Original Article

DOI: 10.7860/JCDR/2022/55065.16193

Considerations for Testing of COVID-19 in Travellers under Quarantine- A Retrospective Study from Palakkad District, Kerala, South India

Community Section

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ABSTRACT

Introduction: Until sufficient herd immunity is generated in the population, contact tracing, testing, and quarantining should be continued as key interventions in breaking the chain of transmission of Coronavirus Disease 2019 (COVID-19).

Aim: To identify appropriate strategies for testing of the travellers, who were coming from high-risk areas by analysing patterns of testing among COVID-19 positive returnees.

Materials and Methods: A retrospective cohort study was conducted in Community Medicine Department, Government Medical College, Palakkad, Kerala, India, during 25th September 2020 to 15th October 2020, using the secondary data available from the database of COVID-19 Contact Tracing Cell (CCTC) to determine the testing pattern among the laboratory confirmed cases of COVID-19 positive returnees in Palakkad district. Only COVID-19 positive travellers returning to Palakkad district in May 2020 were included in the study, thus the sample size obtained was 122. Data regarding age, gender, co-morbidity, presence of symptom and time of its onset, time of swab collection and reporting of results which were collected by CCTC were analysed. The Statistical Package for the Social Sciences (SPSS) version 20.0 was used to analyse the data collected by CCTC. Quantitative variables were summarised as means with standard deviations and median with interquartile ranges. Qualitative variables were summarised as percentages.

Results: Between arrival and swab collection there was mean duration of 6.9±3.8 days and a median duration of seven days among the total positive returnees. Among the asymptomatic cases, the mean duration was found to be 7.4±3.6 days for the same. Between day 10 and day 12 of quarantine, 79%-91% of the cases have given swabs for Reverse Transcription Polymerase Chain Reaction (RT-PCR) testing. This had yielded 90% positive reporting within 14 days of quarantining. Total 10 cases were diagnosed after 14 days of quarantine due to late swab collection while in quarantine. Mean duration between symptom onset and swab collection among 22 symptomatic cases was 1.9±1.6 days (median=2 days).

Conclusion: Testing of asymptomatic returnees from high risk area may be initiated (swab collection) by day 10 as swabs collected around 10th day of quarantine capture maximum number of positive cases. A delayed initiation for testing may prolong the time taken for diagnosis. Those who have tested negative during 14 days of quarantine should self-monitor for symptoms and reduce contact with high risk persons for one more week.

Keywords: Coronavirus disease 2019, High risk persons, Pandemics, Reverse transcription polymerase chain reaction

INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was first reported from patients presented with pneumonia, who were linked to Wuhan Sea food market in China in December 2019 [1]. It soon spread to various countries and was declared pandemic by World Health Organisation (WHO) on 11th March 2020 [2].

Kerala reported the first Coronavirus Disease 2019 (COVID-19) case in India on January 27, 2020 [3]. In the two years after then, the state recorded 53,78,831 total cases with a 97.11% recovery rate and 0.95% fatality rate as of 17th January 2022 [4]. In the state, vaccination programmes are still running strong. As of 17th January 2022, Kerala had achieved coverage of 99.8% of the first dose and 82.3% of the second dosage of COVID-19 vaccine for those aged 18 and higher [4]. The state has begun administering precautionary vaccine doses to adults over the age of 60 and frontline workers. So far, the COVID-19 vaccination has been administered to 76.9% of Kerala's population [4].

Meanwhile, the emergence of novel genetic mutations and variants poses a substantial threat to public health [5]. Breakthrough infections and immune escape mechanisms are still being researched. Contact tracing, testing and quarantining and isolating positive cases should remain as important methods for halting transmissions until the population has developed considerable herd immunity against the emerging strains of SARS-CoV-2 [6].

Quarantining, testing, and tracing the contacts of positive patients were important strategies of state's response to COVID-19, when interstate and non resident Keralites returned to the state throughout the early phases of the epidemic [7]. As per the guidelines existing then, all high risk contacts were advised quarantine for a period of 28 days and low risk contacts were advised quarantine for a period of 14 days [8].

The district of Palakkad, which shares the state's border with Tamil Nadu, was at significant danger due to the enormous number of interstate travellers [9]. Researches analysing the testing pattern are not reported from the state of Kerala. The current study aimed to investigate the testing pattern and suggest appropriate testing strategies for COVID-19 positive returnees in Central Kerala's Palakkad district.

