Clinical Profile and Outcomes of Coronavirus Disease 19 (COVID-19) Patients who Underwent Hemoperfusion (HP) in a Tertiary COVID-19 Referral Hospital: A Descriptive Study

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ABSTRACT

Introduction. As of February 4, 2021, a total of 530,118 COVID-19 cases were recorded in the Philippines with a fatality rate of 2.1%. Significant morbidity from COVID-19 is caused by hyperinflammation. Hemoperfusion (HP), which adsorbs inflammatory cytokines, has been performed in the Philippine General Hospital (PGH) as an adjunct to management given to COVID-19 patients.

Objectives. This study aimed to describe the clinical and laboratory profile, ventilatory support, therapeutic regimens, and outcomes of COVID-19 patients who underwent hemoperfusion in PGH.

Methods. The COVID-19 patient electronic database (April to September 2020) of the Division of Nephrology was reviewed and we included patients with COVID-19 who underwent hemoperfusion. Demographic, clinical, and laboratory data as well as therapeutics and outcomes were described.

Results. Sixty-six patients with COVID-19 underwent hemoperfusion. The majority were male (59.1%) with an average age of 61.3 years (SD 15). Hypertension was the most common comorbidity (62.1%). Acute kidney injury (AKI) requiring dialysis comprised 28.8% while 33.3% had diagnosed chronic kidney disease (CKD). The majority were critical COVID-19 cases who had acute respiratory distress syndrome (ARDS) (56.1%). The mean baseline inflammatory marker levels (Il-6, CRP, LDH, ferritin) were elevated. Post-HP inflammatory markers decreased except for IL-6 among patients who died. Most patients were mechanically ventilated (54.5%). Steroids were the most common medications administered (71.2%). Mortality occurred in 62.1% of the patients. The average length of hospital stay was 20.8 days (SD 19.5), duration from admission to first HP 5.9 days (SD 5.8), and 15.3 days (SD 17.4) from first HP to death or discharge.

Conclusion. Our study showed the characteristics of patients with COVID-19 who underwent HP. Majority were hypertensive men in their early 60s with critical COVID-19 disease. The mean inflammatory markers were elevated with a decrease in most markers post-hemoperfusion (except for IL-6 among those who died). Despite this, mortality was still high and the average length of hospital stay was long.

Keywords: hemoperfusion, hemadsorption, blood purification, COVID-19

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INTRODUCTION

COVID-19 in the Philippines

Infection with severe acute respiratory coronavirus 2 (SARS-CoV-2), better known as COVID-19, has become a global pandemic. As of February 4, 2021, there was a total of 530,118 COVID-19 cases in the Philippines and the Department of Health (DOH) reported 10,942 deaths from COVID-19 with a calculated fatality rate of 2.1%.[1] In response, the Philippine General Hospital (PGH) was designated as a COVID-19 Referral Center on March 30, 2020, reporting a total of 2,689 admissions of COVID-19 confirmed, suspect, and probable cases as of February 4, 2021, and 476 deaths ever since its designation as a referral center.[2]

Hyperinflammation in COVID-19: The Cytokine Release Syndrome and Inflammatory Markers

High levels of pro-inflammatory cytokines are found in COVID-19 patients and this is thought to play an important role in its pathogenicity.[3] The intensity of the inflammatory response reflects a balance between proinflammatory cytokines and their receptors or inhibitors. Excess inflammatory cytokines have led to relative organ dysfunction and morbidity and mortality. This phenomenon is referred to as the cytokine release syndrome (CRS) or cytokine storm.[4]

The key inflammatory markers usually measured in COVID-19 are interleukin-6 (IL-6), C-reactive protein (CRP), and ferritin. Levels are characteristically increased in COVID-19 especially in the setting of CRS. A study involving 191 patients with COVID-19 hospitalized in Jinyuntan Hospital and Wuhan Pulmonary Hospital in China noted that the serum ferritin level was persistently higher among non-survivors compared to survivors.[5] A study involving 305 patients with COVID-19 in China found that elevated CRP had a significant positive association with in-house mortality.[6] In another study done wherein various inflammatory markers were measured and correlated with COVID-19 patient outcomes, IL-6 has been the one most associated with respiratory failure and the need for mechanical ventilation especially with values above 80 pg/mL.[7] Interleukin-6 values have also been used to monitor disease progression.[8]

