Clinical Management of Severe Acute Respiratory Infection (SARI) when COVID-19 Disease is suspected

Patil Aarti[1], Dadewad swapnali[2], Mansi Patilghote[3], Renuka R. Deshpande[4]
[1,2,3] *B.Pharmacy third Year Student, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512, Maharashtra, India*
[4]*Assistant Professor, Department of Pharmaceutics, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512, Maharashtra, India*

***Abstract*- Acute viral respiratory infections (AVRI) are a leading cause of morbidity and mortality among all age groups globally. Except for Influenza virus and Respiratory Syncytial virus, mostly viral aetiology of AVRI remains undiagnosed. Lately, human coronaviruses (HCoVs) have emerged as an important aetiology of AVRI. A laboratory based retrospective cross sectional study was conducted in which respiratory samples (throat swabs) of patients (n ¼ 864), with Influenza negative SARI, of all age groups between Jan 2011–Dec 2012 were tested for HCoVs including MERS-CoV using Conventional and real time PCR assays. The prevalence of HCoV among SARI cases was 1.04% (9/864) [95% CI: 0.36–1.72]. Of these four (44.44%) were identified as HCoV OC43, three (33.33%) as HCoV NL63 and two (22.22%) as HCoV 229E. No HCoV HKU1 was detected. The samples were also negative for SARS-CoV and MERS-CoV. The results of this study documents low prevalence of human corona viruses in SARI cases in south western India and the absence of highly pathogenic human coronavi-ruses. As the study included only SARI cases the prevalence reported could be an under estimate when it is extrapolated to community.**

***Index terms*- COVID-19, influence virus**

INTRODUCTION

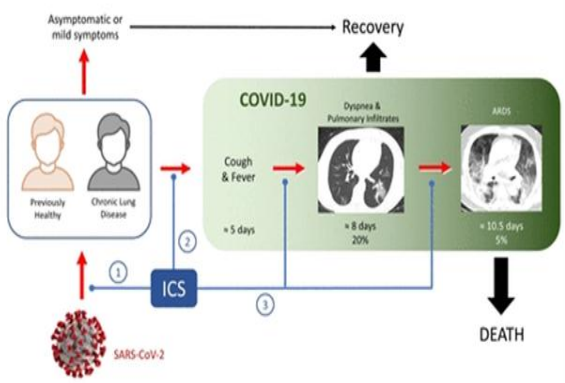
Acute respiratory illnesses (ARI) are a major health problem in people of all ages, according to the World Health Organization (WHO) [Dominguez et al., 2009]. Lower respiratory tract infections particularly contribute to the world's disease burden [Dominguezet al., 2009]. Except for Influenza virus and Respiratory Syncytial virus, mostly viral aetiology of AVRI remains undiagnosed. Human coronaviruses (HCoVs) have a history way back in the late 1960s, identified as a group of viruses with potential to infect humans and animals [Principi et al., 2010]. Six human coronaviruses have been identified till date, which are HCoV-229E, HCoV-HKU1, HCoV-NL63, HCoV-OC43, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and the recent Middle East Respiratory Syndrome coronavirus (MERS-CoV). Four human coronaviruses HCoV-229E, HCoV-HKU1, HCoV-NL63, and HCoV-OC43 have been found to be associated with a wide range of respira-tory symptoms, including fatal outcomes such as pneumonia and bronchiolitis. Specifically, HCoV-NL63 has been associated with croup [Abdul-Rasool and Fielding, 2010] and HCoV-HKU1 with febrile convulsion [Gaunt et al., 2010]. The worldwide epidemic of SARS in 2002–2003, due to a newly discovered coronavirus, the SARS-CoV (SARS-associated coronavirus), reinforced the interest into the Coronaviridae family [Geller et al., 2012]. Globally more than 8,000 cases were reported during the 2002–2003 SARS epidemic, which affected 30 countries across five continents with a case fatality rate of 9% [Bhatnagar et al., 2008]. Ten years after the detection of SARS-CoV, a novel coronavirus known as MERS-CoV was discovered in 2012 [Corman et al., 2012]. The nearest human coronavirus related to MERS-CoV is SARS-CoV [Khan, 2013]. Though HCoVs were identified as respiratory pathogens, hardly any data was available on their role in respiratory infections till 2003. There is no data available in literature on HCoV from India.

