# Experience in establishing a high-risk biocontainment facility in response to COVID-19 pandemic under resource constrain settings

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## Article Info

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## Abstract

The health care systems in resource limited countries are facing major challenges in dealing with Coronavirus disease (COVID-19). In Bangladesh, a steady increase in the number of COVID-19 cases since its first report on March 8, 2020, has led to an increased demand for COVID-19 detection facilities throughout the country. The detection of severe acute respiratory syndrome (SARS-CoV-2), the causative organism of COVID-19 and a highly infectious group 3(three) organism, requires a high biocontainment laboratory with a certain standard prerequisite infrastructure. This study describes the necessary steps for establishing and running a COVID-19 laboratory under resource constraint settings. Our experience indicates that, with collaborative efforts, funding, and technical support from locally available expertise, it is feasible to set up an optimally functional biocontainment facility with an acceptable quality performance despite several short comings.

## Introduction

In late December 2019, an outbreak of an unexplained respiratory illness was reported from the Hubei province of Wuhan, China. On January 7th, 2020, the Chinese authority declared that the agent responsible for this illness is a novel Coronavirus (CoV). Based on its similarity to SARS-CoV (2002-2003), the Coronavirus study group of the International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2, and world health organization (WHO) named this disease as COVID-19.[1] Gradually, the rapid emergence of SARS-CoV-2 globally compelled the WHO to declare it as a pandemic on March 11, 2020. The first COVID-19 case in Bangladesh was confirmed on March 8, 2020, by the Institute of Epidemiology, Disease Control and Research (IEDCR). Infections remained low until March, but a steep rise was observed from April.[2] On March 18th, 2020, the WHO declared that the main principle for controlling COVID-19 epidemics was to isolate, test, treat, and trace. To meet the demands, detection of SARS-CoV-2 RNA were conducted to identify COVID-19 patients.[3] Since the beginning of this pandemic, many countries have been overwhelmed with their weak healthcare systems, particularly low-to-middle-income countries (LMICs) like Bangladesh. To control a pandemic like COVID-19, public awareness and public health approach for prevention are the key factors to be followed. When massive testing facilities were required for the successful containment of SARS-CoV-2, it created enormous pressure for Bangladesh to initiate the rapid establishment of testing laboratories with maintaining biosafety precautions.

SARS-CoV-2 is a respiratory pathogen that is responsible for COVID-19 and manifests mainly as a respiratory disease. Suspected cases should be tested for the virus with nucleic acid amplification tests such as real-time reverse transcription-polymerase chain reaction ( RT-PCR). Specimens from the respiratory tracts were chosen as samples for laboratory detection of SARS-CoV-2 RNA.[4] Additionally, these laboratory detection systems for COVID-19 required massive biosafety, bio engagement, and biocontainment protocol to provide timely and effective diagnostics services.[5]

Despite all the difficulties, the Ministry of Health and Family Welfare, government of Bangladesh (MOHFW, GOB) decided to increase the SARS-CoV-2 testing capacity throughout the country.[6] During that time, Bangabandhu Sheikh Mujib Medical University (BSMMU) came forward as an autonomous body to provide testing support. It would not have been possible without the active initiation from BSMMU administration to allocate funds and allotment of necessary supplies and equipment by the Central Medical Stores Depot (CMSD) of Directorate General of Health Services (DGHS) to set up a COVID-19 laboratory under the Department of Virology. Thus, the purpose of this article is to describe the strategies and efforts made during the establishment of COVID-19 at a tertiary care center and the various challenges encountered during the ongoing maintenance with limited resources.

