JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Challenges in the establishment of a biosafety testing laboratory for COVID-19 in Bangladesh

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Abstract
At the beginning of the coronavirus disease 2019 (COVID-19) pandemic in Bangladesh, there was a scarcity of ideal biocontainment facilities to detect the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a risk group of 3 organisms. Molecular detection of SARS-CoV-2 must be performed in a BSL-2 laboratory with BSL-3-equivalent infection prevention and control practices. Establishing these facilities within a short timeframe proved to be an enormous challenge, including locating a remote space distant from the university campus to establish a laboratory, motivating the laboratory staff to work with a novel pathogen without any prior experience, allocation of funds for essential equipment and accessories, and arrangement of a safe waste management system for environmental hazard reduction. This report also highlights several limitations, such as the facility's architectural design that did not follow the biosafety guidelines, lack of continuous flow of funds, and an inadequate number of laboratory personnel. This article describes various efforts taken to overcome the challenges during the establishment of this facility that may be adopted to create similar facilities in other regions of the country. Establishing a BSL-2 laboratory with BSL-3-equivalent infection prevention and control practices will aid in the early detection of a large number of cases, thereby isolating persons with COVID-19, limiting the transmission of SARS-CoV-2, and promoting a robust public health response to contain the pandemic.

Key words: COVID-19; SARS-CoV-2; biosafety laboratory; challenges.

J Infect Dev Ctries 2021; 15(12):1833-1837. doi:10.3855/jidc.14415

(Received 28 November 2020 – Accepted 17 June 2021)

Introduction

On March 11, 2020, the World Health Organization (WHO) declared that the suppression of the coronavirus disease-19 (COVID-19) pandemic must be through isolation, treatment, and tracing [1]. Numerous severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) RNA detection centers are required to meet this demand. At the onset of this pandemic, health systems in resource-limited settings, such as Bangladesh faced a significant challenge in managing the situation. After the first case was detected on March 8, 2020, the Ministry of Health and Family Welfare (MOH&FW) of the Government of Bangladesh decided to initiate COVID-19 identification and expand SARS-CoV-2 testing laboratories throughout the country to control the spread of the virus [2]. In response, the Bangabandhu Sheikh Mujib Medical University (BSMMU) took the initiative to provide COVID-19 molecular testing support through the Department of Virology. Until March 31, 2020, the Institute of Epidemiology, Disease Control and Research was the sole recognised COVID-19 testing facility in the country [3].

SARS-CoV-2, the causative organism of COVID-19, belongs to the risk group three (RG3) infectious agents; it should be handled in a Biosafety Level-3 (BSL-3) containment facility that permits the manipulation of pathogens transmitted via aerosols [4]. There were limited biocontainment facilities in Bangladesh before the onset of this pandemic that could be transformed to handle SARS-CoV-2. The purpose of this study is to describe the efforts taken to overcome the challenges faced during the establishment and operation of a molecular testing laboratory for COVID-19 in resource-constrained settings.

Planning phase

Initially, relevant guidelines on COVID-19, biocontainment laboratory, biosafety levels, real-time reverse transcriptase-polymerase chain reaction (RT-PCR), and infection prevention and control (IPC) circulated by the Centers for Disease Control and

Prevention (CDC) [5] and the WHO [6] were considered for the planning and establishment of a COVID-19 testing laboratory. Additionally, the risk assessment steps were thoroughly followed to reduce the operational risk hazards while maintaining a functional biosafety laboratory at a minimal cost [7,8]. As SARS-CoV-2 is an RNA virus that belongs to a group of RG3 organisms, it should be handled in a BSL-3 facility. However, it can be considered that non-propagative work with SARS-CoV-2 RNA would be safe to be dealt with in a BSL-2 facility with additional aerosol precautions [9]. Thus, to initiate COVID-19 testing within a short time, considering the gravity of the situation, a BSL-2 facility was planned, and aerosol precautions were taken based on BSL-3-equivalent personal safety measures.

