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COVID-19 death and kidney disease in a multiracial Asian country

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Abstract

Introduction: COVID-19 infection and kidney disease (KD) carry a considerable risk of mortality. Understanding predictors of death and KD may help improve management and patient outcome.

Methods: This is a prospective multicentre observational study conducted in a multiracial Asian country to identify predictors of death and acute kidney injury (AKI) in hospitalized COVID-19 patients from January to June 2020.

Results: A total of 6078 patients were included in this study. Mean age was 37.3 (±16.8) years, 71% were male, 59.4% Malay, 6.7% Chinese, 2.3% Indian and 31.7% other ethnicities. AKI was seen in 3.5% of patients while 1.6% had pre-existing chronic kidney disease (CKD). Overall case fatality rate (CFR) was 1.3%. Patients with KD (AKI and CKD) had CFR of 20%. Many factors were associated with increased risk of death and AKI. However, significant predictors of death after adjustment for covariates were age (>70 years), Chinese ethnicity, diabetes mellitus (DM) and KD. Adjusted predictors of AKI were age (>51 years), DM and severity at presentation. Chinese were 2.58 times more likely to die ($p = .036$) compared to Malay. Centre capacity to manage, ventilate and dialyze patients significantly influenced death. Among those with AKI, the most common symptoms were fever, cough, and dyspnea. They had lower absolute lymphocyte count, were more likely to be admitted to ICU, required more ventilation and longer hospitalization.

Conclusion: Patient and centre factors influence death and AKI among COVID-19 patients. This study also demonstrates death disparities across different racial groups and centre capacities in this multiracial Asian country.

KEYWORDS
COVID-19, death, ethnicity, kidney disease, risk factors

SUMMARY AT A GLANCE

This study found that COVID-19 has disproportionately impacted vulnerable populations: elderly, those with kidney disease, diabetes, and certain ethnic group. There were also death discrepancies in centre's capacity to manage, ventilate and dialyze patients.

1 | INTRODUCTION

As of 1st July 2021, 181 722 790 confirmed cases of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated coronavirus disease 2019 (COVID-19) have been reported globally, including 3 942 233 deaths.[1] Studies have highlighted various risk factors associated with death and kidney disease (KD) in COVID-19 patients. In the west, high incidences of COVID-19 infection and mortality were reported to affect various ethnic groups differently, especially among minorities. This was mainly attributed to the lack of access to healthcare facilities and socio-economic reasons.[2,3]

Studies have shown that Asian minorities have comparable case fatality rate (CFR) with white people while other ethnic minorities like Black and Latinos have higher CFR.[4] With an abundance of different racial groups within Asia, it is possible for each race to have different risk factors associated with COVID-19 mortality. Unfortunately, literature elaborating on the mortality of different races within Asia is scarce. This could be because most studies pool Asian races together instead of analysing them independently.

Malaysia is unique in this sense as our 32.75 million population consists of three major racial groups in Asia, namely the Malays (69.7%) from the Malay Archipelago, the Chinese (22.5%) from East Asia and the Indians (6.8%) from South Asia, the Kadazan, Iban and Dayak from Borneo. This study was conducted to identify patient factors, comorbidities and centre factors linked to COVID-19 deaths and acute kidney injury (AKI) in our unique multiracial Asian population.

2 | METHODS

This is a prospective multicentre observational study involving data from 18 hospitals in Malaysia designated to treat COVID-19. Patients aged 12 years and above, who were admitted from January to June 2020, following positive reverse transcription polymerase chain reaction (RT-PCR) test were included in this study. Patient demographics including gender, age, race, clinical data, laboratory data and outcome were collected until their day of discharge. This study was approved by the Medical Research and Ethics Committee (NMRR-21-59-57 908).

The COVID-19 Management Guideline of the Ministry of Health, Malaysia was developed based on the consensus of an expert panel. Patients were managed by infectious disease teams in accordance with this guideline which was the common practice of all centres. Staging was based on clinical severity as per Malaysia's COVID-19 guidelines. Stage 1: asymptomatic; Stage 2: symptomatic without pneumonia; Stage 3: pneumonia without hypoxia; Stage 4: pneumonia with hypoxia requiring oxygen supplementation; Stage 5: critically ill. Stage 1 & 2 is of mild disease, whereas stage 3 onwards is of severe disease.[5]

In order to ensure that death statistics in Malaysia is in accordance with WHO guidelines, accurate classification of COVID-19 death is crucial. Causality of death due to COVID-19 was ascertained based on Ministry of Health guidelines that was developed following discussions with infectious disease medical specialists, forensic medical specialists and the national committee of COVID-19 mortality review.

The criteria for the classification of "Death due to COVID-19" for hospitalized patients is as follows:

1. COVID-19 positive case that has been confirmed through laboratory tests (RT-PCR or similar);
2. Death resulting from clinically compatible disease;
3. No clear alternative cause of death that is not related to COVID-19 infection (Examples: death due to trauma, road traffic accident or suicide);
4. No period of complete recovery from COVID-19 between illness and death; and
5. Even with pre-existing disease (e.g., cancer), it is death due to COVID-19 if the reason for the severe course is due to COVID-19 infection.[1,5]

KD in this article includes both new AKI patients and existing CKD patients. AKI and CKD were defined using modified KD Improving Global Outcomes (KDIGO) definition as previously used[6] or captured in case mix at respective institutions. AKI is defined as:

1. An increase in serum creatinine of 0.3 mg/dl (26.5 mmol/L) within 48 h OR;
2. An increase in serum creatinine to more or equal to 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days OR;
3. Urine output of <0.5 ml/kg/h for 6 h.

Development of de novo CKD is defined as kidney damage or an eGFR<60 ml/min/1.73 m^2 present on at least two occasions for >3 months. Progression of pre-existing CKD is defined as decline in eGFR >15% or a decrease in eGFR >5 ml/min/1.73 m^2 over 12 months.

Liver injury is defined as deranged liver enzymes with or without deranged international normalized ratio (INR) or bilirubin. Bacteraemia is defined as culture positive with or without raised white cell count (WCC), raised C-reactive protein (CRP), signs and symptoms of infection. Cardiac complication includes endocarditis, cardiac arrythmia, cardiac ischemia, congestive heart failure and cardiac arrest. Coagulopathy is defined as abnormality of the haemostasis compartments such as thrombocytopenia, abnormally high-prothrombin time (PT)/INR or activated partial thromboplastin time.

