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Assessing Quality Indicators for the COVID-19 RTPCR in a Molecular Laboratory

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A B S T R A C T

A quality indicator is a tool that enables the user to quantify the quality of a selected aspect of care by comparing it with a set benchmark. The objective of this study was to review quality indicators for COVID-19 molecular testing at S.S. Institute of Medical Sciences and Research Centre and to compare with the predefined quality indicators in order to improve the performance of the molecular laboratory and to initiate the corrective and preventive measures. Over the period of one year we assessed different quality indicators collected from the molecular laboratory of a tertiary care hospital in Central Karnataka which has processed 36000 throat swabs for the diagnosis of COVID-19. Twelve quality indicators under pre-analytical, analytical and post analytical stage were assessed for the quality by referring it with the select criteria. Missing test request form / specimen (1.36/1000) was the most common inconsistency observed during the assessment of pre-analytical indicators followed by specimen inadequacy (0.194/1000), duplicate specimen referral forms (SRF) generated in ICMR portal (0.277/1000) and color change in the viral transport medium. In analytical phase, non-conformity with QC was seen in 2.83/1000 samples. In post analytical phase, excessive turnaround time was seen in 0.75/1000 samples followed by revised reports due to transcription error (0.38/1000) and duplicate reports (0.13/1000). The results of assessment of quality indicators in the molecular laboratory explicitly supports that laboratory could keep the incidence of errors to the minimum level by following proper corrective and preventive measures. Thus, catering quality laboratory services during devastated COVID pandemic year.

Keywords

Quality indicators, Molecular Laboratory, COVID-19, Root cause analysis, Corrective measures and preventive measures

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Introduction

Quality indicators are standardized evidence based measures of health care quality that can be used for continuous improvement of laboratory services[1]. Assessing the quality of laboratory services using quality indicators or performance measures requires a systematic,

transparent, and consistent approach to collecting and analyzing data[2,3].

A comprehensive approach would address all stages of the laboratory total testing process, with a focus on the areas considered most likely to have important consequences on patient care and health outcomes[4,5]. Quality indicator data should be collected over time to identify, correct, and continuously monitor problems and improve performance and patient safety by identifying and implementing effective interventions and for the purpose of increased consistency and standardization of key processes among clinical laboratories[6].

The objective of this study was to review quality indicators for COVID-19 molecular testing at S.S. Institute of Medical Sciences and Research Centre and to compare with the predefined quality indicators in order to improve the performance of the molecular laboratory and to initiate the corrective and preventive measures.

Materials and Methods

S.S. Hospital is a tertiary care hospital which is a part of S. S. Institute of Medical Sciences and Research Centre which is located in Davanagere, Karnataka, India.

Hospital has central diagnostic laboratory and molecular laboratory which is NABL accredited. Since May 2020 till April 2021 molecular laboratory has received thirty-six thousand nasopharyngeal and oropharyngeal swab from Government setups and private hospital for the diagnosis of COVID-19 by RTPCR.

The samples were received by our technical staff from 8:00 am to 1:00 pm and processed subsequently. The laboratory staff recruited for sample receipt makes an entry including the time the sample is received by the lab. The samples were numbered at the reception counter accordingly.

After screening the samples for any preanalytical errors[6,7], the analytical process begins. After sample preparation and RNA extraction[8] and RTPCR test was conducted as per the kit insert. Positive control and no template control was added in the reaction. Results were interpreted as per the manufacturer's instructions. Covid results were entered in the ICMR portal and reports were issued. In order to assure quality in the testing, laboratory participated in the external quality assurance programs[2] and inter laboratory quality assurance with the reference laboratory.

We have chosen some of these quality indicators criteria as applicable to the inspection of the functioning of our Molecular laboratory.

Pre-analytical indicators[2,3,7]

Specimen inadequacy

Illegible information on specimen container

Color change in the VTM

Duplicate SRF generated in ICMR portal

Specimen container information error (Patient information not matching with the SRF details)

Missing test request form / specimen

Improper packing

Analytical indicators[2]

Proficiency testing performance

Non conformity with Quality control

Post-analytical indicators [2,9-11]

Turnaround time [TAT]

Revised reports due to transcription error

Duplicate reports generated as a result of reports not reaching the clinicians.

