# A retrospective cross-sectional study on the risk factors and survival outcome of End Stage Kidney Disease patients receiving regular maintenance haemodialysis with COVID-19 infection in Hospital Enche' Besar Hajjah Khalsom, Kluang

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**ABSTRACT**

**Introduction: COVID-19 pandemic has affected healthcare services around the globe as hospitals were turned into designated hospitals to accommodate high risk groups of patients with COVID-19 infection including end stage kidney disease (ESKD) patients. In Malaysia, there was insufficient data on COVID-19 infection among ESKD patients. This study aims to determine factors and survival outcomes associated with COVID-19 infection among ESKD patients in a designated COVID-19 hospital in Malaysia.**

**Methods and Materials: A retrospective cross-sectional study involving 80 haemodialysis (HD) patients recruited from March 2020 till March 2021. Patients' information and results was retrieved and evaluated. Risk factors affecting the COVID-19 mortality were analysed using a one-way analysis of variance (ANOVA) and binary logistic regression.**

**Results: The mean age of the patients was 54 years who were predominantly Malays (87.5%) and living in rural areas. Majority of them had comorbidities such as diabetes mellitus (71%) and hypertension (90%). The most common presentations were fever (46%) and cough (54%) with chest radiographs showing bilateral lower zone ground glass opacities (45%). A quarter of the study population were admitted to the intensive care unit, necessitating mechanical ventilation. This study found that 51% of the patients were given steroids and 45% required oxygen supplementation. The COVID-19 infection mortality among the study population was 12.5%. Simple logistic regression analysis showed that albumin, Odd Ratio, OR=0.85 (95% Confidence Interval, 95%CI: 0.73, 0.98)) and absolute lymphocyte count OR=0.08 (95%CI: 0.11, 0.56) have inverse association with COVID-19 mortality. C-reactive protein OR=1.02 (95%CI: 1.01, 1.04), lactate dehydrogenase OR=1.01 (95%CI: 1.00, 1.01), mechanical ventilation OR=17.21 (95%CI: 3.03, 97.67) and high dose steroids OR=15.71 (95%CI: 1.80, 137.42) were directly associated with COVID-19 mortality.**

**Conclusion: The high mortality rate among ESKD patients receiving HD was alarming. This warrants additional infection control measures to prevent the spread of COVID-19 infection among this vulnerable group of patients. Expediting vaccination efforts in this group of patients should be advocated to reduce the incidence of complications from COVID-19 infection.**

**KEYWORDS:**
*ESKD, haemodialysis, COVID-19 infection, end stage kidney disease, Malaysia*

## INTRODUCTION

As the world marches into the year 2021 with the introduction of COVID-19 vaccines, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to devastate health and livelihoods worldwide. This enveloped RNA betacoronavirus, first identified at the end of 2019 in Wuhan, has since rapidly turned into a pandemic affecting countries throughout the world including Malaysia.[1] The disease burden of COVID-19 is high and has crippled most of the healthcare system worldwide.

The clinical presentation of COVID-19 varies widely. Most of the patients infected remain asymptomatic while others develop acute respiratory distress syndrome (ARDS) and multiple organ failures.[2] Many risk factors have been found which may influence the prognosis of patients with COVID-19. Poor prognosis is linked to risk factors such as old age, kidney diseases, hypertension, diabetes mellitus, cancer, chronic respiratory and cardiovascular diseases.[3]

The COVID-19 pandemic has not spared patients with end stage kidney disease (ESKD) . As these patients have multiple other comorbidities, they are more vulnerable and susceptible to COVID-19 infection. This is more apparent in the higher risk of cross infectivity in respective haemodialysis (HD) centres due to recurrent physical presence at healthcare facilities and physical proximity among patients during HD.[4] At the same time, patients needing dialysis have abnormalities in their innate and adaptive immune systems, which put them at a higher risk of adverse outcomes.

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In the Malaysian, almost 86.2% of the 45,937 ESKD patients receive renal replacement therapy (RRT) in the form of haemodialysis.[5] These patients have been receiving regular dialysis primarily from privately owned HD centres (50.2%), and government centres (30.0%) and centres run by non-governmental organisation (19.7%). Since the start of the pandemic, various recommendations and standard operating procedures by local experts have been drafted to prevent the emerging clusters of COVID-19 infection among dialysis patients and staffs.[6] Despite these efforts, incidences of COVID-19 infection among ESKD patients remain worrying.