Hemoperfusion as Adjunct Therapy

Hemoperfusion or hemadsorption is a blood purification technique that has been proposed to remove excess cytokines to blunt the effects of the cytokine storm such as in septic states.[9] It has also been used in life-threatening intoxication with drugs, elemental metals, and industrial toxins.[10] This is done using different resin pore sizes of a sorbent material inside a hemoperfusion cartridge which allows the removal of a wide spectrum of molecular weights. The cartridge is connected in series to an extracorporeal blood circuit (as in hemodialysis) to facilitate treatment. Compared to conventional hemodialysis, it does not significantly remove small molecules such as electrolytes nor does it aid in intravascular volume management. It can be used as an add-on therapy to hemodialysis especially when dealing with substance intoxication or sepsis.[11] The hemoperfusion cartridge used in the PGH is the MG 350 (BioSun Medical Technology Co., Ltd., China) which is made up of a polystyrene resin adsorbent. According to its product insert, it is capable of removing toxins, cytokines (IL-6, IL-8, TNF-α), bilirubin, beta 2 microglobulins, and other middle molecular-sized substances (500-5000 daltons) via adsorption.[12]

The largest randomized controlled trial on hemoperfusion was EUPHRATES in 2018, which concluded that in adult septic patients, there was no difference in 28-day mortality with hemoperfusion compared to standard therapy.[13] Because of this, hemoperfusion is not considered a standard of care in non-COVID septic states. There is no published RCT yet on hemoperfusion in COVID-19. Individual case reports showed improvement in patient outcomes in terms of oxygenation, IL-6 levels, and survival after hemoperfusion was used as an adjunct to standard of care.[14] A case series in Iran has documented ten COVID-19 patients who underwent hemoperfusion with improvement in inflammatory markers and oxygenation.[15] Whether these laboratory outcomes translated to better clinical outcomes cannot be concluded yet. Ongoing COVID-19 hemoperfusion registries in the USA using different hemoperfusion cartridges have been registered (NCT04391920, NCT04413955)[16,17] and may give us more information in the future.

The considerable burden of disease and high mortality caused by COVID-19 warrant exploring interventions to improve patient outcomes, particularly in severe and critical COVID-19 cases due to the limited interventions that can be given to these patients aside from standard of care. The paucity of data on hemoperfusion in COVID-19 and the lack of RCTs limit its use to adjunct to usual care especially if other therapeutics have already been exhausted. Hemoperfusion is one of the treatments given to patients with COVID-19 in PGH and to date, this will be the first study to describe a fairly large number of patients who underwent hemoperfusion with COVID-19 as an indication. This preliminary descriptive study aims to describe the clinical profile, laboratory profile, ventilatory support, therapy, and outcomes of patients with COVID-19 who underwent hemoperfusion in the PGH.

METHODS

This was a descriptive study that reviewed the COVID-19 patient electronic database of the Division of Nephrology from April 2020 to September 2020 (Figure 1). Data from all adult COVID-19 cases who underwent hemoperfusion was included in the study. Data were excluded