2.1 | Statistical analysis

Mean and standard deviation (SD) was used to represent normally distributed continuous variables, while median and interquartile range (IQR) was used to represent non-normally distributed continuous variables. Categorical variables were expressed in frequency and percentage (%). Mortality rate was expressed using CFR, which is calculated by dividing the number of deaths due to COVID-19 in a group of test-positive individuals over the period of study duration by the total number of individuals in that group. This value is then multiplied by

100 to yield a percentage value. CFR eases comparison with other studies as it is commonly used to estimate the proportion of deaths among identified COVID-19 cases.

The main outcomes of interest are death and AKI. Unadjusted and adjusted odds ratio of death and AKI was determined using univariate and multivariate logistic analysis and expressed using odds ratio (OR) and 95% confidence interval (CI). Potential confounders include demographic data such as age, gender, race, comorbidities like hypertension, diabetes mellitus (DM), chronic cardiac disease, obesity, KD, chronic pulmonary disease, severity of presentation, laboratory parameters like haemoglobin (Hb), platelet, WCC, absolute lymphocyte count (ALC), serum creatinine, ICU admission, mechanical ventilation and centre factors like the number of COVID-19 patients managed by respective hospitals, number of ventilated patients and provision of kidney replacement therapy (KRT). These confounders were selected based on clinical importance and significance from previously published studies. Statistical analysis was performed using Kruskal Wallis test, Mann–Whitney U test, Chi Square and Fisher's exact test. p value of <0.05 was taken as significant. Data analysis was performed using SPSS version 20.0 and STATA software version 13.

3 | RESULTS

3.1 | Baseline Characteristics

From January to June 2020, there were a total of 6078 patients who were hospitalized for COVID-19 infection. Their mean age was 37.3 (±16.8) years, 4303 (70.8%) of them were male, 3609 (59.4%) of them were Malay, 405 (6.7%) were Chinese, 138 (2.3%) were Indian and 1926 (31.7%) were of other races. Out of the total number, 312 (5.1%) had KD. Within this group, 100 (1.6%) patients had CKD while 212 (3.5%) patients developed AKI. The mean age of patients with CKD and AKI were 59.6 (±12.2) and 56.2 (±15.2) years respectively. Hypertension was seen in 768 (13.3%) of non-KD patients, 81 (81%) of CKD patients and 105 (49.5%) of AKI patients while DM was seen in 454 (7.9%) of non-KD patients, 60 (60%) of CKD patients and 85 (40.1%) of AKI patients. One hundred and forty-two (2.5%), 27 (27%) and 27 (12.7%) incidence of chronic cardiac disease was seen among non-KD, CKD and AKI patients respectively (Table 1).

3.2 | Presenting symptoms and laboratory results

Presenting symptoms of patients with KD (CKD, AKI) were fever (51 [51%], 129 [60.9%]), respiratory symptoms like cough (54 [54%], 137 [64.6%]), shortness of breath (24 [24%], 51 [24.1%]), gastro-intestinal symptoms like diarrhoea (15 [15%], 44 [20.8%]), nausea and/or vomiting (10 [10%], 14 [6.6%]) (Table 1). About 80% of non-KD patients presented asymptomatically (stage 1: 2948 (51%) and with mild symptoms (stage 2: 1815 (31.5%), whereas about 75% of KD patients presented with severe disease (CKD patients COVID-19 stage 3: 26 [26%], stage 4: 24 [24%], stage 5: 14 [14%]; AKI patients COVID-19- stage 3: 34 [16%], stage 4: 61 [28.8%], stage 5: 34 [16%]). Median ALC among non-KD patients was 2.20 (1.70, 2.80) cell/μl, 1.30 (0.90, 1.82) cells/μl among CKD patients and 1.40 (1.01, 2.00) cell/μl among AKI patients. Duration of hospitalization was 11 (8, 14), 14 (10, 28) and 14 (9, 24) days among non-KD, CKD and AKI patients respectively. There were 1.3% non-KD patients, 39% CKD patients and 44.3% AKI patients admitted in ICU. Mechanical ventilation was required by 0.5% non-KD patients, 32% CKD patients and 40.6% AKI patients (Table 2).

3.3 | Treatment and management

Steroid treatment was given to 27 (0.5%) of non KD patients, 11 (11%) of CKD patients and 17 (8%) of AKI patients. Six hundred and ninety-seven (12%), 54 (54%) and 107 (50%) of patients were administered with antiviral medication within the non-KD, CKD and AKI groups respectively (Table 2). Among patients with KD, the median proportion of those who required KRT was 8.9%. The provision of KRT between hospitals varied widely, with 18.58% as the upper limit of the interquartile range (Table 3).

3.4 | Risk factors for AKI

Unadjusted risk factors for AKI were age, race, comorbidities such as hypertension, DM, obesity, chronic cardiac disease, chronic pulmonary disease and severity (stages) of COVID-19 infection upon presentation (Table 4). After adjusting for other confounders, age, DM and severity upon presentation were found to be significant predictors of AKI. Individuals who were older than 51 years had higher risk of AKI [51–70 years, OR: 3.22 (95% CI: 1.87, 5.55), $p < .001$], [≥71 years, OR: 4.72 (95% CI: 2.28, 9.76), $p < .001$]. DM had an independent association with AKI [OR: 1.90 (95% CI: 1.29, 2.80), $p = .001$]. Patients presenting with severe COVID-19 symptoms were also more likely to develop AKI [stage 3, OR: 2.46 (95% CI: 1.44, 4.22), $p = .001$, stage 4, OR: 4.15 (95% CI: 2.26, 7.63), $p < .001$ and stage 5, OR: 3.93 (95% CI: 1.70, 9.08), $p = .001$]. Complications linked to AKI were liver injury [OR: 2.65 (95% CI: 1.74, 4.05), $p < .001$] and acute respiratory distress syndrome (ARDS) [OR: 2.82 (95% CI: 1.57, 5.08), $p = .001$]. Patients who developed AKI were almost six times more likely to require mechanical ventilation [OR: 5.72 (95% CI: 3.13, 10.45), $p < .001$] when compared to non-AKI patients (Table 4).

