

# Symptomatology and Epidemiologic Characteristics of COVID 19 Patients in Kerala, India

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## ABSTRACT

### BACKGROUND

The wide range of symptoms of COVID-19 has brought out extensive researches across the world to enable early case detection. Very few studies in India give an overall view of the case scenario of any state. Our study aims to look into the symptomatology and epidemiological characteristics of COVID-19 patients of Kerala.

### METHODS

A cross sectional study was conducted among the COVID-19 patients reported in Kerala till 31<sup>st</sup> March 2020. Contact details of patients were obtained from Kerala State Disaster Management Authority (KSDMA). Patients were contacted over phone to obtain consent and to collect information regarding demography, contact and symptomatology.

### RESULTS

Among 202 patients in this study, 154 (76.2 %) were foreign returnees and 48 (23.8 %) acquired disease by local transmission. The mean age was 36.5 ( $\pm$  13.9) years and majority were males (80.2 %). The most common symptoms reported were fever (n = 90, 45 %), cough (n = 54, 27 %), sore throat (n = 44, 22 %), diarrhoea (n = 29, 14.5 %) and anosmia (n = 24, 12 %), while 39 (19.3 %) patients were asymptomatic. Presumptive median incubation period was 6 (IQR = 4) days and median duration of symptoms was 4 (IQR = 6) days. The proportion of asymptomatic, mild, moderate and severe cases were 19.3 %, 68.8 %, 8.9 % and 3 % respectively. Hypertension (adjusted OR = 3.5, (1.1 - 11.2), p = 0.03) and locally acquired infection (adjusted OR = 2.8, (1.1 - 7.1) p = 0.03) were significant predictors of severity of the disease on logistic regression. Case fatality rate was 0.99 %.

### CONCLUSIONS

Mild and nonspecific symptoms and short duration of illness should not be overlooked in COVID-19 and high suspicion should be maintained as a large segment of infections are asymptomatic. The focus should be on insulating the elderly and those with comorbid conditions.

### KEY WORDS

Symptoms, Epidemiology, COVID 19, SARS CoV 2, Comorbidities, Cross Sectional Study, Kerala, India

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## BACKGROUND

The world is witnessing one of the greatest challenges, COVID-19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Since its emergence in China, it took barely few months to become a pandemic and the virus has spread across the continent, infecting more than 3 million and killing more than 2 lakhs globally as of April 2020.<sup>1</sup>

The first case of COVID 19 in India was reported by the end of January in the State of Kerala in a student who returned from Wuhan, China.<sup>2</sup> The situation in India worsened with surge of more than 40,000 cases and more than 1000 deaths in three months.<sup>2</sup> Though Kerala spotted an initial increase of the COVID 19 cases, the State could flatten the curve by last week of April.<sup>3</sup>

The demeanor of SARS CoV-2 in different parts of the world heedless of the technologic, scientific and medical advancements of the nations has been an affair of great discussion. The diversity of symptoms of the disease ranging from no or mild symptoms to severe pneumonia and other complications, makes it a topic of extensive research. With umpteen research works on the characteristics of the COVID-19 from across the world, it is critical to study the epidemiological and clinical pattern in the State.<sup>4</sup> A state level inspection of the case scenario is imperative in planning resources and escalating preparedness. In this context, our study aims to look into the symptomatology and epidemiological characteristics of COVID-19 patients of Kerala.

## METHODS

A cross sectional study was conducted among the patients diagnosed with COVID-19 in Kerala till 31<sup>st</sup> March, 2020. Permission for accessing the data from the COVID-19 database was obtained from Kerala State Disaster Management Authority (KSDMA). KSDMA is a statutory non-autonomous body which plans for the capacity building in the event of COVID turning into a disaster. The study was approved by Institutional Ethics Committee of Government Medical College, Thiruvananthapuram (HEC. No. 03 / 18 / 2020 / MCT).

