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ORIGINAL ARTICLE

# Acute kidney injury and in-hospital mortality among patients with COVID-19 in Ghana – a single-centre study

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## ABSTRACT

**Introduction:** Acute kidney injury (AKI) occurs in patients with coronavirus disease 2019 (COVID-19) and is associated with high mortality, but this has not yet been described in Ghana. We therefore record here the proportion of COVID-19 patients with AKI, and determined the corresponding mortality, in a tertiary-level hospital in Ghana.

**Methods:** We conducted a retrospective study of all patients admitted to the Komfo Anokye Teaching Hospital, with a diagnosis of COVID-19 proven by reverse transcriptase polymerase chain reaction (RT-PCR), from March 2020 to February 2021. Demographics, clinical findings and laboratory investigations were recorded and summary statistics used to describe the data. Predictors of mortality were established by multiple logistic regression.

**Results:** The study involved 250 patients, of whom 129 (52%) were males, with a mean age of 56.3 ± 17.4 years. AKI occurred in 123 (49%). The most common causes of AKI were pre-renal AKI and ischaemic ATN – 65 (73%) and 37 (30%) cases, respectively. Haemodialysis was required in 6 (5%) cases.

The in-hospital mortality of all the COVID-19 patients was 71 (31%). The predictors of in-patient mortality in multivariate analysis were hyperglycaemia (OR = 18.48 [95%CI (2.0 –165.2], P = 0.009), severe COVID-19 (OR = 31.3 [95% CI 1.53–635.5], P = 0.025), elevated white blood cell count (OR = 1.32 [95% CI 1.09–1.59], P = 0.004), lymphopenia (OR = 0.16. [95% CI 0.03–3.26], P = 0.027) and not AKI (OR = 0.79 [95% CI 0.45–1.34], P = 0.380). Stage 3 (severe) AKI, however, occurred in 39 (32%) cases and was significantly associated with mortality [OR = 2.41 (95% CI 1.05–5.49, P = 0.036)] as compared to those with mild–moderate AKI in a sub-analysis.

**Conclusion:** AKI is common in hospitalized patients with COVID-19. Stage 3 AKI was associated with increased in-hospital mortality. Predictors of mortality were severe COVID-19 disease, lymphopenia and hyperglycaemia.

**Keywords:** SARS-CoV-2; acute kidney injury; chronic kidney disease; mortality; sub-Saharan Africa.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, affects multiple organs including the lungs, heart, digestive tract, blood, nervous system and the kidneys [1]. Fortunately, over 80% of cases are asymptomatic or have mild symptoms and will recover without medication or hospitalisation [2]. The mortality rates across Africa are generally lower than in Europe, Asia and the Americas [3]. The reasons for the relatively lower burden of COVID-19 in sub-Saharan Africa remains unclear but has been suggested to be as a result of low testing capacity as well as genetic and environmental factors [4].

When complicated by kidney disease, COVID-19 is associated with increased mortality [5]. The risk factors associated with severe COVID-19 disease and increased mortality include older age, hypertension, diabetes and coronary heart disease. Acute kidney injury (AKI) has been described to vary from 5.1% to 15% in hospital

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admissions on the general wards [2] and in 49.5% of patients with acute respiratory distress syndrome (ARDS) in another, multi-centre study [6]. The mechanisms by which COVID-19 causes kidney disease are many. Most are described as indirect causes, though an early study suggested the direct renal involvement by SARS CoV-2. This study recorded that the virus was isolated in urine and causes glomerulonephritis [7]. There is evidence to suggest that COVID-19 causes collapsing glomerulopathy in sub-saharan Africa [8], with the name COVID-19-associated nephropathy (COVAN) being proposed [9]. A case series, however, showed acute tubular necrosis (ATN) as the predominant pathology causing AKI with no evidence of SARS-COV-2 in the biopsied kidneys [10].

