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Original Research Paper

# Role of Xpert Xpress SARS-CoV-2 assay in emergency patient care: Experience from a tertiary care hospital

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**ABSTRACT:**
The pandemic of coronavirus disease gripped whole of the world, knowing no boundaries. The virus attained proficient human-to-human transmission owing to the low fidelity of RNA-dependent reverse transcriptase (RdRp). Besides the symptomatic patients, asymptomatic carriage became greater matter of concern, underlining the connotation of early diagnosis. The same is pertinent not only to curtail the transmission, but also to prevent the delay in management of patients necessitating emergency interventional care for other medical/surgical conditions. However, the patient care cannot be conceded awaiting the COVID status of patients using RT-PCR, which has turnaround time (TAT) of 6-8 hours. To combat this situation, FDA verified emergence use authorization (EUA) for rapid and POCT tests like Cepheid GeneXpert, Hologic Panther Fusion SARS-CoV-2 assay, GenMark ePlex SARS-CoV-2 assay and Abott ID Now. In our tertiary care centre, in order to divulge COVID status of all the patients presenting to emergency, Xpert Xpress SARS-CoV-2 assay with TAT of 45 minutes was deployed 24 x7, to prevent the delay in management.

***Keywords: COVID 19, Xpert Xpress SARS-CoV-2 assay, emergency, turnaround time, RT-PCR***

## INTRODUCTION:

Coronavirus disease (COVID-19) emerged in wet markets of Wuhan, China in December 2019 and eventually gripped whole of the world (1). The agent implicated in this apocalyptic pandemic was discerned to be severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an enveloped RNA virus, having ~89% of homology with SARS-related bat coronavirus, which belongs to group 2b-betacoronavirus of family *Coronaviridae* and order Nidovirales (2). The primary mode of transmission is via droplet and fomite spread, though aerosol transmission is also contemplated.[3] Other secondary routes of transmission include gastrointestinal and vertical transmission, though isolation from urine and blood has also been reported (3). Patients usually present with fever, myalgia, cough and sore throat, which can culminate into dyspnoea and respiratory failure in severe cases (4). Owing to the low fidelity of RNA-dependent reverse transcriptase (RdRp), the virus has attained high virulence and a proficient human-to-human transmission, with a prohibitive reproduction number ($R_0$). Apart from the symptomatic patients, asymptomatic carriage of the virus is a matter of paramount concern, thereby, underlining the significance of early diagnosis to curtail the transmission in community (5).

The most alarming situation intensifying the disquiet was the rising trend of infection amongst health care workers (HCWs) (6). In light of rising trend among HCWs, there was a pertinent prerequisite for stringent guidelines pertaining use of personal protective equipment (PPE) and rapid testing of patients necessitating emergency interventional care. Owing to the regulated supply of PPE, these couldn't be


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employed for care of all. Moreover, the patient care cannot be conceded for the same, awaiting the COVID status, using real-time polymerase chain reaction (RT-PCR), with turnaround time (TAT) of 6-8 hours. TAT is critically relevant in situations of emergency interventions, shortage of medical personnel, personal protective equipment and isolation wards. Moreover, the pandemic accorded with influenza season in many realms, where it became imperative to have point-of-care test (POCT) in place, to discern patient profiles, accelerate the management of patients admitted for other health tribulations and to implement effective health control measures. This necessitated the requisite for sample-to-answer platforms for rapid diagnosis.

As virus keeps on evolving with time, the emergency responses need to meet the testing requisite. World health organization (WHO) and Center for Disease Control and Prevention (CDC) incriminated early diagnosis and quarantining of cases as the primary overarching armors to prevent and curb the rapid ongoing transmission, as an adjunct to universal masking and stringent hand-hygiene (7). In addition, to strengthen the capacity building, there was an urgent need to exalt the testing platforms, to lessen anticipated TAT. Food and drug administration (FDA) verified emergence use authorization (EUA) for rapid and POCT tests like Cepheid GeneXpert, Hologic Panther Fusion SARS-CoV-2 assay, GenMark ePlex SARS-CoV-2 assay and Abott ID Now.

To divulge COVID status of all the patients before any emergency intervention at our centre, Xpert Xpress SARS-CoV-2 assay was deployed 24 x7, so that appropriate treatment can be given, as results were available in 45 minutes.