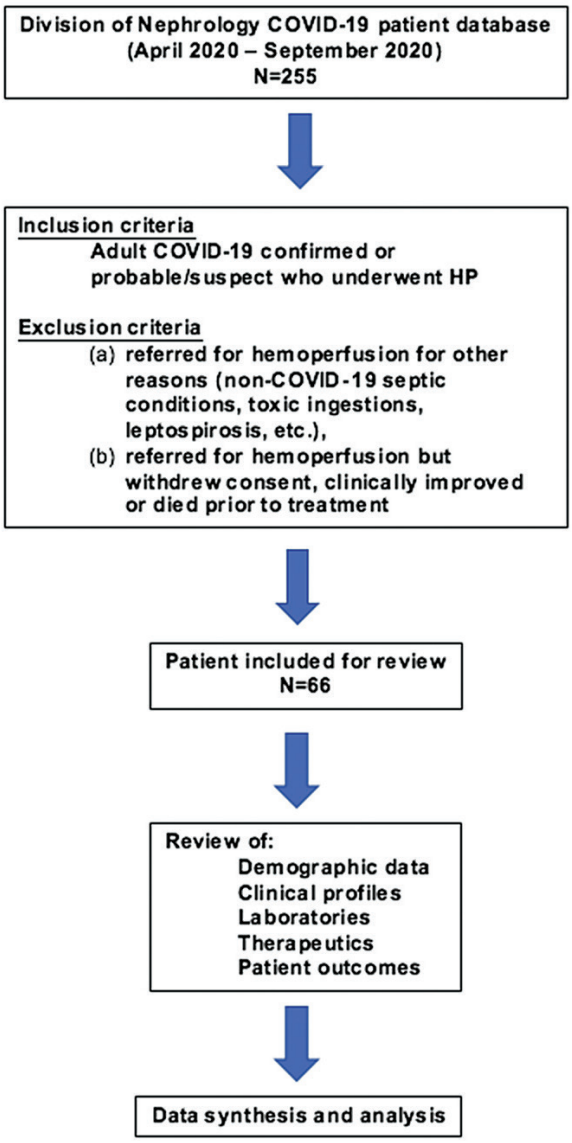

Figure 1. Study Framework.

if: (a) the patients were referred for HP for other reasons such as non-COVID- 19 septic conditions, toxic ingestions, leptospirosis, etc., (b) the patients were referred for HP but the procedure was not done due to withdrawal of consent, clinical improvement or died before treatment. We reviewed patient records and extracted the following information from the database: demographic and clinical profile of COVID-19 patients in terms of age, sex, COVID severity, medical co-morbidities, baseline/admission laboratories including inflammatory markers (IL-6, CRP, ferritin), oxygen support, other COVID-19 therapies (steroids, antivirals, tocilizumab, convalescent plasma therapy), length of hospital stay, time to admission and HP, time to HP and discharge/death, and patient outcomes.

The Division of Nephrology has released an HP protocol in COVID-19 for use in the PGH (Appendix). This document aimed to guide physicians in making decisions on whether they should refer patients to nephrology for hemoperfusion and was based on the April 2020 US FDA emergency use authorization for the use of hemoperfusion in COVID-19 patients.[18]

Indication(s) to hemoperfusion:

All patients, 19 years old and above, with confirmed COVID-19 disease and any one of the following conditions:

- Severe disease, defined as:
  - Dyspnea or RR ≥30 and/or
  - SpO_2 ≤ 93% and/or
  - Oxygenation PaO_2/FiO_2 ratio ≤ 300 mmHg not fully explained by volume overload (cardiac failure, renal disease, excessive hydration) and/or
  - Lung infiltrates ≥ 50% within 24-48 hours
- Life-threatening respiratory failure
- Septic shock

Contraindication(s) to hemoperfusion:

- Any pre-existing advanced medical disease with a life expectancy less than 1 month
- Treatment deemed clinically futile. Conditions which may include but are not limited to the following:
  - Cerebrovascular accident (CVA) with poor functional status
  - Post cardiopulmonary arrest
  - Malignancy ≥ stage 3
  - Advance care directives that include "do not intubate" (DNI) or "do not resuscitate" (DNR) status
- Patients with very low platelet counts (< 20,000/μL)
- History of heparin-induced thrombocytopenia
- Unable to insert vascular access for any reason (e.g., position, coagulopathy)
- Any pre-existing contraindication to extracorporeal therapy
- Known allergies to extracorporeal circuit components (polystyrene/divinylbenzene, polycarbonate, polypropylene, silicone, and polyester)

PGH Hemoperfusion Protocol

The HP protocol (Appendix) utilizes the MG 350 cartridge. After central vascular access is secured, the patient is connected to a dialysis machine or a blood pump machine which, instead of (or in addition to) a dialyzer, will incorporate an MG 350 cartridge into the extracorporeal circuit. Each session lasts 2–3 hours: 1 session on the first day, 1 session on the second day, and 1 session on the third day. The nephrologist may add a session on top of the recommended in the protocol depending on the patient status. Unfractionated heparin at 5000 units is used to prime the HP circuit. The blood flow rate is regulated at 200 mL/min. The choice of anticoagulation is prescribed at the discretion of the nephrologist depending on the patient's clinical condition.