3.5 | Case fatality rate

The overall CFR was 1.3%. Chinese patients had higher CFR compared to other races (Chinese 3.7%, Malay 1.3%, Indian 1.4% and other races 0.7%). CFR for those with KD was notably higher (20.2%). Chinese patients with KD were more likely to die with CFR of 32.4%, followed by other races (21.1%), Malays (18.2%) and Indians (15.4%) [OR: 3.76 (95% CI: 1.63, 8.68), $p < .002$] (Table 5).

TABLE 1 Baseline characteristics, presenting symptoms and COVID-19 severity among hospitalized COVID-19 versus kidney disease patients

			KD (N = 312)		
	Total N = 6078	No KD (N = 5766)	CKD N = 100 (1.6%)	AKI N = 212 (3.5%)	*p* value[d]
Age, mean (SD)	37.3 (16.8)	36.2 (16.2)	59.6 (12.2)	56.2 (15.2)	.0001[a]
Age group, n (%)					<.0001[b]
≤30 years	2607 (42.9)	2585 (44.8)	1 (1.0)	21 (9.9)	
31–50 years	1945 (32.0)	1876 (32.6)	21 (21.0)	45 (21.3)	
51–70 years	1351 (22.2)	1174 (20.4)	60 (60.0)	117 (55.2)	
≥71 years	174 (2.9)	127 (2.2)	18 (18.0)	29 (13.7)	
Male gender, n (%)	4303 (70.8)	4043 (70.0)	77 (77.0)	183 (86.3)	<.0001[b]
Ethnicity, n (%)					<.0001[b]
Malay	3609 (59.4)	3403 (59.0)	68 (68)	138 (65.1)	
Chinese	405 (6.7)	370 (6.4)	14 (14)	21 (9.9)	
Indian	138 (2.3)	125 (2.2)	7 (7)	6 (2.8)	
Other Malaysian	1926 (31.7)	1868 (32.4)	11 (11)	47 (22.2)	
Presence of comorbidity, n (%)					
Hypertension	954 (15.7)	768 (13.3)	81 (81.0)	105 (49.5)	<.0001[b]
Diabetes mellitus	599 (9.9)	454 (7.9)	60 (60.0)	85 (40.1)	<.0001[b]
Chronic cardiac disease	196 (3.2)	142 (2.5)	27 (27.0)	27 (12.7)	<.0001[b]
Obesity	95 (1.6)	83 (1.4)	3 (3.0)	9 (4.3)	.004[c]
Chronic pulmonary disease (except asthma)	35 (0.6)	26 (0.5)	3 (3.0)	6 (2.8)	<.0001[c]
Presenting symptoms, n (%)					
Fever	1821 (30.0)	1641 (28.5)	51 (51.0)	129 (60.9)	<.0001[b]
Cough	1958 (32.2)	1767 (30.7)	54 (54.0)	137 (64.6)	<.0001[b]
Shortness of breath	322 (5.3)	247 (4.3)	24 (24.0)	51 (24.1)	<.0001[b]
Diarrhoea	316 (5.2)	257 (4.5)	15 (15.0)	44 (20.8)	<.0001[b]
Nausea and/or vomiting	116 (1.9)	92 (1.6)	10 (10.0)	14 (6.6)	<.0001[c]
Anosmia	166 (2.7)	163 (2.8)	1 (1.0)	2 (1.0)	.133[b]
Ageusia	40 (0.7)	40 (0.9)	0 (0.0)	0 (0.0)	.569[c]
Case severity upon admission, n (%)					
Stage 1: Asymptomatic	2996 (49.3)	2948 (51.1)	20 (20.0)	28 (13.2)	<.0001[b]
Stage 2: Symptomatic without pneumonia	1882 (31.0)	1815 (31.5)	15 (15.0)	52 (24.5)	
Stage 3: Pneumonia without hypoxia	856 (14.1)	796 (13.8)	26 (26.0)	34 (16.0)	
Stage 4: Pneumonia with hypoxia	236 (3.9)	151 (2.6)	24 (24.0)	61 (28.8)	
Stage 5: Critically ill	63 (1.0)	15 (0.3)	14 (14.0)	34 (16.0)	

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; SD, standard deviation.
[a]Kruskal-Wallis test for continuous variables.
[b]Chi squared test.
[c]Fisher's exact test for categorical variables.
[d]*p* value is obtained by comparing Non kidney disease patients, CKD patients and AKI patients.

3.6 | Risk factors for death

3.6.1 | Patient factors

Unadjusted risk factors for death were age, race, comorbidities such as hypertension, KD, DM, obesity, cardiac and pulmonary disease. After adjusting for other variables, age, race, KD and DM were found to be significant predictors for death. Patients aged between 51–70 years old had 7.7 times higher risk of death [OR: 7.71 (95% CI: 1.69, 35.22), $p < .008$] when compared to those aged <30 years old. The risk of death was 30 times higher for individuals more than 70 years of age [OR: 29.38 (95% CI: 6.08, 142.03), $p < .001$] when compared to those aged <30 years old. The odds of dying were 2.22 times more in diabetic patients [OR: 2.22 (95% CI: 1.20, 4.11),

TABLE 2 Clinical and laboratory parameters among hospitalized COVID-19 versus kidney disease patients