### Case Definitions

A COVID 19 positive patient is defined as an individual with a throat swab or nasopharyngeal swab sample positive for SARS CoV-2, using RT-PCR test at a COVID-19 testing centre in Kerala. A COVID 19 patient with a recent history of travel to a country with local transmission and tested positive in maximum incubation period (14 days) is considered as an imported case. A person with history of contact with a known positive case of COVID-19 within last 14 days, tested positive is considered as a local case. The presumptive incubation period was determined from the details of primary cases as the interval between the earliest date of contact of the transmission source and the earliest date of symptom onset.

## Data Source, Collection and Data Analysis

We obtained the contact details of 241 COVID-19 patients of Kerala from the KSDMA COVID-19 database. The patients were contacted over phone, explained about the study and willingness enquired. Patients who were not willing to give oral consent, foreign tourists and those who didn't answer the call after two attempts were excluded from the study. The interview was done over telephone and using a semi structured questionnaire. Data were collected regarding demography, contact and travel history, symptoms, comorbidities, details of testing, hospitalisation and discharge. As all patients who tested positive were admitted with IP care at a COVID treatment centre irrespective of the clinical severity till their RT PCR test become negative, according to the State's guideline, severity of symptoms was assessed based on patient's / immediate care giver's perception. Patients were classified into three categories-mild, moderate and severe based on the perception of need for OP / home management, IP care and critical care.

We analysed the data using SPSS (IBM SPSS Statistics for Windows, Trial Version 26.0. Armonk, NY: IBM Corp) software. The data was consolidated and continuous variables were presented as mean (SD) or median (IQR) and categorical variables as frequency (%). We used Chi square test or Fishers exact test and Man Whitney U test to compare differences. To explore the predictor of disease severity, multivariable logistic regression model was used.

## RESULTS

Out of the 202 patients reported in this study, 154 (76.2 %) patients travelled from countries with local transmission (67 % from Middle East countries, 7.5 % from European countries and 2 % from other countries) and rest of the patients had contact with a foreign returnee (23.8 %, n = 48). The mean age of the patients was 36.5 ( $\pm$  13.9) years of which nine (4.5 %) patients were aged more than 60 years. The proportion of elderly ranged from 0.6 % among the foreign returnees to 16.7 % among the locally transmitted cases (Figure 1). While most of the patients were males (80.2 %, n = 162), there was a significant difference in the gender distribution between COVID 19 cases who were foreign returnees and the ones who acquired disease through local transmission. There were 8 (5.2 %) females in the former group and 32 (66.6 %) females among the latter. Maximum cases were reported from the northern districts in the state, namely Kasaragod and Kannur (Figure 2)

Analysing the 48 patients who acquired COVID-19 through local transmission, presumptive median incubation period was estimated to be 6 (IQR = 4) days. Among them 34 (70.8 %) patients had close household contact and six (12.5 %) patients travelled with a COVID-19 patient in a closed vehicle. There were eight patients (16.7 %) who were secondary contacts of an imported case and the linking primary contact was also diagnosed with COVID-19.

All patients were admitted in COVID isolation units attached to tertiary care centres at district level. Common symptoms reported were fever (n = 90, 45 %), cough (n = 54, 27 %) and sore throat (n = 44, 22 %).

