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Original Research Article

IDENTIFY PREDICTORS OF INFLUENZA AMONG SEVERE ACUTE RESPIRATORY INFECTION (SARI) PATIENTS FROM TERTIARY CARE HOSPITALS, IN MUMBAI, INDIA - A PROSPECTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Background: An identification of key predictors in influenza epidemics is of much interest for the implementation of effective public health response strategies, The study has tried to develop causal relationships between clinico-epidemiological parameters and influenza positivity followed by identification of influenza positivity predictors among Severe Acute Respiratory Infection (SARI) cases.

Materials and Methods: This is prospective study with collecting clinico epidemiology, medical history after taking consent and assent. Pearson's chi-square test was performed to assess the association between exposure variables and influenza positivity, and logistic regression was used to examine the relationship with the outcome variables. The results are presented as odds ratios (ORs).

Results: In a 6 month period, a total of 302 participants were enrolled. Off them 43 (14.2%) were influenza positive. A significant correlation was observed between influenza positivity and clinico-epidemiology parameters viz. age (p=0.005), symptoms viz. breathlessness (p=0.057), clinical parameter viz. respiratory rate (p=0.012), O2 saturation (p=0.010), wheeze (p=0.000), medical history viz. tuberculosis (p=0.037), hypertension (p=0.055) by chi square test. Sore throat (OR=2.68, 95%CI: 0.97-7.37), diarrhoea (OR=2.73, 95%CI: 0.62-11.98), respiratory rate (OR=1.38, 95%CI: 0.46-4.14), O2 saturation (1.86, 95%CI: 0.73-4.69), wheeze (OR=4.53, 95%CI: 1.38-14.83), diabetes (OR=1.17, 95%CI: 0.28-4.86) showed causal association with influenza positivity. Sore throat (p>z=0.06), wheeze (p>z=0.01) were the only predictor found to be predictor for influenza positivity.

Conclusion: Although sore throat, diarrhoea, respiratory rate < 24, O2 saturation <99, wheeze, diabetes showed causal association with influenza positivity. Sore throat and wheeze were the only response variables were found to be influenza predictors.

Keywords: SARI, clinico-epidemiology, influenza positivity predictors, Mumbai.

INTRODUCTION

Influenza A or "the flu," is a vaccine-preventable disease Influenza.[1] Globally, seasonal influenza infects as many as 1 billion people per year making it one of the most common infectious respiratory viruses, after the common cold.[2] Besides it has created global public health crisis with 290,000 to

650,000 deaths every year through respiratory complications.[1,2] Influenza A (H1N1 and H3N2 subtypes) and B viruses (Victoria and Yamagata lineages) cause infections in humans.[3]

In order to understand the burden of influenza disease, estimate mortality and morbidity, and for informed decision-making on health policy and resource allocation, World Health Organization (WHO) tracks seasonal influenza viruses and makes recommendations for vaccines through a large global network called Global Influenza Surveillance and Response System (GISRS). This network also strengthens laboratory surveillance to prepare for and respond to outbreaks.[2]

In July 2021, the Indian Council of Medical Research (ICMR) established a country-wide integrated Influenza Like infection (ILI) and Severe Acute Respiratory Infection (SARI) for influenza and SARS-CoV-2 in India in community and hospital settings through 21 geographically representative network of government-supported Laboratories to determine burden of the diseases as well as for pandemic preparedness. The existing surveillance activities for ILI/SARI in the state, implemented through the IDSP and Viral Research & Diagnostic Laboratory Networks (VRDLN), have generated the trend of infections and predicted early warning signals for respiratory infections.[4] When surveillance for influenza carried out in India in 2021-2022, a total of 34,260 cases of influenza-like illness (ILI) and Severe acute respiratory infection (SARI) were reported from 4 July 2021 to 31 October 2022.[5]