AKI is associated with mortality of up to 91.7% in severe infections [11]. COVID-19 has been shown to increase the need for dialysis with the potential for the spread of infection in haemodialysis units as patients are in an enclosed space for prolonged periods of about four hours during haemodialysis sessions [12]. Guidelines have therefore been drawn up by the African Association of Nephrology (AFRAN) for the prevention and management of kidney disease patients in Africa [13]. However, the management of kidney disease associated with COVID-19 is challenging in Ghana [14] because there are gross inequities among patients with COVID-19 in low-income settings, especially when dialysis is required [15].

The proportions of AKI in patients with COVID-19 have not been described in Ghana, according to our knowledge. We therefore set out to describe patients who were victims of the pandemic, the proportion of those with AKI and also to determine the in-patient mortality as well as the predictors of mortality among COVID-19 patients at the Komfo Anokye Teaching Hospital (KATH).

## MATERIALS AND METHODS

We conducted a retrospective observational study of all patients with COVID-19, diagnosed with reverse transcriptase polymerase chain reaction (RT-PCR), in the 23-bed Highly Infectious Isolation Unit (HIIU) of the KATH. Data were collected from the medical records of patients with COVID-19 admitted between March 2020 and February 2021. Subjects were excluded from the study if they did not have kidney function tests done or had no recorded evidence of the state of their kidney function.

## STUDY SITE AND STUDY POPULATION

KATH is a 1200-bed tertiary-level health facility which serves as the referral site for complicated medical and surgical cases in the northern half of Ghana. Patients with COVID-19 were confirmed by RT-PCR on naso-pharyngeal swab by the Kumasi Centre for Collaborative Research (KCCR) or the KATH laboratory, using an Applied Biosystems 7500 PCR machine.

Patients were mainly referred to the HIIU after clinical and RT-PCR diagnosis of COVID-19 was confirmed according to WHO criteria [16]. Laboratory investigations including full blood count, erythrocyte sedimentation rate (ESR), renal function test and liver function test were requested for most patients. Chest X-rays and electrocardiograms (ECG) were requested in some cases. Patients with severe and critical disease had serum ferritin, C-reactive protein (CRP) and D-dimer requested to aid management. Computerised tomography pulmonary angiography was requested for those with suspected pulmonary embolism.

Demographic data – including history of comorbidities such as hypertension, diabetes mellitus, chronic kidney disease, human immunodeficiency virus (HIV) infection and malignancies – were also documented. Clinical findings such as pulse, blood pressure and respiratory rate were also recorded. The data on patients who required and those initiated on haemodialysis were all extracted from the patients' medical records. Patients whose oxygen saturation was below 94% were placed on oxygen either via nasal prongs or non-rebreather mask and the levels titrated until oxygen saturation was greater than or equal to 94%.

All patients were put on azithromycin tablets, zinc tablets, vitamin C supplements and subcutaneous low-molecular-weight heparin. Initially, patients were treated with hydroxychloroquine. Those requiring oxygen were given intravenous 8 mg dexamethasone 8-hourly for 5–10 days. Patients with severe or critical disease were given 400 mg intravenous tocilizumab and/or remdesivir 200 mg stat and then continued with 100 mg daily for 4 days.

## DISCHARGE CRITERIA

At the beginning of the pandemic, these criteria included negative PCR results for COVID-19 from at least two consecutive tests 14 days after admission. A third laboratory test was recommended on the 21st day for subjects who remained positive for SARS CoV-2. This requirement was, however, reviewed after the WHO changed the criteria for discharge in May 2020 [17]. Asymptomatic patients were therefore discharged after 14 days of no symptoms without the requirement of a negative PCR test for COVID-19.

## DEFINITIONS

Severe COVID-19 is defined as a respiratory rate greater than 30 cycles per minute, hypoxia with oxygen saturation

of less than 92% and or greater than 50% lung involvement on X-ray examination [16]. Acute kidney injury stages 1–3 were diagnosed according to the KDIGO criteria [18]. Mild–moderate AKI was defined as stages 1 and 2 and severe disease was defined as AKI stage 3, according to the KDIGO criteria [18]. Chronic kidney disease (CKD) was defined according to the KDIGO criteria [19]. Anaemia was defined according to the WHO criteria. Lymphopenia was defined as total lymphocyte count of less than 1.0 x 109/L on admission.