This study explored the clinical condition, management, and survival outcomes of ESKD patients who had contracted COVID-19 infection and were admitted to a designated COVID-19 hospital in Johor, Malaysia.

## MATERIALS AND METHODS

*Study design and methodology*

A retrospective cross-sectional study was conducted to assess the risk factors and survival outcome of End Stage Kidney Disease (ESKD) patients receiving regular maintenance haemodialysis with COVID-19 infection at Hospital Enche' Besar Hajjah Khalsom, Kluang (HEBHK).

*Study area*

HEBHK is a 268-bed hospital located in the district of Kluang, Johor which serves a population of 320,000. It is a hospital with intensive care units and has several major disciplines such as internal medicine, surgical, orthopaedics, paediatrics, and obstetrics and gynaecology. Since March 2020, HEBHK had been converted to a centralised COVID-19 hospital for the whole state of Johor. The objective was to pool these patients in a hospital for better monitoring and treatment.

Patients who tested positive via nasopharyngeal or oropharyngeal real-time polymerase chain reaction (RT-PCR) COVID-19 swab test were contacted and sent to HEBHK. Patients admitted to the hospital were isolated in the designated isolation wards with full history clerking and blood taken upon admission (within 24 hours) by the attending medical officer. They were stratified according to the protocol guidelines "COVID-19 Training Slides", implemented by the Ministry of Health, Malaysia. These guidelines were set by a team of experienced infectious disease consultants in Malaysia to help clinicians with risk stratification, monitoring of patients and monitoring of blood parameters, use of steroids and antiviral therapy in COVID-19 patients. The guideline also categorised COVID-19 patients into 5 categories. Category 1 is defined as asymptomatic, Category 2 as symptomatic with no evidence of pneumonia, Category 3 as symptomatic with evidence of pneumonia, Category 4 as symptomatic with evidence of pneumonia and requiring oxygen supplementation, and lastly, Category 5 as critically ill with multiorgan failure. Blood investigations taken included also for full haematology profiles, renal profiles, liver function tests, C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin and arterial blood gas. A chest radiograph was ordered to determine the stage of pneumonia. Demographic information (age, gender, weight, height, body mass index, and pre-existing medical diseases) was also collected.

Patients were reviewed on a daily basis until they were discharged from the COVID-19 treatment pathway (transferred to another hospital for continuation of therapy for non-COVID-19 related health issues). All the patients were observed for at least 10-14 days depending on each individual's clinical condition of individual patient, chest radiograph changes and severity of the disease. They were given an appointment in the outpatient clinics of their respective district hospitals for health evaluation 1 month after discharge.

*Inclusion and exclusion criteria*

The inclusion criteria are ESKD patients tested positive for SARS-CoV-2 age ≥18 years old and who have received >3 months of regular HD admitted to HEBHK. Those who are on continuous ambulatory peritoneal dialysis (CAPD) were excluded.

*Patient Recruitment*

Data of patients who were admitted to HEBHK from March 2020 to March 2021 and met the inclusion and exclusion criteria were retrieved.

*Definition of variables*

Patients were classified as being from an urban area if the combined population of the area is greater than 10,000 people and at least 60% of the population is engaged in non-agricultural activities.

*Ethics, consents and permissions*

In compliance with ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice Guideline, all patients in this study were anonymised and numbered accordingly. No identifiers of patients were collected or used in the analysis.

This study was reviewed and approved by the Malaysian Medical Research Ethics Committee (NMRR-20-2729-57507). This is a study involving data collection through medical records, therefore informed consent from patients is not required.

*Statistical Analysis*

The statistical analysis was performed using SPSS Statistics for Windows, version 17.0 (SPSS Inc, Chicago, IL, USA). All data were presented as a mean±standard deviation (SD), while non-normal distributed variables were shown as median and interquartile range (IQR). Categorical variables have been shown as n (%). The continuous variables' differences in outcomes were measured using a one-way analysis of variance (ANOVA), while the categorical variables were measured using the chi-square test. For non-parametric variables, Mann-Whitney test was used. Multiple regression for all significant factors on univariate analysis was not done. The sample size for this study was 80 with 16 significant factors. The application of multivariate regression analysis requires over 100 cases for the model to have sufficient power (around 0,80).[7] Simple binary logistic was applied with stepwise forward selection [odds ratio, OR; 95%