Definition of Terms

COVID-19 case: Reverse transcriptase polymerase chain reaction (RT-PCR) confirmed for COVID-19 in a test that was conducted in a national or subnational reference laboratory and/or DOH-certified testing facility.[19]

Hemoperfusion (HP): Part of an array of treatment strategies under "Extracorporeal Organ Support" (ECOS) wherein blood is passed through a cartridge containing adsorbent particles (either charcoal or resins) used in sepsis or in life-threatening intoxication with drugs, elemental metals, and industrial toxins.[21, 22]

Length of hospital stay: Time from patient admission to the time the patient is discharged or the patient died.

COVID-19 disease classification:[20]

Mild: fever, cough, fatigue, anorexia, myalgias, and other non-specific symptoms such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, loss of smell (anosmia), or loss of taste (ageusia) preceding the onset of respiratory symptoms; no signs of pneumonia or hypoxia.

Moderate: with signs of non-severe pneumonia but the respiratory rate (RR) 21–30/minute, SpO_2 > 92% on room air

Severe: with severe pneumonia or severe acute respiratory infection: fever, cough, dyspnea, RR > 30/minute, severe respiratory distress or SpO_2 ≤ 92% on room air

Critical: onset within one week of known clinical insult (pneumonia) or new or worsening respiratory symptoms, progressing infiltrates on chest x-ray or chest CT, with respiratory failure not fully explained by cardiac failure or fluid overload (adults with acute respiratory distress syndrome); sepsis or septic shock.

Data Management and Analysis

Descriptive statistics were used to summarize the data. Results were reported as medians and interquartile ranges or means and standard deviations, as appropriate. Categorical variables were summarized as counts and percentages. No imputation was made for missing data.

Ethical Considerations

This study was approved by the University of the Philippines Manila Research Ethics Board (UPMREB). No personal or identifying information was recorded for the patient records included in the study. Each patient had a designated numerical code. Only the principal investigators and the fellows of the Division had access to the electronic database. All information and data collected were kept confidential by the investigators. All forms of data collected from the COVID database for use in the study will be electronically deleted permanently (including backup copies) and was checked for complete deletion by a fellow from the Division of Nephrology not involved in the study. Data was for deletion one year from the end of the study.

RESULTS

Sixty-six patients were included in the study (Table 1). The majority were men with an average age of 61.3 years (SD 15). Hypertension was the most common medical comorbidity (62.1%). Acute kidney injury (AKI) requiring dialysis comprised 28.8% while 33.3% had diagnosed chronic kidney disease (CKD). Patients diagnosed with AKI already have AKI on referral to nephrology and may not necessarily have had AKI on hospital admission. The majority of referred patients were critical COVID-19 cases (56.1%) on referral (not necessarily on admission). Baseline IL-6, CRP, LDH, and ferritin were all elevated (Table 2). The PaO_2/FiO_2 ratios (PF ratio) and absolute lymphocyte counts (ALC) were low. Most patients had bilateral pneumonia on chest radiographs.

The majority of patients were mechanically ventilated (54.5%) (Table 3). Steroids were the most common medications administered (71.2%). Only a small percentage of patients were given remdesivir (9.1%) versus tocilizumab

Table 1. Demographic and clinical profile of patients who underwent hemoperfusion (N=66)

Sex, Male, n (%)	39 (59.1)
Age, average years (SD)	61.3 (±15)
Comorbidities, n (%)	
Hypertension	41 (62.1)
Diabetes	21 (31.8)
Dyslipidemia	2 (3.0)
CVD	4 (6.1)
Malignancy	4 (6.1)
Lung disease	2 (3.0)
None	12 (48)
AKI, n (%)	29 (43.9)
Dialytic	19 (28.8)
CKD, n (%)	22 (33.3)
Dialytic	11 (16.7)
Neither AKI/CKD, n (%)	25 (37.9)
Cause of ESKD, n (%)	
DM	3 (27.3)
HTN	6 (54.5)
Gout	1 (9.1)
CGN	1 (9.1)
COVID Severity, n (%)	
Mild	0
Moderate	8 (12.1)
Severe	21 (31.8)
Critical	37 (56.1)