## MATERIALS AND METHODS:

This was a single-centre, prospective study aimed to discern the COVID-19 status of all the patients who required any emergency services. Nasal, nasopharyngeal or throat swabs were collected from patients using dacron, rayon or nylon swabs. The desired sample was collected with gentle rotatory movements and was immediately placed in 3 ml universal viral transport medium (VTM). The samples were transported as soon as possible, in an adequately maintained cold-chain. The testing was carried out using manufacturer's instructions. The contents of VTM were mixed by inverting the VTM five times. 300 µl of the specimen was transferred from VTM to sample chamber of the assay cartridge, which is then, scanned and loaded into the GeneXpert platform. Subsequent to the testing, the samples were aliquoted and stored at -80°C. Testing by Xpert Xpress SARS-CoV-2 assay was conducted 24x7 for period of 4 months.

### Cepheid Xpert Xpress SARS-CoV-2 assay:

Xpert Xpress SARS-CoV-2 assay is a fully automated in-vitro cartridge-based platform for qualitative detection of SARS-CoV-2 nucleic acid using real-time PCR principle. The assay incorporates sample preparation; extraction, amplification and detection of the target sequences in a single step in a self-contained cartridge, with two internal controls; sample processing control (SPC) and probe check control. The assay is based on principle of real-time reverse transcription PCR amplification targeting E (envelope) and N2 (nucleoprotein) genes. SPC ought to be positive with a cycle threshold (ct) of less than 40 for the test to be valid. If only E gene is positive, it is considered as a presumptive positive result (inconclusive), N2 alone or with E gene is considered as confirmatory positive result (8). The results were available in 45 minutes with this assay.

## RESULTS:

The total number of patients included in the present study was 2,794. Maximum number of samples were tested from emergency trauma services (27.1%), trailed by emergency medical services (24.4%), neurosurgery (11.8%), emergency gynaecological procedures (10.2%), surgeries (10.1%), paediatrics (5%), cardiac emergencies (5%), symptomatic ILI-patients (2.5%), orthopaedic emergencies (3.1%), emergency ophthalmic procedures (1.5%), intensive care units (1%), otolaryngological procedures, plastic surgeries (0.5% each) and health care workers (0.3%). 2% of samples were referred from other hospitals. Average age of patients included in the study was 39.47 years with male-to-female ratio of 1.8:1. The demographic details divulged that 42.12% of the patients were residents of Punjab, 21.87% of Haryana, 14.75% of Chandigarh, 12.85% of Himachal Pradesh, 4.97% of Uttar Pradesh, 1.07% of Jammu and Kashmir, 0.75% of Uttarakhand, 0.72% of Bihar, 0.57% of Rajasthan and 0.07% of Delhi, 0.036% of Assam, Kerala, Jharkhand, Ladakh, Manipur, Tamil Nadu and West Bengal each.

Of these 2,794 patients, eighty- eight (3.14%) were positive and three (0.11%) had an inconclusive or presumptive positive result. The average age of positive patients was 41.41 years with male-to-female ratio of 1.8:1. Maximum rate of positivity (54.54%) was noted amongst the residents of Punjab, followed by 21.59% from Chandigarh, 11.36% from Haryana, 4.54% from Uttarakhand and UP each and 1.14% from J&K, Kerala, Bihar and H.P each. The most common co-morbidity associated with COVID-19 was chronic renal disease noted in 7.95% of patients, hypertension and cardiac disease in 5.7% each, diabetes mellitus in 4.5%, chronic liver disease in 2.27%, and chronic lung disease in 1.1% of the patients. The symptoms were noted in merely 22.72% of patients, while 77.27% of these patients were asymptomatic and COVID-19 was divulged as a result of pre-operative work-up for emergency surgeries.