**Table I: Demography, Radiological Imaging and Management of 80 haemodialysis patients**

| Patient's characteristics | All (N, %) | Alive (n, %) | Dead (n, %) | p-value |
|---|---|---|---|---|
| Age, mean±SD | 54.41±12.3 | 54.13± 2.57 | 56.40±10.34 | 0.588 |
| Gender | | | | 0.035 |
| Female | 41 (51.2) | 39 (55.7) | 2 (20.0) | |
| Male | 39 (48.8) | 31 (44.3) | 8 (80.0) | |
| Race | | | | 0.613 |
| Malay | 70 (87.5) | 61(87.1) | 9 (90.0) | |
| Chinese | 5 (6.3) | 5 (7.1) | 0 (0) | |
| Indian | 5 (6.3) | 4 (5.7) | 1 (10.0) | |
| Place of Residence | | | | 0.104 |
| Urban | 26 (32.5) | 25 (35.7) | 1 (10.0) | |
| Rural | 54 (67.5) | 45 (64.3) | 9 (90.0) | |
| BMI (kg/m$^2$), mean±SD | 26.43±5.7 | 26.62±5.90 | 25.13±3.75 | 0.441 |
| Causes of ESKD | | | | 0.816 |
| Diabetes Mellitus (DM) | 3 (3.8) | 3 (4.3) | 0 (0) | |
| Hypertension (HTN) | 17 (21.3) | 14 (20.0) | 3 (30.0) | |
| Glomerulonephritis | 4 (5.0) | 4 (5.7) | 0 (0) | |
| Others | 1 (1.3) | 1 (1.4) | 0 (0) | |
| DM and HTN | 55 (68.8) | 48 (68.6) | 7 (70.0) | |
| COVID-19 category (on admission) | | | | 0.002 |
| Category 1 | 10 (12.5) | 10 (14.3) | 0 (0) | |
| Category 2 | 9 (11.3) | 9 (12.9) | 0 (0) | |
| Category 3 | 33 (41.3) | 31 (44.3) | 2 (20.0) | |
| Category 4 | 18 (22.5) | 15 (21.4) | 3 (30.0) | |
| Category 5 | 10 (12.5) | 5 (7.1) | 5 (50.0) | |
| Comorbids | | | | |
| Diabetes | 57 (71.3) | 50 (71.4) | 7 (70.0) | 0.926 |
| Hypertension | 72 (90) | 63 (90.0) | 9 (90.0) | 1.000 |
| Dyslipidaemia | 35 (43.8) | 30 (42.9) | 5 (50.0) | 0.670 |
| Cerebral vascular events | 3 (3.8) | 1 (1.4) | 2 (20.0) | 0.004 |
| Cardiovascular diseases | 10 (12.5) | 7 (10.0) | 3 (30.0) | 0.074 |
| Others | 16 (20) | 15 (21.4) | 1 (10.0) | 0.398 |
| Duration of dialysis (years)a, mean±SD | 3.0 (4.85) | 2.4 (5) | 4.5 (4.0) | 0.153 |
| Education level | | | | 0.382 |
| None | 5 (6.2) | 5 (7.1) | 0 (0) | |
| Primary | 22 (27.5) | 21 (30.0) | 1 (10.0) | |
| Secondary | 43 (53.8) | 36 (51.4) | 7 (70.0) | |
| Tertiary | 10 (12.5) | 8 (11.4) | 2 (20.0) | |
| Symptoms on admission | | | | |
| Fever | 37 (46.2) | 30 (42.9) | 7 (70.0) | 0.107 |
| Fatigue | 7 (8.8) | 4 (5.7) | 3 (30.0) | 0.011 |
| Cough | 43 (53.8) | 37 (52.9) | 6 (60.0) | 0.672 |
| Shortness of breath | 25 (31.2) | 18 (25.7) | 7 (70.0) | 0.005 |
| Chest pain | 2 (2.5) | 2 (2.9) | 0 (0) | 0.588 |
| Nausea | 6 (7.5) | 5 (7.1) | 1 (10.0) | 0.748 |
| Radiological imaging | | | | |
| Pneumonia/Consolidation | | | | 0.028 |
| Left | 8 (10.0) | 7 (10.0) | 1 (10.0) | |
| Right | 8 (10.0) | 6 (8.6) | 2 (20.0) | |
| Bilateral | 11 (13.8) | 7 (10.0) | 4 (40.0) | |
| None | 53 (66.2) | 50 (71.4) | 3 (30.0) | |
| Ground glass opacities | | | | 0.193 |
| Left | 11 (13.8) | 9 (12.9) | 2 (20.0) | |
| Right | 9 (11.3) | 9 (12.9) | 0 (0) | |
| Bilateral | 36 (45.0) | 29 (41.4) | 7 (70.0) | |
| None | 24 (35.0) | 23 (32.9) | 1 (10.0) | |
| Treatment and Management | | | | |
| Antibiotics usage | 46 (57.5) | 37 (52.9) | 9 (90.0) | 0.026 |
| Antibiotics duration (Days), mean±SD | 9.5±4.5 | 9.5±4.9 | 9.7±2.8 | 0.916 |
| Steroid usage | | | | 0.004 |
| Low dose steroid | 8 (10.0) | 8 (11.4) | 0 (0) | |
| High dose steroid | 33 (41.2) | 24 (34.3) | 9 (90.0) | |
| None | 39 (48.8) | 38 (54.3) | 1 (10.0) | |
| Steroid duration throughout hospitalisation (days), mean±SD | 14.32±5.83 | 15.38±5.72 | 10.56±4.75 | 0.026 |
| Oxygen supplementation | 36 (45) | 26 (37.1) | 10 (100) | <0.001 |
| ICU admission | 20 (25) | 13 (18.6) | 7 (70.0) | <0.001 |
| ICU duration (Days) (only 20 patients), mean±SD | 11.7±7.0 | 12.3±8.1 | 10.6±4.8 | 0.612 |
| Mechanical ventilation | 19 + 1*(25) | 12 (17.1) | 7 + 1*(80.0) | <0.001 |
| Inotrope usage | 20 (25) | 12 (17.1) | 8 (80.0) | <0.001 |
| Total days of hospitalisation (Days) , mean±SD | 15.93±7.41 | 16.43±7.43 | 12.40±6.62 | 0.108 |