			KD (N = 312)		
	Total N = 6078	No KD (N = 5766)	CKD N = 100 (1.6%)	AKI N = 212 (3.5%)	*p* value[d]
Admission vital signs, median (IQR)					
Systolic BP (mmHg)	128.0 (117.0, 139.0)	128.0 (117.0, 138.0)	141.0 (125.0, 157.0)	132.0 (118.0, 147.0)	.0001[a]
Diastolic BP (mmHg)	78.0 (70.0, 86.0)	78.0 (70.0,86.0)	75.0 (67.0, 84.0)	78.0 (88.0, 87.0)	.1538[a]
		85.0 (76.0,94.0)			
Fever (≥37.5 °C), n (%)	549 (9.1)	748 (13.0)	25 (25.0)	58 (27.4)	<.0001[b]
Tachycardia (≥100 bpm), n (%)	827 (13.6)	466 (8.1)	25 (25.0)	54 (25.5)	<.0001[b]
Tachypnoea (≥21 bpm), n (%)	431 (7.1)	336 (5.8)	25 (25.0)	70 (33.0)	<.0001[b]
Laboratory tests, median (IQR)					
Haemoglobin (g/dl)	14.4 (13.2, 15.4)	14.4 (13.2,15.4)	11.8 (9.8, 13.3)	13.9 (12.7, 15.2)	.0001[a]
Platelet ($\times 10^9$/L)	264 (219, 316)	267 (221317)	218 (173, 279)	216 (167, 276)	.0001[a]
Absolute neutrophil count (cells/ul)	4.34 (3.20, 5.70)	4.30 (3.20,5.69)	5.20 (3.40, 7.80)	4.80 (3.50, 6.90)	.0001[a]
Absolute lymphocyte count (cells/ul)	2.20 (1.62, 2.80)	2.20 (1.70,2.80)	1.30 (0.90, 1.82)	1.40 (1.01, 2.00)	.0001[a]
Serum urea (mmol/L)	3.7 (3.0, 4.6)	3.6 (3.0,4.4)	12.4 (7.7, 20.1)	5.5 (4.5, 8.3)	.0001[a]
Serum sodium (mmol/L)	139 (138, 141)	139 (138141)	137 (133, 139)	137 (134, 139)	.0001[a]
Serum potassium (mmol/L)	3.8 (3.5, 4.1)	3.8 (3.5,4.0)	4.3 (3.8, 4.8)	3.9 (3.5, 4.3)	.0001[a]
Serum creatinine (μmol/L)	78 (65, 90)	77 (64,88)	257 (154, 682)	115 (97, 132)	.0001[a]
Medication, n (%)					
Steroid	55 (0.9)	27 (0.5)	11 (11.0)	17 (8.0)	<.0001[c]
Antiviral drugs	858 (14.1)	697 (12.1)	54 (54.0)	107 (50.5)	<.0001[c]
Hydroxychloroquine	1725 (28.4)	1573 (27.3)	50 (50.0)	102 (48.1)	<.0001[b]
Chloroquine	89 (1.5)	76 (1.3)	3 (3.0)	10 (4.7)	.001[c]
Tocilizumab	7 (0.1)	3 (0.1)	3 (3.0)	1 (0.5)	<.0001[c]
Complications					
Liver injury	411 (6.8)	320 (5.6)	20 (20.0)	71 (33.5)	<.0001[b]
Acute respiratory distress syndrome	147 (2.4)	38 (0.7)	27 (27.0)	82 (38.7)	<.0001[b]
Bacteraemia	45 (0.7)	7 (0.1)	10 (10.0)	28 (13.2)	<.0001[c]
Arrythmia	44 (0.7)	11 (0.2)	13 (13.0)	20 (9.4)	<.0001[c]
Heart failure	23 (0.4)	7 (0.1)	7 (7.0)	9 (4.3)	<.0001[c]
Coagulopathy	13 (0.2)	2 (0.0)	2 (2.0)	9 (4.3)	<.0001[c]
Outcome					
Duration of hospitalization, days	11 (8,15)	11 (8,14)	14 (10, 28)	14 (9, 24)	.0001[a]
Admission to ICU	207 (3.4)	74 (1.3)	39 (39.0)	94 (44.3)	<.0001[b]
Mechanical ventilation	149 (2.5)	31 (0.5)	32 (32.0)	86 (40.6)	<.0001[b]
Death (CFR)	77 (1.3)	15 (0.3)	15 (15.0)	47 (22.2)	<.0001[b]

Abbreviations: AKI, acute kidney injury; BP, blood pressure; CFR, case fatality rate; CKD, chronic kidney disease; ICU, intensive care unit; IQR, interquartile range; SD, standard deviation.

[a]Kruskal-Wallis test for continuous variables.

[b]Chi squared test.

[c]Fisher's exact test for categorical variables.

[d]*p* value is obtained by comparing Non kidney disease patients, CKD patients and AKI patients.

$p = .011$] compared to non-diabetic patients. Patients with KD had 42 times higher chances of dying [OR: 42.00 (95% CI: 21.58, 81.73), $p < .001$] compared with patients without KD (Table 6).

Chinese were found to have 2.58 times higher risk of death when compared to Malay [OR: 2.58 (95% CI: 1.06, 6.260), $p = .036$] (Table 6). A large proportion of Chinese were beyond 51 years old (33.3%), had more DM (8.6%) and KD (8.6%). A huge percentage of Chinese also presented with more severe disease (stage III to V: 36.5%), required more ICU admission [27 (6.7%)] and ventilatory support [19 (4.7%)] compared to other races (Table 7).

TABLE 3 Distribution of kidney disease, kidney replacement therapy and death in 18 hospitals

Hospital	Total COVID-19 patients	Total KD[a] N = 312 (%)	Total KRT N = 38 (%)	Total death N = 77 (%)
1	2575	125 (4.9)	15 (12.0)	13 (0.5)
2	455	33 (7.3)	1 (3.0)	12 (2.6)
3	467	28 (6.0)	4 (14.3)	15 (3.2)
4	200	21 (10.5)	2 (9.5)	4 (2.0)
5	324	20 (6.2)	5 (25.0)	4 (1.2)
6	136	12 (8.8)	1 (8.3)	9 (6.6)
7	56	11 (19.6)	0	0
8	225	10 (4.4)	1 (10.0)	4 (1.8)
9	767	10 (1.3)	2 (20.0)	7 (0.9)
10	144	8 (5.6)	3 (37.5)	3 (2.1)
11	99	7 (7.1)	0	1 (1.0)
12	106	5 (4.7)	0	1 (0.9)
13	110	5 (4.5)	0	1 (0.9)
14	85	4 (4.7)	3 (75.0)	1 (1.2)
15	197	4 (2.0)	0	0
16	4	3 (75.0)	0	0
17	112	3 (2.7)	1 (33.3)	1 (0.9)
18	16	1 (6.3)	0	1 (6.3)
Median (IQR) percentage		5.8 (4.55, 7.25)	8.9 (0, 18.58)	1.1 (0.90, 2.08)

Abbreviations: IQR, interquartile range; KD, kidney disease; KRT, kidney replacement therapy.
[a]CKD and AKI.

3.6.2 | Centre factors

The risk of death was found to be higher in centres managing less patients [<200 patients, OR: 3.32 (95% CI: 1.09 10.13), $p = .035$] after adjustment for other confounders (Table 6).

