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Review Article

COVID-19 and the clinical chemistry laboratory: experience from a dedicated COVID-19 laboratory

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ABSTRACT

The ongoing coronavirus disease 2019 (COVID-19) pandemic has presented major challenges to health care workers including laboratory professionals. Clinical laboratories play a critical role in this challenging environment by providing information to clinicians regarding prognosis, disease severity, and response to therapy apart from the diagnosis of COVID-19. Clinical chemistry laboratories inhabit central role in the management of COVID-19 through assessing the biochemical and inflammatory profile. It has been emphasised by many health organisations that health care workers are at high risk with COVID-19 outbreak. Sharing and updating of personal experiences regarding the laboratory safety is essential to minimise the risk of laboratory personal working in this crisis. Hence, in this review article, we documented our experiences in setting up a dedicated COVID-19 clinical chemistry laboratory and the biosafety aspects followed in our setup. This review article will provide information to clinical biochemists and laboratory professionals to establish a safety laboratory environment during this COVID-19 pandemic.

1. Introduction

Coronavirus disease 2019 (COVID-19) which is declared as a global pandemic by the World Health Organization (WHO) is the third corona virus outbreak in the last 20 years, after severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[1,2] Although initial reports claimed that COVID-19 infection is less severe than SARAS, the recent epidemiological and clinical reports clearly shows COVID-19 is severe. WHO reported 17,918,582 confirmed cases of COVID-19 including 6, 86,703 deaths till 4th August, 2020 and in India, it was 18, 55,745 confirmed cases with 38,938 deaths. Early diagnosis, isolation of positive cases and treatment with appropriate treatment protocol are the global strategies to tackle this COVID-19 pandemic.[3,4] Diagnostic laboratories play an important role in the above approaches in early diagnosis, risk assessments and managements.

It has been emphasised by many health organisations that health care workers are at high risk with COVID-19 outbreak.[5] It is documented that 10.7% of healthcare workers among the total number of COVID-19 patients are infected.[6] This alarming figures prompted us to make guidelines for bio safety procedures to protect health care workers including laboratory personnel. Infection and quarantine of health care workers cause additional burden to health care services due to shortage of manpower. Though, clinical chemistry laboratory and biochemical parameters are not directly involved in the diagnosis of COVID-19, they play a vital role in evaluating disease severity, co-morbidity and prognosis in COVID-19 management.[7,8] World Health Organisation (WHO), International Federation of Clinical Chemistry (IFCC) and Indian Council of Medical Research (ICMR) have given many guidelines in safety aspects for laboratory personnel to minimise the risk in the laboratory.[9,10] However, updates and sharing of personal experiences are always required to enrich our knowledge on this aspect. Hence, in this review article we documented our experiences in setting up a dedicated COVID-19 clinical

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chemistry laboratory and the biosafety aspects followed in our laboratory. This article will be helpful to establish or to improve the biosafety aspects of clinical chemistry laboratories involved in COVID -19 battle.

2. Importance of Clinical Laboratories and Biochemical Parameters in COVID-19 Management

The clinical laboratories play a crucial role in assessing severity of disease, choosing the suitable treatment options and monitoring the response in addition to diagnosis of COVID-19. Though the nucleic acid amplification tests (NAATs) carried out by virology/molecular biology laboratories are currently the gold standard for diagnosing suspected cases of COVID-19,[11] management of patients mainly depends on haematological, inflammatory and biochemical parameters.[12,13] The biochemical and inflammatory parameters assayed by clinical chemistry laboratories help the clinicians in their decision making and assessing response to their treatment.

