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CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH SEVERE ACUTE RESPIRATORY INFECTION (SARI) DURING COVID PANDEMIC OF A TERTIARY CARE HOSPITAL IN CHENNAI

Pulmonary Medicine

Vengada Krishnaraj S.P* — Associate Professor, Department Of Respiratory Medicine, Government Stanley Medical College, Chennai, Tamilnadu, India.*Corresponding Author

Roshan Kumar. M — Assistant Professor, Department Of Respiratory Medicine, Government Stanley Medical College, Chennai, Tamilnadu, India.

Vinod Kumar. V — Professor, Department Of Respiratory Medicine, Government Stanley Medical College, Chennai, Tamilnadu, India.

Reetu Singh G — Post Graduate, Department Of Respiratory Medicine, Government Stanley Medical College, Chennai, Tamilnadu, India.

ABSTRACT

BACKGROUND: SARI is one of the clinical manifestations of COVID-19 disease. As per WHO SARI is defined as an acute respiratory infection with a history of fever or measured fever of ≥ 38 C°; and cough with onset within the last 10 days and requires hospitalization. **AIMS/OBJECTIVES:** To describe clinical characteristics and factors associated with the clinical outcome of patients presenting with SARI at our hospital. **METHODOLOGY:** This is a record-based cross-sectional study that included all cases admitted in the SARI ward in Government Stanley Hospital, a tertiary care center in Chennai designated for the management of case definition and screened for SARS-CoV-2/COVID-19 between 15th March 2020 and 15th December 2020.**RESULTS:** A total of 246 patients were included in the study period from 15th March to 15th May 2020. The median age was 49.4 years and 56.9% were males. The most common symptom was fever (69.1%) followed by cough (62.6%), Breathlessness (62.6%), and sore throat (52.8%) in our study. Of this 4 (1.8%) were tested positive for COVID-19. Of the 5 (2.1 %) patients who expired. **CONCLUSION:** In our single-center tertiary the incidence of COVID-19 among the SARI patients done between March-May 2020 showed an incidence rate of 1.8%

KEYWORDS

Sari, Survival, Clinical Characteristics, Viral Infection

INTRODUCTIONS

Dual infections with other respiratory viral infections have been found in SARS and MERS cases. At this stage, we need detailed microbiologic studies in all suspected cases. Both URT and LRT specimens can be tested for other respiratory viruses, such as influenza A and B (including zoonotic influenza A), respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, enteroviruses (e.g. EVD68), human metapneumovirus, and endemic human coronaviruses (i.e. HKU1, OC43, NL63, and 229E). [1] LRT specimens can also be tested for bacterial pathogens, including Legionella pneumonia In hospitalized patients with confirmed nCoV infection, repeat URT and LRT samples should be collected to demonstrate viral clearance. The frequency of specimen collection will depend on local circumstances but should be at least every 2 to 4 days until there are two consecutive negative results (both URT and LRT samples if both are collected) in a clinically recovered patient at least 24 hours apart. If local infection control practice requires two negative results before removal of droplet precautions, specimens may be collected as often as daily. [2] In patients with moderate or severe ARDS, higher PEEP instead of lower PEEP is suggested. PEEP titration requires consideration of benefits (reducing atelectrauma and improving alveolar recruitment) vs. risks (end-inspiratory overdistension leading to lung injury and higher pulmonary vascular resistance). Tables are available to guide PEEP titration based on the FiO2 required to maintain SpO2.[3] A related intervention of recruitment maneuvers (RMs) is delivered as episodic periods of high continuous positive airway pressure [30–40 cm H2O], progressive incremental increases in PEEP with constant driving pressure, or high driving pressure; considerations of benefits vs. risks are similar. Higher PEEP and RMs were both conditionally recommended in a clinical practice guideline. [4]For PEEP, the guideline considered an individual patient data meta-analysis of 3 RCTs. However, a subsequent RCT of high PEEP and prolonged high-pressure RMs showed harm, suggesting that the protocol in this RCT should be avoided. [5]High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure.[6] The risk of treatment failure is high in patients with MERS treated with NIV, and patients treated with either HFNO or NIV should be closely monitored for clinical deterioration. HFNO systems can deliver 60 L/min of gas flow and FiO2 up to 1.0; pediatric circuits generally only handle up to 15 L/min, and many children will require an adult circuit to deliver adequate flow.[7] Compared to standard oxygen therapy, HFNO reduces the need for intubation. Patients with hypercapnia (exacerbation of obstructive lung disease, cardiogenic pulmonary edema), hemodynamic instability, multi-organ failure, or abnormal mental status should generally not receive HFNO, although emerging data suggest that HFNO may be safe in patients with mild-moderate and non-worsening hypercapnia[8,9]