* Patient demised at Emergency Department

[a] Data not normally distributed, median and IQR reported, non-parametric- Mann-Whitney test was used

**Table II: Laboratory parameters of 80 haemodialysis patients**

| Laboratory Parameter | All (N=80) | Alive (n=70) | Dead (n=10) | P=value |
|---|---|---|---|---|
| Sodium (mmol/L) | 135.21±4.0 | 135.30±3.88 | 134.60±4.81 | 0.604 |
| Potassium (mmol/L) | 4.18±0.8 | 4.20±0.76 | 4.05±1.06 | 0.573 |
| Urea (mmol/L) | 19.41±8.5 | 18.87±8.26 | 23.19±9.99 | 0.136 |
| Chloride (mmol/L) | 95.47±4.7 | 95.94±4.59 | 92.2±3.94 | 0.017 |
| Creatinine (µmol/L) | 850.81±367.1 | 841.61±365.41 | 914.30±392.54 | 0.562 |
| Heamoglobin (g/dl) | 9.88±1.7 | 9.80±1.64 | 10.39±2.07 | 0.309 |
| White blood cell ($10^3$/µL) | 7.16±2.9 | 7.10±2.87 | 7.58±2.94 | 0.625 |
| Absolute Lymphocyte Count (ALC) ($10^3$/µL) | 1.27±0.7 | 1.35±0.644 | 0.70±0.49 | 0.003 |
| Platelet ($10^3$/µL) | 239.03±115.7 | 244.49±121.54 | 200.8±48.72 | 0.267 |
| Absolute Neutrophil Count (ANC) ($10^3$/µL) | 5.22±3.0 | 4.96±2.83 | 7.03±3.47 | 0.038 |
| Monocytes ($10^3$/µL) | 0.55±0.3 | 0.57±0.25 | 0.37±0.24 | 0.021 |
| Total Bilirubin (µmol/L) | 10.25±4.0 | 10.00±3.86 | 11.96±3.96 | 0.145 |
| Total Protein (g/L) | 75.78±6.9 | 75.86±6.86 | 75.20±7.32 | 0.780 |
| Albumin (g/L) | 35.96±4.6 | 36.42±4.32 | 32.80±5.12 | 0.018 |
| AST (U/L)[a] | 21.00 (16.00) | 19.00 (10.00) | 35.50 (99.75) | 0.009[c] |
| ALT (U/L)[a] | 13.00 (14.00) | 12.00 (13.00) | 24.50 (39.75) | 0.008[c] |
| ALP (U/L) | 119.67±76.7 | 122.28±79.19 | 101.00±55.67 | 0.413 |
| Ferritin (µg/L)[b] | 1865.70 (2469.25) | 1455.00 (2815.00) | 3132.20 (3226.50) | 0.063[c] |
| CRP (mg/L)[a] | 30.70 (66.10) | 23.75 (49.58) | 187.50 (168.50) | <0.001[c] |
| LDH (U/L) | 292.74±195.8 | 264.37±128.66 | 482.80±195.78 | 0.001 |

