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Management of COVID-19 Related Paediatric Blood Samples in a Clinical Haematology Laboratory

Running Title: Management of COVID-19 Related Paediatric Blood Samples

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There is currently limited knowledge about the transmission risks of the SARS-CoV-2 virus and its associated disease COVID-19 from routine clinical specimens. The first study to be published on the initial 41 cases of COVID-19 infections admitted in Wuhan detected SARS-CoV-2 RNA in the blood of 6/41 (15%) of patients (Huang *et. al*., 2020) . However, another study conducted on 1070 clinical specimens collected from confirmed COVID-19 patients in China showed the highest positive rates of SARS-CoV-2 from rRT-PCR testing of respiratory specimens such as bronchoalveolar lavage, sputum and nasopharyngeal swabs (32% - 93%). In contrast, only 1% of blood specimens and none of the urine specimens tested positive (Wang et. al., 2020). Although the rates of viraemia appear to be low, it nonetheless poses a risk of potential respiratory transmission to laboratory staff via aerosolization of blood specimens during specimen processing steps such as centrifugation and vortexing. Paediatric specimens pose a particular challenge as automated analysers cannot handle small volume samples from paediatric-sized tubes, necessitating manual handling of specimens. The Haematology Laboratory at the Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital processes over 130 000 paediatric samples annually. Our laboratory received the first sample from a suspect COVID-19 patient on 22 January 2020 and processed samples from a confirmed COVID-19 patient on 5 February 2020. From January to March 2020, we processed approximately 1700 samples from paediatric patients with suspected or confirmed COVID-19 infection. In this paper, we describe the specimen management policy for handling and processing COVID-19 related blood samples in our laboratory, and highlight the challenges of working with paediatric samples during this period.

Materials and Methods

Risk Assessment

Our laboratory had existing biosafety guidelines for specimen management from patients with emerging respiratory pathogens (SARS-CoV and MERS-CoV). In early January 2020, the Ministry of Health in Singapore alerted healthcare practitioners of the emergence of a novel respiratory infection in Wuhan (Wong *et. al*., 2020) . Following the announcement, we performed a series of risk assessments based on identification of potential hazards and available laboratory equipment and facilities. Our guidelines were regularly reviewed when documents from the Ministry of Health, Singapore (Ministry of Health, Singapore, 2020), World Health Organization (WHO) (World Health Organization, 2020) and the Centres for Disease Control and Prevention (CDC) (Centres for Disease Control and Prevention, 2020) relating to laboratory biosafety when handling COVID-19 specimens became available. We reviewed each test offered in our laboratory and made the decision to either require consultations with the laboratory haematologists for tests with a higher risk profile or not to offer tests which could not be performed safely based on our risk

assessments (Table 1). We redesigned the laboratory workspace such that dedicated analysers closest to the Class II biological safety cabinet (BSC) were used for COVID-related specimens in an area separated from the rest of the laboratory.

Use of Appropriate Paediatric Tubes for Specimen Collection

Prior to the COVID-19 outbreak, paediatric blood specimens were collected in Becton Dickinson (BD) Microtainer EDTA microtubes. However, this required open mode sampling on the Sysmex XN-1000 analyser in use at our laboratory, and would have subjected staff to the risk of aerosol exposure. We had previously performed a validation study using the BD Microtainer MAP (Microtube for Automated Process) Microtube, which is an alternative collection tube with a membrane cap allowing automated sample piercing and analysis without cap removal. Early on in the outbreak, a decision was made to switch specimen collection tubes to the MAP Microtube, avoiding the need to manually handle specimens in open mode. Paediatric blood samples for coagulation assays are collected in 3.2% sodium citrate Greiner Bio-One MiniCollect® 9NC tubes. Although the tube has a membrane cap allowing for automated closed mode analysis, the coagulation analyser in use at our laboratory (STA Compact Max) is not equipped with the optional cap-piercing system. **Specimens for blood gas analysis are collected in heparinized syringes (Becton Dickinson (BD) A-Line™ Blood Gas Analysis Syringe).**

Transport and Labelling of COVID-Related Samples

Even before receiving specimens in the laboratory, close communication with clinical areas is essential to ensure safe transport and appropriate labelling of specimens. At our institution, a Disease Outbreak Task Force (DOTF) was set up to coordinate management of suspect and confirmed COVID-19 patients, with representation from the laboratory to design protocols and communicate updates around laboratory-related issues. Specimens had to be double-bagged, labelled appropriately as COVID-19 related specimens and hand-delivered to the laboratory to avoid loss or misplacement of specimens. The pneumatic tube system was not used due to the risk of specimen loss and spillage.