The routine biochemical investigations like blood glucose, urea, creatinine and electrolytes are required to assess the co-morbid conditions such as diabetes mellitus and renal dysfunction in COVID-19 patients. The arterial blood gas analysis (ABG) is the crucial biochemical investigation required for the risk assessment and management of COVID-19 patients. Assay of inflammatory markers such as ferritin, C-reactive protein (CRP), interleukin (IL) 6, fibrinogen and myoglobin are the indices of so called cytokine storm in COVID-19 patients. These markers support clinicians in risk assessment, titration of drug doses and assessment of disease prognosis. Cardiovascular dysfunction in COVID-19 patients due to viral myocarditis or cytokine driven myocardial injury is assessed by the assay of lactate dehydrogenase (LDH), creatinine kinase (CK) -MB, natriuretic peptides and cardiac troponin I (cTnI). Though, hepatic injury in COVID-19 patient remains ambiguous, numerous studies have shown elevated transaminases levels in COVID-19 patients. Nevertheless, it is important that liver function should be assessed for those who are on antiviral treatment. It is obvious that the biochemical parameters and inflammatory markers estimated by clinical chemistry laboratories play a crucial role in risk assessment, drug selection and titration and monitoring the response to the treatment in COVID-19 patients.

3. About Our Hospital and Clinical Chemistry Laboratory

Indira Gandhi Medical College and Research Institute (IGMC&RI) is located in Puducherry UT, India. This Government medical college, functions with 18 speciality. The Government of Puducherry declared, IGMC&RI as a dedicated COVID-19 hospital to manage the COVID-19 pandemic. The diagnostic divisions of this medical college hospital is comprising of clinical biochemistry, pathology and microbiology laboratories. The department of microbiology established the Viral Research and Diagnostic Laboratory (VRDL) under ICMR, Ministry of Health & Family Welfare, and Government of India. The pathology laboratory functions with its divisions comprising of haematology, histopathology, cytology and blood bank.

The clinical biochemistry laboratory which functions 24X7, performs average 1800 tests per day. Clinical Biochemistry laboratory is equipped with fully automated clinical chemistry analysers (AU480-Beckmen Coulter Ltd& EM200-Transasia Bio-Medicals),Semi automated clinical chemistry analysers (Chem5X- Transasia Bio-Medicals & Prietest-Robonik India pvt ltd), Arterial Blood Gas Analysers (Cobasb121-Roche Diagnostics&i- STAT-Abbort Rapid Diagnostics), Electrolyte Analyser (ISE Acculyte – Compact Diagnostics) and semi-automated coagulometer (ACT- 4 channel - Compact Diagnostics). The administrative and technical supervision of our clinical biochemistry laboratory is managed by faculty members and tutors of the department. The reliability of the laboratory results is ensured by the internal quality control (BIO-RAD) and participation in the External Quality Assurance Scheme, Christian Medical College Hospital (CMC), Vellore, India.

4. Dedicated COVID-19 Clinical Chemistry Laboratory

As a dedicated COVID laboratory, all appropriate measures were taken while setting up the laboratory to prevent infections from the infectious materials and onward transmission. The routine clinical chemistry laboratory was transformed into COVID laboratory with two zones (Figure 1). Both the zones are designated as infectious and only laboratory personnel with the necessary protective equipments are permitted into these zones. The orange zone (infectious area) is consisting of entrance, staff room, donning room and wash room. The red zone (highly infectious area) is comprising of reception cum despatch, analytical area and doffing room.

The laboratory staffs posted on duty are entering into staff room through the entrance. The staff room is provided with an intercom, hand wash facility and very limited furniture. The laboratory personnel are instructed to switch off the air-conditioner in the staff room, keep the windows open and maintain the social distancing. After washing their hands with soap, they are entering into donning room. Only two persons are permitted inside the donning area at a time, where the required protective equipments are arranged sequentially. They are all well trained in donning and doffing Personal Protective Equipments (PPE) and Standard Operating Procedure (SOP) displayed in the donning room.