TABLE I. Demographic Characteristics of SARI Cases and Confirmed HCoVs Cases From Jan 2011–Dec 2012 (n = 864)

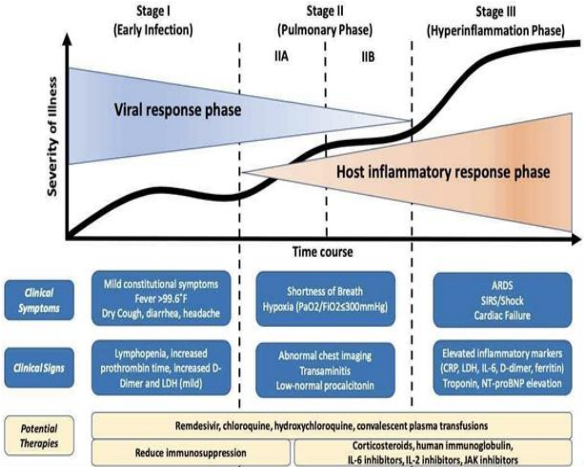
Features	Description	All SARI cases % N (n = 864)	Human coronavirus OC 43 %N (n = 4)	Human coronavirus NL63 %N (n = 3)	Human coronavirus 229E %N (n = 2)
Age in years					
	Mean (SD)	24.3 (21.9)	26.25 (8.098)	33.67 (26.83)	13.25 (18.03)
	Median (IQR)	20 (3–40)	23.5 (21.–35.0)	24 (13–64)	13.25 (0.5–26)
Sex					
	Male	436 (50.5%)	1 (25.0%)	2 (66.7%)	1 (50.0%)
	Female	428 (49.5%)	3 (75.0%)	1 (33.3%)	1 (50.0%)
Place					
	Kerala state(INDIA)				
	Kozhikode	339 (39.2%)	1 (25.0%)	2 (66.7%)	1 (50.0%)
	Kasargod	33(3.8%)	1 (25.0%)	–	–
	Malappuram	35 (4.1%)	1 (25.0%)	–	–
	Trissur,	68 (7.9%)	1 (25.0%)	–	–
	Other districts	207 (23.8%)	–	–	–
	Karnataka state(INDIA)				
	Bangalore	18 (2.1%)	–	–	1 (50.0%)
	Dakshina Kannada,	31 (3.6%)	–	1 (33.3%)	–
	Other districts	133 (15.4%)	–	–	–

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019. Genetic sequencing of the virus suggests that it is a beta coronavirus closely linked to the SARS virus (1).While most people with COVID-19 develop only mild or uncomplicated illness, approximately 14% develop severe disease that requires hospitalization and oxygen support, and 5% require admission to an intensive care unit (1). In severe cases, COVID-19 can be complicated by the acute respiratory distress syndrome (ARDS), sepsis and septic shock, multi organ failure, including acute kidney injury and cardiac injury (2). Older age and co-morbid disease have been reported as risk factors for death, and recent multivariable analysis confirmed older age, higher Sequential Organ Failure Assessment (SOFA) score and d-dimer > 1 µg/L on admission were associated with higher mortality. This study also observed a median duration of viral RNA detection of 20.0 days (IQR 17.0–24.0) in survivors, but COVID-19 virus was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days (3, 4). Building on evidence-informed guidelines developed by a multidisciplinary panel of health care providers with experience in the clinical management of patients with COVID-19 and other viral infections, including SARS and MERS, as well as sepsis and ARDS, this guidance should serve as a foundation for optimized supportive care to ensure the best possible chance for survival and to allow for reliable comparison of investigational therapeutic interventions as part of randomized controlled trials (5, 6).There are few data on the clinical presentation of COVID-19 in specific populations, such as children and pregnant women. In children with COVID-19 the symptoms are usually less severe than adults and present mainly with cough and fever, and co-infection has been observed (7, 8). Relatively few cases have been reported of infants confirmed with COVID-19; those experienced mild illness (9). There is currently no known difference between the clinical manifestations of COVID-19 pregnant and non-pregnant women or adults of reproductive age. Pregnant and recently pregnant

women with suspected or confirmed COVID-19 should be treated with supportive and management therapies, as described below, taking into account the immunologic and physiologic adaptations during and after pregnancy.