MATERIALS AND METHODS

A retrospective cohort study was done by Community Medicine Department, Government Medical College, Palakkad, Kerala, India, during the period 25/09/20-15/10/20, using the secondary data available from the database of COVID-19 Contact Tracing

Cell (CCTC) to determine the testing pattern among the laboratory confirmed cases of COVID-19 positive returnees in the month of May 2020, in Palakkad district. The research was approved by the Institutional Ethics Committee (IEC) GMC Palakkad (vide letter no. IEC/GMCPKD/15/20/69).

Inclusion and Exclusion criteria: Only COVID-19 positive travellers who returned to Palakkad district in May 2020 were included in the study. Those cases with incomplete data required for study were excluded from the study.

Procedure

COVID-19 Contact Tracing Cell (CCTC) had been functioning under the Department of Community Medicine, Government Medical College (GMC), Palakkad for tracing the contacts of COVID-19 cases positive cases in the district. CCTC collected information about demographic variables, clinical characteristics and co-morbidities, testing, travel, contacts made during period of incubation, assessed risk of the contacts and advised measures according to risk categorisation by doing telephonic interviews.

As expatriates returned and the borders were re-opened in May 2020, allowing returnees to enter the state, the cases reported in Palakkad district during that month (May) were investigated [10,11]. Travellers returning to Palakkad accounted for 122 cases (87%) of the total 140 COVID-19 positive cases reported in the district in May 2020. Only COVID-19 positive travellers who returned to Palakkad district were included in the study, thus the sample size obtained was 122.

Variables regarding co-morbidity, presence of symptoms with time of onset, time of swab collection and time of reporting were investigated as these were important parameters for timely diagnosis, isolation and case management. Those cases with incomplete data on the above mentioned variables were planned to be excluded from analysis.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) version 20.0 was used to analyse the data collected by CCTC. Quantitative variables were summarised as means with standard deviations and median with interquartile ranges. Qualitative variables were summarised as percentages.

RESULTS

There were 122 COVID-19 positive travellers in the month of May 2020 in Palakkad district. Total 22 positive returnees (18%) had symptoms such as fever, cough, sore throat and myalgia. The baseline characteristics of the returnees in given in [Table/Fig-1]. All the returnees were following quarantine as per guideline [8].

Variables	Number (%)
Gender	
Male	103 (84.4)
Female	19 (15.5)
Symptoms	
Present	22 (18)
Absent	100 (82)
Co-morbidity*	
Present	26 (21.3)
Absent	96 (78.7)
Type of traveller	
Domestic	26 (21.3)
International	96 (78.7)

[Table/Fig-1]: Baseline characteristics of COVID-19 positive returnees.
*Diabetes Mellitus, hypertension, cardiovascular disease and cancer

Pattern of testing: Among all study participants, COVID-19 was diagnosed by RT-PCR testing of nasal swabs [12]. Swabs were taken at the nearest Government Health Facility and forwarded to the nearest tertiary care centre having an RT-PCR laboratory for testing. [Table/Fig-2] shows some patterns of timings with respect to diagnosis of COVID-19 among the positive returnees.

Variables	Mean±SD days	Median (IQR) days	Range (days)
Interval between last day of travel and symptom onset (n=22, symptomatic cases)	4.1±2.6	3 (2-7)	1-8
Interval between arrival and swab collection (n=122)	6.9±3.8	7 (4.7-9)	0-15
Interval between arrival and swab collection (n=100, asymptomatic cases)	7.4±3.6	7 (5-9.75)	0-15
Interval between arrival and swab collection (n=22, symptomatic cases)	4.9±3.9	4.5 (1.75-7)	0-15
Interval between symptom onset and swab collection (n=22, symptomatic cases)	1.9±1.6	2 (0-3.25)	0-6
Interval between swab collection and reporting (n=122)	2.4±0.7	2 (2-3)	1-7
Interval between arrival and reporting (n=122)	9.4 7±4.0	9 (7-12)	2-20
Interval between symptom onset and reporting (n=22, symptomatic cases)	4.2±1.8	4.5 (2.25-6)	1-7

[Table/Fig-2]: Temporal patterns with respect to diagnosis of COVID-19 among the cases.

Among the 22 symptomatic travellers, the mean and median duration between last day of travel (assuming it to be the last day of exposure) and symptom onset was 4.1±2.6 days and three days, respectively. Among 100 asymptomatic travellers, mean duration between arrival and swab collection was 7.4±3.6 days. Among 22 symptomatic travellers, mean duration between arrival and swab collection was 4.9±3.9 days. Mean duration between symptom onset and swab collection among 22 symptomatic cases was 1.9±1.6 days. The results were reported after mean duration of 2.4±0.7 days following swab collection in all cases. The distribution of time of onset of symptom, the time of swab collection, the time of diagnosis (reporting) with respect to day in quarantine is given in [Table/Fig-3-5], respectively.