## Facility launch and expansion

*Risk assessment and guidance preparation*

Risk assessment (RA) is an integral part in the construction of any biocontainment laboratory. The purpose of RA is to conduct risk control, reduce the severity and frequency of accidents, and minimize the risk of biosafety laboratory operations with minimal cost.[7] Hence, we went through a risk assessment procedure as thoroughly as possible before establishing a laboratory. We followed the risk assessment steps laid down by the Bangladesh Biosafety and Biosecurity Guidelines for Handling and Disposal of Bio-hazardous Materials[8] and consulted our faculties and local experts in this field. From the prevailing guidelines, it was learned that SARS-CoV-2 RNA virus belongs to the risk group-3 (RG3) organism. RG3 agents are those that are associated with serious or lethal human disease for which preventive or therapeutic interventions may not be available or may have few emergency use listed drugs for clinical use for severely ill patients.[9] Based on the Bio risk level (BSL) of the organism, we considered that non-propagative work with SARS-CoV-2 RNA virus would be safe if dealt in BSL II taking enhanced personal precautions (BSL III level protections). Besides, several factors were taken into consideration namely bio-characteristics and potential risk of exposure, laboratory practices and procedures, efficiency and knowledge of laboratory staffs in hazard identification and mitigation, proper use/handling of safety equipment, and appropriate facility designing to avoid any events of unfortunate biocontainment failure, etc. A set of search terms were prepared covering in topics of COVID-19, bio-containment laboratory, biosafety levels, Real-time RT-PCR, Infection prevention and control (IPC), etc. for guidelines and Standard operating procedure (SOP) preparation. In addition, relevant guidelines circulated from WHO[10], CDC[11], DGHS[12], IEDCR[13] were also considered for protocol preparation on molecular detection of SARS-CoV-2 RNA and establishment of a COVID-19 testing laboratory. As per several documental reviews, we have prepared laboratory guidance and SOP on laboratory detection of SARS-CoV-2 RNA detection[14] and followed it religiously to maintain our COVID-19 laboratory.

***Manpower and training***

The pioneered members of the COVID-19 laboratory of BSMMU consisted of 10-12 people, headed by the Chairman of the Department of Virology, BSMMU. The other laboratory members included faculties, virologists, MD virology residents, scientific officers, medical technologists, and support staff. Apart from the University manpower and project-linked staff, many people volunteered during the establishment and maintenance of the laboratory.

Before the commencement of the laboratory function, all the members had in-campus practical training on the basic techniques and skills to operate in this enhanced biocontainment laboratory. In particular, the participants were trained to acquire knowledge on maintaining biosafety precaution at all times, use of personal safety equipment (use of surgical musk and N95 musk, use of face shield/ goggles,donning-doffing of personal protective equipment (PPE)), sample collection techniques from nasopharyngeal/ throat site, molecular detection using SARS-CoV-2 reagents and real-time instrument for SARS-CoV-2 RNA & reporting, safe waste disposal and regular decontamination, and maintenance of the instruments and laboratory as a whole. During practical training, all participants voluntarily worked and were regularly monitored for the reliability and quality of the COVID-19 result generated by them. A standard operating procedure described in short by flow charts was kept at the working bench and was maintained by all laboratory personnel during work.

*Selection of the laboratory place*

To avoid interaction between suspected COVID-19 patients and non-COVID-19 patients, a completely separate building from the main university campus was selected for the establishment of a fever clinic along with COVID-19 Laboratory (Figure 1). It is an old building, known as the proposed BSMMU administrative block (former Betar Bhabon, Bangladesh Betar). The laboratory section was placed at the corner end of the 1$^{st}$ floor of the building, which is free of any people movement. A designated sample collection area for COVID-19 testing was placed on the ground floor along with the fever clinic rooms. Several sample collection booths were set up to reduce crowding in the area

Figure 1: The Four-storied building in which COVID-19 laboratory is located.

### *Laboratory equipment*

In the beginning, all the minimum necessary items and equipment was listed, and the required equipment were provided by CMSD, DGHS, and University Authority. Few other equipments were purchased directly from the local vendors as per the specifications. The start-up equipment consisted of a single Real-time PCR (now two in number), Biosafety Cabinet (BSC) Class II (now two in number), a PCR cabinet, Dry shaking heating block, vortex mixer, refrigerated centrifuge, 2-8°C refrigerator, -20°C freezer. After the installations of the Real-time PCR and BSC Class II, the instruments were duly calibrated and certified by the local expert. Additionally, the personal safety equipment was delivered by both DGHS and University hospital office, and few consumables were purchased from the local market.

*Facility Designing and laboratory Infrastructure*

The area for the laboratory section was divided into stationary storage and donning area, specimen handling and work area, amplification room, doffing and decontamination area. Open space with outside communication was in use for report delivery purposes. Every step was taken considering that good microbiological laboratory practices (GMLP) and standard precautions could be maintained at their best (Figure 2).