Risk of death was lower in centres which provided more kidney replacement therapy (KRT) [KRT support ≥3, OR: 0.37 (95% CI: 0.17, 0.790), $p = .010$] (Table 6).

The capacity for centres to manage ventilated patients was also found to affect death significantly. Compare to centres with ≤4 capacity for ventilated patients, centres with 5–8 capacity for ventilated patients, the unadjusted OR for death was 2.38 while the adjusted OR was 6.04 (95% CI: 1.69, 21.61, $p = .006$), and centres with ≥9 capacity for ventilated patients the unadjusted OR for death was 1.59 with adjusted OR of 6.00 (95% CI: 1.31, 27.38, $p = .021$) (Table 6).

4 | DISCUSSION

The purpose of this study was to identify predictors of death and AKI in multiracial COVID-19 patients. Adjusted predictors for death were race, age, KD and DM. Centre factors were also found to significantly influence death. Adjusted risk factors for AKI among COVID-19 patients were age, DM and disease severity at presentation.

The CFR reported in Asian countries was 1%–2% while the CFR in Europe was 4%–5%.[7] Our study revealed CFR of 1.3%. European reports showed CFR of 15%–60% in KD patients[8–12] while in Asia, patients with KD had CFR of 25%–86%.[13] In our study, KD patients had CFR of 20%. This was closer to the lower range of European and Asian CFR. Risk factors associated with death reported in literature include KD (AKI + CKD), haematuria, dialysis, organ transplant, hypoglycaemia, DM, heart disease, older age, chronic obstructive pulmonary disease, gender, elevated baseline creatinine, leucocytosis, and hypercholesterolemia.[9,14–16] Although some of these factors appeared to be significant in our univariate analysis, after correction for other confounders with multivariate analysis, age, ethnicity, KD and DM were found to be independent predictors of death in COVID-19 patients.

Reports have revealed higher risk of mortality among male patients.[15,16] Our study however, did not show such gender preponderance. The association between age and COVID-19 deaths has garnered extensive attention.[9,12] Among our patients, those aged 70 and above had almost 30 times higher chances of dying. From a geroscience perspective, Promislow explained how age-related reduction in inflammatory and immune response could result in cytokine storm following excessive release of pro-inflammatory cytokines.[17]

DM has been described as a predictor of morbidity and mortality in COVID-19 patients.[15] In our study, diabetic patients were 2.22 times more likely to die of COVID-19 infection compared to non-diabetic patients. Though the exact mechanism is unknown, there are some postulations. The immune response and cytokine profile of patients with type-2 DM was found to be higher than non-diabetics.[18]

TABLE 4 Significant risk factors for AKI related to COVID-19

	Unadjusted OR		Adjusted OR	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age group				
<30	Ref		Ref	
31–50 years	2.92 (1.73, 4.91)	<.001	1.67 (0.95, 2.90)	.067
51–70 years	11.68 (7.30, 18.67)	<.001	3.22 (1.87, 5.55)	<.001
≥71 years	24.63 (13.71, 44.25)	<.001	4.72 (2.28, 9.76)	<.001
Gender				
Male	Ref			
Female	0.37 (0.25, 0.56)	<.001	NS	—
Ethnicity				
Malay	Ref			
Chinese	1.38 (4.36, 7.62)	.185	NS	—
Indian	1.14 (5.19, 9.25)	.753	NS	—
Others	0.63 (3.18, 7.54)	.007	NS	—
Comorbidities				
Hypertension	5.77 (4.36, 7.62)	<.001	NS	—
Diabetes mellitus	6.93 (5.19, 9.25)	<.001	1.90 (1.29, 2.80)	.001
Chronic cardiac disease	4.89 (3.18, 7.54)	<.001	NS	—
Obesity	3.01 (1.49, 6.08)	.002	NS	—
Chronic pulmonary disease	5.83 (2.39, 14.19)	<.001	NS	—
Severity				
Stage I: Asymptomatic	Ref		Ref	
Stage II: Symptomatic without pneumonia	3.01 (1.89, 4.79)	<.001	2.54 (1.57, 4.11)	<.001
Stage III: Pneumonia without hypoxia	4.38 (2.64, 7.27)	<.001	2.46 (1.44, 4.22)	.001
Stage IV: Pneumonia with hypoxia	36.95 (23.03, 59.28)	<.001	4.15 (2.26, 7.63)	<.001
Stage V: Critically ill	124.28 (66.88, 230.93)	<.001	3.93 (1.70, 9.08)	.001
Complications				
Liver injury	8.12 (5.98, 11.02)	<.001	2.65 (1.74, 4.05)	<.001
Acute respiratory distress syndrome	55.87 (38.63, 80.80)	<.001	2.82 (1.57, 5.08)	.001
Bacteraemia	51.98 (27.96, 96.65)	<.001	2.87 (1.29, 6.36)	.009
Mechanical ventilation	63.90 (44.10, 92.60)	<.001	5.72 (3.13, 10.45)	<.001

Abbreviations: CI, confidence interval; NS, not significant; OR, odds ratio.

This may lead to severe disease and even death. Micro and macrovascular complications associated with diabetes such as nephropathy and coronary artery disease could also influence the outcome of COVID-19 patients.

Mortality reporting in the top 10 countries with high COVID-19 case notification, surprisingly did not require race related information.[19] Nevertheless, racial differences have been reported as a contributing factor of death in the west.[2–4,20] A systemic review and meta-analysis by Sze S et al showed pooled hazard ratio of 1.19 for risk of mortality in Asian minorities with COVID-19 infection in the US and UK.[20] Centers for Disease Control and Prevention (CDC) reported similar rate ratios of positive COVID-19 cases, hospitalizations and death in Asian non-Hispanic persons compared to White non-Hispanic persons.[4] In Western Asia, a study involving 405 COVID-19 patients showed notably higher mortality rates among minority South Asians compared to the local Arab population.[21]

Our study is the first to report differences within a multiracial Southeast Asian population. Chinese had 2.58 times higher mortality rate compared to Malay. Although the exact reason may not be ascertained, both genetic and non-genetic differences may play an interchangeable role.[22] Selection bias with over representation of individuals with higher risk of death among the Chinese was unlikely as our cohort was almost representative of the actual racial distribution in Malaysia. Chinese in Malaysia have educational background that is at par with other races. They mainly reside in urban areas (93.6%) compared to the overall population (79.8%). Their mean monthly household income is 9900 Malaysian Ringgit while the mean monthly household income of the overall population is 7900