Time of symptom onset with respect today in quarantine (n=22)	Number (%)
<5 days	13 (59)
6-10 days	9 (41)

[Table/Fig-3]: Time of symptom onset with respect to day in quarantine among symptomatic returnees.

Time of swab collection	Asymptomatic cases (n=100) Number (%)	Symptomatic cases (n=22) Number (%)
<5 days	17 (17)	11 (50)
5-10 days	62 (62)	9 (41)
11 days	7 (7)	0
12 days	5 (5)	0
13 days	2 (2)	01 (4.5)
≥14 days	7 (7)	01 (4.5)

[Table/Fig-4]: Time of swab collection with respect to number of days in quarantine among positive returnees.

Time of diagnosis	Asymptomatic cases (n=100) Number (%)	Symptomatic cases (n=22) Number (%)
<5 days	14 (14)	10 (45.5)
5-10 days	65 (65)	8 (36.3)
11-14 days	13 (13)	2 (9.1)
>14 days	8 (8)	2 (9.1)

[Table/Fig-5]: Time taken for diagnosis (reporting) with respect to number of days in quarantine among positive returnees.

Among total 122 COVID-19 positive returnees, there were 10 cases whose results were positive after 14 days of quarantine. Certain characteristics pertaining to testing of the 10 cases are shown in [Table/Fig-6].

S. No.	Presence of symptoms before swab collection	Day of swab collection after arrival	Time taken for reporting
1.	No	14th	2 days
2.	Yes	14th	2 days
3.	No	14th	2 days
4.	No	15th	2 days
5.	No	9th, 15th	2 days (second swab)
6.	No	15th	2 days
7.	No	14th	2 days
8.	No	14th	3 days
9.	Yes	13th	4 days
10.	No	12th	4 days

[Table/Fig-6]: Details of returnees reported positive case after 14 days of quarantine.

Only two cases out of 10 showed symptoms before swab collection. Among those cases reported after 14 days majority of the cases (7 out of 10), testing was initiated on or after 14th day of quarantine. This was coupled with 2-4 days delay in reporting. Mean days for reporting after swab collection was 2.5 days. Case no: 5 may be identified as a false negative result on first testing done on 9th day which was later turned positive on 15th day swab as he was retested when his co-traveller turned positive.

DISCUSSION

Majority of Kerala's COVID-19 positive cases were from the returnees to the state from abroad and other states within India during the months May 2020 to June 2020 [11]. Similar trend was observed in the current study; 87% of total cases reported in the month of May in Palakkad district were returnees.

An 82% of returnees in the present study were asymptomatic. These results are in line with many other researches published globally where the proportion of asymptomatic COVID-19 was more than 50% [13-15]. The WHO also suggests 80% of infections are mild or asymptomatic [16]. But certain studies have identified the prevalence of asymptomatic COVID-19 cases below 50% also [17-19]. A series of systematic reviews and meta-analysis revealed that the proportion of tested positive for COVID-19 who never developed symptoms ranged from 8.44% to 39% [17,18,20]. This variation may be explained by differences in definition of asymptomatic cases, accuracy of testing methods and duration of follow-up [21].

Among symptomatic travellers the mean and median time duration between day of travel (assuming it to be the last day of exposure) and symptom onset was 4.1±2.6 days and 3 (IQR 2-7) days respectively. This may be considered as a proxy indicator of incubation period for the disease among returnees. Different studies have reported ranges of mean incubation periods varying from 4.6 to 6.4 days which were based on different methods of assessment like earliest exposure to onset, exposure interval to onset and other methods [22-24]. In majority of the published literature, mean/median incubation period is reported to be around five days [24-26]. Because of lack of confirmation with respect to day of exposure, the current study assumed the day of travel to Kerala as the day when exposure would have happened. None of the travellers were symptomatic on the day of travel.

Mean duration of time between arrival and swab collection was 6.9±3.8 with median of seven days among the total positive returnees. Among the asymptomatic cases the same was found to be 7.4±3.6 days. By day 10 and day 12 of quarantine 79%-91% of the cases have given swabs for RT-PCR testing. This had yielded 90% positive reporting within 14 days of quarantining allowing for an average two days time for reporting from nearest Government Tertiary Care Centre.