[a] Median and IQR is reported for this variable.
[b] Ferritin levels are available for 40 subjects, 31 of whom are alive and 9 of whom are deceased.
[c] Mann-Whitney test was used for non-parametric data

**Table III: Simple logistic regressions of mortality risk factors in 80 haemodialysis patients**

| Factor | OR | 95% CI | p-value | Adjusted OR* | Adjusted 95% CI | Adjusted p-value |
|---|---|---|---|---|---|---|
| Age (years) | 1.02 | 0.96, 1.08 | 0.583 | | | |
| Gender | 0.20 | 0.39, 1.00 | 0.520 | | | |
| High dose steroid | 14.25 | 1.70,119.70 | 0.050 | 15.71 | 1.80,137.42 | 0.045 |
| BMI (kg/m$^2$) | 0.95 | 0.84,1.08 | 0.437 | 0.96 | 0.83, 1.12 | 0.608 |
| Fever | 3.11 | 0.74,13.04 | 0.121 | 2.83 | 0.64, 12.51 | 0.169 |
| Cough | 1.34 | 0.35, 5.16 | 0.672 | 2.23 | 0.52, 10.10 | 0.271 |
| Mechanical Ventilation | 19.33 | 3.64,102.65 | 0.001 | 17.21 | 3.03, 97.67 | 0.001 |
| ALC ($10^3$/µL) | 0.08 | 0.01,0.50 | 0.007 | 0.08 | 0.11, 0.56 | 0.011 |
| Albumin (g/L) | 0.85 | 0.74,0.98 | 0.025 | 0.85 | 0.73,0.98 | 0.027 |
| CRP (mg/L) | 1.02 | 1.01,1.03 | <0.001 | 1.02 | 1.01, 1.04 | 0.001 |
| LDH (U/L) | 1.01 | 1.00, 1.01 | 0.031 | 1.01 | 1.00, 1.01 | 0.041 |

Age and gender adjustments were made.
* Adjusted odds ratio (OR) to age and gender

confidence interval (95%CI)] to identify factors associated with mortality among ESKD COVID-19 patients in this study. Based on national COVID-19 data, adjustments were made for age and gender because age and gender were known to affect mortality.[8] A p-value of <0.05 was considered significant.

## RESULTS

A total of 80 ESKD patients who were admitted to HEBHK for COVID-19 infection from March 2020 to March 2021 were enrolled into the study. There was almost an equal distribution of male and female patients. The mean age was 54 (±12) years old with 67% of them staying in rural areas. Malays made up the largest cohort of patients at 87.5%, followed by Chinese (6.3%) and Indians (6.3%). Their level of education was mostly up to primary (27.5%) and secondary school level (53.8%). In terms of comorbidities, 68.8% of the participants developed ESKD due to both hypertension and diabetes mellitus. A total of 35 (43.8%) patients had dyslipidaemia. The mean BMI was 26.43kg/m$^2$. Ten patients (12.5%) had a history of cerebrovascular accident (CVA) and another three (3.8%) had a history of cardiovascular disease (CVD). The median duration of patients receiving haemodialysis was 3 years with an interquartile range of 4.85 years.

The majority of the patients admitted to the hospital were categorised as Stage 3 (with pneumonia changes) and above; 41.3% of them had stage 3 COVID-19 infections, 22.5% is in stage 4 (requiring oxygen supplementation) and 12.5% in stage 5 (multi-organ failure). Most common reported presenting symptoms were cough (53.5%), fever (46.2%) and shortness of breath (31.2%).

The mean total white cell count was 7.16x$10^3$/µL with mean absolute lymphocyte count of 1.27x$10^3$/µL. Mean ferritin level (n=40) was high with 3621.87µg/L, mean CRP value was 62.83mg/L. Radiographic abnormalities, especially ground glass opacities were common among ESKD patients in this study. On chest radiographs, 36 (45%) patients had bilateral ground glass opacities, 11 (13.8%) had left sided

