1)	84 (59.6)	33 (58.9)	0.04*
Productive cough	64 (25.6)	5 (9.4)	54 (38.3)	10 (17.9)	0.12
Congestion	127 (50.8)	10 (18.9)	31 (22)	9 (16.1)	0.56
Sore throat	117 (70.8)	7 (13.2)	21 (14.9)	8 (14.3)	0.26
Head ache	58 (23.2)	6 (11.3)	37 (26.2)	22 (39.3)	0.05*
Myalgia	67 (26.8)	10 (18.9)	24 (17.0)	9 (16.1)	0.13
Joint pain	29 (11.6)	5 (9.4)	11 (7.8)	4 (7.1)	0.61
Nasal discharge	161 (64.4)	31 (58.5)	89 (63.1)	33 (58.9)	0.37
Sneezing	59 (23.6)	11 (20.8)	37 (26.2)	13 (23.2)	0.28
Conjunctivitis	6 (2.4)	2 (3.8)	6 (4.3)	2 (3.6)	0.17
Fatigue	31 (12.4)	7 (13.2)	31 (22)	11 (19.6)	0.05*
Anorexia	84 (33.6)	14 (26.4)	51 (36.2)	17 (30.4)	0.307
Shortness of breath	34 (13.6)	2 (3.8)	11 (7.8)	6 (10.7)	0.05*
Shortness of breath on exertion	43 (17.2)	3 (5.7)	13 (9.2)	6 (10.7)	0.05*

\* $p < 0.05$  is significant.

**Table III.** Hospital visits and admission by C19VS.

Variables	All	Group 1	Group 2	Group 3	p-value
<b>Total No. of hospital visits</b>					
1	14 (5.6)	3 (5.7)	4 (2.8)	7 (12.5)	0.05*
2	21 (8.4)	5 (9.4)	7 (5.0)	9 (16.1)	
3	41 (16.4)	3 (5.7)	17 (12.1)	21 (37.5)	
4	57 (22.8)	1 (1.9)	15 (10.6)	41 (73.2)	
None	117 (46.8)	41 (77.4)	40 (28.4)	36 (64.3)	
<b>Hospital admission</b>	13 (5.2)	1 (1.9)	8 (5.7)	4 (7.1)	0.213

\* $p < 0.05$  is significant.

2022, of which 53 (21.2%) received only one dose of the C19V. In the literature, the fully vaccinated people against COVID-19 with last dose of primary series per 100 population worldwide is 63.46 and boosted is 28.96<sup>5</sup> compared to 56.4 and 26.4, respectively, among the study participants. Similar findings were reported in a study<sup>18</sup> done on HCWs, which shows that 81.71% of them received both doses; however, 18.29% took only the initial dose.

Among the samples of the present study, 43.2% were aged 51–65 years, 56.4% got 2 doses of C19V and 30% had  $\geq 2$  comorbidities such as diabetes (22.8%), hypertension (28.4%) and ionically, 77.2% of them were using chronic medications. A slightly different finding was reported in a study<sup>18</sup>, in which 42.36% are in the 31–40 age range and 29.39% are in the above 50 age range. Even though getting a yearly flu shot has many benefits, only about 50% of US citizens do so<sup>20</sup>. In the current study, only 3.6% of the samples received the vaccine, which was very low comparatively.

Among the samples of present study, 86% had the IARI symptoms for more than 7 days and there were significant differences ( $p < 0.05$ ) found between the groups with C19V status, such as duration of illness, cough, headache, fatigue, shortness of breath and shortness of breath on exertion. Among the 250 samples, 133 visited the hospitals

for one or more times and there was significant difference ( $p < 0.05$ ) among groups. According to earlier research<sup>22–25</sup>, the flu patient's clinical presentation, severity, and outcome depend on their demographics, medical history, kind of virus, and other factors, and the most frequent symptoms were dyspnea, cough, fever, and sore throat. In contrast to the present study, the average duration of fever and its accompanying systemic symptoms is 3 days, which extend up to 8 days. After the fever has subsided, cough and general malaise may last for up to 2 weeks<sup>3,26,27</sup>. In the present study, the duration of the illness and number of hospital visits varied according to the C19V status which is one of the most significant findings. There could be several independent or linked explanations for this significant association, including a possible antigenic drift or antigenic shift. Secondly, the reported relationship might have happened by accident, be connected to seasonal respiratory virus infections<sup>28,29</sup>, or be mechanistically unrelated, according to another theory explaining the negative association. However, there are already well-known advantages of these vaccinations, immunization against COVID-19 and flu, must be urged to minimize hospitalization and related consequences. To ascertain whether there is a causal relationship between C19V uptake and IARI, additional virological, epidemio-