METHODOLOGY:

This is a record-based cross-sectional study that included all cases admitted in the SARI ward in Government Stanley Hospital, a tertiary care center in Chennai designated for the management of case definition and screened for SARS-CoV-2/COVID-19 between 15th March 2020 and 15th December 2020. As of the WHO surveillance case definitions for SARI were implemented as follows, acute respiratory infection with a history of fever or measured fever of ≥ 38 C°; and cough; with onset within the last 10 days; and requiring hospitalization. An enrollment form was used to collect data from enrolled eligible patients including patient demographics, medical history, clinical signs and symptoms, comorbidities, reported influenza vaccine status, recent travel history, treatment, clinical course, and outcome. Patients with incomplete medical records were excluded. hospitalized patients meeting the WHO case definition for SARI were enrolled. Nasopharyngeal/oropharyngeal (NP/ OP) swabs were collected and samples were tested using RT-PCR for influenza A, B, respiratory syncytial virus (RSV), human metapneumovirus (hMPV), parainfluenza virus (PIV 1,2,3,4), adenovirus, bocavirus, coronavirus, enterovirus, rhinovirus, and atypical bacteria. Data were analyzed to calculate positivity rates for viral pathogens and determine which pathogens related to severe outcomes or resulted in death.

STATISTICALANALYSIS

Data analyses were conducted using the software SPSS (Statistical Package for the Social Science; IBM Corp, NY, USA); version 22. Data were summarized using median (range) for quantitative variables and number and percent for qualitative variables. Comparison between groups was done using the Chi-square test for qualitative variables, independent sample t-test for normally distributed quantitative variables, while the Mann-Whitney U test was used for quantitative variables that are not normally distributed. Only variables with statistically significant univariate association with severe outcomes were included in multivariate regression analysis. All tests were two-

sided, and differences with $p < 0.05$ were considered significant.

RESULTS

The median age of patients positive for SARS.Cov.2 tests (39 years) was comparable to that of patients negative for the tests (46 years). In patients positive for SARS.Cov.2 tests, 14 were females (36.8%) and 24 were males (63.2%). However, a higher proportion of male patients (12/16, 75%) was found in those negative SARS.Cov.2 tests (4/16, 25%). Fever was the main initial symptom both in SARS.Cov.2 tests positive (65.8%) or negative (68.8%) patients. Similarly, comparisons of additional symptoms between positive and negative patients for SARS.Cov.2 tests, such as cough (31.6% vs 31.3%), diarrhea (5.3% vs 6.3%), chill (5.3% vs 0%), sore throat (2.6% vs 0%), chest tightness (5.3% vs 12.5%), dyspnea (7.9% vs 12.5%), rhinorrhea (2.6% vs 0%, fatigue (18.4% vs 12.5%), inappetence (5.3% vs 6.3%), expectoration (5.3% vs 6.3%), nervous (0% vs 6.3%), nausea (2.6% vs 0%), muscle ache (5.3% vs 6.3%), and globus sensation (2.6% vs 0%) also failed to detect a perceptible difference. All the medical staff performed chest CT.scans at the time of admission. Remarkably, chest CT images were missing in two nucleic acid.positive patients and were suggested virus.infected pneumonia in 52 out of 54 inpatients. Among those 52 patients, 11 were manifested as common.type, while the rest 41 cases were characterized as severe./critical.type patients. It was noted that the typical CT images derived either from common.type or severe./critical.type patients with COVID.19 were characterized by the ground glass.like shadows (63.6% vs 78.1%), fibrous stripes (54.6% vs 51.2%), patchy shadow (36.4% vs 43.9%), and pleural thickening (18.2% vs 29.3%). Other imaging features included nodules (18.2% vs 24.4%), consolidation (18.2% vs 9.8%), and pleural effusion (9.1% vs 9.8%). Of note, severe./critical.type patients were featured by the higher severity of lymphadenitis (29.3% vs 9.1%) and interstitial thickening (7.3% vs 0%) but with no significant difference. Furthermore, a significantly higher proportion of patients positive for SARS.Cov.2 tests displayed patchy shadow (19/36, 52.8%) in the CT.cans than that of patients negative for the tests (3/16, 18.8%, $P = .022$). Analysis of the lesion sites in CT.scans revealed that that severe-/critical-type of patients were more likely to exhibit lesions in the right lung (61% vs 18.2%; $P = ·012$) of the upper lobe of the right lung (31.7% vs 0%; $P = ·028$)

