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FULLENGTH

# Improving turnaround time of molecular diagnosis of Middle East respiratory syndrome coronavirus in a hospital in Saudi Arabia

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**Background:** There have been 2562 laboratory-confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) in 27 countries, with a case fatality rate of 34.5%. Data on the turnaround time (TAT) are lacking. We report TAT for MERS-CoV samples over time.

**Methods:** This is a monocentric study and the TAT for the reporting of 2664 MERS-CoV polymerase chain reaction (PCR) results were calculated in hours from the time of the receipt of respiratory samples to the reporting of the results.

**Results:** The mean TAT±standard deviation was significantly lower in 2018 compared with previous years (19.25±13.8). The percentage of samples processed within 24 h increased from 42.3% to 73.8% in 2015 and 2018, respectively ($p<0.0001$). The mean TAT was 19.2 h in 2018 and was significantly lower than previous years.

**Conclusions:** The TAT for the MERS-CoV results decreased during the study period. Timely reporting of MERS-CoV PCR results may aid in further enhancing infection control measures.

**Keywords:** Middle East respiratory syndrome coronavirus, MERS-CoV, turnaround time

## Introduction

In the past 6 y a total of 2562 laboratory-confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) were reported to the World Health Organization (WHO) from 27 countries, with an associated case fatality rate of 34.5%.[1] Most cases have arisen in the Middle East, particularly the Kingdom of Saudi Arabia, and there was a large hospital-associated outbreak in the Republic of Korea in 2015.[2–6] Exposure to dromedary camels has been recognized by the WHO as a risk factor in primary cases, but the exact mechanisms of transmission are unclear. Rigorous application of nationally defined infection prevention and control measures has reduced the levels of healthcare facility–associated outbreaks.[6] The gold standard for MERS-CoV is reverse transcription polymerase chain reaction (RT-PCR) testing. The main reasons to have a better and faster laboratory diagnostic test of viral infections are to initiate appropriate therapeutic options and to isolate patients who require isolation. Fast and immediate isolation would decrease secondary transmissions in the community as well in healthcare settings. In addition, specific viral diagnosis would allow the discontinuation of empiric antimicrobial therapy. The Saudi Arabian Ministry of Health (MOH) guidelines state that all samples from suspected MERS-CoV patients must be sent to an MOH designated regional laboratory. There are five regional laboratories for testing in the Kingdom: in Makkah, Madinah, Jeddah, Riyadh and Dammam.[7] The turnaround time (TAT) for samples collected in the same city where a laboratory is located is an average of 1 d and is about 2 d from one region to another.[7] However, data on turnaround times are lacking. The molecular laboratory in our institution was the first to be granted permission to do MERS-CoV PCR testing outside these designated laboratories. Thus, in this study, we calculate the TAT for all result of MERS-CoV samples and compare the results over time.

## Methods

The study was conducted at one of the first hospitals to deal with MERS-CoV infection. From 1 April 2013 to 3 June 2013,

there were 99 patients meeting the case definition of suspected MERS-CoV and 17 cases were positive for MERS-CoV by PCR.[8–11] In the years 2012–2016, the molecular diagnostic laboratory (MDL) at the hospital tested samples from 2657 patients who were admitted or screened for MERS-CoV, with a positivity rate of 0.74%.[10]

In this study we collected available information for all samples received at the MDL for MERS-CoV testing from January 2014 to June 2018. The collected information included the time and date of receiving the samples and when the results were available. The TAT is defined differently based on the type of test and the methodology of testing. The TAT may be defined as the time from ordering the test to the time of reporting. However, to avoid the lag time between the order and the actual collection of samples, we defined the TAT as the time between receipt of the sample by the MDL and the time of reporting the results in the electronic medical system.[12] The TAT was calculated in hours.

Patients underwent nasopharyngeal swabs using Dacron-flocked or deep respiratory samples (tracheal aspirates and bronchoalveolar lavage) in case of patients requiring intensive care unit care. These samples were tested for MERS-CoV using real-time RT-PCR.[13] The PCR amplification targeted the upstream E protein (*upE* gene) and ORF1a for confirmation. A positive test is indicated if both assays are positive.[14] In case of discordance between the *upE* gene and ORF1a, or if the result was judged a weak positive, then another clinical sample was requested and analysed.

In order to decrease the TAT, the following were instituted: rapid delivery of specimens to the MDL, adding additional staff to the MDL and extending the number of shifts to cover evenings and weekend. In addition, we developed a team-based approach for the collection of clinical samples by the introduction of a nursing-led protocol for the collection of nasopharyngeal swabs.[15]

In the initial year, only two staff were working in the MDL and were performing only one run per day. To decrease the TAT, additional microbiology staff were trained to perform the MERS-CoV PCR test. Subsequently we increased the number of runs that were performed per day. In addition, the MERS-CoV PCR test was performed on weekends. Electronic monitoring of the TAT was set up in the laboratory information system and the report was monitored on a daily basis. Here we analyse the impact of these interventions on the TAT for MERS-CoV testing.

Statistical analysis was done using Minitab (version 17; Minitab, State College, PA, USA). We generated a histogram of the TAT and calculated the mean and standard deviation (SD) of TAT for each year of the study. We compared the means per year using analysis of variance (ANOVA) and the yearly grouping information using the Tukey method for the mean and SD. A p-value $<0.05$ was considered significant.

## Results

During the study period there were 2664 samples processed in the MDL. The mean age of the included patients was 63.2±22.2 y and there were 1417 (53.2%) male patients. The most common TAT was 16.5–28.75 h for 39.3% of the samples.

