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Original Research Article

Clinico-demographic analysis of symptomatic versus asymptomatic COVID -19 Patients: A one year retrospective study from a tertiary care center in Kashmir, India

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ABSTRACT

Introduction: SARS-CoV-2 causing COVID 19 disease has emerged as one of the most infectious pathogen known to humans, causing severe acute respiratory illness (SARI) along with MERS and Influenza A/H1N1. The proportion of asymptomatic and mild illness is significantly higher and a minimal proportion of individuals develop a severe disease. Albeit, more cases of COVID-19 are from India, but the data regarding clinical epidemiology of COVID-19 in India is very low. In this backdrop, the present study was aimed to evaluate the clinical/epidemiological characteristics and outcomes of asymptomatic vs. symptomatic COVID-19 patients.

Material and Methods: All relevant clinical and demographic and epidemiological information was recorded over a period of one year From March 2020 to march 2021. A total of 217,665 samples from clinically suspected cases of COVID-19 were collected and using upper respiratory tract swabs. RT PCR assay was conducted according to the manufacturer's instructions for the detection of RNA from SARS-CoV-2 present in the nasal pharyngeal swabs of from the patients suspected of COVID-19.

Results: Out of the total 217,665 samples, 133474 (61.3%) were males and 84,191 (38.7%) were females. Among the 24,009 (11%) tested positive cases for SARS-CoV-2 infection, 15,254 (63.5%) were males and 8755 (36.5%) were females. The age group between 30 – 39 years showed high positivity and the fever was the most common symptom. Among the positive cases 60% were asymptomatic and 40% were symptomatic. Male patients, patients above 60 years of age and with comorbid conditions were more symptomatic. Children with <10 years age and positive patients with age group of 10 -19 were asymptomatic.

Conclusion: In our study, the proportion of asymptomatic COVID-19 was higher with male preponderance. Thus the higher number of asymptomatic positive patients with increased chance of transmission is missed on symptom-based screening calls for adherence to preventive measures. Thus, effective measures must be taken among the asymptomatic cases to halt the transmission of disease, prevent death and alter the course of this epidemic.

1. Introduction

On December 31, 2019 a cluster of pneumonia cases was seen in Wuhan, China and was reported to WHO, by the Wuhan Municipal Health Commission.[1] This pneumonia was caused by unknown agent identified later as a new type of Coronavirus now known as Severe Acute Respiratory Syndrome Coronavirus-2(SARS-CoV-2).[2]World Health Organization declared it as a global pandemic On March, 2020 over 173 million cases of

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COVID-19 have been reported globally with over 3.7 million deaths.[3] The first positive case of COVID-19 was reported from Kashmir region on 18th March, a 65 year old lady from Srinagar who had a travel history from Saudi Arabia. Coronaviruses have been associated with outbreaks earlier as well, in Asia and in Middle East over the past decades. Severe Acute Respiratory Syndrome emerged in the winter of 2002 in southern China. Middle East Respiratory Syndrome began to emerge in 2012 from Saudi Arabia. In 2019, SARS CoV-2 emerged and became a worldwide, emergency and pandemic.[4]With the overall fatality rate of around 2%, the mortality of COVID-19 far less than SARS, or MERS.[5] Human to human transmission is higher and the main route of transmission being aerosol mode of transmission. Faeco-oral, blood borne, mother to child and animal to human transmissions have also been reported.[6] Within three days, the viral RNA can be detected by RT PCR in the affected patient and RT PCR remains positive for one to two weeks for asymptomatic persons and up to three weeks or more for patients with mild to moderate disease.[7] While as in some patients with severe disease it can be much longer. The course of Coronavirus disease is usually divided into three phases. The first with cough, fever, wheezing fatigue, headache, diarrhea, and dyspnea, consistent with upper respiratory tract infection. The second phase with rapid appearance of bilateral pneumonia and infiltrates with variable degree of hypoxia and the last third phase with respiratory failure, which leads to death.[8]This virus multiplies in the upper respiratory tract, and the peak viral load is reached even before the symptom onset. As a result, asymptomatic individuals can also transmit. In those who are symptomatic, the manifestations range from mild to severe, requiring intensive care. Studies have shown that the proportion of asymptomatic and mild illness is significantly higher and a tiny proportion of individuals develop a severe disease.[9]

Therefore, to analyze and compare the clinical and demographic dynamics of symptomatic with asymptomatic COVID patients in detail is important. So that effective measures can be taken to halt the transmission of disease, prevent death and alter the course of this epidemic. This study, one of the first of its kind in our region will give us a perspective into clinic-demographics of symptomatic vs asymptomatic patients as well as the prevalence and risk factors in COVID 19 patients.