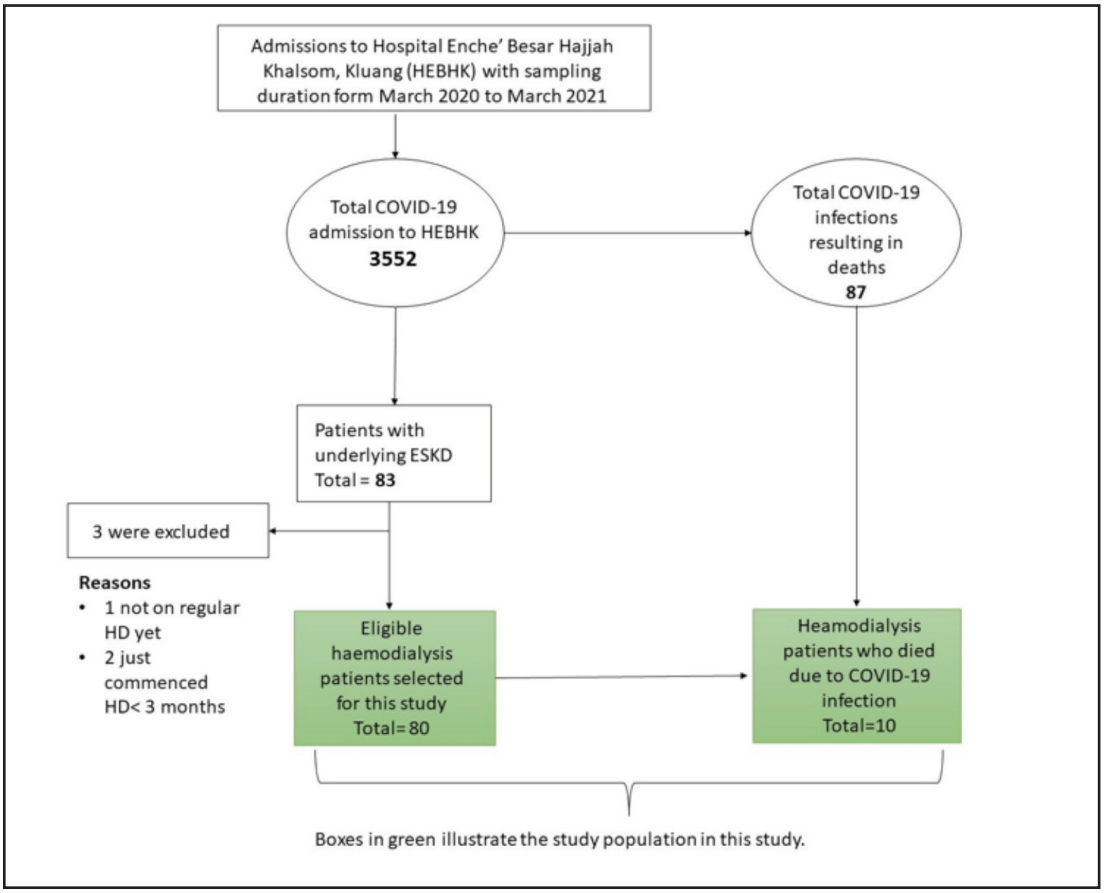


**Fig. 1:** Selection of study population from March 2020 to March 2021 in HEBHK.

ground glass opacities and 9 (11.3%) had right sided ground glass opacities. About one third of those 27 (33.8%) had concomitant pneumonia or consolidation changes.

A total of 46 (57.5%) ESKD patients had received antibiotics for a mean duration of 9.5 days. A total of 33 (41%) required high dose steroid (intravenous methylprednisolone 1mg/kg/day) while eight (10 %) were given low dose steroid (intravenous dexamethasone 6mg daily) during the hospitalisation. Almost half (45%) required oxygen therapy during their stay and a quarter (25%) required intubation and inotropes. The mean duration of hospitalisation and ICU stay were 15.92 days and 11.7 days respectively. Twenty (20) ESKD patients were admitted into the ICU; 19 of whom required mechanical ventilation.

A total of 10 (12.5%) ESKD patients in this cohort succumbed due to COVID-19 infection. Seven deaths were reported in the intensive care unit (ICU) and two deaths were reported in the COVID-19 ward. There was one ESKD male patient who died in the emergency department after contracting category 5 COVID-19 infection. His COVID-19 PCR swab test later turned out to be positive after his demise. All the patients who died from COVID-19 infection received mechanical ventilation except for two patients in the COVID-19 ward. One of the two patients who were not ventilated refused active resuscitation or intubation, while the other patient's clinical condition rapidly deteriorated in the ward despite prompt resuscitation.