With PPE they are moving to the reception area, where the samples are received. The samples are taken inside the

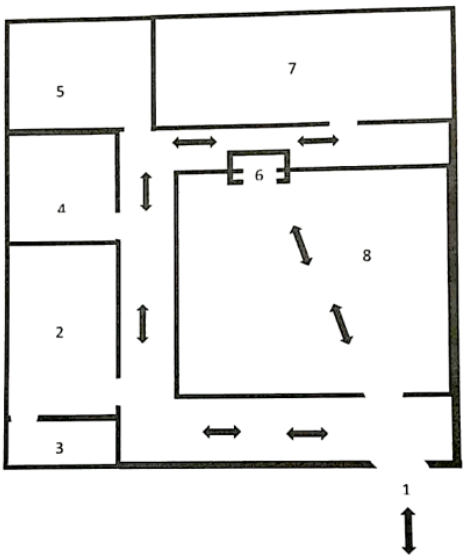

Fig. 1: Floor map for COVID clinical laboratory

1- Lab entrance, 2- Staff room, 3- Rest room, 4- Donning room, 5- Doffing room, 6-Reception cum Despatch, 7- Analytical area, 8- Atrium
1,2,3,4 & 8 are designated as yellow zone (Infectious area);
5,6 & 7 are designated as red zone (Highly infectious area).

analytical area, after making entry in the register. Samples are disinfected and analysed inside the analytical lab as described below. The reports are kept in the registration desk for despatch then they are moving to the doffing area for the removal of PPE. After removing PPE they are entering into the staff room where they wash their hands and Wash (Rest) room is also in the vicinity of staff room so, they can take bath. Alcohol based hand sanitizer (WHO-formulation 2), 1% Lysol, 0.5% hypo solution, cotton and tissue rolls are kept in the staff room, donning room, doffing room and analytical area. Intercoms were removed from the laboratory except staff room to prevent cross contamination and infection. Dust bins with double layered yellow covers, sprayed with 1% Lysol are kept in the staff room, reception, analytical area, doffing room and rest room. Disposable pens are kept in the reception and analytical area and these pens are discarded after every shifts. Instruments which are not required for the analysis of COVID-19 parameters (eg. Hot air oven, pH meter, electronic balance, cyclomixer, etc..), backup instruments and furniture were removed from laboratory.

5. Biosafety Practices, Trainings and Standard Operating Protocols

As soon as it was declared as a dedicated COVID hospital by the Government, the laboratory staff were called for a meeting and sensitised to the COVID-19 disease, its pathogenesis, transmission, symptoms etc.,. The technicians were motivated to become confident and courage as many of them were initially scared to work in a COVID laboratory. The laboratory personnel were explained about the steps taken by the department to ensure their personal safety and protection against the infection. The importance of clinical chemistry laboratory and biochemical investigations in the management of the patients with COVID-19 was also explained to them.

Training programs on donning and doffing of PPE and Do's and Don'ts in the COVID laboratory were conducted to the laboratory personnel. They were also explained in detail about setting up of COVID laboratory, their movements with in different zones of the lab and activities in the zones. Besides, the training programmes were video recorded and sent to the laboratory personnel to watch as and when required. SOPs were prepared for hand washing, donning and doffing of PPE, sample collection, transportation, receiving, analysis, dispatch of reports and decontamination of waste. These SOPs were demonstrated to the laboratory personnel and the laminated copies are kept in the respective areas.

The laboratory personnel were instructed to use the rear side entrance and the main entrance of the hospital is exclusively for the patients. They were instructed to come for duty with minimum requirements and advised to avoid watch, hand bags, food and water. Eating, smoking, storing food and application of cosmetics in the laboratory are strictly prohibited and 300 ml disposable water bottle is supplied. Drinking of water is permitted only in the staff room not in the other areas of the laboratory.

Roster was divided into four shifts with each 6 hours. 1^{st} shift is from 8.00 AM to 2.00 PM, 2^{nd} shift is from 2.00 PM to 8.00 PM, 3^{rd} shift is from 8.00 PM to 12.00 PM and the 4^{th} shift is from 12.00 PM to 8.00 AM. One technician and one lab attender are posted for each shift and the technicians are provided with complete PPE which contains, cover all, N95 mask, goggles, hood (head cover) and shoe cover. The lab attenders are provided with N95 mask, face shield (prepared by the department with OHP sheets), surgical disposable gown, hood and shoe cover. The N95 masks are reused thrice with the gap of 72 hours between the subsequent use. Weekly roster for the laboratory personnel is prepared with 6 hours for each shift and after completing one week duty they are given 14 days quarantine. Pregnant woman, immune comprised and other high risk group for COVID-19 are not posted for laboratory duty and their service is utilised for purchase of reagents, intending the laboratory requirement, maintenance of stock and statistics, etc., in the department. Faculty of the department are in coordination with the personnel posted in the laboratory over intercom and mobile phones. Besides, the faculty are visiting the laboratory as and when required with appropriate protective equipments. In case of any break

down of instruments, service engineers are called and they are provided with PPE to attend the breakdown.