2. Materials and Method

This was a hospital based cross sectional based study conducted at Virology unit of Department of Microbiology, Government Medical College and associated hospitals, Srinagar. All relevant clinical and demographic and epidemiological information was recorded over a period of one year From March 2020 to march 2021.Patients with acute respiratory infection, influenza like illness, severe acute respiratory infection, High risk contacts and asymptomatic close contacts of COVID-19 patients, hospitalized patients, pregnant women, Traveler who fulfilled the ICMR screening criteria were screened for SARS CoV-2 by RT PCR and were included in this study. A positive result on real time PCR of nasopharyngeal / oropharyngeal swab was taken as a confirmed positive case of COVID-19. A total of 217,665 samples from clinically suspected cases of COVID-19 were collected and processed at VRDL division of our laboratory. Following Proper sample collection protocols and procedures is the cornerstone of the diagnosis of COVID-19. Therefore, Samples were collected under all recommended protocols as recommended by CDC. For initial diagnosis of SARS its recommended by CDC to collect upper respiratory tract specimens which include the following: nasopharyngeal swabs, oropharyngeal swabs, nasal mid turbinate swabs, nasopharyngeal aspirates and saliva and lower respiratory specimens like sputum, BAL tracheal aspirate, lung biopsy and Plural fluid were also included. In this study Nasopharyngeal swabs were taken from deep nostrils using a dry synthetics swab stick. The swab was inserted along the floor of the nostril parallel to the palate and back to the nasopharynx. It was left in place for a few seconds and rotated 3 times. The swab was then slowly removed and tip was placed in vial containing three ml of viral transport media while breaking the applicator stick. It was subsequently transported to COVID testing lab at 4 degree Celsius as quickly as possible.

Samples from various districts of the state were received at our laboratory and were processed under appropriate biosafety level precautions. RT PCR assay was conducted according to the manufacturer's instructions for the detection of RNA from SARS-CoV-2 present in the nasal pharyngeal swabs of the patients suspected of COVID-19.RNA extraction and purification was done from all the samples using Invitrogen Purelink viral RNA/DNA mini kit by Thermo Fisher scientific with each kit containing 50 reactions. This extracted and purified RNA was reverse transcribed to cDNA and subsequently amplified using ABI 7500 Fast DX RT-PCR Thermocycler. The kit was a two-step kit wherein the E gene was used for screening. All samples which came positive for screening were confirmed by a secondary reaction targeting the ORF and RdPR genes as per the NIV protocol. Over a period of one year various other kits from different manufacturers were also used for example, modified Thermo Fisher Taq Path COVID-19 SARS-CoV-2 (ORF1ab,N,S gene detection), labgun COVID-19 assay (RdRP,E,IC DETECTION) . To ensure the integrity and verification of RT PCR assay results an internal control was analyzed for each sample, Also, one replicate of positive control and one replicate of negative control was tested in each batch. A cycle threshold (CT VALUE) value of less than 35 was defined as positive and

CT value have greater or equal to 40 was defined as negative test results. A CT value from 35 to less than 40 was reported as inconclusive, and a repeat sampling was requested from such patients.

3. Results

A total of 2,17,665 samples from clinically suspected cases of COVID-19 were collected and analyzed at the VRDL division of our department over a period of one year from, March 2020 to March 2021. Of the 217665 patients, 130559(60%) were asymptomatic, and 87066 (40%) were symptomatic (Table 1). Out of them 133474 (61.3%) were males and 84,191 (38.7%) were females (Table 2). The overall mean age was 34.3 years. 3,730 (1.7%) patients had presented with severe acute respiratory illness (SARI) when tested for SARS- CoV-2 (Table 6). Of the total 217665 patients, 24,009 (11%) tested positive for SARS-CoV-2 infection by RT- PCR, among them 15,254 (63.5%) were males while 8755 (36.5%) were females (Table 3). The mean age observed was 35.3 years. Also, 2,748 results were declared Inconclusive (according to the kit manufacturer's instructions) and 886 specimens were rejected for various reasons (Table 3). The highest positivity was observed in the age group of 30 – 39 years (n=5297, 22%), followed by 20 -29 years (n=4885, 20.4%). On comparing the clinical manifestations of symptomatic vs. asymptomatic patients, male patients were significantly more symptomatic than female patients (Table 4). Amongst lab confirmed positive cases, fever was the most common symptom, and was present in (1.7%) patients, followed by cough (41%) and fatigue / malaise was reported by 37% of patients (Table 5). Also among positive cases, associated comorbidities were present in 5580 (23.2%) patients, of which Hypertension (n=2593, 10.8%) was the most common, followed by COPD (n=1176, 4.9%) and Diabetes mellitus (n=960, 4%). 120 patients with malignant conditions also tested positive for SARS-CoV-2 infection (Table 5). 1118 patients (25%) of the positive patients above 60 years of age were seen to be symptomatic. Among children of age less than 10 years 91.3% were asymptomatic.92.4% of COVI-19 positive patients in age group of 10 -19 were asymptomatic. Also 51.3% positive patients with one or more comorbidity were symptomatic. (Table 6). Further, there was no significant (p=0.589) association number of comorbidities and symptomatic and asymptomatic COVID-19 positive patients (Table 7).