The data show that 51.6% of samples were reported in <24 h (Table 1). The percentage of samples processed within 24 h increased from 42.3% to 73.8% in 2015 and 2018, respectively ($p<0.0001$). The mean TAT was compared for different years (2014–2018) using the Tukey method (Table 2) and ANOVA with a p-value <0.0001 (Table 2). The mean TAT was significantly lower in 2018 compared with previous years (19.25±13.8; $p<0.0001$).

## Discussion

In this study we evaluated the TAT of PCR testing for MERS-CoV. Over the study period there was a significant improvement in the TAT, with a reduction from >23 h to 19.2 h. This is an important improvement in the TAT, as one of the cited limitations of PCR testing is the long time to get the results.[16] Although the results of PCR tests were available in a short time in the latter years of the study, the impact of this on infection control could not be evaluated. The cited reasons for faster laboratory diagnostic testing of viral infections are to initiate appropriate therapeutics and to institute the required isolations. Fast and immediate isolation will decrease secondary transmissions in the community as well in healthcare settings. However, there are other considerations in isolation precautions, such as the likelihood of having MERS based on the clinical presentation. It is difficult to predict which patients will be positive for MERS based on clinical[8] and even when using a standardized screening protocol.[7] It was shown that a single negative nasopharyngeal swab does not rule out MERS-CoV infection[17] and that three respiratory samples are needed to achieve 98% sensitivity.[17]

There are other important issues for practicing physicians and infection control staff to consider when dealing with suspected MERS patients.

In a survey of multiple laboratories in South Korea, the median TAT was 5.29 h in 26 medical institutions and the median time was <6 h for about 57% of laboratories.[12] In a study from Qatar, the TAT decreased from 3 d to 1 d using an enhanced protocol.[18] We were able to decrease the TAT from 24 h to about 19 h by rapid delivery of specimens to the MDL, increasing the virology technical staff and extending the number of shifts to cover evenings and weekend. Additional steps to optimize swab collection could result in further decreasing the TAT. Such a strategy could be done by the introduction of a nursing-led protocol for the collection of nasopharyngeal swabs.[15]

Recommendations for scaling up molecular testing for MERS-CoV include the need to have effective laboratory testing within a short period of time. In addition, there is always room to expedite and shorten the time of MERS-CoV testing by the use of an enhanced laboratory algorithm and the utilization of dedicated teams. Mapping the process of laboratory testing for MERS-CoV or other emerging infectious diseases would aid in determining ways to decrease the TAT of laboratory tests. Since this is a retrospective study, other factors contributing to the TAT were not included. Such factors include the time needed by the MDL staff to validate and release results once these were completed. Such an analysis of these reports is an important way to decrease the TAT.[19,20] We also did not study the effect of reducing the TAT on the length of the hospital stay. In a previous study, decreasing the laboratory TAT was associated with a decrease in the

**Table 1.** TAT of the MERS-CoV samples

| TAT (h) | 2014, n (%) | 2015, n (%) | 2016, n (%) | 2017, n (%) | 2018, n (%) | All years, n (%) |
|---|---|---|---|---|---|---|
| <6 | 1 (20) | 6 (1.4) | 24 (2.7) | 11 (1.3) | 105 (20.2) | 147 (5.5) |
| 6–12 | 0 (0) | 27 (6.5) | 95 (10.6) | 99 (12) | 72 (13.9) | 293 (11) |
| 12–24 | 3 (60) | 144 (34.5) | 333 (37.2) | 305 (37) | 206 (39.7) | 991 (37.2) |
| >24 | 1 (20) | 241 (57.7) | 444 (49.6) | 411 (49.7) | 136 (26.2) | 1233 (46.3) |
| All | 5 | 418 | 896 | 826 | 519 | 2664 |

**Table 2.** TAT per year

| Year | Samples, n | Mean | SD | 95% CI | Grouping[a] |
|---|---|---|---|---|---|
| 2014 | 5 | 23.02 | 17.13 | 10.06 to 35.98 | A |
| 2015 | 418 | 29.416 | 14.747 | 27.999 to 30.83 | A B |
| 2016 | 896 | 28.236 | 16.162 | 27.268 to 29.20 | B |
| 2017 | 826 | 26.984 | 13.78 | 25.976 to 27.99 | A B C |
| 2018 | 519 | 19.251 | 13.779 | 17.979 to 20.53 | C |

[a]Grouping information was done using the Tukey method. In the grouping column, if the rows do not share a letter then this indicates that there is a significant difference in the means.

emergency room length of stay.[19] We also did not study the effect of any additional automation of the results on the TAT, but such automation is associated with a reduction in the TAT.[20] In addition, we did not look at the contribution of the need to do any stat MERS-CoV PCR testing during the study period. However, we believe that measuring the mean and understanding the TAT in laboratory tests are important to decrease variation and speed up the results.[20] Other possible contributing factors to increased TAT that we did not include in this study are sample collection and transportation.[21] As we incorporated multiples of the mentioned interventions at the same time, it was not possible to further analyse the contribution of each to the reduction in the TAT. All contributing factors could be studied and improved to reduce the TAT in laboratories utilizing a Lean Six Sigma methodology.[22]

In conclusion, the TAT for the MERS-CoV results decreased over time during the study period, with more results being reported within 24 h in 2018 compared with 2015. Timely reporting of MERS-CoV PCR results may aid in further enhancing infection control measures and prioritizing those who test positive for early detection, surveillance of contacts and therapy.

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**Competing interests:** None declared.

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**Data availability:** Data are available from the corresponding author upon request.

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