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Brief Communication

A retrospective analysis of COVID-19 diagnosis results obtained by rapid antigen tests and RT-PCR: Implications for disease management

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ABSTRACT

There is a need for understanding and establishment of the most appropriate testing algorithm for COVID-19 diagnosis in asymptomatic high-risk groups. Here, we present a retrospective analysis of RT-PCR results obtained from 412 cases tested negative for coronavirus disease 2019 (COVID-19) by rapid antigen testing method. Among 178 (43.2%) asymptomatic individuals, 44.9% of the high risk contacts, 12.2% of police custody individuals, 22.22% of the pregnant women and 33.33% of individuals hospitalised for preoperative or other medical conditions showed RT-PCR positivity. Our results suggest a need for focussed and intensive (multi-modality) testing in groups at high risk for SARS-CoV-2 infection.

1. Introduction

Several screening and confirmatory tests are available for the detection of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1–3]. Screening tests like rapid antigen test (RAT) can identify the population at high risk [4]. Though, RAT has lower sensitivity, is comparatively cost-effective, rapidly deployable and faster [1]. RAT reduces the dependence on real time reverse transcriptase polymerase chain reaction (RT-PCR), where cost of the RT-PCR kits and technical expertise are major concerns [5]. RAT is helpful if done at early stage of infection where viral load is high. Such individuals if isolated faster can limit the disease spread [1]. However, antigen levels may drop below the limit of detection in specimens collected beyond 5–7 days of onset of the symptoms [6].

Since, screening by RAT is associated with false negative results, RT-PCR still remains the "gold standard" for diagnosis of SARS-CoV-2 infection as it detects pathogen based on amplification of target genes using specific primers [5,7]. It is an accurate, reliable and more sensitive method. As per guidelines, suspected cases with antigen negative reports need to be further evaluated with RT-PCR and the interval between collection of samples for the two tests should be less than two days [6,8].

2. Methods

Here, we present a retrospective analysis of RT-PCR results obtained from 412 cases tested negative for coronavirus disease 2019 (COVID-19) by RAT. All cases were referred from Municipal Corporations and Government hospitals of Mumbai and its periphery, during 7th July - 7th August 2020 to COVID-19 testing laboratory at ICMR-NIRRH, Mumbai. RAT data and characteristics of patients like age, gender, clinical presentations and underlying medical conditions were extracted from ICMR Specimen Referral Form (SRF) for COVID-19. All samples were processed for RNA extraction and analysed by various RT-PCR platforms and kits. The testing was done as per the manufacturer's protocol.

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Table 1
RT-PCR outcomes among asymptomatic and symptomatic antigen negative tested COVID-19 cases.

RT-PCR results	Asymptomatic	Symptomatic (N = 234)	
	N = 178 (100%)	Multiple symptoms N = 190 (100%)	Single symptom N = 44 (100%)
Positive	48 (26.9)	74 (38.9)	17 (38.64)
Negative	125 (70.2)	104 (54.74)	27 (61.36)
Inconclusive	5 (2.81)	12 (6.31)	Nil

Abbreviations: N, number, %, percentage.

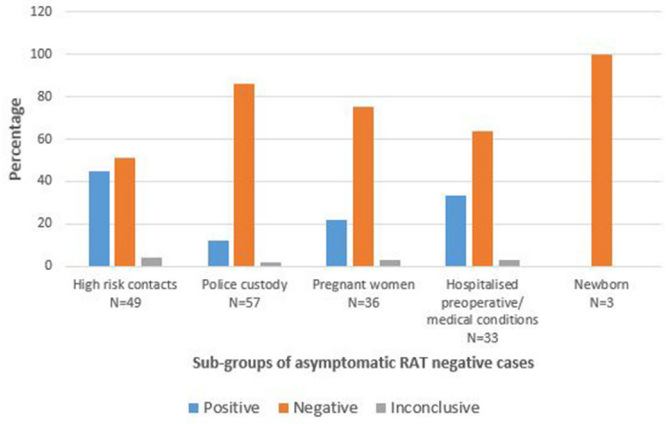

Fig. 1. Distribution of asymptomatic rapid antigen test negative cases and their RT-PCR outcomes (N=178) as positive, negative and inconclusive for different sub-groups.