4. Discussion

SARS-CoV-2 is placed in the genera Beta Coronavirus and subgenus Sarbecovirus. SARS-CoV-2 causing COVID 19 disease has emerged as one of the most infectious pathogen known to humans, causing severe acute respiratory illness (SARI) along with MERS and Influenza A/H1N1. Initial studies from China demonstrated COVID-19 to be a respiratory illness with a spectrum ranging from mild illness (81%), severe respiratory distress (14%) and critical illness in 5%, with a case fatality rate (CFR) of around 2.4%.[9] The COVID-19 pandemic has had a major impact on clinical microbiology laboratories in the past one year. The ongoing pandemic has affirmed the importance of the laboratory diagnosis of SARSCoV- 2 infection in order to diagnose, limit the spread, and promptly treat those patients who have a serious infection. Our institute has reported close to one third (32%) of the total positive cases from Kashmir division and around 18.8% cases of the whole state, indicating a high burden and the magnitude of work that has been carried out by the department of Microbiology, GMC, Srinagar. In our study an overall positivity rate of 11% observed, majority of the positive cases were males (63.5%), while 36.5% were females. The mean age observed was 35.3 years and the median age was 32 years (Range 0 – 98 years). The highest positivity was observed in the age group of 30 – 39 years (22%), followed by 20 -29 years (20.4%), and 40 – 49 (16.9%). In a similar study by Khan M, et al. in Peshawar, Pakistan it was found that among 121 RT-PCR positive patients, 70.25% were male, while 29.8% were females, and the majority of the cases were between 25 to 60 years old.[10] Patients testing positive for SARS-CoV-2 infection in our study were younger (median age=32 years) when compared to those in China (median age=56 years)[11] and New York (median age=63 years).[12] In most of the developing countries, males are the working members in majority of the households, thereby exposing themselves in work places and explaining the higher preponderance. The high infection rates among adolescents and young adult population can be attributed to the higher outdoor exposure and subsequent chances of them getting infected from cases in crowded areas, events and work places. In the present study, 40% of total positive cases were symptomatic at the time of testing for SARS-CoV-2. Fever (62%), cough (41%), Fatigue/Malaise (37%) were the predominant symptoms, while gastrointestinal symptoms (3.6%) were relatively infrequent. In a similar study conducted by Soni et al. the common presenting complaints were fever in 37(77.1%) followed by cough in 26 (54.2%) patients.[13] In another study conducted by Wu et al. who reported fever, cough and sputum production as the predominant symptoms among patients requiring hospitalization with COVID-19.[14] These observations are quite similar to our findings. In a study from New Delhi, India by Gupta et al. symptoms were observed in 42.9% of cases with fever an cough being the most common.[15] Fever as the predominant symptom in overwhelming cases indicates an early Interleukin mediated systemic response to initial infection or a localized inflammatory response to the respiratory tract infection.[16] In our study, 23.2% of total SARS-CoV-2 positive cases had some underlying medical condition or comorbidity.