CVD, Cerebrovascular disease; AKI, Acute kidney injury; CKD, Chronic kidney disease; ESKD, End-stage kidney disease; DM, Diabetes mellitus; HTN, Hypertension; CGN, Chronic glomerulonephritis

Table 2. Baseline laboratory test results

Laboratory Parameter	Mean (SD or %)
hsCRP (mg/L, NV 1.0-3.0)	130.0 (88.8)
Ferritin (ng/mL, NV 17.9-464)	2117.3 (1967.8)
LDH (U/L, NV 120-246)	644.6 (273.3)
IL–6 (pg/mL, NV 0-50)	363.7 (627.6)
PF ratio (NV≥400)	177.6 (97.2)
WBC count (%)	12.0 (8.8)
ALC (NV 1000-4800)	863.7 (535.9)
Chest radiograph findings	
Unilateral pneumonia	N=3 (4.5%)
Bilateral pneumonia	N=54 (81.8%)
Diffuse pneumonia	N=9 (13.6%)

hsCRP, High-sensitivity C-reactive protein; LDH, Lactate dehydrogenase; IL-6, Interleukin-6; PF ratio, PaO_2/FiO_2 ratio; WBC, White blood cell count; ALC, Absolute lymphocyte count

Table 3. Therapeutic modalities and ventilator support

Therapeutic Strategy	n (%)
O_2 support	
MV	36 (54.5)
HFNC	23 (34.8)
Nasal cannula	1 (1.5)
None	6 (9.1)
HCQ/CQ	7 (10.6)
Ritonavir	16 (24.2)
Remdesivir	6 (9.1)
Steroids	47 (71.2)
Tocilizumab	33 (50.0)
CPT	12 (18.2)

MV, Mechanical ventilator; HFNC, High-flow nasal cannula; HCQ/CQ, Hydroxychloroquine/chloroquine; CPT, Convalescent plasma therapy

Table 4. Clinical outcomes and different clinical time variables

Outcomes	
Died, n (%)	41 (62.1)
Discharged alive, n (%)	25 (37.8)
Length of hospital stay, average days (SD)	20.8 (19.5)
Days from admission to HP, average days (SD)	5.9 (5.8)
Days from HP to death/discharge, average days (SD)	15.3 (17.4)

(50%), though it should be noted that remdesivir was used more frequently during the latter part of the year. Hydroxychloroquine (HCQ) was given in 10.6% of the patients. Ritonavir was given in 24.2% of patients.

The majority of the patients who underwent hemoperfusion expired (62.1%) (Table 4). The average duration from admission to the first session of HP was 5.9 days (SD 5.8), and from the first HP session to death or discharge was 15.3 days (SD 17.4). Not all patients had both pre- and post-HP inflammatory markers and only those with both values were included for analysis in Table 5. Except for IL-6 among those who died, all post-HP inflammatory markers showed a decrease from pre-HP values.

DISCUSSION

Inflammatory markers and other laboratory measures in COVID-19

Our study showed the average baseline laboratories of patients with COVID-19 who underwent HP. Markers were elevated and all showed decrease following hemoperfusion except for IL-6 among patients who died. Case series and reports on the use of HP in COVID-19 patients commonly measured inflammatory markers such as CRP, ferritin, LDH, and IL-6 as well as other laboratory investigations such as PF ratio, lymphocyte counts, and SpO_2 to quantify the effects of hemoperfusion. These markers are associated with different patient outcomes. The observational study by Jørgensen (2021) showed a relationship between high IL-6 values and higher risk for severe respiratory failure among COVID-19 patients.[23] Elevated inflammatory markers to include IL-1Ra, IL-6, IL-8, IL-17a, IP-10, and MCP-1 were also related to AKI and 30-day mortality among COVID-19 patients.[24] Hemoperfusion is theorized to decrease inflammation caused by the cytokine storm of COVID-19 by clearing these cytokines through adsorption. In a series describing HP among 5 severe to critical COVID-19 patients, post-HP CRP and IL-6 decreased and only one of these patients died.[25] The average PF ratio also increased among all HP-treated patients with COVID-19 in a Japanese case series.[26] The relationship between an improvement in laboratory parameters and patient outcomes (survival, liberation from MV, discharge from ICU) should be studied in RCTs.