Table 1: Basic Demographic Details Of The Study Population

Demographic details		Values (n=246)
Age (years) (Mean±sd)		49.42±13.97
Gender N(%)	Female	106 (43.1%)
	Male	140 (56.9%)
Smoking status N(%)	Smokers	49 (19.9%)
	Non Smokers	197 (80.1%)
Comorbidities N(%)	No comorbidities	179 (72.8%)
	Bronchial asthma	3 (1.2%)
	CAD	1 (0.4%)
	COPD	4 (1.6%)
	DM	18 (7.3%)
	Hypothyroidism	4 (1.6%)
	SHT	1 (0.4%)
	Seizure Disorder	15 (6.1%)
	2comorbidities	15 (6.1%)
	>2 comorbidities	6 (2.4%)

Table 2: Age Categorisation Of The Study Population

Age Group	Values (n=246) N (%)
< 20 years	3 (1.2%)
21 to 40 years	68 (27.6%)
41 to 60 years	125 (50.8%)
61 to 80 years	48 (19.5%)
> 81 years	2 (0.8%)

Table 3: Symptomatic Status Of The Study Population

Symptoms	Values (n=246) N (%)
Fever	170 (69.1%)
Cough	154 (62.6%)
Breathlessness	154 (62.6%)
Sore throat	130 (52.8%)
Diarrhea	90 (36.6%)

Table 4: Covid 19 Swab Positivity Status Of The Study Population

Swab type	Positivity status N (%)
Oral Swab	2 (0.8%)
Nasopharyngeal Swab	2 (0.8%)

Table 5: Lab Investigation & Radiography Status Of The Study Population

Investigations		Values (n=246) N (%)
CBC	Normal	55 (22.4%)
	Anaemia	1 (0.4%)
	Leukocytosis	2 (0.8%)
	Lymphocytosis	26 (10.6%)
	Lymphopenia	133 (54.1%)
	Neutrophilia	22 (8.9%)
	Thrombocytopenia	7 (2.8%)
CXR / CT	Normal study	29 (11.8%)
	B/L infiltrates	21 (8.5%)
	Diffuse GGO	9 (3.7%)
	Peripheral GGO	187 (76.0%)

Table 6: Various Outcomes Of The Study Population

Outcome	Values (n=246) N (%)
Recovered & Discharged	241 (97.9%)
Died	5 (2.1%)

Table 7: Association Between Swab Positivity & Outcome In The Study Population

Swab status	Outcome		p-value
	Discharged	Death	
Positive	1 (0.4%)	1 (0.4%)	0.000***
Negative	240 (97.6%)	4 (1.6%)	

Table 8: Association Between Chest Xray/ Ct Findings & Outcome In The Study Population:

Findings	Outcome N(%) (n=246)		p value
	Discharged	Death	
Normal study	28 (11.3%)	1 (0.4%)	0.009**
B/L infiltrates	21 (8.5%)	0	
Diffuse GGO	7 (2.8%)	2 (0.8%)	
Peripheral GGO	185 (75.2%)	2 (0.8%)	

p Value < 0.05 –significant*,<0.01 – very significant**, <0.001 – Very highly significant***

DISCUSSION

In comparison to non-viral infected individuals, viral-infected SARI ones had significantly predominant signs and symptoms at presentation. [10]Particularly, they had significant viral prodromal symptoms, as well as tachypnea, wheezes, and convulsions (p=0.000 each). Among individual viral pathogens, SARI patients with influenza had more significant tachypnea (p= 0.038), wheezes (p=0.000), and abnormal breath sounds (p= 0.023), than those with non-influenza viral infections. Patients whose specimens were collected within 5 days of the onset of symptoms were more likely to have a viral pathogen detected than those whose specimens were collected later (73% versus 36%, p = 0.047). [11]Fifty-three percent of patients had at least one underlying medical condition. These comorbidities included chronic respiratory disorders (asthma, COPD, bronchiectasis, and immotile cilia syndrome), cardiac disorders (heart failure congenital heart diseases, and cardiomyopathy), neuromuscular disorders (epilepsy, cerebral palsy, and myopathies), hematological disorders (thalassemia), endocrine disorders (diabetes mellitus, hypothyroidism, and morbid obesity), renal disorders (end-stage renal disease), and liver disorders (liver cirrhosis and hepatic failure).[13]Patients with comorbidities (n = 570, 53%) were significantly older compared to those with no comorbidities (median age: 54 versus 3, $p < 0.001$). Additionally, they were significantly more likely to be symptomatic.In terms of comorbidities, patients with and without viral detection differed significantly in the frequencies of chronic respiratory (p=0.002), endocrine (p=0.000), hepatic (p=0.002), and neuromuscular disorders (p=0.001).[14] Among individual viral pathogens, SARI patients with para-influenza virus had significant endocrine (p= 0.004), and neuromuscular disorders (p=0.012), than those with non-para-influenza viral infections [15].For influenza vaccination history; 832/1,075 (77.4%) cases did not receive the vaccine within the 12 months before hospital admission, while 243/1,075 (22.6%) were reported as unknown for an influenza