Table 1: Symptomatic andasymptomatic cases among the study participants

Total no of patients	Asymptomatic patients, n (%)	Symptomatic patients, n (%)
217665	130599(60%)	87066(40%)

Table 2: Gender distribution among the study participants

Gender	No of Patients (%)
Males	133474(61%)
Females	84191(38.6%)

Table 3: Outcome of COVID-19 testing among the study participants

Total no of patients tested	Total positives	Total negatives	Total no of inconclusive and rejected samples
217665	24009(11%)	190022	3634

Table 4: Association between gender and COVID-19 symptom

Parameter (gender)	Asymptomatic	Symptomatic	P value
Male (n=15043)	7522(50.0%)	7521(49.99%)	0.004
Female n=(8663)	6671(77%)	1992(22.99%)	

Table 5: Comorbidities and Presenting symptoms among the COVID-19 positive patients

Clinical Features	No of Patients (%)
Comorbidities in positive patients	
Hypertension	2593(10%)
COPD	1176(4.8%)
Diabetes Mellitus	960(3.9%)
Cardiovascular Diseases	480(1.99%)
Hypothyroidism	72(0.2%)
Malignancies	120(0.49%)
CKD	144(0.49%)
Pulmonary Tuberculosis	24(.09%)
Pancreatitis	11(.045%)
Multiple Comorbidities	1560(6.49%)
Presenting Symptoms	
Fever	14886 (62%)
Cough	9844 (41%)
Fatigue or Malaise	8884 (37%)
Myalgia	5763 (24%)
Shortness of Breath	4003 (16.6%)
Headache	2641(11%)
Chills and Rigor	1680(7%)
Loss of Smell/Taste	1273 (5.3%)
Nasal Congestion	960 (4%)
Sore Throat	720 (3%)
Rhinorrhea	480 (2%)
Diarrhoea	480 (2%)
Nausea and Vomiting	242 (1%)
Abdominal Pain	140 (0.6%)

Table 6: Comorbidities among the symptomatic and Asymptomatic COVID-19 positive patients

Comorbidities	Symptomatic	Asymptomatic	Total
No	18901(8.48%)	4297(18.52%)	23198
One or greater than One	248(48.63%)	262(51.37%)	510

Table 7: Association between number of Comorbidities among the symptomatic and Asymptomatic COVID-19 positive patients

Number of comorbidities	Asymptomatic	Symptomatic	P value
0 (n=18326)	9713(53%)	8613(47%)	
1 (n=5683)	3643(64.1)	2040(35.9%)	0.589
Greater than 1 (n=1560)	953(61.1%)	607(38.9%)	

Hypertension 10.8% was the most common, followed by COPD 4.9% (1.4% ILI & 3.5% SARI) and Diabetes mellitus 4%. 6.5% patients had multiple comorbidities. In another study by Soni et al. 29.8% patients had associated comorbid condition of varying severity, this included hypertension in 16.6%, diabetes in 14.9% and chronic renal disease in 2.6% patients.[13] Gupta et al. reported hypertension in 23.4% as the most common comorbidity among COVID-19 patients.[15] These findings are in concordance with the findings of our study. An overall increased risk among people with comorbid conditions, particularly chronic lifestyle related diseases have put an added burden on an already high mortality and morbidity numbers associated with COVID-19.

Asymptomatic transmission of COVID-19 was initially described in household contacts of positive patients from China.[17] The percentage of asymptomatic COVID-19 in positive patients from China ranged from 1.2-11%.[18] However, the rate of individuals with asymptomatic COVID-19 depends highly on the testing strategies as asymptomatic individuals are unlikely to report to the hospital. In a study from south India by Gupta et al. all travelers were screened irrespective of the symptoms and were admitted irrespective of the severity, the percentage of asymptomatic individuals was seen to be higher (59%). This was similar to our finding were 60% patients were asymptomatic.[19] The spectrum of symptomatic patients with COVID-19 ranges from mild to severe. In a large report from China, the proportion of mild patients among all symptomatic patients was 81%. The risk factors for severe disease in patients with COVID-19 range from cardiovascular disease, diabetes mellitus, hypertension, chronic lung disease and immunosuppressive conditions. In a study, the mean number of comorbidities in patients who died was 2.7.[20] In another study; the mortality rate was significantly higher in those with comorbidities than those without comorbidities.[21] Similar to our study, male sex was associated with more severe illness.[22] Older age has also been associated with symptomatic disease which is in line with the present study.[20]

5. Conclusion

The possibility of transmission from asymptomatic cases which form a significant proportion of total positive patients but are missed on symptom-based screening calls for adherence to preventive measures such as physical distancing, frequent hand washing, wearing of masks in the community and universal masking. Since patients with asymptomatic and mild illness have excellent outcomes without any therapeutic interventions, unnecessary and unproven medications should be avoided in such patients. These patients can also be managed in-home isolation (with monitoring) to decrease the burden on tertiary care hospitals.

6. Acknowledgements

None.

7. Conflict of Interest

None to declare.

8. Funding Sources

None.

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