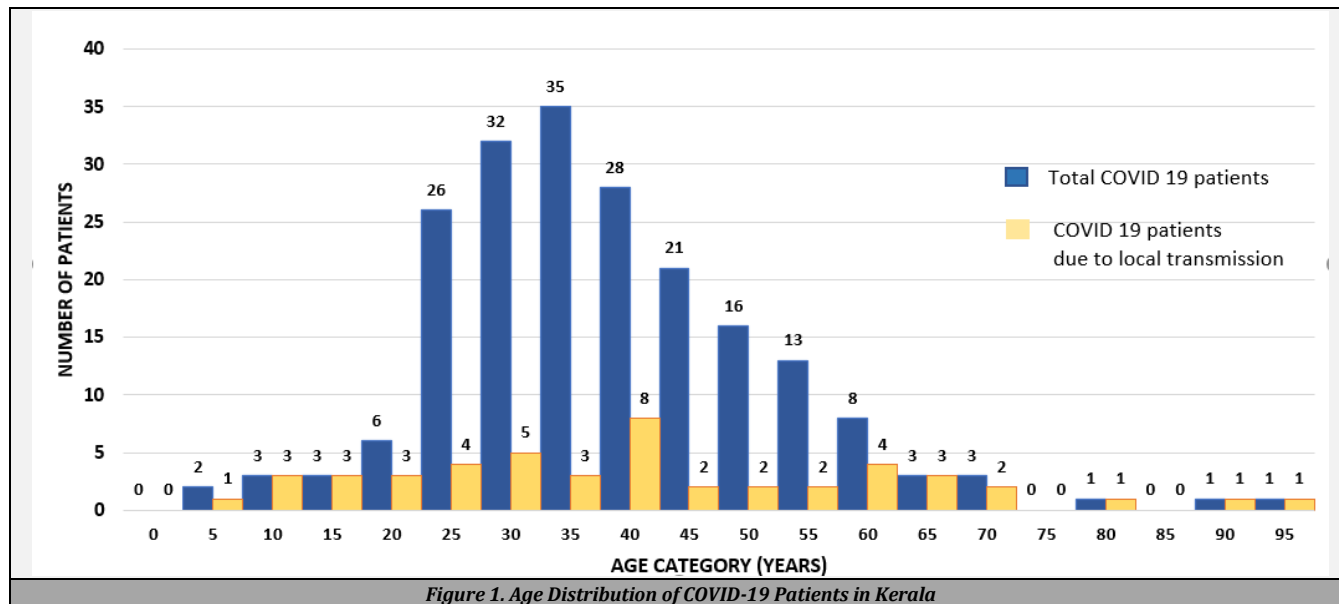


Figure 1. Age Distribution of COVID-19 Patients in Kerala

Diarrhoea was reported by 29 (14.5 %) and anosmia by 24 (12 %) patients. One fifth of (39, 19.3 %) patients did not report any symptoms at all and even in 163 symptomatic, majority (108, 66.3 %) had only two symptoms or less. The locally transmitted cases reported a significantly higher proportion of fever (n = 28, 63.6 %) than among foreign returnees (40.5 %, p = 0.007). On the other hand, while 18.3 % of the foreign returned COVID-19 patients developed sore throat, the proportion was only 5.5 % among the locally transmitted patients (p = 0.011). Thirty (19 %) among the symptomatic patients reported duration of symptoms for only one day and in most patients, the symptoms lasted for less than one week. Median duration of symptoms was 4 (IQR = 6) days. Associated comorbidities were present in 49 (24.3 %) patients, the most common comorbidity being diabetes followed by hypertension and respiratory comorbidities. (Table 1).

	Frequency	Percentage
Asymptomatic	39	19.3
<b>Symptoms</b>		
Fever	90	45
Cough	54	27
Sore throat	44	22
Diarrhoea	29	14.5
Headache	28	14
Rhinitis	25	12.5
Anosmia	24	12
Myalgia	15	7.5
Fatigue	14	7
Breathlessness	9	4.5
Tastelessness	7	3.5
Abdominal pain	2	1
Reduced sleep	2	1
Vomiting	2	1
<b>Duration of Symptoms (n = 163)</b>		
1 day	30	19.0
2 days to 1 week	87	55.1
1 week to 2 weeks	34	21.5
more than 2 weeks	7	4.4
<b>Comorbidities (n = 202)</b>		
Present	49	24.3
Absent	153	75.7
<b>Coexisting Chronic Diseases (n = 202)</b>		
Diabetes mellitus	21	10.5
Hypertension	19	9.4
Respiratory Comorbidities	14	6.9
Dyslipidaemia	9	4.5
Cardiac comorbidities	5	2.4
Others	7	3.5