**Table IV.** Logistic regression models for extended IARI symptoms according to C19VS.

COVID-19 vaccination status	Unadjusted		Model 1		Model 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Group 1	1		1		1	
Group 2	2.13 (0.89, 7.53)	0.69	2.01 (0.63, 4.89)	0.413	1.76 (0.66, 6.07)	0.41
Group 3	9.17 (3.01, 29.0)	<b>0.05*</b>	5.13 (1.37, 14.91)	0.021	4.96 (1.41, 16.2)	<b>0.034*</b>

OR – Odds Ratio; CI – Confidence Interval; \* $p < 0.05$  is significant. \*Model 1: Adjusted for potential confounders: number of comorbidities and chronic conditions. (DM, HT, CVS, asthma, COPD). \*Model 2: Adjusted for all factors in Model 1 and flu vaccination status.

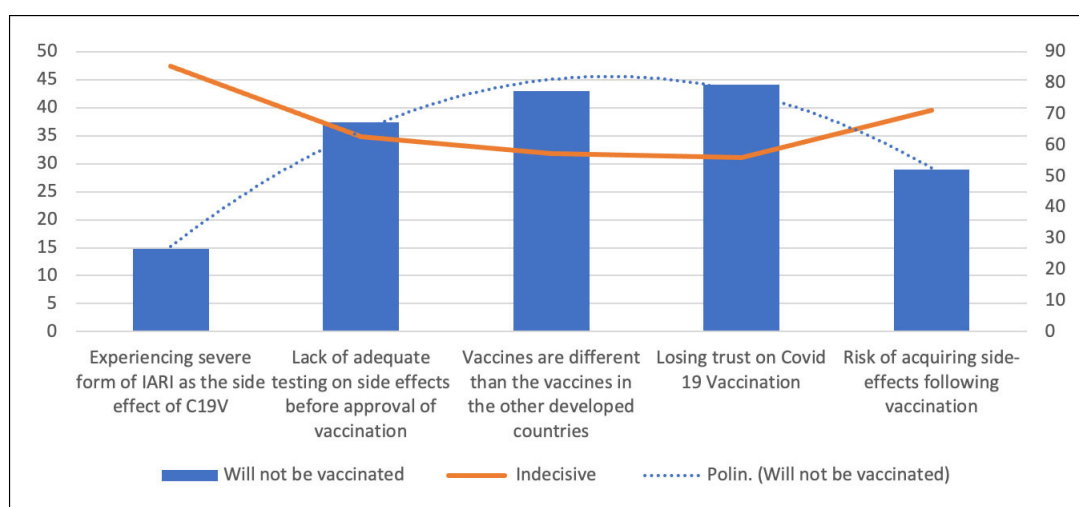


Figure 1. Attitude on COVID-19 vaccination.

logical, and observational studies are required.

In the present study, the logistic regression analysis shows that there are significant differences between the groups at  $p < 0.05$  with the number of comorbidities, chronic conditions such as DM, HT, CVS, asthma and COPD. Similarly, the extended IARI symptoms and hospital visits were significantly high among Group 3 samples (OR=9.17, 95% CI=3.01-29.0) and the same trend remained significant after the adjustment of number of comorbidities, the chronic conditions (OR=5.13, 95% CI=1.37-14.91) with the additional adjustment of flu vaccination status (OR=4.96, 95% CI=1.41-16.2). Though there is almost no researched data on the latent effect of C19V status vs. IARI, there are studies<sup>12,30-33</sup> showing that numerous documented ocular side effects, such as facial nerve palsy, abducens nerve palsy, new-onset Graves' disease, episcleritis, anterior scleritis, anterior uveitis (AU), multifocal choroiditis, central serous retinopathy (CSR), etc., presented immediately after receiving the C19V. Rare adverse effects like myocarditis, costochondritis, seizures, hematuria, menstrual disorders, appendicitis, MIS-C, etc., were also reported<sup>20</sup>.

As the COVID-19 vaccinations play a significant role in limiting the transmission and effects of infectious diseases, we have no intention of disputing its overwhelming public health advantages<sup>34</sup>. Similarly, the occurrence of adverse effects also calls for careful evaluation. Public and healthcare professionals frequently express skepticism against vaccines, with side effects following immunization serving as the main obstacle<sup>35</sup>. Promoting acceptance necessitates having frank conversations about potential impacts as well as

reiterating the advantages for the person, their family, and the society<sup>36</sup>. It is critical to address these distinctive obstacles to vaccine acceptance based on community dynamics, societal elements, and vaccine detractors<sup>37,38</sup>.