Analysis of the results: The incidence of errors is expressed in frequency/1000 specimen[2]

Results and Discussion

Incidence of pre-analytical error is depicted in table-1. Over the period of one year, a total of 2.13/1000 samples were rejected. Out of which 1.36/1000 samples were rejected due to missing samples/request form, 0.27/1000 samples were due to duplicate SRF generated, 0.19/1000 samples were rejected due to specimen inadequacy, 0.16/1000 were rejected due to change in color in viral transport medium, 0.05/1000 due to mismatch information on VTM and SRF, 0.05/1000 due to improper packing and 0.027/1000 due to illegible handwriting on VTM (Table-1).

Incidence of analytical errors are depicted in table-2. Lab participated in the proficiency testing and inter laboratory quality assurance over the period of one year and results were in concordance with the reference laboratories. 2.833/1000 samples did not comply to the quality control parameters. 0.972/1000 samples were retested due to non-conformity of positive control (0.444/1000) and non-template control (0.5277/1000) and with the quality control parameters. 1.86/1000 samples did not show amplification for the Rnase P (internal control). Incidence of post analytical errors are depicted in table-3. Analysis of total turn around time revealed that 0.75/1000 samples could not be reported within the stipulated time frame of 24 hours. In COVID-19 testing transcription error is classified as uploading erroneous result in the ICMR portal. In one-year period 12 number of negative reports were reported as positive with a frequency of 0.381/1000 negative samples. The number of duplicate reports generated during the study year was 5 with a frequency of 0.13/1000.

Pre-analytical variables account for majority of the laboratory errors incurred[7], and encompass the time from when the test is ordered by the physician until the sample is ready for analysis[12]. Most errors often occur before the samples are analysed[6], especially, in case of COVID pandemic where fear factor plays an important role in the commitment of the health care personnel. Hence, there is an urgent need for proper accountability to improve test quality by reducing the pre-analytical variables.

In the present study, over the period of one year, 2.13/1000 pre-analytical errors were documented. Out of which significant proportion of errors were due to missing samples or missing SRF. Root cause analysis revealed that SRF generation, packing and transportation were done by different team. It was brought to the notice of the concerned in-charge regarding the lack of coordination among different team and advised a proper co-ordination among the team to minimise the incidence. Next most common pre-analytical error observed was duplicate SRF generation (0.27/1000) which could be due to issue with the ICMR portal, internet connectivity and miss-spelt name of the patient. It was advised to collect aadhar card while entering SRF details. Other criteria for sample rejection was change in the color of the VTM indicating contamination. The tubes were visually inspected for signs of bacterial growth such as color change (with phenol red specifically, a yellowing of the initial pink color indicative of acidification, frequently because of bacterial growth), turbidity, or presence of floccules

when tapped or vortexed. 0.16/1000 specimens showed change in the color which could be due to improper closure of the lid of the tube during specimen transportation. 0.199/1000 specimen were rejected due to insufficient volume which might have raised due to sample leakage.

0.027/1000 samples were rejected due to illegible handwriting/ smudging of patient information on the VTM. Root cause analysis revealed that during the sample preparation stage, hypochlorite was sprayed to disinfect the tube. Technicians were advised to avoid spraying hypochlorite over the tube(s). After corrective and preventive measures, we didn't notice such incidence.

In order to assure quality in the testing, laboratory participated in the external quality assurance programs and inter laboratory quality assurance with the reference laboratory. Results were 100% in concordance with the proficiency testing provider(s) indicating benchmark performance at all analytical parameters.

2.83/1000 samples did not comply to the quality control parameters. 0.97/1000 samples were retested due to non-conformity of positive control and non-template control with the quality control parameters. Root cause analysis revealed this could be due to repeated freeze-thaw cycles leading to reagent deterioration. Corrective measures were initiated reinforcing to use cold blocks while handling the reagents and storage of the QC vials with a strict maintenance to cold chain. For variable results with NTC, nuclease free water was changed and test were rerun with the standards for optimization. Rnase P (internal control) did not amplify in 1.86/1000 samples. Internal control amplification failure may be due to inhibition; hence the RNA extracts were serially diluted in 1:10 dilution and the test were rerun and the results were in conformity with the QC standards[13].