Table 1. Symptomatology and Details of Associated Comorbidities of 202 COVID-19 Patients in Kerala (Diagnosed till 31<sup>st</sup> March 2020)

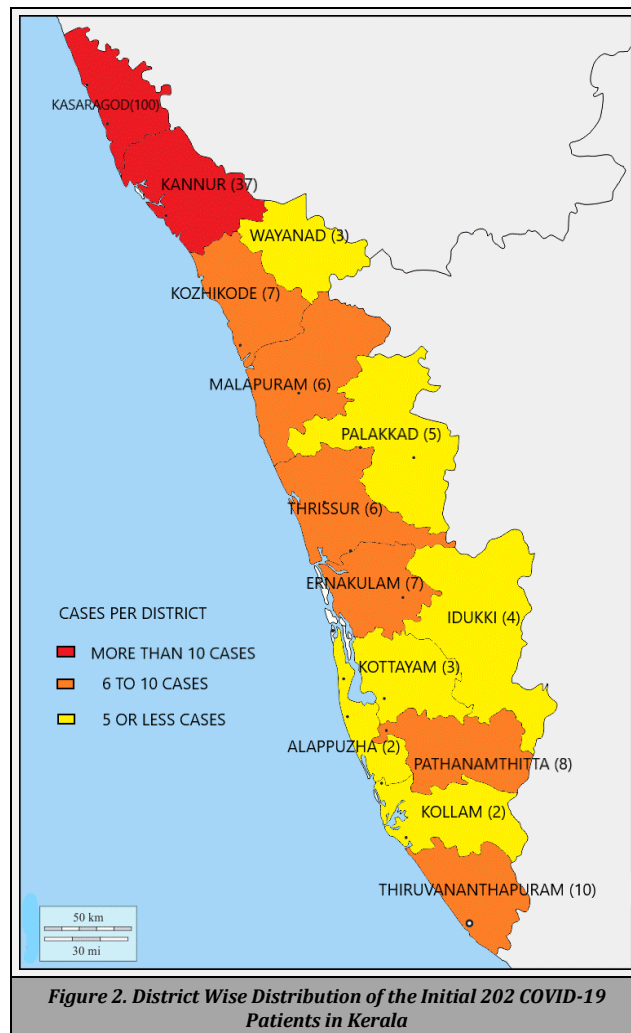


Figure 2. District Wise Distribution of the Initial 202 COVID-19 Patients in Kerala

Among the 202 patients the proportion of asymptomatic, mild, moderate and severe cases were 19.3 % (n = 39), 68.8 % (n = 139), 8.9 % (n = 18) and 3 % (n = 6) respectively. Critical care was required only in six (3 %) cases. Distribution of disease severity showed an increasing proportion of severity with age (Figure 3). The patients were classified into two groups based on the reported severity of illness.