Mumbai, is a metropolitan city and homes 23.598 million people, of India.[6] It is densely populated, with most of its inhabitants living in congested conditions. All these factors lay the ground for the fast spread of any infectious disease.[6] In 2015, due to heavy rainfall, the outbreaks of influenza and leptospirosis were reported in the city with considerable mortality.[7] The past history indicated that it is necessary to monitor the trend of influenza and clinical complications associated with it in the city as due to growing population and change in climate.[8] A robust formal viral surveillance network can prevent the next pandemic.[9] Several experts have advocated for integrated surveillance of influenza and other respiratory viruses with epidemic and pandemic potential as a necessity for better preparedness of public health systems.[8]

Although diagnostics and therapeutics have evolved, deciding which patients to be tested and how to be treated is a perplexing situation for clinicians as there is no single symptom or sign with adequate sensitivity to make informed clinical decisions.[9,10] It is estimated that only 30% of clinical judgement can accurately diagnose influenza.[11] This problem can be resolved with increasing the pre-test probability of influenza with the highest risk of morbidity, avoid excessive testing and treatment.[2]

Towards this a respiratory virus surveillance has been deployed in Mumbai city.[4]

MATERIALS AND METHODS

A Severe Acute Respiratory Infections (SARI) case was defined as a patient presenting with a reported and measured fever of ≥38°C and cough, with onset within the last 10 days and requiring hospitalization.[12] Patients meeting case definitions of SARI and ready to give consents were enrolled.[13] Ten SARI samples were collected per week.

The study design and its objectives were explained to prospective participants in the local language by clinicians, and informed consent/assent were sought from the participant, guardian of children and relatives of patients for individuals unable to consent. The clinical samples viz. Nasopharyngeal (NP) or Oropharyngeal swab(OP) were collected from the patients by trained clinicians in a viral transport medium.[14] The requisite information was obtained from patients including demographic data and relevant medical history, using a predesigned case record form. The SARI patients were followed up throughout the course of their hospitalization to establish the outcome of the illness.

After collecting NP/OP swabs from the patients, the swabs were placed in Virus Transport Medium (VTM) and transported to the Virus Research and Diagnostic Laboratory (VRDL) located in the Kasturba hospital for Infectious Disease, Mumbai in a cold chain within 12 hours of sample collection. The nucleic acid from the samples was extracted using automated extraction method (HimediaMag32, India) on the same day. The extracted nucleic acid was further subjected to Polymerase Chain Reaction (Himedia InstaQ96, India) for Influenza A and Influenza B using validated kits. The reports were dispatched to study hospital within 24 hours of testing. Statistical analysis was carried out using STATA version 18. Categorical variables were presented as frequency distribution and percentages. Pearson's chi-square test with a 95% confidence interval was performed to assess the association between influenza positivity and relevant clinico-epidemiology.[14] Clinico-epidemiology parameters showing significant association were further analysed using logistic regression to determine their relationship with influenza positivity, and the results are presented as odds ratios (ORs).

RESULTS

In a 56 month period, a total of 302 participants were enrolled. Of these, 177 (58%) were males and 124 (42%) females. In terms of age, 20-59years old age group was predominant with more than 65% of population. In SARI, the median age was for non-paediatric population (>12 years) found to be 45 years with quartile q1=29 years, q3=58 years. However, when paediatric population (<12 years) was separated from adult population the median age was found to be 7 years (q1=0.1 years years, q3=7.5 years).

From 302 study participants, 43 (14%) were found to be influenza positive. Influenza positivity was reported mainly in adults followed by paediatric population followed by geriatric population [Table 1].

In terms of influenza positivity, none of the exposure variables showed presence, greater than 5% hence no significant correlation was reported [Table 1].

Among influenza-positive participants, the most commonly reported symptoms were fever (90%), cough (90%), sore throat (74%), breathlessness (53%), headache (32%), and bodyache (30%) (Table 2). In terms of clinical diagnosis, bronchopneumonia (25%), acute febrile illness (13.95%) and chronic obstructive pulmonary disease (11.6%) were predominant.