Despite the COVID-19 outbreak ultimately slowing down and a growing number of people becoming vaccinated, a significant number of people continued to be impacted with COVID-19 misinformation, which represents a serious co-factor to COVID-19 pandemic. The WHO also uses the term "infodemic" to describe "false and misleading information that leads to misunderstanding, risk-taking behaviors, and mistrust of health officials"<sup>38-40</sup>. Since most individuals currently seek out COVID-19 information online and through social media, the issue is exacerbated. According to research<sup>39,40</sup>, 72% of US population sought out information about COVID-19 from online news and social media sites. A loss of faith in research, expert recommendations that are based on evidence, governmental actions, and public health responses to COVID-19 were all caused by this misinformation<sup>40</sup>.

Our findings highlight a great concern regarding the attitude of the IARI patients towards C19V; it has emerged that among the Group 1 and 2, there is an unwillingness to get vaccinated further because of losing trust on C19V, lack of adequate testing to monitor side effects, and using different vaccines. The results also shows that about 66.4% of the patients were indecisive about getting vaccinated further. The fact that these side effects started to manifest after vaccination is most likely just an unfortunate coincidence.

Despite this, a careful analysis and framing the list of vaccine side effects along with comparative risk labeling to highlight the latent adverse events of C19V, can increase vaccine adoption and minimize hesitancy<sup>41-43</sup>. Hence, comprehensive population-based studies integrating clinical and virological data over more than one season should help to identify causative relationship of C19V with IARI accurately. Additionally, it is the social duty of those who receive the vaccine to assess the probability of small, non-life-threatening side events against the potential benefits of C19V against a severe, life threatening disease.

### **Limitations**

The following limitations are acknowledged.

- Because this was an independent study looking at in-depth self-reported symptoms, the study investigators did not formally confirm or verify the type of vaccines study participants had taken or the claimed symptoms of those participants.
- The reported adverse events summarized here should not be regarded as a causal link because the data are self-reported in nature.
- Although some respondents' symptoms of pre-existing chronic medical conditions may have contributed to these adverse events, it may also be an unfortunate coincidence from the previous underlying medical issues unrelated to the vaccine. Some respondents may have incorrectly blamed the vaccine for the clinical features and the clinical course of IARI.
- Direct comparison is limited because the data collection was restricted to a small sample size in one hospital.
- The negative effects should be better understood by comprehensive, substantial population-based studies that integrate clinical and virological data related to mutations, resistance of the viruses, on more than one season.

### **Conclusions**

As the impact that C19V will have during the future flu season is a significant area of uncertainty, we investigated whether there was any relationship between C19V and IARI outcome in the early flu season of 2022. We observed that IARI symptoms, hospitalizations, and disease duration vary considerably with C19V status, and research participants expressed hesitation about getting the vaccine. It has been challenging to reach any definitive conclusions regarding the effects of C19V on IARI. Hence, conducting extensive, substantial population-based studies that integrate clinical and

virological data from more than one season are absolutely required, although the majority of adverse effects reported were mild and temporary.

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### **Ethics Approval**

Institution Ethical Committee gave an ethical clearance with IEC/LCN/2022-09 dated 20.07.2022.

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### **Informed Consent**

Written informed consent was obtained from the participants of the study to publish this paper.

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### **Availability of Data and Materials**

The data presented in this study is available on request from the corresponding author.

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### **Authors' Contributions**

All authors have read and agreed to the published version of the manuscript. Premalatha Paulsamy: conceptualization, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing-original draft, writing-review and editing. Shadia Hamoud Alshahrani: conceptualization, formal analysis, methodology, project administration, resources, software, supervision, validation, visualization, writing-original draft, writing-review and editing. Mohammad Hamdi Abuadas: conceptualization, methodology, project administration, resources, software, supervision, validation, visualization, writing-original draft, writing-review and editing. Zainab Fatehi Albikawi: conceptualization, formal analysis, funding acquisition, methodology, project administration, resources, software, supervision, validation, visualization, writing-original draft, writing-review and editing. Prema Balusamy: conceptualization, data curation, methodology, project administration, validation, writing-original draft, writing-review and editing. Mervat Mostafa Arrab: data curation, methodology, project administration, validation, visualization, writing-review and editing. Krishnaraju Venkatesan:



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