TABLE 5 Case fatality rates by race and KD in 6078 COVID-19 Patients

	CFR, %		Unadjusted OR				Adjusted OR			
			Overall		With KD[a]		Overall		With KD[a]	
	Overall	With KD[a]	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Overall	1.28	20.2								
Malay	1.28	18.2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Chinese	3.73	32.4	2.98 (1.65, 5.38)	<.001	2.14 (0.96, 4.78)	.062	3.76 (1.63, 8.68)	0.002	1.61 (0.14, 4.34)	.763
Indian	1.45	15.4	1.13 (0.27, 4.70)	.867	0.82 (0.17, 3.84)	.797	0.23 (0.03, 2.02)	0.184	1.76 (0.34, 9.03)	.496
Others	0.73	21.1	0.57 (0.31, 1.03)	.064	1.20 (0.58, 2.48)	.630	1.90 (0.84, 4.28)	0.121	3.80 (0.68, 21.12)	.127

Abbreviations: CFR, case fatality rate; KD, kidney disease.
[a]CKD and AKI.

Malaysian Ringgit.[23,24] Despite this, their mortality rate is higher than other races. Contributing factors from our study points towards older age and the presence of comorbidities like KD as the possible explanation for their increased risk of death. Their life expectancy is 75.4 years (male) and 80.5 years (female) while the overall life expectancy in Malaysia is 72.6 years (male) and 77.6 years (female). Furthermore, their COVID-19 presentation was more severe, with lower ALC compared to other races.

When this disease first emerged, focus was mostly on pulmonary manifestations as its mode of transmission was through the respiratory tract. However, symptoms related to other organ involvement begun to surface soon after. Extra-pulmonary involvement and its association with patient outcome has received much more scrutiny ever since. In our cohort, 3.5% of patients developed AKI. Some studies had higher prevalence of AKI while others were similar to ours. With the clinical presentation of COVID-19 infection broadly variable, it is hardly surprising that AKI prevalence has such a wide range (5.1%–70.7%).[13] Risk factors for AKI in COVID-19 patients reported in literature include male gender, advanced age, body mass index (BMI), hypertension, DM, ARDS, CKD, cardiovascular disease, peripheral vascular disease, haematological malignancy, severity of illness, transaminitis, elevated trop-I, elevated c-reactive protein, d-dimer, ferritin, lactate dehydrogenase, procalcitonin, triglycerides, neutrophil count and total white count, ventilation, ICU admission and need for vasopressors.[8,11,25–27] While some of these factors may have appeared in our univariate analysis, advanced age, DM and severity at presentation were the only independent risk factors for AKI following multivariate analysis.

With about 10% of the world's population suffering from CKD, it has emerged as a huge public health concern.[6,28] If left unmonitored, this "silent killer" may lead to end stage KD, development of cardiovascular disease and even sudden death.[29] Many studies have demonstrated that pre-existing CKD was a significant contributing factor to severity (OR 3–3.3) and mortality (28%–41%) in COVID-19 patients.[9,11,30–32] In our cohort, 1.6% of patients presented with underlying CKD and along with 3.5% of patients with AKI, KD patients had CFR of 20%. According to Henry and Lippi, patients with CKD had three times higher risk of developing severe COVID 19 infections.[30] ERA-EDTA council and ERACODA working group highlighted that dialysis (3.7×), organ transplant (3.5×) and advanced CKD (2.5×) were three of the top four risk factors associated with COVID-19 deaths.[14] A study by Collado et al showed that COVID-19 infected patients with advanced CKD with or without AKI had a tendency to present with more respiratory symptoms like cough and dyspnoea.[10] This was similar to our findings. The prevalence of cardiovascular disease among patients with KD could worsen fluid overload and lead to exacerbation of respiratory symptoms.[2] Gastrointestinal symptoms were also commonly seen among our KD patients. Presence of uraemia may further aggravate gastrointestinal symptoms like nausea and vomiting.

There is a paucity of literature associating centre effect and COVID-19 mortality. In general, bigger hospitals and haemodialysis facilities have been associated with lower patient mortality rates.[33] In

TABLE 6 Significant risk factors for death related to COVID-19

	Unadjusted OR		Adjusted OR	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Patient factors				
Age				
<30	Ref		Ref	
31–50 years	6.05 (1.31, 28.04)	.021	2.09 (0.41, 10.55)	.373
51–70 years	40.83 (9.86, 169.05)	<.001	7.71 (1.69, 35.22)	.008
>70 years	218.33 (51.23, 930.54)	<.001	29.38 (6.08, 142.03)	<.001
Malay	Ref		Ref	
Chinese	2.98 (1.65, 5.38)	<.001	2.58 (1.06, 6.26)	.036
Indian	1.13 (0.27, 4.70)	.867	0.25 (0.03, 2.10)	.199
Others	0.57 (0.31, 1.03)	.064	1.82 (0.78, 4.26)	.166
Comorbidities				
Kidney disease	96.32 (54.02, 171.73)	<.001	42.00 (21.58, 81.73)	<.001
Diabetes mellitus	11.02 (6.98, 17.38)	<.001	2.22 (1.20, 4.11)	.011
Cardiac disease	12.39 (7.34, 20.92)	<.001	NS	—
Hypertension	9.78 (6.12, 15.65)	<.001	NS	—
Obesity	4.92 (1.93, 12.54)	.001	NS	—
Pulmonary disease	5.06 (1.19, 21.55)	.028	NS	—
Number of patients				
≥200	Ref		Ref	
<200	1.45 (0.85, 2.46)	.174	3.32 (1.09, 10.13)	.035
Capacity for ventilated patients				
≤4	Ref		Ref	
5–8	2.38 (0.92, 6.16)	.075	6.04 (1.69, 21.61)	.006
≥9	1.59 (0.63, 4.04)	.330	6.00 (1.31, 27.38)	.021
Number of KRT support				
<3	Ref		Ref	
≥3	0.51 (0.32, 0.80)	.003	0.37 (0.17, 0.79)	.010

Abbreviations: CI, confidence interval; KRT, kidney replacement therapy; NS, not significant; OR, odds ratio.

this study, centre capacity to treat more patients and ability to provide more KRT were found to be associated with lower mortality. The reason for this is yet to be determined. However, there are some possible explanations. Lower risk of death in larger centres could be a reflection of the presence of better facilities and more experienced medical staff. Despite being statistically insignificant, our univariate analysis showed that centres with less ventilation capacity and centres with larger ventilation capacity had lower risk of death compared to centres with medium ventilation capacity. However, after adjusting for patient demographics, centres with medium and larger ventilation capacity had six times higher risk of death compared to centres with less ventilation capacity. This could be because centres with less ventilation capacity, manage fewer and less severe patients thus have lower risk of death. Further studies should be done to evaluate the association between centre ventilation capacity and mortality.