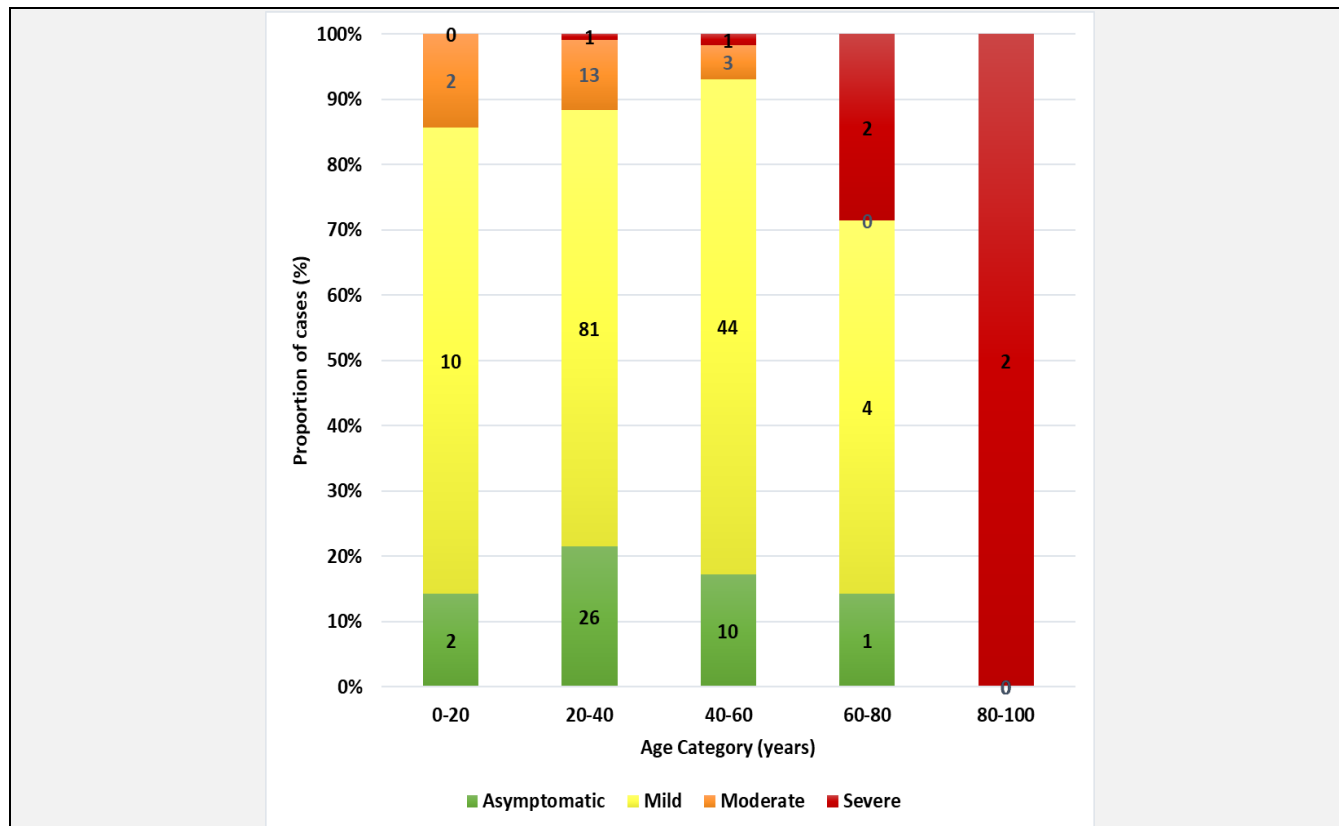


Figure 3. Disease Severity of Covid-19 Patients Distributed across the Age Groups

Features	Severity	Mild*	Moderate / Severe	P-Value	Odds Ratio (95 % CI)
	More than 60 (n = 9)	5 (55.6)	4 (44.4)		
Transmission	Foreign returnee (n = 154)	141 (91.6)	13 (8.4)	0.007	3.2 (1.3 - 7.8)
	Local transmission (n = 48)	37 (77.1)	11 (22.9)		
Comorbidities					
Hypertension	Present (n = 18)	12 (66.7)	6 (33.3)	0.009	4.8 (1.6 - 14.7)
	Absent (n = 184)	167 (90.7)	17 (9.3)		
Respiratory comorbidities	Present (n = 14)	10 (71.4)	4 (28.6)	0.06	3.5 (1.01 - 12.4)
	Absent (n = 188)	169 (89.8)	19 (10.2)		
Cardiac disease	Present (n = 4)	3 (75)	1 (25)	0.39	2.65 (0.26 - 26.61)
	Absent (n=198)	176 (88.8)	22 (11.2)		
Diabetes Mellitus	Present (n = 21)	19 (90.5)	2 (9.5)	1.0	0.8 (0.17 - 0.367)
	Absent (n = 181)	160 (88.3)	21 (11.7)		
Dyslipidaemia	Present (n = 9)	7 (77.8)	2 (22.2)	0.28	2.33 (0.45 - 11.94)
	Absent (n = 193)	172 (89.1)	21 (10.9)		