vaccination status.In comparison to non-viral infected individuals, viral-infected SARI ones had significantly lower rates of pneumonia (p=0.004) and admission to the ICU (p=0.000).[16] Patients with influenza virus tended to have significantly different rates of admission to the ICU (p=0.045), and mechanical ventilation (p=0.001), in comparison to those with non-influenza infections. With regards to complications, viral-infected SARI patients had significant differences for developing respiratory failure (p=0.033), and acute respiratory distress syndrome; ARDS (p=0.011), in comparison to those without viral infections.[17]Overall mortality in SARI-positive patients was 24/1,075 (2.2%) and peaked at 1% in 2014. Overall, only 2(8%) were adults, while 22 (92%) were children. Among children, 18(75%) were aged <5 years. Overall, two-thirds (16/24) had comorbidities. All patients who died were admitted to the ICU and mechanically ventilated. Notably, all patients who died tested positive for a viral pathogen; twelve were positive for RSV, four for influenza virus, two for adenovirus, one for hMPV, one for PIV, and four for mixed viral infections, respectively. Among those who died, there was a significant difference between those with (2.2%) and without (5%) viral detection (p = 0.005). [18]Among individual viral pathogens, SARI patients with RSV and influenza had significant deaths (p= 0.045 and 0.006), in comparison to those with non-RSV and non-influenza viral infections. No mortality was reported for patients with atypical bacteria.[19] Logistic regression was used to further examine associations with severe outcomes in SARI-positive individuals with complete demographic data and clinical risk factors. By univariate analysis, individuals with positive results for rhinovirus and adults >18 years were more likely to experience a severe outcome than those not infected with rhinovirus (OR 4.975, 95% CI 2.431-17.812, p=0.024) and children <18 years (OR 10.357, 95% CI 5.895-18.197, p=0.000), respectively.Multivariate analysis confirmed these results where individuals with positive results for rhinovirus and adults >18 years were more likely to experience a severe outcome than those not infected with the rhinovirus (OR 4.807, 95% CI 2.981-16.112, p=0.025) and children <18 years (OR 11.716, 95% CI 7.225-18.998, p=0.000), respectively. [20]We observed that, SARI cases <5 years were significantly more likely than older patients to be infected with each of the pathogens examined, particularly for RSV and influenza. As the majority of enrolled patients were children (83%), this is not unexpected since these pathogens have a strong association with this age group. This is inconsistent with data that nearly 80% of children are exposed to RSV by age two, 100% to hMPV by age five, and 90% to hPIV by age five. Furthermore, hPIV is a significant etiology of LRTI in children, second only to RSV, and adenoviruses are the second most common viral pathogen in children under two years of age. [21]Patients with positive viral detection had better clinical outcomes than those with no viral detection, in terms of pneumonia, ICU admission, and overall mortality. Furthermore, compared to patients with no virus identified, patients with RSV-positive infection were significantly less likely to have pneumonia, to be admitted to the ICU, mechanically ventilated, and had less mortality. [23]Interestingly, analyses to assess associations with severe outcomes in the current study revealed that no infections were independently associated with those outcomes, even after controlling for age and associated medical comorbidities. [24]Despite the predominance of RSV infections among SARI-positive cases (45%), there was strong evidence that individuals with RSV and influenza were less likely to experience a severe outcome than those not infected with each of these pathogens. Furthermore, individuals with multiple infections were no more likely than those with infection with a single pathogen to experience severe outcomes. [25]Multivariate logistic regression analysis confirmed that individuals with positive results for rhinovirus and adults >18 years were more likely to experience a severe outcome than those not infected with rhinovirus and children <18 years, respectively. However, because of the low prevalence of rhinovirus (2%) and adults (8.8%) in this study, further larger studies are needed to confirm these associations.[26]

CONCLUSIONS:

Comparing the clinical course, complications, and outcomes between viral-infected cases and non-viral detected controls showed interesting results. Patients with identified viruses had significantly lower rates for ICU admission, hospital stay, length of mechanical ventilation, and overall mortality than those without identified viruses. However, there were no differences between ARDS and mechanical ventilation. Most of the patients had normal chest radiographs on admission, while computed tomography chest showed the characteristic findings in over two-thirds. Almost half of our patients recovered while 5% died. This is an initial experience only and an increased patient cohort will provide further information.

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