Mean duration between symptom onset and swab collection among 22 symptomatic cases was 1.9±1.6 days (Median 2, IQR 0-3.25) which indicates testing was initiated on second day after symptom onset. Median duration of symptom onset to sample collection was two days (IQR 1-4) among positive results in a study based on Indian Council of Medical Research laboratory surveillance network in India from March 2020 to January 2021 [27]. From a systematic review of individual participant data, regarding time during infection when COVID-19 is detectable by RT-PCR, the highest percentage virus detection was from nasopharyngeal sampling between 0 and 4 days postsymptom onset at 89% {95% Confidence Interval (CI) 83 to 93} dropping to 54% (95% CI: 47 to 61) after 10 to 14 days [28]. In all symptomatic returnees, testing should be initiated immediately with symptom onset. This will help in early diagnosis, reducing the complications and interrupting the transmissions [29]. All the symptomatic returnees had a milder course of disease and short duration of stay in hospital.

Mean duration between swab collection and reporting was 2.4±0.7 (Median 2, IQR 2-3) in the present study. Median duration between testing to data entry for positive results was 0 days (IQR 0-1) across different states in India from March 2020 to January 2021 [27]. The state of Kerala had a median duration of five days (IQR 1-15) for entering positive results according to the same study [27].

Results of 10 cases came positive after 14 days of quarantine. Among them testing was initiated on or after 14th day of quarantine for seven persons. From the findings in the current study, the authors are of the opinion that, testing of asymptomatic returnees, if done around 10 days of quarantine would cover double the median incubation period. This will help to capture the positive cases early among the returnees. Positivity mandates isolation, which will limit further spread of disease.

A single negative result may not rule out the disease status of returnees; as the test is not 100% sensitive [30]. It is to be noted that the pretest probability of the disease is high especially among people from red zone areas and those who are symptomatic. Case no: 5 may be identified as a false negative result on first testing done on 9th day due to only moderate sensitivity (around 63% positive rate for nasal swab of COVID-19 patients) [31]; or it could be an outlier with regard to duration of infection following exposure as evidenced by positive second swab result on 17th day. Infection could have happened around or outside the maximum incubation period of 14 days in the case as an outlier; the chance for this is as low as 101/10000 cases [14]. These evidences reinforce the point; a negative result around 12 days of quarantine should not impart a false sense of security in high-risk suspects [32].

From the sociological point of view, being asymptomatic is a reason for breach in quarantine restrictions observed among the returnees [33]. This can increase the number of primary and secondary contacts. A late testing coupled with delayed reporting may increase the onward transmission; thus the burden on the system and families [34].

Strict quarantine of minimum 14 days is to be ensured when testing all returnees is not feasible. Considering the possibility of false negative results, negative person should self-monitor for symptoms and reduce close contact with high-risk persons for one more week.

Testing of asymptomatic returnees may be initiated (swab collection) early around 10-12 days of quarantine as it will cover double the incubation period and capture maximum number of positive cases. It will also prevent the patient from making unintentional contacts after 14 days and lower the risk of contact transmission. Even if tested negative by RT-PCR while in quarantine, all asymptomatic returnees need to strictly self-monitor for symptoms and reduce contact with high risk people for one more week owing to the possibility of a false negative result. Further investigation into the probability of transmission beyond 14 days following exposure is recommended, and for those who are not tested while in quarantine, extending its duration beyond the authorised period may be considered accordingly.

Limitation(s)

As the study was based on secondary data, the information regarding clinical characteristics and co-morbidities could not be verified by the investigators. Impact of delayed testing could not be estimated by the present investigation.

CONCLUSION(S)

Majority of the COVID-19 positive returnees were asymptomatic. Average duration between symptom onset and swab collection among symptomatic cases was two days. Among the total COVID-19 positive returnees, swabs were collected for RT-PCR testing on day 7 of quarantine (median duration). By day 10 and day 12 of quarantine 79%-91% of the cases had given swabs for RT-PCR testing. This had yielded 90% positive reporting within 14 days of quarantining.

Acknowledgement

Authors acknowledge the District Health Authority, Palakkad, Principal, Director, Head of Department and faculty of Community Medicine (GMC Palakkad), Medico-social workers, JHI/JPHNs and volunteer medical students (GMC Palakkad), nodal officer of COVID 19 control cell, Nodal officers of COVID First Line Treatment Centres (CFLTCs), and most importantly our patients for the support and valuable inputs.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 20, 2022
- Manual Googling: Jan 31, 2022
- iThenticate Software: Mar 22, 2022 (3%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 19, 2022**
Date of Peer Review: **Feb 02, 2022**
Date of Acceptance: **Mar 23, 2022**
Date of Publishing: **Apr 01, 2022**