Table 2. Univariate Analysis of Factors Associated with Severity of Covid-19

\*Includes Asymptomatic Patients also

Asymptomatic and mild cases fell into the first group & moderate and severe cases were grouped into the second. Table 2 shows the significant factors associated with the severity of COVID 19 infections on univariate analysis using chi square test. Hypertension (adjusted OR = 3.5, (1.1 - 11.2), p = 0.03) and locally acquired infection (adjusted OR = 2.8, (1.1 - 7.1) p = 0.03) were found to be significant predictors of

severity of the disease on logistic regression. Univariate analysis to test association of individual symptoms with severity of COVID-19 using chi square test showed dyspnoea, cough, headache and fatigue were significantly associated with moderate / severe illness compared to mild cases (Table 3). Two among 202 COVID-19 patients succumbed to death, thus bringing the case fatality rate to 0.99 %. Both the patients were males, above 60 years old, had comorbidities including hypertension and cardiac / respiratory illness, developed complications and required ventilator support.

Symptoms	Severity	Mild	Moderate / Severe	P-Value	Odd's Ratio (95 % CI)
	Absent (n = 68)	63 (92.6)	5 (7.4)		
Cough	Present (n = 55)	44 (80.0)	11 (20)	0.04	2.64 (1.02 - 6.83)
	Absent (n = 104)	95 (91.3)	9 (8.7)		
Sore throat	Present (n = 44)	40 (90.9)	4 (9.1)	0.481	0.66 (0.21 - 2.11)
	Absent (n = 115)	100 (86.8)	15 (13.2)		
Diarrhoea	Present (n = 29)	25 (86.2)	4 (13.8)	0.754	1.22 (0.37 - 3.97)
	Absent (n = 130)	115 (88.4)	15 (11.6)		
Myalgia	Present (n = 15)	12 (80)	3 (20)	0.39	1.98 (0.51 - 7.79)
	Absent (n = 144)	128 (88.8)	16 (11.2)		
Anosmia	Present (n = 24)	20 (83.3)	4 (16.7)	0.49	1.59 (0.49 - 5.27)
	Absent (n = 135)	120 (88.8)	15 (11.2)		
Rhinitis	Present (n = 25)	22 (88)	3 (12)	1	0.99 (0.27 - 3.71)
	Absent (n = 134)	118 (88)	16 (12)		
Headache	Present (n = 28)	21 (75)	7 (25)	0.04	3.28 (1.16 - 9.24)
	Absent (n = 131)	119 (90.8)	12 (9.2)		
Dyspnoea	Present (n = 9)	4 (44.4)	5 (55.6)	0.001	12.05 (2.90 - 50.13)
	Absent (n = 150)	136 (90.6)	14 (9.4)		
Fatigue	Present (n = 14)	8 (57.1)	6 (42.9)	0.002	7.56 (2.27 - 25.15)
	Absent (n = 145)	132 (91.0)	13 (9)		
Tastelessness	Present (n = 7)	6 (85.7)	1 (14.3)	1.0	1.23 (0.14 - 10.82)
	Absent (n = 152)	134 (88.1)	18 (11.9)		
Reduced sleep	Present (n = 2)	2 (100)	0 (0)	1	0.88 (0.83 - 0.93)
	Absent (n = 157)	138 (87.8)	19 (12.2)		
Vomiting	Present (n = 2)	2 (100)	0 (0)	1	0.88 (0.83 - 0.93)
	Absent (n = 157)	138 (87.8)	19 (12.2)		
Abdominal pain	Present (n = 2)	2 (100)	0 (0)	1	0.88 (0.83 - 0.93)
	Absent (n = 157)	138 (87.8)	19 (12.2)		