1. Screening and triage: early recognition of patients with SARI associated with COVID-19 Screening and triage: Screen and isolate all patients with suspected COVID-19 at the first point of contact with the health care system (such as the emergency department or outpatient department/clinic). Consider COVID-19 as a possible etiology of patients with acute respiratory illness under certain conditions (see Table 1). Triage patients using standardized triage tools and start first-line treatments. Remark 1: Although the majority of people with COVID-19 have uncomplicated or mild illness (81%), some will develop severe illness requiring oxygen therapy (14%) and approximately 5% will require intensive care unit treatment. Of those critically ill, most will require mechanical ventilation (2, 10). The most common diagnosis in severe COVID-19 patients issevere pneumonia. Remark 2: Early recognition of suspected patients allows for timely initiation of appropriate IPC measures (see Table 3). Early identification of those with severe illness, such as severe pneumonia (see Table 2), allows for optimized supportive care treatments and safe, rapid referral and admission to a designated hospital ward or intensive care unit according to institutional or national protocols. Remark 3: Older patients and those with comorbidities, such as cardiovascular disease and diabetes mellitus, have increased risk of severe disease and mortality. They may present with mild symptoms but have high risk of deterioration and should be admitted to a designated unit for close monitoring. Remark 4: For those with mild illness, hospitalization may not be required unless there is concern about rapid deterioration or an inability to promptly return to hospital, but isolation to contain/mitigate virus transmission should be prioritized. All patients cared for outside hospital (i.e. at home or non-traditional settings) should be instructed to manage themselves appropriately according to local/regional public health protocols for home isolation and return to a designated COVID-19 hospital if they get worse (https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts)



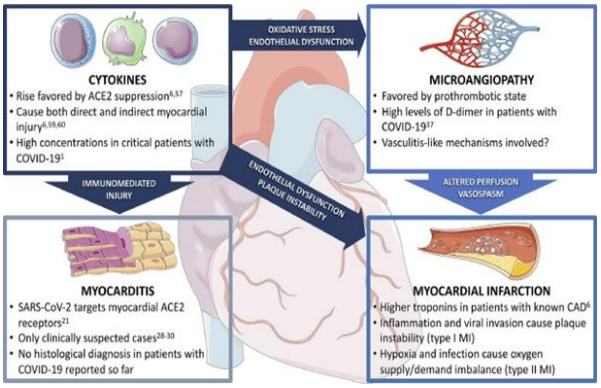
RESULTS

A total of 1706 cases of influenza virus negative SARI were referred to MCVR during the study period. Of the 864 cases included, the mean age was 24.3 (SD ¼ 21.9), median age was 20 (IQR ¼ 3–40) and the male to female ratio was 1:1 (Table I). Geographically, 21.2% of SARI cases were from Karna taka and 78.8% from Kerala States of India. Of the 864 samples tested, only nine samples were positive for HCoVs and the prevalence was 1.04% (95% CI: 0.36–1.72). The mean age of confirmed cases was 25.8 (SD ¼ 17.5) and the median age was 24.0 (IQR ¼ 16.5–32.0). Of the nine confirmed cases, four were positive for HCoV-OC43, three were positive for HCoV-NL63 and two were positive for HCoV-229E (Table I). Seven confirmed cases were seen in 2011 and only two cases were positive in 2012. No MERS-CoV was detected. Since, the pan coronavirus positive samples already revealed the

HCoV types, the need to further screen for SARS CoV was negated.

DISCUSSION

This study reports low prevalence of HCoV among SARI cases from south west India during the period January 2011 to December 2012. This is in concordance with the findings of a similar study from Thailand [Dare et al., 2007]. However the prevalence reported here is less when compared to studies conducted in similar age groups in Brazil and United Kingdom [Dare et al., 2007; Gaunt et al., 2010; Cabecca et al., 2013]. But these studies included all respiratory infections and were not limited to SARI cases. While majority of HCoVs are associated with mild acute respiratory infection and our samples included only SARI cases, this could be the possible reason for the observed low prevalence of HCoVs in this study. Further, tropical climate in Southwest India also may have contributed to the low prevalence.



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AUTHOR DETAIL:

Patil Aarti Vitthalrao
Student of B.pharmacy 3rd year, Latur College of Pharmacy, Hasegaon

Dadewad swapnali sanjiv
Student of B.pharmacy 3rd year, Latur College of Pharmacy, Hasegaon

Mansi Mukundraj Patilghote
Student of B.pharmacy 3rd year, Latur College of Pharmacy, Hasegaon

Renuka R. Deshpande,
Assistant Professor, Department of Pharmaceutics, Latur College of Pharmacy, Hasegaon