Sample processing room was equipped with two biosafety cabinets, BSC-II (Class II), and one PCR cabinet. BSC-II was dedicated for sample processing and acts as a primary containment device, whereas the PCR cabinet was for master mix and 96 well PCR reaction plate preparation. Heat block and vortex mixture machine were placed inside BSC-II to avoid contamination through aerosol generation while processing samples. Due to space constraints, the centrifuge machine was placed outside BSC, but proper precaution was in practice following the guidelines for infectious materials handling procedure. The sample processing room was also equipped with a refrigerator and freezer to preserve samples and PCR kit and, several biohazard waste bins were kept to discard waste material for further decontamination. Upon receiving samples, they were taken directly to BSC-II for marking, and then samples were being processed accordingly. Specimen collection processes were followed as per the SARS-CoV-2 detection kits instructions. While working in this section, all the laboratory personnel wore full PPE safety gear as per the IPC protocol, and their duration of stay was restricted to four hours to avoid any kind of accidental incident for working for a longer duration. Both before and after the work, regular cleaning and decontamination were done, and ultraviolet light was installed and turned on for 10 minutes as a part of the room decontamination process (Figure 3).

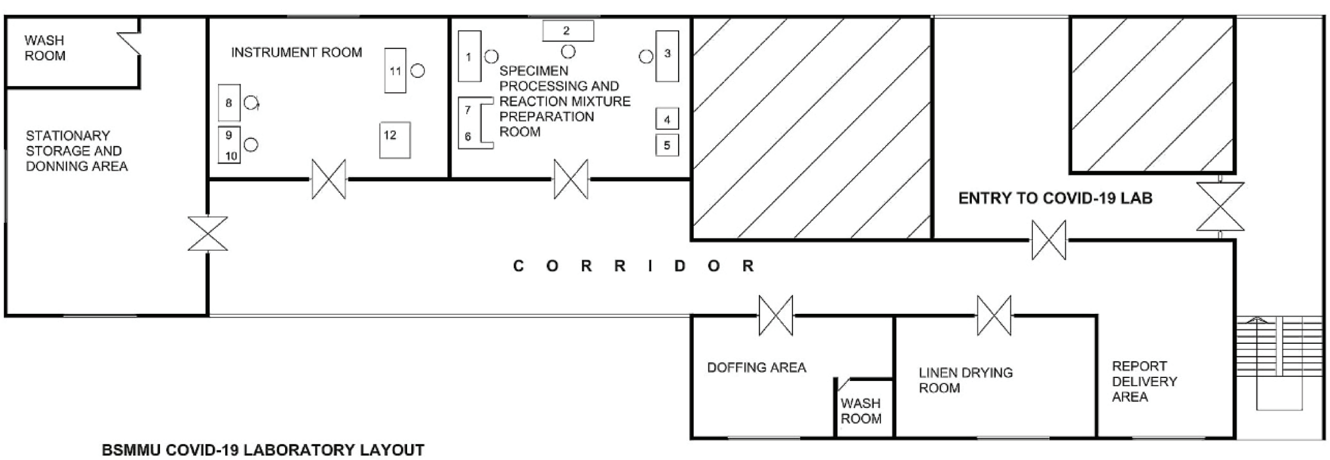


Figure 2: Architectural design and equipment at the BSMMU COVID-19 laboratory.

- Specimen processing and reaction mixture preparation room: biosafety cabinet Class II [1, 2], PCR cabinet [3], refrigerator [4], -20 OC freezer [5], refrigerated centrifuge [6], water bath [7]
- Instrument room: Real-time PCR and accessories [8, 9, 10], GeneXpert [11], computer [12]

Figure 3: Specimen processing and reaction mixture preparation room.