Table 3. Significant Symptoms Associated with Severity of Covid-19

## DISCUSSION

In the present study, among the initial 202 COVID-19 patients of Kerala, about three fourths of the patients were foreign returnees and the rest acquired infection through local transmission. Majority were from the Middle East countries followed by European countries reflecting the pattern of international return during this time period. The mean age of cases in our study were lower compared to most of the studies from the country and abroad.<sup>5-8</sup> Proportion of elderly were significantly more among locally acquired cases. Infection appears to have trickled into more vulnerable groups as local transmission occurred from young infected immigrants like elsewhere.<sup>9,10</sup> Male gender predominated in the study population as in most populations with large number of imported cases. When the disease transmission increases locally, gender usually shows an equitable distribution in the population.<sup>1,5</sup> On the contrary, among the locally transmitted cases, our study showed a higher number of cases among the female gender compared to males. This may be because of a higher proportion of females among the household contact and the risk of close contact may be more for the female spouses as most of the infected immigrants appeared to be men. Though Kannur and Kasaragod districts had a notably high number of cases compared to other districts, the major proportion of cases in both the districts were imported. This shows that even with high number of imported cases, early detection and response can aid in preventing wide local transmission.

The median incubation period reported by most of the international articles is around 5 days and a meta-analysis by Borges do Nascimento et al estimates it at 4.5 - 4.7 days.<sup>11-14</sup> Our study estimated the presumptive median incubation period at 6 days with an interquartile range of 4 days. Since around three fourth of the locally transmitted cases were family members who came in contact with the expatriates on the very first day of their arrival, the day of their arrival itself were treated as the first possible contact. It can slightly over estimate the actual incubation period. Transmission to family members showed that the emphasis should not be confined to isolating the person from the community but also should focus on strict isolation within the family (room quarantine). Slightly longer median incubation period could also be viewed in the context of less severity of the disease as severity of disease has an inverse relationship with duration of incubation period. Apart from household, transmission occurred largely in closed air conditioned vehicles. A closed air conditioned space is found to provide an optimum environment for transmission of the virus. The strong airflow in the closed space can help in propagating the droplets to wider distances.<sup>15,16</sup> Qifang Bi et al reported household contact and travelling together to be the major predictors of transmission.<sup>10</sup>

The results of our study emphasised the mild nature of the disease in majority of the cases with one fifth of the patients reporting no symptoms and around one-fifth of the symptomatic showing symptoms for only one day. Even this number can be an underreporting of asymptomatic cases as they may usually be a fall out of the screening criteria in the absence of a strong epidemiological link. The larger proportion of asymptomatic and mild cases reported in our study compared to many international studies may be due to the

better case detecting mechanisms in Kerala and the low case load enabling testing and screening of asymptomatic and mild cases.<sup>6,17</sup> However studies reporting population screening had come out with high rates of asymptomatic in COVID 19. A study to estimate the proportion of asymptomatic by Nishiura et al among people evacuated from Wuhan estimated it at 41.6 %.<sup>18</sup> A study from an Indian tertiary care centre in the initial phase of outbreak reported a proportion of 42.9 %.<sup>8</sup>

The most common symptom experienced by our study participants was fever followed by cough. Cough and fever were most common symptoms reported by Indian Council of Medical Research (ICMR) in country wide study.<sup>19</sup> Though the pattern of symptoms were comparable to the literature across the globe, the proportions were notably low. Most studies reported fever in more than three fourth of the participants whereas in our study only 45 % of patients gave a history of fever. Even among the symptomatic patients the proportion of fever was only 55 %. Similarly, all other symptoms including cough, sore throat, breathlessness and gastrointestinal symptoms were proportionately low among the COVID-19 patients in our study. However, the proportion who reported anosmia was higher than most studies.<sup>11-12,20-21</sup> There may be an overlap with rhinitis induced anosmia and it was not ruled out in our study. A recent multicentre European study estimated around 80 % of COVID 19 patients without nasal obstruction or rhinorrhoea had olfactory disturbance suggesting it to be a major and sometimes initial symptom.<sup>22</sup>