## DISCUSSION:

The COVID-19 left no stone unturned to expose the carcass of our health care system with a catastrophic rise in number of cases everyday. To combat this rise in morbidity and mortality, CDC and Indian Council of Medical Research (ICMR) constantly updated the guidelines for testing strategy of COVID-19 to ensure maximum coverage of the populace (9). The current diagnostic modalities accessible for testing across the globe are based either on molecular techniques or antigen detection. Molecular tests are the mainstay of diagnosis of COVID-19 and RT-PCR is considered as the gold standard testing modality. RT-PCR testing can either be of open or closed platform, the open one being commercially available RT-PCR, which is currently being exploited at a large scale. Closed platforms of RT-PCR include plethora of commercial kits that have also been validated by Indian council of Medical Research (ICMR) and Food and Drug Administration (FDA) under emergence use authorization (EUA) viz Cepheid cartridge-based nucleic acid amplification test (CBNAAT) GeneXpert, TruNat, Roche COBAS 6800/8800 targeting E and *RdRp* gene and ID Now (Abbott) platforms targeting *RdRp* gene.[18] Of these tests, few are LAMP-based; digital PCR, droplet PCR, dual kinetic assay, real-time reverse transcription isothermal amplification test, CRISPR-based, NGS-based and dual LFA and PCR-based (10). Open RT-PCR platforms are cost-effective but have several bottlenecks inherently associated with them, owing to the tedious, time-consuming RNA extraction and PCR run, making turnaround time (TAT) ~6-8 hours. The modest resolution to these tailbacks could be rapid antigen detection kits, however, these kits are cladding the issues of low sensitivity, in spite of being highly specific, thereby, eliminating their role in emergency settings. On the contrary, antibody detection kits hold no significance in testing strategy and are helpful merely in sero surveys. The futility of these antigen and antibody detection kits paved the path for point-of-care molecular tests like Xpert Xpress SARS-CoV-2 assay.

In the present study, Xpert Xpress SARS-CoV-2 was used as the diagnostic modality for detection of SARS-CoV-2 in pre-operative situations, owing to TAT of 45 minutes with hands-on time of 1-2 minutes. Many studies have shown 100% agreement between commercially available PCRs and Xpert Xpress SARS-CoV-2. A multicentric study in China revealed positive percent agreement of 96.1% and negative percent agreement of 96.2% between Xpert Xpress SARS-CoV-2 and approved real-time PCR assays in oropharyngeal swabs (11). Another study from US has divulged positive percent agreement and negative percent agreement of 99.5% and 95.8% respectively (12). Besides these, another chief advantage of Xpert Xpress SARS-CoV-2 is its lower limit of detection (LoD), provided as 250 cp/ml by the manufacturer, while few studies have found LOD to be as low as 8.26cp/ml and 0.0100 PFU/ml (13,14). The variation in LOD is attributed to varied methods of detection for input concentrations. Moreover, Xpert Xpress SARS-CoV-2 assay has outperformed other commercially available diagnostic platforms in terms of sensitivity. A recent study has been conducted to compare three POCT viz Cepheid Xpert Xpress SARS-CoV-2 assay, GenMark ePlex SARS-CoV-2 assay and Abott ID Now, with a reference standard, Hologic Panther Fusion SARS-CoV-2 assay. Of all these assays, Xpert Xpress SARS-CoV-2 assay performed superior to the rest, with 98.3% clinical sensitivity compared to 87.9% of ID Now and 91.4% of ePlex. The LoD was also noted to be the least (100 copies/ml) for Xpert Xpress SARS-CoV-2 assay, in contrast to 20,000 and 1,000 copies/ml for ID Now and ePlex. The least discrepant results were reported with Xpert Xpress SARS-CoV-2 assay, thereby, underlining the role of Xpert Xpress SARS-CoV-2 assay in rapid testing (15). Few studies have also demonstrated the acceptable agreement between Xpert Xpress SARS-CoV-2 assay and Roche Cobas SARS-CoV-2 assay, bestowing Xpert Xpress SARS-CoV-2 assay as the superlative POCT with a high sensitivity, low LoD, reliable results and ability to test multiple samples in a single go (16).

Xpert Xpress SARS-CoV-2 assay has also been exploited and validated for detection of SARS-CoV-2 in stool samples and study has demonstrated an acceptable agreement. Moreover, the study has also proposed to include the same in testing algorithm of highly suspected patients with negative result from upper respiratory tract samples, owing to the inability to detect SARS-CoV- 2 in upper respiratory tract samples two-to-three weeks post-symptoms (17). Similar studies have been conducted using saliva as an acceptable alternative, owing to its non-invasive nature, ease of collection, less need of PPE for sampling and a good agreement value (positive percent agreement of 96% and negative percent agreement of 99%) (18).

Owing to the risks posed by asymptomatic patients in transmission dynamics of SARS-CoV 2 and to prevent the injudicious use of PPE, it was initially pertinent to test all the patients being admitted to hospitals for COVID-19 for emergency care. Simultaneously, emergency procedures can't be kept on foothold due to unavailability of the COVID status, thereby, making Xpert Xpress SARS-CoV-2 as the most appropriate alternative for testing in such scenario. The most appropriate application of this test is in critical care hospitals, where rapid triage decisions have to be made for appropriate patient disposition and lifesaving management of patients. On the contrary, commercially available RT-PCR has relatively higher TAT, entailing multiple steps of decontamination, RNA extraction, master mix preparation and PCR. Moreover, owing to low throughput of Xpert Xpress SARS-CoV-2 assay and high-cost of testing per

sample, the use of Xpert Xpress SARS-CoV-2 assay remains restricted.