3. Results

Out of 412 RAT negative samples, 139 (33.7%) were positive, 256 (62.14%) were negative and 17 (4.13%) were inconclusive by RT-PCR. Of these 412 RAT negative cases, 234 were symptomatic and 178 were asymptomatic (**Table 1**). The latter include, individuals undergoing antenatal visits, surgery and those who were high-risk contacts. Of the 234 symptomatic patients 91(38.8%) showed positivity, 131(55.55%) showed negativity and 12(5.1%) were inconclusive on RT-PCR. The samples reported initially inconclusive by RT-PCR were repeated and 17 (4.13%) of which remained inconclusive after retesting. The percentage of positivity in RT-PCR was similar (38.9% and 38.64%) in individuals with single or multiple symptoms. Of the 178 asymptomatic individuals negative for RAT, 48 (26.96%) were positive, 125 (70.22%) were negative and 5 (2.81%) were inconclusive on RT-PCR. Of these, 49 (27.5%) were high risk contacts of confirmed case of COVID-19, 57 (32%) were from police custody, 36 (20.2%) were pregnant women, 3 (1.69%) were newborns and 33 (18.53%) were admitted preoperative or for other medical conditions. The RT-PCR outcome for these asymptomatic groups is shown in Fig. 1.

In older age group (61–80 years) around 46% of RAT negative cases were positive by RT-PCR (**Supplementary Fig. 1**). Among 412 RAT negative cases, 89 (21.6%) had pre-existing comorbidities like diabetes, hypertension, cardiovascular disease, chronic renal disease, malignancy etc. Out of them, 32 (35.95%) individuals were positive by RT-PCR.

4. Discussion

In the retrospective analysis of RT-PCR data of 412 RAT negative cases, 139 (33.7%) were positive by RT-PCR, maybe because of lower sensitivity of RAT. As per the literature, the percentage of false negative SARS-CoV-2 result is high in RAT [6,9]. A study reported 89.9% (95% CI 85.4%–94.4%) of sensitivity and 97.6% (95% CI 96.5%–98.5%) of specificity by RAT in symptomatic patients, whereas, only 50.0% (95% CI 36.0%–63.0%) of sensitivity and 99.6% (95% CI 99.1%–99.9%) of specificity in asymptomatic individuals [10]. 234 (56.8%) of RT-PCR positive individuals were symptomatic in the form of fever, sore throat, breathlessness, cough, body ache, diarrhoea and vomiting. Out of 178 asymptomatic patients showing negative RAT results, 48 (26.96%) were positive on RT-PCR. Both tests in 46 out of these 48 individuals were carried out on the same day, ruling out the possibility of RT-PCR positivity following post RAT infection. The impact of SARS-CoV-2 infection is more with co-morbidities, elderly, pregnant women etc. [11,12] In our study, among 44.9% of the high risk contacts, 12.2% of police custody individuals, 22.22% of the pregnant women and 33.33% of individuals hospitalised for preoperative or other medical conditions showed RT-PCR positivity.

There is limited data on usage of RAT in asymptomatic individuals to detect or exclude COVID-19, or to determine infectious status of previously confirmed cases [6]. In our study, the date of onset of symptoms was not known in many cases as it was not a mandatory field in the ICMR specimen referral form. However, the date of RAT and collection of the sample for RT-PCR was the same. Hence comparison of these are possible. Moreover, the RAT for COVID-19 showed lower sensitivity than RT-PCR test both for symptomatic (single or multiple symptoms) and asymptomatic infection. Confirmation of antigen negative tested individuals by RT-PCR especially for asymptomatic or high-risk groups is critical for prompt isolation and clinical management. Our results suggest need for focussed and intensive (multi-modality) testing in groups at high risk for SARS-CoV-2 infection and strongly support the use of RT-PCR as the first line of testing instead of RAT in asymptomatic high-risk group.

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Conflicts of interest

There are no conflicts of interest.

CRediT authorship contribution statement

Kiran Munne: Concepts, Design, Definition of intellectual content, Literature search, Funding acquisition, Data acquisition, Statistical analysis, Writing – original draft, Manuscript preparation. **Venkanna Bhanothu:** Concepts, Design, Definition of intellectual content, Literature search, Funding acquisition, Data acquisition, Data curation, Formal analysis, Data analysis, Statistical analysis, Writing – original draft, Manuscript preparation. **Anjali Mayekar:** Design, Definition of intellectual content, Literature search, Funding acquisition, Data acquisition, Data curation, Formal analysis, Data analysis, Writing – original draft, Manuscript preparation. **Shantanu Birje:** Data curation, Formal analysis, Data analysis. **Vikrant Bhor:** Data curation, Formal analysis, Data analysis. **Vainav Patel:** Definition of intellectual content, Writing – review & editing, Manuscript editing. **Smita D. Mahale:** Definition of intellectual content, Writing – review & editing, Manuscript editing, Manuscript review. **Shailesh S. Pande:** Concepts, Design, Definition of intellectual content, Writing – original draft, Manuscript preparation, Writing – review & editing, Manuscript editing, Manuscript review, Guarantor.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://

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