Table 5. Pre- and post-hemoperfusion inflammatory markers

Inflammatory Marker	Died			Discharged		
	Pre	Post	% Decrease	Pre	Post	% Decrease
IL-6 (pg/mL) (N=7)	352.1	996.9	-183.1	395.3	162.6	58.9
LDH (U/L) (N=50)	726.7	666.1	8.3	601.9	488.9	18.8
Ferritin (ng/mL) (N=50)	1971.8	1372.3	30.4	2251.2	1570.9	30.2
hsCRP (mg/mL) (N=26)	139.1	36.2	74.0	155.7	29.3	81.2

IL-6, Interleukin-6; LDH, Lactate dehydrogenase; hsCRP, High-sensitivity C-reactive protein

Clinical comorbidities and therapeutic modalities other than hemoperfusion

Hypertension was the most common comorbidity seen among our patients with COVID-19. This is similar to previous studies by Anderberg (2021) and Rampino (2020) that also reported hypertension as the most common comorbidity among patients with COVID-19 who underwent hemoperfusion. It is noted that a sizable percentage (48%) of our patients do not have any comorbidities, which is similar to the study by Asgharpour (2020) wherein 40% of the COVID-19 patients were well before infection. Future studies can investigate if the presence or absence of comorbidities affect outcomes among COVID-19 patients who underwent hemoperfusion. Data from our study showed that steroids were still the most commonly given medications among patients with COVID-19. This study compiled data from COVID-19 patients relatively early in the pandemic and some of the drugs described in this study such as hydroxychloroquine, chloroquine, and convalescent plasma therapy are no longer used based on newer data.[27]

Timing of hemoperfusion

Our study showed that the average duration from admission to the first session of HP was 5.8 days (SD 5.9). At present, there is still no recommendation for the ideal timing of HP in COVID-19. It is proposed that it should be performed at the earliest possible time to blunt the effect of a surge in cytokines before severe clinical manifestations occur. Previous studies done in patients with non-COVID-19 sepsis, septic shock, and post-operative septic conditions have used HP 3-12 hours after randomization. These studies were not able to see a correlation between mortality and the timing of HP.[28,29] As it is an invasive procedure with concomitant procedural risks, more definitive data are needed to recommend giving HP at the earliest possible time.

Clinical outcomes

Our study showed that the majority of COVID-19 patients who underwent hemoperfusion died (62.1%) while survival to discharge was seen in 36.4%. An early, single-center study in the Philippines reported a mortality rate of 21% among a general cohort of COVID-19 patients,[30] which is similar to another study in a single tertiary center catering to an underserved-inner city population in the United States (21.5%).[31] The previously cited case series by Asgharpour (2020), Ramipino (2020), and Katagiri (2020) on hemoperfusion and COVID-19 showed varying reports in mortality rates (25–80%), which is in part due to the small sample size of these studies. The high disparity in mortality between the general population with COVID-19 and the patients in our study can be explained by the finding that the majority of the patients with COVID-19 who underwent hemoperfusion in our study were critical COVID-19 cases (56.1%). This might explain the higher mortality rate since the patients who underwent HP were usually those who are already at the critical stage of COVID illness.

The average length of stay of patients who underwent hemoperfusion in PGH was 20.8 days (SD 17.4). No follow-up, post-discharge data was collected for those who had hemoperfusion and survived to discharge. According to the DOH, the mean length of stay for patients hospitalized from COVID-19 was 16.00 days for those who recovered and 7.27 days for those who died.[32] At present, no available studies explicitly cited the number of patients with COVID-19 who underwent hemoperfusion and were discharged.

Limitations

Since this is only a descriptive study of the experience of a tertiary institution in performing HP among patients with COVID-19, we cannot make any association between HP and patient outcomes. Further RCTs are needed to establish the role of hemoperfusion in COVID-19 management. We recommend that future studies explore the relationship between the timing of hemoperfusion, type of hemoperfusion cartridge used, number of hemoperfusion sessions, levels of inflammatory markers, and how these affect meaningful outcomes such as mortality, mechanical ventilator-free days, and length of hospitalization. Data from this study can be used in future studies to further define the role of hemoperfusion in COVID-19.