Other hypothesis could be due to higher concentration of the template which is quite a normal phenomenon in the respiratory specimen, this leads to competitive inhibition during amplification cycle. In this scenario, because of higher concentration of template / target pathogen, they consume the ingredients of the PCR reaction faster because of their higher concentration, eventually they dominate the reaction and leaving the internal control (submissive) behind[14]. Hence we often note very weak or no amplifications in such conditions which could be resolved by diluting the extract of the specimen.

The post-analytical factors measuring the quality of our laboratory are illustrated in Table 3. We do not have an automated sample transport system in our hospital and also our laboratory received samples from Government set ups also; hence the samples were delivered by a manual courier and the results were entered in the ICMR portal and reports were delivered by a manual courier. We have set a benchmark of 24 hours as the TAT for category A samples[15], since COVID-19 being a critical test and 48 hours for category B and C samples keeping in mind all the steps involved in sample delivery, analysis, validation, and finally report dispatch[2,12,13].

A total of 0.75/1000 samples could not be reported within the stipulated time frame. Out of 27 delayed reporting the root cause analysis revealed 21 samples (0.58/1000) SRF were fetched by other COVID laboratories.

Table.1 Analysis of the Incidence of Pre-analytical Quality Indicators

Quality Indicators	Frequency
Specimen inadequacy	0.199/1000
Illegible information on specimen container	0.027/1000
Color change in the VTM	0.16/1000
Duplicate SRF generated in ICMR portal	0.27/1000
Specimen container information error (patient information not matching with the SRF details)	0.05/1000
Missing test request form/missing specimen	1.36/1000
Improper packing	0.05/1000

Table.2 Analysis of the Incidence of Analytical Quality Indicators

Quality Indicators	Frequency
Proficiency testing performance	100% concordance
Non conformity with QC	2.83/1000

Table.3 Analysis of the Incidence of Post-Analytical Quality Indicators

Quality Indicators	Frequency
Excessive turnaround time (TAT)	0.75/1000
Revised reports due to transcription error	0.38/1000
duplicate reports generated by the laboratory as a result of reports not reaching the clinicians	0.13/1000

Hence the results could not be uploaded in the ICMR portal in time, but the reports were mailed to district surveillance officer and also to the ICMR customer service to update the same. 0.16/1000 did not qualify TAT criteria due to delayed report entry in online portal due to technical glitch.

Analysis of transcription error revealed that 0.38/1000 negative samples were reported as positive over the period of one year. Root cause analysis unmasked that inspite of true negative result, during data entry stage in the ICMR portal, the result was entered as positive. As the ICMR portal doesn't give the option to change the positive result, such transcription errors were immediately notified to concerned authority regarding the authenticity of the results and email was sent to ICMR support team to revise the results. As the preventive measures, concerned data operators were re-oriented to the results entry in the ICMR portal and a request was given to procure sample management system and interfacing ICMR approved third party softwares with the ICMR portal for error free entries.

Number of duplicate reports dispatched was also analysed as another quality indicator of our services. Hard copy of the report generated for private testing was collected by the patient attendants at the sample collection centre and for inpatient the reports were handed over by the nursing staff in-charge of sample collection. However, Due to some lapses on the part of the staff involved in handing over the reports and also due to

restriction at the covid wards, 0.13/1000 reports were not added to the case sheet of the in-patient. As the result duplicate reports were issued on demand by the treating clinicians.

The idea of quality indicators has transformed the field of laboratory medicine. These analytical and extra analytical indicators are of utmost importance in decreasing errors occurring throughout the total testing process, to improve patient safety and also in the comparison of individual laboratory performance with the aim of improving laboratory quality. Over the period of one year by identifying and monitoring quality indicators regularly we have set up a benchmark in keeping errors to the minimum in the diagnosis of COVID-19.

Limitation of the study

Not many/no literatures are present on quality indicators in molecular laboratory. Hence, the findings of the present study were not correlated with such similar studies.

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