**CONCLUSION:**

Xpert Xpress SARS-CoV-2 assay was the most suitable sample-to-answer platform for precise and rapid testing of patients during initial waves of pandemic, which accords appropriate use of PPE and isolation resources, simultaneously complimenting the superlative regulation of therapeutic interventions.

**Conflict of interest**: None

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**REFERENCES**:

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395:497-506.
2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020 Mar;579(7798):270-273.
3. Sun J, Zhu A, Li H, Zheng K, Zhuang Z, Chen Z, et al. Isolation of infectious SARS-CoV-2 from urine of a COVID-19 patient. Emerg Microbes Infect. 2020 Dec;9:991-993
4. CDC. Coronavirus Disease 2019 (COVID-19) [Internet]. Centers for Disease Control and Prevention. 2020. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/respirators-strategy/crisis-alternate-strategies.html
5. D'Arienzo M, Coniglio A. Assessment of the SARS-CoV-2 basic reproduction number, R0, based on the early phase of COVID-19 outbreak in Italy. Biosaf Health. 2020 Jun;2:57–9.
6. Wang Y, He Y, Tong J, Qin Y, Xie T, Li J, et al. Characterization of an Asymptomatic Cohort of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infected Individuals Outside of Wuhan, China. Clin Infect Dis. 2020 Nov 19;71(16):2132-2138
7. Fusco FM, Pisaturo M, Iodice V, Bellopede R, Tambaro O, Parrella G, et al. COVID-19 among healthcare workers in a specialist infectious diseases setting in Naples, Southern Italy: results of a cross-sectional surveillance study. J Hosp Infect. 2020 Aug;105(4):596-600
8. Xpert® Xpress SARS-CoV-2 has received FDA Emergency Use Authorization. Available from: https://www.cepheid.com/coronavirus
9. COVID-19 | Indian Council of Medical Research | Government of India. Available from: https://icmr.nic.in/content/covid-19
10. Current Molecular and Antigen Tests with FDA EUA Status. Johns Hopkins Center for Health Security. Available from: https://www.centerforhealthsecurity.org/resources

/COVID-19/molecular-based-tests/current-molecular-and-antigen-tests.html

11. Hou H, Chen J, Wang Y, Lu Y, Zhu Y, Zhang B, et al. Multicenter Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 Assay for the Detection of SARS-CoV-2 in Oropharyngeal Swab Specimens. J Clin Microbiol. 2020 Jul 23;58(8):e01288-20
12. Loeffelholz MJ, Alland D, Butler-Wu SM, Pandey U, Perno CF, Nava A, et al. Multicenter Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 Test. J Clin Microbiol. 2020 Jul 23;58:e00926-20
13. Zhen W, Smith E, Manji R, Schron D, Berry GJ. Clinical Evaluation of Three Sample-to-Answer Platforms for Detection of SARS-CoV-2. J Clin Microbiol. 2020 Jul 23;58(8):e00783-20. doi: 10.1128/JCM.00783-20.
14. Moran A, Beavis KG, Matushek SM, Ciaglia C, Francois N, Tesic V, et al. Detection of SARS-CoV-2 by Use of the Cepheid Xpert Xpress SARS-CoV-2 and Roche cobas SARS-CoV-2 Assays. J Clin Microbiol. 2020 Jul 23;58:e00772-20
15. Phan T, Mays A, McCullough M, Wells A. Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 test for bronchoalveolar lavage. J Clin Virol Plus. 2022 Jun;2(2):100067.
16. Szymczak WA, Goldstein DY, Orner EP, Fecher RA, Yokoda RT, Skalina KA, et al. Utility of Stool PCR for the Diagnosis of COVID-19: Comparison of Two Commercial Platforms. J Clin Microbiol. 2020 Jul 1; 58: e01369-20
17. McCormick-Baw C, Morgan K, Gaffney D, Cazares Y, Jaworski K, Byrd A, et al. Saliva as an Alternate Specimen Source for Detection of SARS-CoV-2 in Symptomatic Patients Using Cepheid Xpert Xpress SARS-CoV-2. J Clin Microbiol. 2020 May 15; 58: e01109-20