Development and establishment phase

Guidance documents and standard operating procedures (SOPs) for laboratory detection of SARS-CoV-2 RNA were prepared [10] and followed during the functioning of the COVID-19 laboratory. The start-up equipment consisted of real-time reverse transcription–polymerase chain reaction (RT-PCR) (Applied Biosystems QuantStudio 5 and 7500 Real-Time PCR System, Thermo Fisher Scientific Inc. USA), GeneXpert Systems (Cepheid, USA), biosafety cabinet (BSC)-Class II (Esco Lifesciences, Singapore), PCR cabinet (BIOBASE, China), dry shaking heating block, water bath, vortex mixer, refrigerated centrifuge, 2-8 °C refrigerator, and -20 °C freezer. The pioneer members of the COVID-19 laboratory comprised faculties, residents, scientific officers, medical technologists, project-linked personnel, support staff, and volunteers and were headed by the Chairman of the Department of Virology. All members underwent on-campus training in basic techniques and skills required to operate the instruments and practiced IPC in a high-containment laboratory before the commencement of operations in the COVID-19 laboratory. In particular, the participants were trained to maintain biosafety precautions at all times, the use of personal safety equipment according to the CDC guidelines, sample collection techniques from the nasopharynx/throat, molecular detection of SARS-CoV-2 RNA using reagents and instruments, safe waste disposal, and regular decontamination and maintenance of the instruments.

Figure 1. The four-storied building in which the COVID-19 laboratory is located.

Figure 2. Naso-pharyngeal swab collection for COVID-19 testing.

Operational phase

A building completely separate from the main university campus was selected to establish the COVID-19 laboratory to avoid intermingling among suspected and non-COVID-19 patients. The chosen building is an old structure that belongs to the proposed BSMMU administrative Block-1 (Figure 1). The laboratory was established at the far end of the first floor of the building to limit the number of people in the area. A designated sample collection area for COVID-19 testing was set up on the ground floor (Figure 2). Several sample collection booths were constructed, and the long queue of patients was systematized by creating prior online bookings for the daily testing slots.

This laboratory received samples of suspected COVID-19 patients after evaluation at the fever clinic, health care workers who developed COVID-19-like symptoms, and patients admitted under the hospital's COVID-19 and non-COVID-19 sections as directed by the University authority. Collection, transportation, and processing of samples followed by RT-PCR testing were performed according to SOP guidelines. First, nasopharyngeal swabs were collected from patients, and each swab was inserted into a sample storage tube containing 2 mL of normal saline with an RNase inhibitor. In the laboratory, these samples were processed using heat-inactivation and buffer-based extraction methods. Real-time RT-PCR was performed using a SARS-CoV-2 detection system (PCR-fluorescence probing) that utilised *ORF1ab* and *N* genes as targets for the qualitative detection of SARS-CoV-2 RNA. In addition, internal control targeting the *RNase P* gene was used to monitor sample collection, sample handling, and molecular processes to avoid false-negative results. A cycle threshold (Ct) value of > 40 cycles indicated negative results, and the lowest limit of detection was 200 copies/mL. The organization of the COVID-19 laboratory is shown in Figure 3.

The results of the tested samples were sent to the Management Information System (MIS) under the Directorate General of Health Services (DGHS) that was added to the National Coronavirus COVID-19 Dashboard in 2020 [11]. Data shared with MIS and DGHS were analyzed for COVID-19 detection frequency in terms of locality, age-gender particulars, recovery, and death numbers and compared with other areas of the country that are included on the National Coronavirus COVID-19 Dashboard, 2020, and circulated with a press release. Electronically generated testing reports can be downloaded by the patients using a web-based link from the DGHS website, and the results were notified to each individual via text messages from a BSMMU-authorised mobile number [12].

The daily sample turnover at this facility usually depends on the rate of infections in the country, publicised in the daily press released by the DGHS; a high rate of infection or high death rate due to COVID-19 makes more people screen for the disease when they feel symptomatic. By May 31, 2021, about 144,067 samples were tested for COVID-19 in this laboratory, and on average 3,000 samples were received weekly for testing.

None of the laboratory personnel had laboratory-associated COVID-19 infections. However, many admitted that they were infected through contact with family members or friends, probably resulting from unenthusiastic health safety [13].

Discussion

The experience of establishing a COVID-19 testing center in Bangladesh indicates that collaborative efforts of all stakeholders, funding from the local budget, and the technical expertise of in-house researchers and scientists enabled the development of a biocontainment laboratory within a short time and permitted operations with acceptable quality in a resource-constrained situation. The establishment of a COVID-19 testing center in the premises of the BSMMU was an enormous challenge, but it started functioning as a molecular COVID-19 laboratory within a short period.