Respiratory rate <24/tachypnea, pulse rate <100/dyspnea, O2 saturation <99, axillary temperature>38/fever, wheeze, were reported in 36.11%, 39.47%, 64.86%, 94.74% and 74.42% respectively. More than 90% of influenza positive patients reported tuberculosis, diabetes, and hypertension as a comorbidity [Table 2].

A significant association was observed between viral positivity and clinico-epidemiology parameters viz. Age (p=0.005), symptoms viz. breathlessness (p=0.057), clinical parameter viz. Respiratory rate (p=0.012), O2 saturation (p=0.010), wheeze (p=0.000), medical history viz. tuberculosis (p=0.037), hypertension (p=0.055) by chi square test [Table 2].

Sore throat (OR=2.68, 95% CI: 0.97-7.37), diarrhoea (OR=2.73, 95%CI: 0.62-11.98), respiratory rate (OR=1.38, 95%CI: 0.46-4.14), O2 saturation (1.86, 95%CI: 0.73-4.69), wheeze (OR=4.53, 95%CI: 1.38-14.83), diabetes (OR=1.17, 95%CI: 0.28-4.86) showed causal association with influenza positivity. Sore throat (P>z=0.06), wheeze (P>z=0.01) were found to be predictor for influenza positivity [Table 3].

Table 1: Symptom profile of influenza suspects reported to the Molecular diagnostic laboratory from Mumbai based tertiary care hospital in 2025 (N=302)

Variables	Negative	Positive	Total	*P*
	N=259	N=43	N=302	
Age Group				
<9	8 (3.0)	6(13.9)	14 (4.6)	0.005
10-19	30 (11.5)	8 (18.6)	38 (12.5)	
20-59	170 (65.6)	24 (55.8)	194 (64.2)	
60+	51 (19.6)	5 (11.6)	56 (18.5)	
Gender				
Male	151 (58.5)	26 (60.4)	177 (58.8)	0.811
Female	107 (41.4)	17 (39.5)	124 (41.2)	
Exposure Variables				
Smoker in Family				
Yes	39 (15.0)	4 (9.3)	43(14.2)	0.317
No	220 (84.9)	39 (90.7)	259 (85.7)	
Animal Exposure				
Yes	7 (2.7)	0 (0.0)	7 (2.32)	0.275
No	252 (97.3)	43 (100)	295 (97.6)	
Number of Family Member Sleeping in Room				
1-2	10 (7.1)	0 (0.0)	10 (6.02)	0.151
3+	129 (92.8)	27(100)	156(93.9)	
Birds Exposure				
Yes	20 (7.7)	1 (2.3)	21 (6.9)	0.198
No	239 (92.2)	42(97.6)	281(93.0)	
Travel History				
Yes	8 (3.0)	0 (0.0)	8 (2.6)	0.243
No	251 (96.9)	43 (100)	294 (97.3)	
Farm Animal Exposure				
Yes	7 (2.7)	0 (0.0)	7 (2.32)	0.275
No	252 (97.3)	43 (100)	295 (97.6)	

Table 2: Clinical profile of influenza suspects reported to the Molecular diagnostic laboratory from Mumbai based tertiary care hospital in 2025 (n=302)

Background Variable	Negative	Positive	Total	*P*
	N=259	N=43	N=302	
Symptom profile				
Fever				
Yes	227 (87.6)	39 (90.7)	266 (88.0)	0.567
No	32 (12.3)	4(9.3)	36(11.92)	
Rigors				
Yes	5 (1.93)	0 (0.0)	5 (1.66)	0.358
No	254 (98.0)	43 (100)	297 (98.3)	
Sputum				
Yes	28(10.8)	7(16.2)	35(11.5)	0.300
No	231 (89.1)	36 (83.7)	267 (88.4)	