CONCLUSIONS

Our study showed the characteristics of patients with COVID-19 who underwent HP in terms of demographics, clinical comorbidities, baseline laboratory exams, ventilatory and therapeutic interventions, and clinical outcomes in the PGH, a tertiary COVID-19 referral center. The majority were hypertensive men in their early 60s with severe to critical COVID-19 disease. The mean inflammatory markers (IL-6, CRP, LDH, ferritin) were elevated with a decrease in most markers post-hemoperfusion (except for IL-6 among those who died). Despite this, mortality was still high and the average length of hospital stay was long.

Statement of Authorship

SARM contributed to the protocol development, data gathering, data analysis, and manuscript writing. JanASM, JenASM, and ESM contributed to the protocol development. ESM reviewed and approved the manuscript. CFCU contributed to data gathering.

All authors approved the final version submitted.

Author Disclosure

All authors declared no conflicts of interests.

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APPENDIX

UP-PGH Division of Nephrology Protocol on the Use of Hemoperfusion for Patients with COVID-19

Rationale:

Critically-ill patients with COVID-19 pneumonia may present with a dysregulated immune response, producing the so-called "cytokine storm" with varying degrees of organ damage. Hemoperfusion may be given as adjunctive therapy to reduce inflammatory cytokines, improve hemodynamic stability (reduce vasopressor support) and reduce oxygen support among ventilated patients, although robust evidence is still lacking.

Indications for Hemoperfusion (with or without kidney replacement therapy), in any of the following:

All patients, 19 years old and older, with confirmed COVID-19 disease and any one of the following conditions:

- Severe disease, defined as:
  - Dyspnea or RR ≥30 and/or
  - SpO_2 ≤ 93% and/or
  - Oxygenation PaO_2/FiO_2 ratio ≤ 300 mmHg not fully explained by volume overload (cardiac failure, renal disease, excessive hydration) and/or
- Lung infiltrates ≥ 50% within 24-48 hours
- Life-threatening respiratory failure
- Septic shock

Contraindication(s) for Hemoperfusion:

- Any pre-existing advanced medical disease with life-expectancy less than 1 month
- Treatment deemed clinically futile
  - Conditions which may include but not limited to the following:
    - Cerebrovascualr accident (CVA) with poor functional status
    - Post cardiopulmonary arrest
    - Malignancy ≥ stage 3
    - Advance care directives that include "do not intubate" (DNI) or "do not resuscitate" (DNR) status
- Patients with very low platelet counts (< 20,000/μL)
- History of heparin-induced thrombocytopenia
- Unable to insert a vascular access for any reason (position, coagulopathy, etc)
- Any pre-existing contraindication to extracorporeal therapy
- Known allergies to extracorporeal circuit components (polystyrene/divinylbenzene, polycarbonate, polypropylene, silicone and polyester)

Vascular access:

HD compatible AV graft/fistula or permanent venous access catheter; if none, refer to TCVS for insertion of venous catheters (preferably triple lumen)

1. Femoral catheter length MUST be > 20 cm
2. IJ catheter at least French 11

Hemoperfusion Orders:

Blood Flow Rate: recommended: 200mL/min
Cartridge: HA 330 or MG 350
Prime with 5000 units Heparin
Anticoagulation: Enoxaparin 0.4 cc (unless with contra-indications)
Duration: 3 hours

- Hemoperfusion should be done first before the dialysis modality of choice.
- If the system clots after at least 2 hours of hemoperfusion, may terminate the procedure.