Around one fourth of the study participants had one or more comorbidities and the most common was diabetes followed by hypertension and respiratory illness. The pattern shows minor variations from the morbidity pattern in general population as hypertension is more prevalent in Kerala than diabetes mellitus.<sup>23</sup> Many studies have reported a significantly increased risk of hospitalization and death due to COVID 19 in diabetics. However, the role of diabetes in increasing the risk of infection is not fully understood.<sup>24</sup>

Majority (68.8 %) of patients reported to have mild illness which otherwise would have required home based or outpatient treatment only. This when coupled with the asymptomatic cases comes to around 88 %. The proportion of moderate / severe disease is just below 12 % and this was the group of people whose symptoms would otherwise need hospitalisation as per the patient perspective. Data across the globe shows a predominance of moderate severity among the hospitalised cases and severe cases requiring critical care are above 10 %.<sup>9,16,25</sup> The pattern of severity and requirement of ventilator support in our study was comparable to the observations made by Tabata et al from the outbreak on board in the Diamond Princess Cruise Ship, Japan.<sup>26</sup>

The severity of symptoms were found to be increasing with age. Other significant factors were presence of hypertension and respiratory comorbidities. These findings are in concordance with most of the published studies on comorbidities.<sup>27,28</sup> A significant association of diabetes with severity of illness was not established in our study unlike the study by Zhou et al.<sup>29</sup> A meta-analysis on effect of comorbidities on severity of COVID 19 identifies hypertension (OR 2.36), respiratory system disease (OR 2.46) and cardiovascular disease (OR 3.42) to be significantly associated with severity of illness and fails to demonstrate a significant association with diabetes.<sup>24</sup> Dyspnoea and cough, the symptoms reported in higher proportion by the moderate /

severe group of the current study may be related to alveolar damage and may represent a severe form of illness. A study by Kunhua Li et al showed a significant association of dyspnea, chest pain, high grade fever and cough with severity of COVID 19 assessed by clinical criteria.<sup>30</sup>

The case fatality rate (CFR) of COVID 19 in India varies across states from less than 1 % to more than 20 %.<sup>2</sup> The CFR in Kerala (< 1 %) is one among the lowest in the country. This rate is comparable to the CFR reported from the outbreak in the Cruise ship 'Diamond Princess' in Japan.<sup>31</sup> Excluding China where the outbreak began, Italy, Iran and South Korea had the highest number of cases and deaths by mid-March and by the end of April, USA and Spain topped the list in number of cases. However, Italy continued to have the highest CFR which is above 10 %.<sup>32</sup>

In conclusion, majority of COVID-19 cases in Kerala are imported and the milder symptomatology and a lower fatality rate may be due to the health care seeking behaviour of people, extensive surveillance, case detection and rapid response. Our study emphasizes that although fever is the most common symptom of COVID 19, more than half of the cases in Kerala did not report a history of fever. Thus, mild and nonspecific symptoms and short duration of illness should not be overlooked and high suspicion should be maintained even among the asymptomatic with a strong epidemiological link. The focus should rely on reverse quarantine and insulating the elderly and those with comorbid conditions.

### Limitations

Major limitations of our study were that clinical examination features and laboratory parameters were not included and that only subjective data from the patient could be assessed. Since the study included only COVID-19 confirmed cases, the possibility of undetected cases cannot be neglected in estimating proportions.

## CONCLUSIONS

Mild and nonspecific symptoms and short duration of illness should not be overlooked in COVID-19 and high suspicion should be maintained as a large segment of infections are asymptomatic. The focus should be on insulating the elderly and those with comorbid conditions.

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