Sore Throat				
Yes	177 (68.3)	32(74.4)	209(69.2)	0.424
No	82 (31.6)	11 (25.5)	93 (30.7)	
Ear Discharge				
Yes	2 (0.77)	1 (2.33)	3 (0.99)	0.342
No	257 (99.2)	42 (97.6)	299 (99.0)	
Body Ache				
Yes	109 (42.0)	13 (30.2)	122 (40.4)	0.142
No	150 (57.9)	30 (69.7)	180 (59.6)	
Chest Pain				
Yes	40 (15.4)	4 (9.3)	44 (14.5)	0.290
No	219 (84.5)	39 (90.7)	258 (85.4)	
Vomiting Nausea				
Yes	28 (10.8)	8 (18.6)	36 (11.9)	0.144
No	231 (89.1)	35 (81.4)	266 (88.0)	
Breathlessness				
Yes	177 (68.3)	23 (53.4)	200 (66.2)	0.057
No	82 (31.6)	20 (46.5)	102 (33.7)	
Chills				
Yes	17 (6.5)	1 (2.3)	18 (5.9)	0.277
No				
Haemoptysis				
Yes	9 (3.4)	0 (0.0)	9 (2.9)	0.215
No	250 (96.5)	43 (100)	293 (97.0)	
Nasal Discharge				
Yes	84 (32.4)	10 (23.2)	94 (31.1)	0.229
No	175 (67.5)	33 (76.7)	208 (68.8)	
Headache				
Yes	104 (40.1)	14 (32.56)	118 (39.07)	0.344
No	155 (59.85)	29 (67.44)	184 (60.93)	
Malaise Fatigue				
Yes	16 (6.18)	1(2.3)	17(5.6)	0.310
No	243 (93.8)	42 (97.6)	285 (94.3)	
Abdominal Pain				
Yes	7 (2.7)	1 (2.33)	8 (2.65)	0.887
No	252 (97.3)	42 (97.6)	294 (97.3)	
Diarrhoea				
Yes	14 (5.41)	4 (9.3)	18 (5.96)	0.318
No	245 (94.5)	39 (90.7)	284 (94.0)	
Seizures				
Yes	4 (1.5)	0 (0.0)	4 (1.32)	0.412
No	255 (98.4)	43 (100)	298 (98.6)	
Taste				
Yes	21 (8.1)	3 (6.9)	24 (7.9)	0.799
No	238 (91.8)	40 (93.0)	278 (92.0)	
Smell				
Yes	24 (9.2)	1 (2.33)	25 (8.2)	0.126
No	235 (90.7)	42 (97.6)	277 (91.7)	
Respiratory rate				
Respiratory<24	129 (58.6)	13 (36.1)	142(55.4)	0.012
Respiratory>=24	91 (41.3)	23 (63.8)	114 (44.5)	
Pulse				
pulse<100	111 (47.0)	15(39.4)	126(45.9)	0.385
pulse>=100	125(52.9)	23(60.5)	148(54.0)	
O2 saturation				
O2 saturation <99	194(82.9)	24(64.8)	218(80.4)	0.010
O2 saturation >=99	40(17.0)	13(35.1)	53(19.5)	
o2 saturation <95	22(9.4)	2(5.4)	24(8.8)	0.427
o2 saturation >=95	212 (90.6)	35(94.5)	247(91.1)	
Temperature				
axillary temperature<38	221 (95.2)	36(94.7)	257(95.1)	0.889
axillary temperature>=38	11(4.7)	2(5.2)	13(4.8)	
Wheeze				
No	239 (92.2)	32(74.4)	271(89.7)	0.000
Yes	20(7.7)	11(25.5)	31(10.2)	
Crepitation				
No	192 (74.1)	32 (74.4)	224 (74.1)	0.968
Yes	67 (25.8)	11(25.5)	78(25.8)	
Medical History				
Tuberculosis				
No	215 (83.0)	41(95.3)	256(84.7)	0.037

Yes	44(16.9)	2(4.6)	46 (15.2)	
Diabetes				
No	222(85.7)	40(93.0)	262(86.7)	0.190
Yes	37 (14.2)	3(6.)	40(13.2)	
Hypertension				
No	202 (77.9)	39 (90.7)	241(79.8)	0.055
Yes	57(22.0)	4 (9.3)	61 (20.2)	