After every shift, the work surfaces and pipettes were cleaned with hypo solution. Any spillage of samples is immediately cleaned with hypo and the same is informed to the next shift lab staff to take necessary precautions. Every morning, first shift begins with the cleaning of floor and working area of the laboratory and disposal of waste from the instruments.

6. Sample Collection and Transportation

Samples for the various biochemical investigations are collected from emergency ward, isolation ward, COVID ward and ICU. Samples are collected in primary tubes either by duty doctor or staff nurse posted in these wards with PPE. The samples are collected in a clot activator serum tube (BD Biosciences-Red cap) for routine biochemical investigations like glucose, urea, creatinine, electrolytes, ferritin and LFT. Sodium citrate (3.8% w/v) tubes are used for the estimation of fibrinogen and prothrombin time (BD Biosciences-Blue cap). Pre-lithium heparinised syringe (23 gauges) are used for collecting ABG samples.

The primary tubes and requisition forms for the biochemical investigations are legibly filled by the ward staff with complete details like name, age, sex, ward, patient ID and COVID POSITIVE/SUSPECT etc. The primary tubes are placed in a plastic centrifuge tube (secondary container) and kept in the Zip-lock bag to minimise the hazardous due to breakage or spill. Further, these (primary & secondary) containers are kept in a large plastic box (bread box), labelled as biohazard and COVID suspected/confirmed.

The labelled large plastic box and filled up requisition forms are handed over to the lab attender posted for the transportation of sample to the biochemistry laboratory. Delay in transportation of samples and analysis (especially for ABG) is avoided by coordination between the staff in the ward and the technicians in the lab in order to ensure the availability and working condition of the instruments.

7. Receipt of Samples

Sample collected from the different wards by the attenders are handed over to technicians at the reception area. The technician on duty with PPE receive the samples and check for the labelling of samples, information in the request form and any spillage of samples. If any mismatch or discrepancy in sample labelling and requisition form, it is clarified or sample is rejected accordingly. In case of haemolysis, inappropriate collection of blood etc. . . repeat samples are asked from the ward for the rejected samples. The details of the samples received are entered into the register kept in the registration area. A duplicate request form is prepared by the technician and the original is discarded to prevent cross contamination.

8. Disinfection and Analysis of Samples

Samples are disinfected before they are analysed. The primary tube which contains the sample is disinfected with 1% Lysol and then the tube is placed in a UV cabinet for 20 minutes for disinfection of the sample. The sample is kept for 30 minutes for serum separation. As recommended by IFCC, the aerosol generation procedures like centrifugation is avoided where ever possible. The syringes containing ABG samples is disinfected with 1% Lysol and analysed immediately.

9. Decontamination of Samples and Waste

The liquid waste containers of ABG analyser, auto analyser and PT analyser are filled $1/3^{rd}$ of the volume with 0.5% hypo solution. The primary tubes, reaction tubes/cups, tips and syringes are discarded in the dust bin (Lysol sprayed-double layered yellow polythene cover). The PPE used are discarded in the dust bin kept in the doffing area. These wastes are autoclaved and handed over to the waste management department of the institute for incineration.

10. Conclusion

In summary, clinical chemistry laboratories are contributing to the risk evaluation, management and assessment of prognosis in COVID-19 patients by investigating various biochemical and inflammatory markers. Though the laboratory professionals are at the risk of infection, training and adopting the recommended biosafety measures are indispensable to minimise the risk during this pandemic. We are optimistic that sharing of our experience in setting up COVID laboratory will benefit the laboratory professionals to create a safety laboratory environment and better patient care services.

11. Conflict of Interest

None.

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