The strength of this study is that it involves big data from multiple centres in a multiracial country. The data contains a colossal of demographic and clinical information that is important, especially now as the pandemic has projected more questions than answers. Statistical analysis, particularly multivariate regression was more meaningful with the availability of this comprehensive data. This study however, has its limitations. As information was collected and submitted voluntarily from 18 different hospitals to form this database, there were concerns about missing or unavailable data. More kidney specific data, like urinalysis, urine output and details pertaining to KRT would have shed more light on the dynamics of managing COVID-19 patients with KD. Confounders are important for validity of causal inference. There may be other variables, related to the manipulated variable that could influence the dependent variable. Although statistical adjustment for confounders was done in this study, we may not have adequately considered the full range of confounders.

In conclusion, with the findings of this study, we would like to emphasize that the severity, complications and outcome of hospitalized COVID-19 patients are determined by baseline characteristics

TABLE 7 Demographic and clinical characteristic by race

	Total N = 6078	Malay N = 3609 (59.4%)	Chinese N = 405 (6.7%)	Indian N = 138 (2.3%)	Others N = 1926 (31.7%)	*p* value
Age, mean (SD)	37.3 (16.8)	38.0 (17.9)	41.9 (18.5)	44.0 (17.1)	34.7 (13.7)	.001[a]
≥51 years, n (%)	1525 (25.1)	1068 (29.6)	135 (33.3)	50 (35.7)	272 (14.2)	<.001[b]
Male gender, n (%)	4303 (70.8)	2449 (67.9)	223 (55.1)	71 (51.5)	1560 (81.0)	<.001[b]
Comorbidities, n (%)						
Hypertension	954 (15.7)	648 (18.0)	83 (20.5)	40 (29.0)	183 (9.5)	<.001[b]
Diabetes mellitus	599 (9.9)	424 (11.8)	35 (8.6)	33 (23.9)	108 (5.6)	<.001[b]
Chronic cardiac disease	196 (3.2)	130 (3.6)	20 (4.9)	17 (12.3)	29 (1.5)	<.001[b]
Obesity	95 (1.6)	37 (1.0)	9 (2.2)	2 (1.5)	47 (2.4)	<.001[b]
Kidney disease[c], n (%)	312 (5.1)	206 (5.7)	35 (8.6)	13 (9.4)	58 (3.0)	<.001[b]
Chronic pulmonary disease	35 (0.6)	19 (0.5)	3 (0.7)	4 (2.9)	9 (0.5)	<.021[d]
Severity, n (%)						<.001[b]
Stage I–II	4878 (80.3)	2986 (82.7)	254 (62.7)	100 (72.5)	1538 (79.9)	
Stage III–V	1155 (19.0)	595 (16.5)	148 (36.5)	38 (27.1)	374 (19.4)	
Laboratory parameters, median (IQR)						
Haemoglobin (g/dl)	14.4 (13.2,15.4)	14.2 (13.0, 15.2)	13.7 (12.6, 15.0)	13.6 (12.5, 14.9)	14.8 (13.8, 15.8)	.001[a]
Platelet ($\times 10^9$/L)	264 (219, 316)	264 (217, 320)	259 (206, 312)	247 (198, 314)	267 (223, 312)	.036[a]
White cell count ($\times 10^9$/L)	7.50 (6.03, 9.16)	7.3 (5.9, 9.0)	6.7 (5.3, 8.5)	7.58 (6.20, 9.70)	8.0 (6.6, 9.4)	.001[a]
Absolute lymphocyte count (cells/ul)	2.20 (1.62, 2.80)	2.13 (1.60, 2.74)	1.68 (1.20, 2.30)	2.12 (1.69, 2.70)	2.3 (1.8, 2.9)	.001[a]
Serum creatinine (μmol/L)	78 (65,90)	78 (63, 91)	71 (58, 85)	76 (63, 90)	79 (69, 89)	<.001[a]
Intensive support, n (%)						
ICU	207 (3.4)	146 (4.0)	27 (6.7)	4 (2.8)	30 (1.6)	<.001[b]
Ventilator	149 (2.5)	104 (2.9)	19 (4.7)	3 (2.1)	23 (1.2)	<.001[b]
KRT	38 (0.6)	27 (0.7)	5 (1.2)	2 (1.4)	4 (0.2)	<.001[b]
Complications, n (%)						
AKI	212 (3.5)	138 (3.8)	21 (5.2)	6 (4.3)	47 (2.4)	.010[b]
Cardiac	97 (1.6)	56 (1.4)	22 (5.4)	7 (5.1)	16 (0.8)	<.001[b]
Coagulopathy	13 (0.2)	9 (0.2)	2 (0.5)	1 (0.7)	1 (0.1)	<.060[d]
Liver injury	411 (6.8)	198 (5.5)	28 (6.9)	17 (12.3)	168 (8.7)	<.001[b]

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; IQR, interquartile range; KRT, kidney replacement therapy; SD, standard deviation.
[a]Kruskal-Wallis test for continuous variables.
[b]Chi squared test.
[c]CKD and AKI.
[d]Fisher's exact test for categorical variables.

such as age, ethnicity, existing diseases such as chronic KD, DM and complications during hospitalization such as AKI.

COVID-19 patients with KD had higher CFR compared to non-KD patients. Centre factors such as capacity to manage, ventilate and dialyze patients had an effect on mortality in this study. Hence, it is crucial to recognize kidney involvement for all hospitalized COVID-19 patients. The results of this study emphasize the importance of early referral of patients with kidney involvement for co-management with nephrologists. We would also like to recommend a follow up study on all COVID-19 patients with KD, to determine the long-term sequelae of their kidney function. There are important racial differences in mortality among Asian population that needs to be explored further.