Table 3: Predictors of Influenza Positivity Among Severe Acute Respiratory Infection (SARI) Patients

Variable	Odds Ratio	*p*>z	[95% Conf. Interval]	
Age				
10-19	0.25	0.11	0.05	1.33
20-59	0.16	0.02	0.03	0.79
60+	0.21	0.06	0.04	1.07
Gender				
Male	1.00	1.00	0.44	2.29
Cough	1.67	0.54	0.33	8.40
Sore throat	2.68	0.06	0.97	7.37
Diarrhoea	2.73	0.18	0.62	11.98
Vomiting/nausea	1.72	0.36	0.54	5.50
Headache	1.13	0.79	0.45	2.84
Respiratory rate	1.38	0.57	0.46	4.14
O2 saturation	1.86	0.19	0.73	4.69
Temperature	0.66	0.72	0.07	6.15
Pulse	0.69	0.45	0.27	1.80
Wheeze	4.53	0.01	1.38	14.83
Crepitation	0.77	0.58	0.31	1.93
Tuberculosis	0.38	0.23	0.08	1.85
Diabetes	1.17	0.83	0.28	4.86
Hypertension	0.73	0.66	0.18	3.00

DISCUSSION

Since last two decades, government affiliated tertiary care hospitals of Mumbai, test only type C category SARI patients for influenza virus as per government recommendation.[15] However, this type of approach does not give a comprehensive picture of influenza positivity.

Since February 2025, this surveillance has been initiated in Mumbai focussing on public health and clinical aspects along with diagnostics. The study duration was considered from February 2025 to August 2025. The study has four innovative arms. It is the first scientific study carried out in Mumbai with holistic approach taking into consideration SARI cases (10 per week) throughout the year irrespective of seasons. Secondly, the current surveillance did not restrict only to testing but also captured clinico-epidemiology and medical history data. Thirdly, the study tried to find predictors of influenza positivity in the city which has not been tried since last two decades of testing.

In the present study, adults constituted 87% population whilst paediatric comprised 13% population. In a study by Potdar et al, 2023, adult and paediatric population were 69% and 31% respectively.[16] The less number of paediatric population in the current study may be due to convenient sampling undertaken. In current surveillance, a large population with respiratory complications ranged from 20-59 years which may be due to gradual declining functions of lungs related to age.[17,18]

Overall 43 (14%) of SARI participants reported influenza positivity. There could be multiple reasons or limitations for the detection of low burden of viruses such as testing coverage or seasonal changes.[19] Other respiratory viruses viz paramyxoviruses, adenoviruses, rhinoviruses respiratory bacterial infections viz Haemophilus influenzae, Bordetella *sps* could be etiological agents. There are fair chances of the presence of aforementioned pathogens in the sample.[20]

Although age is a confounder, it showed (p=0.005) significant association with influenza positivity particularly with study population of 20-59 years. Literature suggested that those age group 18–49 years, accounts for a large number of symptomatic illnesses and outpatient visits for influenza. For those aged 50–64, the rate of hospitalization and mortality from influenza is significantly higher than for younger adults generating higher influenza-related hospitalization costs.[21]

The present study found that acute wheezing episodes showed significant association with influenza positivity in adult as well as in paediatric group. The study findings are in line with the paediatric respiratory findings by Wilson, (2003).[22] Besides, the patients with wheeze had higher odds 4.53 times of developing influenza and wheeze has also found to be predictor of influenza. Sore throat had 2.68 times odds of having an influenza than any other symptom. Li et al 2023 mentioned that Upper respiratory symptoms, such as sore throat and productive cough, and general symptoms, such as body ache and fatigue, were more predictive in the first half of the week (OR: 1.51–3.25) whereas lower respiratory symptoms, such as shortness of breath and wheezing,

were more predictive in the second half of the week (OR: 1.52–2.52) of Influenza.[23]