Personal Protective Equipment

As there were limited supplies of face shields in our institution, a decision was made by hospital management to reserve the use of face shields for clinically high-risk situations, for example procedures involving suctioning of patients with confirmed COVID-19 infections. When handling and processing COVID-19 related blood samples **in the laboratory**, all staff must don personal protective equipment (PPE) including laboratory coats, disposable gloves, surgical masks and safety googles **which provide a good**

alternative for protection of the face and mucous membranes. All staff are reminded to practice good hand hygiene after processing samples and before leaving the laboratory. **This policy applies round the clock.**

Specimen Handling and Analysis

All COVID-related specimens are initially handled in the Class II BSC. Samples are carefully removed from specimen bags and manually disinfected with Mikrozid®AF (94% Ethanol) wipes with a minimum contact time of 2 minutes. Samples for full blood count are loaded directly into the dedicated Sysmex XN analyser located just beside the BSC. Blood films are manually prepared in the BSC and fixed in 100% methanol for 15 minutes before automated staining by a Hematek stainer. Samples sent for coagulation assays are decapped in the BSC and checked for clots with applicator sticks. The samples are centrifuged using a STI PlasmaPrep centrifuge located within the BSC. Plasma is then aliquoted into Eppendorf tubes which are packed in a clean biohazard bag and hand-carried to the STA Compact Max coagulation analyser for analysis. A splash guard was installed beside the analyser for safe opening of the Eppendorf tubes which are then loaded into the sample drawer of the analyser. **Point-of-care testing for blood gases in paediatric patients at our institution is handled mostly at clinical areas by staff in appropriate PPEs using I-Stat devices (Abbott Laboratories). However, specimens for blood gas analysis which includes measurement of the haematocrit (Table 1) can also be analysed in the laboratory using the CG8+ cartridge on the I-Stat device, with all analysis performed within the BSC.**

Specimen Disposal and Waste Management

All consumables used during processing of COVID-related samples are immediately discarded into the original specimen bags, double-bagged and disposed into a biohazard waste bin. When testing is completed, all specimens are double-bagged with new biohazard bags and stored in a locked container for 3 days before disposal in the biohazard waste bin. When a suspect patient tests positive for COVID-19 from rRT-PCR of respiratory samples, the Haematology Laboratory is informed by the Molecular Microbiology Laboratory within the same laboratory service. Samples from the patient are retrieved and autoclaved the next working day before disposal. Work surfaces inside the BSC are disinfected with Mikrozid® AF wipes after each use. **The Sysmex XN analyser is decontaminated daily with a proprietary 5% sodium hypochlorite solution (CellClean™) when performing daily maintenance and shutdown procedures**. The Stago Compact Max analyser is decontaminated weekly with a higher strength of sodium hypochlorite (0.5%) using the routine maintenance protocol. Biological liquid waste from both analysers are decontaminated with 5% sodium hypochlorite for at least 30 minutes before disposal.

Discussion

The management of COVID-related specimens from paediatric patients poses unique challenges. Samples from children need to be collected in small volume tubes, which may not always be suitable for automated analysis by analysers. Repeated blood sampling is also a challenge in young children, necessitating upfront discussion between clinicians and the laboratory haematologist as to the timing and availability of tests, so that repeated blood-taking procedures are minimized. It is now recognized that children with COVID-19 infections present with less severe symptoms compared to adults, with a case series of more than 2000 children reporting that 13% of confirmed cases were asymptomatic (Dong *et. al*., 2020). A 6-month old infant with confirmed COVID-19 infection identified through family screening remained asymptomatic despite detectable viraemia (Kam *et. al*., 2020). Compared to adults, clinical identification of potential COVID-19 infected children may not be as obvious, adding to the risk of laboratory staff unknowingly handling a blood sample with SARS-CoV-2. This is why we have reiterated to staff in our laboratory on the need to adhere to standard precautions for all samples, including the use of personal protective equipment such as laboratory coats, surgical masks, gloves and fastidious attention to hand hygiene. In this letter, we have shared our experience and challenges with management of COVID-19 related blood specimens from paediatric patients, and hope that this can serve as a guide for other laboratories who need to handle similar specimens.

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Table 1: List of Haematology and Coagulation Tests Offered in the Haematology Laboratory at KK Women's and Children's Hospital

Test	**Specimen Type**	**COVID-19 Status**	
		Suspect	Confirmed
Full Blood Count	Whole blood in EDTA	Test performed with use of enhanced biosafety practices	
Peripheral Blood Film	Whole blood in EDTA		
Coagulation assays Prothrombin time (PT) Activated partial thromboplastin time (APTT) International normalized ratio (INR) Thrombin time (TT) Fibrinogen Anti-Xa assay	Whole Blood in 3.2% sodium citrate		
Blood Gas Analysis on I-Stat Parameters assessed: Sodium Potassium Ionized Calcium Glucose Haematocrit pH PCO_2 PO_2 TCO_2 HCO_3 Base excess	Heparinized syringe	Test performed with use of enhanced biosafety practices	

Erythrocyte Sedimentation Rate (ESR)	Whole blood in EDTA	Discuss with Laboratory Haematologist[1]	Tests NOT performed[2]
Haemoglobin (Hb) Electrophoresis	Whole blood in EDTA		

[1] Clinicians are to discuss the clinical urgency of these tests, and if possible to defer testing or to consider alternative tests until patients are tested negative for COVID-19.

[2] ESR and Hb electrophoresis tests are not performed for confirmed COVID-19 patients as testing involves open centrifugation and aspiration systems which are deemed to be high risk for aerosolization of samples