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REFERENCES

1. World Health Organisation. https://covid19.who.int/. 2021.
2. Abuelgasim E, Saw LJ, Shirke M, Zeinah M, Harky A. COVID-19: unique public health issues facing black, Asian and minority ethnic communities. *Curr Probl Cardiol*. 2020;45(8):100621.
3. Henning-Smith C, Tuttle M, Kozhimannil KB. Unequal distribution of COVID-19 risk among rural residents by race and ethnicity. *J Rural Health*. 2021;37(1):224-226.
4. Centers for Disease Control and Prevention, USA. Risk for COVID-19 Infection, Hospitalization, and Death by Race/Ethnicity. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html.
5. Ministry of Health Malaysia. Clinical Management of Confirmed COVID-19 Case in Adult and Paediatric. www.covid-19.moh.gov.my/garis-panduan/garis-panduan-kkm
6. Goh CY, Visvanathan R, Ong LM, et al. A prospective, multi-centre, observational study to determine the incidence and outcome of acute kidney injury among hospitalized patients in Malaysia. *KI Reports*. 2017;2(4S):S14.
7. Cao Y, Hiyoshi A, Montgomery S. COVID-19 case-fatality rate and demographic and socioeconomic influencers: worldwide spatial regression analysis based on country-level data. *BMJ Open*. 2020;10:e043560.
8. Procaccini FL, Arroyo RA, Ramón MA, et al. Acute kidney injury in 3182 patients admitted with COVID-19: a single center retrospective case–control study. *Clin Kidney J*. 2021;14(6):1557-1569.
9. Portoles J, Marques M, Lopez-Sanchez P. Chronic kidney disease and acute kidney injury in the COVID-19 Spanish outbreak. *Nephrol Dial Transplant*. 2020;35:1353-1361.
10. Collado S, Arenas MD, Barbosa F, et al. COVID-19 in grade 4-5 chronic kidney disease patients. *Kidney Blood Press Res*. 2020;45:768-774.
11. Russo E, Esposito P, Taramasso L, et al. Kidney disease and all-cause mortality in patients with COVID-19 hospitalized in Genoa, northern Italy. *J Nephrol*. 2021;34:173-183.
12. Fanelli V, Fiorentino M, Cantaluppi V, et al. Acute kidney injury in SARS-CoV-2 infected patients. *Crit Care*. 2020;24:155.
13. Ertuglu LA, Kanbay A, Afsar B. COVID-19 and acute kidney injury. *Tuberk Toraks*. 2020;68(4):407-418.
14. ERA-EDTA council and the ERACODA working group. Chronic kidney disease is a key risk factor for severe COVID-19: a call for action by ERA-EDTA. *Nephrol Dial Transplant*. 2021;36:87-94.
15. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *JAMA Intern Med*. 2020;180(10):1345-1355.
16. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 patients in Wuhan. *J Allergy Clin Immunol*. 2020;146(1):110-118.
17. Promislow DEL. A geroscience perspective on COVID-19 mortality. *Biol Sci Med Sci*. 2020;75(9):e30-e33.
18. Zheng M, Wang Z, Guo H, et al. The cytokine profiles and immune response are increased in COVID-19 patients with type 2 diabetes mellitus. *J Diabetes Res*. 2021;952670:1-8.
19. Pareek M, Bangash M, Pareek N, et al. Ethnicity and COVID-19: an urgent public health research priority. *Lancet*. 2020;395(10234):1421-1422.
20. Sze S, Pan D, Nevill CR, et al. Ethnicity and clinical outcomes in COVID-19: a systematic review and meta-analysis. *E. Clin Med*. 2020;29:100630.
21. Ali H, Alshukry A, Marafie SK, et al. Outcomes of COVID-19: disparities by ethnicity. *Infect Genet Evol*. 2021;87:104639.
22. Yildirim Z, Sahin OS, Yazar S, Bozok Cetintas V. Genetic and epigenetic factors associated with increased severity of Covid-19. *Cell Biol Int*. 2021;45(6):1158-1174.
23. Department of Statistics Malaysia. www.dosm.gov.my.
24. Arshad M. Return to education by ethnicity: a case of Malaysia. *Int Jour Econ Man*. 2016;10(1):141-154.
25. Hansrivijit P, Gadhiya KP, Gangireddy M, Goldman JD. Risk factors, clinical characteristics, and prognosis of acute kidney injury in hospitalized COVID-19 patients: a retrospective cohort study. *Medicines (Basel)*. 2021;8(1):4.
26. Phillips T, Stammers M, Leggatt G, et al. Acute kidney injury in COVID-19: identification of risk factors and potential biomarkers of disease in a large UKcohort. *J Nephrol*. 2021;26(5):420-431.
27. Alfano G, Ferrari A, Fontana F, et al. Incidence, risk factors and outcome of acute kidney injury (AKI) in patients with COVID-19. *Clin Exp Nephrol*. 2021;25:1203-1214.
28. Levey AS, Eckardt KU, Tsukamoto Y. Definition and classification of chronic kidney disease: a position statement from kidney disease: improving global outcomes (KDIGO). *Kidney Int*. 2005;67:2089-2100.
29. Tang M. Pulmonary hypertension, mortality, and cardiovascular disease in CKD and ESRD patients: a systematic review and meta-analysis. *Am J Kidney Dis*. 2018;72(1):75-83.
30. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Inter Urol and Nephrol*. 2020;52(6):1193-1194.
31. Sim BLH, Chidambaram SK, Wong XC, et al. Clinical characteristics and risk factors for severe COVID-19 infections in Malaysia: a nationwide observational study. *Lancet Reg Health West Pac*. 2020;4:100055.
32. Ozturk S, Turgutalp K, Arici M, et al. Mortality analysis of COVID-19 infection in chronic kidney disease, haemodialysis and renal transplant patients compared with patients without kidney disease: a nationwide analysis from Turkey. *Nephrol Dial Transplant*. 2020;35:2083-2095.
33. Fareed N. Size matters: a meta-analysis on the impact of hospital size on patient mortality. *Int J Evid-Based Healthc*. 2012;10:103-111.

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