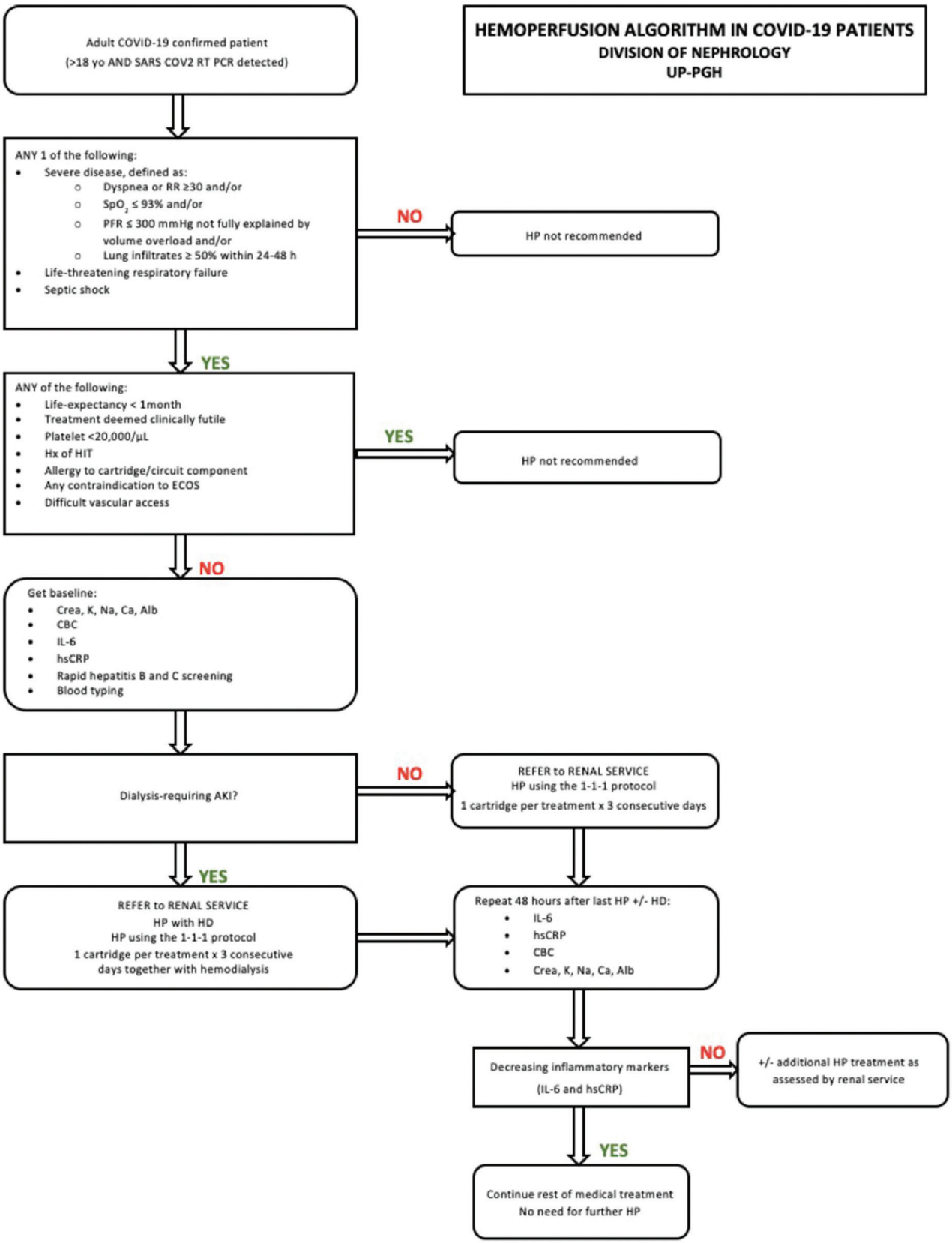
Schedule (1-1-1): One hemoperfusion session daily for 3 days

Removal of Drugs

Hydrophobic drugs may be removed by the device.
There is no available data on the removal of Remdesivir.
Due to the large size of tocilizumab (148 kDa), convalescent plasma antibodies (>150 kDa), and other biologics of similar size, these are NOT expected to be removed by hemoperfusion.

When using Tocilizumab:

- Hemoperfusion should preferably be done first before giving Tocilizumab
  - Day 1 – Hemoperfusion #1 immediately followed by tocilizumab infusion
  - Day 2 – Hemoperfusion #2 (to start 24 hours after giving Tocilizumab)
  - Day 3 – Hemoperfusion #3



HP, hemoperfusion; ARDS, acute respiratory distress syndrome; RR, respiratory rate; PFR, PaO_2/FiO_2 ratio; BMI, body mass index; HIT, heparin-induced thrombocytopenia; ECOS, extracorporeal organ support; CBC, complete blood count; IL-6, interleukin-6; hsCRP, high sensitivity C-reactive protein; PT/PTT, prothrombin time/partial thromboplastine time; AKI, acute kidney injury; HD, hemodialysis