In this cohort, high dose steroid (intravenous methylprednisolone 1mg/kg/day) was given to ill patients (Category 4 and 5) who developed warning signs or required ICU admission. Low dose steroid (intravenous dexamethasone 6mg daily) was served to Category 3 patients with raised inflammatory markers. Following consultation with the infectious disease team, steroids were administered (high or low dose) for five days before being tapered down based on their clinical responses, inflammatory markers and chest radiographs. Steroids were either extended in terms of duration or escalated (change from dexamethasone to methylprednisolone) if patients deteriorated. Antibiotics were administered to 57% of the cohort for secondary bacterial infection. This was due to prolonged steroid usage or hospital acquired infections as they generally spent an average of 15 days in HEBHK.

Table III shows several factors associated with mortality using simple logistic regression. Absolute lymphocyte count (ALC), OR=0.08 (95%CI: 0.11, 0.56) and serum albumin, OR=0.85 (95%CI: 0.73, 0.98) have an inverse association with COVID-19 mortality. COVID-19 mortality was directly associated with C-reactive protein, OR=1.02 (95%CI: 1.01, 1.04), lactate dehydrogenase, OR=1.01 (95%CI: 1.00, 1.01), mechanical ventilation, OR=17.21 (95%CI: 3.03, 97.67), and high dose steroids, OR=15.71 (95%CI: 1.80, 137.42). There was no correlation between age, gender, BMI, or clinical symptoms and mortality rate in this study.

## DISCUSSION

Given their immunocompromised nature, high comorbidity burden and impracticable social distancing restrictions in haemodialysis centres, ESKD patients with various comorbidities were among the most vulnerable population to be infected with COVID-19 infection.[9,10] Several risk factors such as advanced age >65 years old, chronic systemic diseases namely hypertension, diabetes mellitus, and cardiovascular diseases had been attributed to the increased risk of developing severe type and mortality of COVID-19 infections.[11,12] Mortality rates vary between 16-32% based on reported cases around the world.[13] Herein, our study describes the experience in managing ESKD patients with COVID-19 infection in a COVID-19 hospital setting. The cohort in this study represents 1.12% of total haemodialysis patients in the state of Johor, Malaysia.

The initial presentation of COVID-19 infections varies from being asymptomatic to developing severe acute respiratory distress. However, there were some reported cases of atypical presentation involving gastrointestinal symptoms.[14,15] The most common presenting symptoms in our cohort were cough (53.8%) and fever (46.2%). These findings were similar to several other studies conducted in dialysis centres around the world.[16-18] Approximately 12.5% of our cohort remained asymptomatic throughout hospitalisation. Radiological imaging via chest radiograph showed more than half of our cohort had bilateral infiltrates attributed to active COVID-19 infection or chronic underlying volume overload. Thirty three percent (33%) of them developed consolidations probably from the disease itself or secondary bacterial infection due to their immunocompromised state.

From March 2020 to March 2021, Malaysia recorded 1,272 mortalities out of 345,500 confirmed COVID-19 patients representing 0.37%. Data from HEBHK showed a total admission of 3,552 COVID-19 patients with 87 deaths over a similar period. This represented a 2.44% overall mortality rate. On the other hand, this study has shown that the mortality rate from COVID-19 infection among haemodialysis patients stands at 12.5%. Of the ten deaths recorded in HEBHK, four were classified as deaths due to COVID-19, while the remaining six were due to death with COVID-19. In comparison to the overall national mortality rate in Malaysia and HEBHK, the mortality rate among ESKD patients receiving haemodialysis with COVID-19 is 33.8 times and 5.1 times higher respectively. This mortality rate, however, was lower as compared to the meta-analysis done by Kooman et al., on the outcome of dialysis patients with COVID-19 infections in different centres around the world which recorded a mortality rate that ranged from 16.2% to 32.8%.[13]

There were several relevant factors that may have contributed to the lower mortality rate observed in our cohort. ESKD patients who were unwell with warning signs were detected early and alerted to the healthcare authorities for initial surveillance and hospitalisation. Contact tracing of family members of patients and staff was performed swiftly to contain the spread of COVID-19 infections. Admission of this group of patients was prioritised to enable closer monitoring in wards and to minimise the risk of transmission to other ESKD patients or staff at respective HD centres. Strict adherence to national guidelines in managing ESKD patients with COVID-19 infection was practised. In addition, they were monitored for a period of 2 weeks with regular HD in a designated ward. As the majority of our study population presented with Category 3 and above, early detection of warning signs, prompt referral to intensivists and availability of ICU care with mechanical ventilation improved the overall survival rate as well.