An oxygen saturation below 99% in admitted patient indicates a seeking of medical attention, though the range 95–100% is generally considered normal. Oxygen saturation values below 95% are abnormal due to hypoxemia. Therefore, in the present study oxygen saturation below 99% and 55% are investigated. In the present study, hypoxemia did not show significant relationship. Whilst oxygen saturation below 99% showed significant association with influenza positivity. Dyspnea/breathlessness, tachypnea/(Respiratory rate <24) and O2 saturation <99 was recorded in in 53%, 36% and 64% of influenza positive participants. Additionally, breathlessness (p=0.057), respiratory rate (p=0.012), O2 saturation (p=0.010) had a significant association with influenza positivity. Our findings are also consistent with other studies mentioning dyspnea, tachypnea have impact on influenza,[3,24] as they had causal relationship with influenza.

SARI patients with tachypnea had odds of influenza infection (OR=1.38, 95%CI: 0.46-4.14). O2 <99 saturation (1.86, 95%CI: 0.73-4.69) were found to have strong causal relationship with influenza though they were not detected to be predictors.

Rao et al, 2022 in their study found that respiratory rate was useful predictor of severity for acute respiratory infections such in children with tachypnea are more likely to have respiratory infections than children without tachypnea.[3] They have also suggested that respiratory rate is a more reliable predictor of influenza severity than oxygen saturation in children.[3] However, Vasoo et al, 2010 mentioned that respiratory infection, hospitalization or ICU admission hypoxia or requirement for oxygen were also an important risk factor. Besides, only a higher number of high-risk medical conditions, dyspnea, and a lower median oxygen saturation level were predictive of hospitalization.[23] These findings suggest that clinicians' decision to hospitalize had accurately reflected the risk for complicated or severe disease.[23] A report published in Mexico highlighted that dyspnea, tachypnea, and cyanosis were prognostic factors for admission and death in complication with seasonal influenza.[24,25]

In the present study, 52% population was from Intensive Care Unit (ICU) viz. Intensive Respiratory Care Unit (IRCU)/ Medical Intensive Care Unit (MICU). Patients admitted in IRCU had reported hypoxia in greater number therefore were supplied with oxygen and Continuous positive airway pressure (CPAP) as a treatment measures.[26] Moreover, respiratory viral infections can worsen the health conditions of patients. The study reported underlying lung diseases and comorbidity which increased the hospitalization days among some of the patients. Similar findings have been reported by Jankowski et al, 2023.[27]

SARI patients having diarrhoea have more odds of developing influenza (OR-2.73 95%CI: 0.62-11.98). Literature suggested that gastrointestinal symptoms showed significant corelation probably due to lack of administration of the flu vaccine.[28] None of the SARI participants were vaccinated in the current study. Patients were advised to take vaccines after 3 weeks of discharge. The study findings also highlighted that there is a paucity of data pertaining to gastrointestinal symptoms among respiratory viral infections.

Tuberculosis (p=0.037), hypertension (p=0.055) had a significant association with influenza. People with chronic lung diseases (like asthma or COPD), heart disease, hypertension, renal disease, diabetes, tuberculosis or weakened immune systems are more vulnerable influenza.[29]

During the course analysis, it was realized that the study has limitations in terms of power of predictors. The predictive power can be increased by increasing numbers of positive participants. Fortunately it is a prospectives study and it will continue till July 2026. At present findings cannot be considered to comment on influenza predictability for Mumbai. It is advisable to continue the enrolment and check the status after completing two years of surveillance.

CONCLUSION

The study found a low percentage of influenza positivity in the surveillance. The study proposes that sore throat and wheeze are predictors for influenza, whilst tachypnea, hypoxia, and dyspnea can also be indicators of influenza with patients suffering from respiratory complications. Patients with hypertension and diabetes must be tested for influenza if they had complains of respiratory complication. However, the relatively small sample size may have influenced the strength or significance of some variables observed for the city of Mumbai. Achieving balance between rapid diagnostics and clinical findings is crucial for clinical and public health decisions. It is crucial to continue enrolment of patients for longer duration and focus on integrating clinical findings with rapid diagnostic tests in order to develop predictive models.

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