The processed samples prepared in 96 well PCR rack from the sample processing room were transferred to the amplification room, which is a clean zone with a separate entry door. Transferred processed samples in PCR tubes from the working room were placed directly into real-time PCR instrument. At the end of each PCR run, the amplification curve was analyzed as per the manufacturer's instructions, and the results were noted as per the sample identification number. In this section, laboratory members used to practice BSL II level protection, and at the end of work, the room was also decontaminated by turning on the UV light for 10 minutes. Results from daily COVID-19 testing were uploaded into management and information system software dedicated for COVID-19 maintained by DGHS and the individual's result was notified to them via a text message. System generated report can also be downloaded using a web-based link under DGHS, MOHFW.[15]

*Biosafety precaution during doffing and laboratory waste disposal plan*

The doffing area in our laboratory is a separate room with a washroom and decontamination facility. We have arranged a separate biohazard bag for each person in the doffing room with a supply of chlorine spray, 70% ethyl alcohol, disposable gloves, and a medical mask. After completing doffing by following the biosafety protocol, each lab worker seals their biohazard bag and keeps it in an isolated corner for further decontamination by incineration method according to University Hospital protocol. Additionally, a room beside the doffing room was used for linen and re-usable/ washable gown/linen drying. Thus, the anterograde working flow was maintained and good microbiological laboratory practice (GMLP) according to IPC protocol was practiced. All the laboratory wastes generated during this procedure were also sealed in a biohazard bag and disposed of similarly. Here, consumables after use were decontaminated in 10% hypo-chloride solution before being sealed in the biohazard bag.

## Discussion

A great concern when working with a high-risk pathogen like SARS-CoV-2 was to follow infection prevention and control guidelines (IPC) during sample collection, laboratory testing up to waste management. This level of containment is needed to protect laboratory personnel from the risk of infection and prevent the spread of pathogens in the environment.[16] After paying close attention to several laboratory biosafety and practice guidelines[17], on setting up a biosafety laboratory, a well-equipped Biocontainment facility consisted of facility designing, installation of safety equipment's and strict laboratory practices & techniques with the implementation in appropriate biosafety measures were taken. In this pandemic, detection of SARS-CoV-2 RNA was conducted in an enhanced BSL-II laboratory using real-time RT-PCR as per the guidelines. All the laboratory procedures were performed following the standard precautions, and decontamination of waste through the autoclaving method and other measures were done according to the standard waste disposal plan.[18]

Despite our endless effort, we faced quite a few challenges for the ongoing continuation of this high biocontainment infrastructure. The major drawback was that the placement of the COVID-19 laboratory was temporary and we had to compromise with limited space with a weak biosafety chain. Due to its old building structure, we did not get enough time to convert it to a negative pressure sample processing room. So, we had to take the challenge of maintaining the acceptable safety standard and practices. Another major issue was the low number of manpower supporting the activities. Though the laboratory is supervised by University faculties and staff, many of the members were attached from Government and project-linked support temporarily. Additionally, many members also had volunteered in the working process. The absence of monthly stipend/overtime payment failed them to continue service for a longer period. So, rapid turnover of the staff may hamper the ongoing services of the laboratory. As this pandemic situation is new to everyone, any new member added to the facility should be trained properly to avoid any laboratory-associated/acquired infections.[19] Another important challenge to make the laboratory sustainable is continuing funding and supply chain management. The ongoing running and maintenance of an enhanced BSL II laboratory are expensive and complex, and they require real technical expertise.[20] We do not have any clear priority settings neither from the university nor country policy as to how long this service needs to continue as the pandemic is still ongoing and cannot assume as to how long it might continue. But as days pass, this may result in low financing and delay in infrastructure development and equipment maintenance as the flow of funding gets delayed and instruments may go out of order due to overrunning as the number of patients has increased. Strategic framework and goal settings by the government are necessary to ensure continuous and sustainable availability of the resources to maintain the timely procurement and supply chain management. Uncertainty of the continued financial support may cause difficulty in laboratory operation. Immediate robust planning and budget allocation with a quick release of the fund are necessary when required by the authority to maintain such facilities.[21] Thus, these challenges can be overcome by creating a collaborative, goal-directed partnership with several national bodies and persons having expertise in infectious diseases, biosafety, and bio engagement program.

## Conclusion

A global crisis like COVID-19 has posed an insurmountable challenge in the health sector of the whole world not only in Bangladesh. But our experience has taught us that it can be overcome by appropriate ideas and intervention feasible to local set up. The establishment of an enhanced BSL II level laboratory in this pandemic was very challenging for the department of Virology, BSMMU, due to lack of prior experience to work with respiratory pathogens as well as due to lack of financial affluence. However, with a concerted effort, we overcame most of them despite several shortcomings.

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## Conflict of Interest

Authors declare no conflict of interest

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