This study found several risk factors associated with increased risk of mortality. This is similar to findings by Tortonese et al., where CRP and LDH showed a direct association with mortality[18]. Patients with high inflammatory markers were more likely to deteriorate as the cytokine storm may lead to severe respiratory distress. Absolute lymphocyte count has an inverse association with mortality as lymphopenia marked the activation of pro- inflammatory cytokines that lead to increased disease severity.[18] Albumin has been a predictor of mortality in various studies dated to the pre-COVID-19 era. Malnutrition, particularly among the dialysis population has been linked to increased deaths during this pandemic.[20] Multivariate analysis of our cohort showed albumin had an inverse association with mortality. The need for mechanical ventilation also increases the risk of death. Our study did not find an association between age, gender or clinical symptoms with mortality.

Systemic corticosteroid administration has been the mainstay treatment of COVID-19 infection especially during the cytokine storms.[21] The initiation of steroid therapy for COVID-19 patients with Category 4 and above was discussed with infectious disease (ID) consultants and based on the national guideline- Clinical Management of Confirmed COVID-19 Case in Adult and Paediatric, Annex 2e.[22] The duration of steroid administration varied based on clinical condition and inflammatory markers after consulting the ID team. In managing ESKD patients with COVID-19, it was found that administering high doses of systemic corticosteroid such as methylprednisolone was associated with a higher mortality risk. This is likely due to an increased risk of nosocomial infections; either ventilator related or prolonged hospitalisation. High doses of systemic corticosteroid were used mainly among ill patients with severe clinical conditions, those who required oxygen supplementation, longer hospitalisation, ICU care and inotropic support.

The introduction of drugs such as hydroxychloroquine, lopinavir, ritonavir and interferon were hotly discussed and debated by experts around the world. These drugs were suggested as a mode of therapy for patients in the first and second waves of the COVID-19 pandemic in Malaysia. Our cohort was recruited mainly from the third wave of the COVID-19 pandemic in Malaysia whereby steroids and oxygen therapy were the mainstay. The data showed only one ESKD patient received hydroxychloroquine as part of COVID-19 treatment whereas two ESKD patients with SLE had their hydroxychloroquine continued during hospitalisation. Three patients received tocilizumab in this cohort (two died, one alive). Tocilizumab was given to patients with severe disease in the ICU based on ID recommendation. In view of the small number of

prescriptions for hydroxychloroquine and tocilizumab, no proper conclusion or data can be analysed to substantiate the effectiveness of these drugs.

The limitations of this study include a small sample size, the retrospective nature of our data and missing laboratory test results of some patients. The true total number of ESKD patients infected with COVID-19 could not be depicted because ethical approval was only obtained for HEBHK. Although this cohort reflected the true demography of multiethnicity disposition in Malaysia, more data was needed to determine the association between various ethnic groups and the need for hospitalisation based on COVID-19 severity. As this cohort only included patients on regular haemodialysis, no data could be compared between haemodialysis, peritoneal dialysis, and transplant patients.

## CONCLUSION

The findings from this study demonstrates a higher mortality rate among hospitalised patients with ESKD receiving haemodialysis. Several risk factors were identified which contributed to higher mortality rate in this study. These factors were low actual lymphocyte count, low albumin, increased CRP, increased LDH and patients who required mechanical ventilation and high dose steroid. Therefore, patients undergoing haemodialysis are at a high risk of mortality. Strict infection control measures and compliance with standard operative protocols are necessary to limit the spread of COVID-19 among this population in order to lower the risk of mortality in ESKD patients. Advocating and expediting vaccination programmes should be encouraged to reduce the severity and mortality of COVID-19 infections.

## ETHICS APPROVAL

This study has been approved by Malaysian Medical Research Ethics Committee (NMRR-20-2729-57507). This is a study involving data collection through medical records, therefore informed consent from patients is not required.

## CONSENT FOR PUBLICATION

We would like to thank the Director-General of Health, Malaysia for his permission to publish this report.

## AVAILABILITY OF DATA AND MATERIALS

The datasets during and/or analysed during the current study are available from the corresponding author on reasonable request.

## COMPETING INTERESTS

The authors declare that they have no competing interests.

## FUNDING

The authors declare that no funding was received for the publication of this study.

## AUTHORS' CONTRIBUTIONS

CHH, CYH and YYL designed the study. CHH, CYH, YYL and TPS executed and analysed the study. TXT, HY and CPW drafted the manuscript. All the authors read and approved the final manuscript.

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