The initial challenge was to locate an ideal space for a biocontainment facility that limited person-to-person transmission due to the intermingling of COVID-19 patients with non-COVID-19 patients attending the hospital for other health-related services; this was managed by designating a separate building. The second challenge was to motivate the laboratory personnel to deal with a new, unfamiliar pathogen without prior knowledge and to work while wearing

Figure 3. Organization of the COVID-19 laboratory: Specimen processing room (A), RNA isolation and reagent mixture preparation (B), Amplification room (C).

various safety gears. This department has a long experience in molecular detection of blood-borne pathogens [14], and after intensive training, the staff acquired a basic understanding of testing and IPC procedures. The third challenge was to reduce aerosol formation during sample collection and molecular testing to avoid laboratory-associated infections. Preventing contact with the aerosol formed during sample collection was minimised by collecting the samples inside the designated booths or kiosks. In the laboratory, the sample tubes were placed in a dry heating block inside a biosafety cabinet II that degraded the virus envelope, making it non-infectious [15]. Fourthly, there was a shortage of Personal protective equipment (PPE) with accessories during the initial stages because of increased global demand; necessities were met through imports from foreign countries. Subsequently, rapid initiatives taken by the local readymade garments (RMG) industry to manufacture all the components of PPE made safety gear readily available [16]. Fifthly, there was a gradual increase in sample turnover, causing difficulty in delivering results in due time; this issue was resolved by the emergency employment of a few laboratory technologists from DGHS. Lastly, the waste management system was another challenge that was resolved by merging it with the University waste disposal protocol. Hence, all the challenges were overcome, and a COVID-19 testing laboratory has been established that has already earned the confidence of the local community.

Limitations

Despite all efforts, there are certain drawbacks to the COVID-19 laboratory setup. First, the construction of the laboratory was on a temporary basis, and we had to compromise with the old architectural design of the building. For this reason, the laboratory design did not include the ideal biosafety precautions and sequences. Moreover, the sample collection and processing rooms could not be designed as negative pressure rooms with a controlled HEPA-filtered airflow. Furthermore, the establishment lacked a self-closing double-door air-showered facility and a pass-through box between the biocontainment rooms. Additionally, on-site autoclaving and effluent decontamination systems could not be arranged. Second, the duration of the pandemic cannot be predicted; therefore, there have been challenges in bearing the operational expenses of the support and supplies in a resource-constrained situation. Although the essential instruments were obtained and the establishment cost was covered, the uncertainty of continued financial support may hamper the services and maintenance of instruments. A decrease in the efficacy of instruments is already being noticed owing to overuse under the current circumstances. Third, there has been a shortage of labor that persisted despite few appointments, and many staff members were already exhausted as there were no backup laboratory members. Moreover, the lack of short-term assignments or stipends for volunteers and risk allowances for the working personnel at the laboratory failed to motivate them to continue work, as observed in the initial phase [17]. Finally, accreditation of the COVID-19 testing laboratory, necessary for quality assurance and follow-up calibration certification for continued testing and equipment, respectively, could not be obtained due to the ongoing pandemic in the country.

Conclusions

This experience has taught us that, despite several limitations and financial barriers, the concerted efforts of all stakeholders can enable the establishment and functioning of a biocontainment facility that is beneficial to the community in the current pandemic. Nonetheless, it is essential to set long-term goals, and financing should be made available to sustain continuous functioning and improve the quality of COVID-19 laboratories.

Acknowledgements

We are grateful for the support of the Administration, Bangabandhu Sheikh Mujib Medical University (BSMMU), Directorate General of Health Services, Ministry of Health and Family Welfare, and Government of Bangladesh. We sincerely appreciate the tireless contributions of numerous university staff during the establishment and continuance of the services.

Author contribution

Conceptualization: SRUI, ST, SUM; fund acquisition: SUM; designing the facility: SRUI, SUM, MJ, AN, AKG; developing the facility: SRUI, AKG, PD, MAON, SUM; performing the experiments and reporting the results: SRUI, PD, AKG, MAON, TA, AHB; literature search and drafting the manuscript: SRUI, PD, AKG, TA, AHB; data analysis: SS, MAON, AHB; reviewing, editing, and revising the manuscript: SRUI, ST, SS, TA; approving the final version of the manuscript: SRUI, ST.

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Conflict of interests: No conflict of interests is declared.