## STATISTICAL ANALYSIS

The data were exported to the statistical software Stata® 13 for analysis. Categorical variables were summarised as proportions and percentages. Continuous variables were summarised as means and standard deviations when parametric, and median with interquartile range when non-parametric. Student's t-test and the Wilcoxon signed-rank test were used to test for differences for continuous variables when parametric or non-parametric, respectively. The chi-squared test was used to test for differences for categorical variables and Fisher's exact test where the cell was less than 5. Missing values were not included in the analysis. For the AKI stages, ANOVA was used to test for differences when parametric and the Kruskal–Wallis test was invoked for differences when non-parametric when variables were continuous. Patients with severe (stage 3) AKI were then compared with those with mild–moderate AKI in a sub-analysis. Predictors of mortality were established in a multiple logistic regression. A P value of less than 0.05 was considered statistically significant.

## ETHICAL CONSIDERATION

The study was approved by the institutional review board of the Komfo Anokye Teaching Hospital before the start, with IRB number KATH IRB/AP/132/20.

## RESULTS

There were 255 patients with confirmed SARS-CoV-2 infection during the study period; however, 250 patients provided adequate data on a kidney function test or a clinical diagnosis of AKI to be included in the study. There were some missing data in most laboratory variables.

The mean age of patients was 56.3 ± 17.4 years with 129 (52%) males. There were 93 (38%) and 148 (60%) subjects with a history of diabetes and hypertension, respectively, and 24 (10%) patients with a history of chronic kidney disease. The mean respiratory rate for all participants was 28.9 ± 9.4 cycles per minute with a median saturation of peripheral oxygen (SPO2) of 94.0% (88.0–97.0%). There were 81 (34%) patients with hyperglycaemia and 111 (45%) recorded hypertension on examination. A total of 131 (54%) patients were diagnosed with severe COVID-19 (Table 1).

The mean haemoglobin concentration was 11.1 ± 2.8 g/dL and 161 (68%) patients presented with anaemia. The median serum urea was 6.7 (4.2–13.9) mmol/L and serum creatinine was 99 (69–207) µmol/L (Table 1).

Acute kidney injury occurred in 123 (49%) patients. The most common causes of the condition were pre-renal AKI in 65 (52%) and ischaemic acute tubular necrosis in 37 (32%) patients with diagnosis of AKI. There were 41 (33%), 43 (35%) and 39 (32%) cases of AKI stages 1, 2 and 3, respectively The incidence of mortality in AKI stages 1, 2 and 3 were 8 (21%), 11 (26%) and 16 (42%) (P = 0.093), respectively (Table 1). Generally, AKI was not significantly associated with increased mortality as compared to those without AKI [35 (29%) vs. 43 (34%), P = 0.454)].

When dichotomised into AKI stage 3 (severe AKI) and mild–moderate AKI, cases of the former were significantly associated with mortality in a univariate analysis [OR = 2.41 (95% CI 1.05–5.49), P = 0.036] whereas mild–moderate AKI was not. Those with severe AKI manifested significantly higher proportions of hyponatraemia [7(50%) vs. 3(14%), P = 0.026] as well as high serum potassium (5.4 ± 1.0 vs. 4.7 ± 0.7, P = 0.014) as compared to those with mild–moderate AKI (Table 2).

Renal replacement therapy in the form of intermittent haemodialysis was required in 6 (5%) patients with AKI, but 5 (4%) were able to receive dialysis and 50% of those requiring dialysis died on admission.

The in-hospital mortality of all COVID-19 patients was 71 (31%). Mortality was also associated with severe COVID-19 [57 (74%) vs. 73 (44%), P < 0.001], increased respiratory rate on admission [32.2 ± 11.0 vs. 27.4 ± 8.2, P = 0.0002], hyperglycaemia [33 (44%) vs. 48 (29%), P = 0.022], pulse rate [104.2 ± 19.1 vs. 95.2 ± 19.5, P = 0.001], lymphopenia [28 (41%) vs. 32 (21%), P = 0.002], higher white cell count [12.6 (7.2–15.0) vs. 7.9 (6.1–11.7), P = 0.004 and lower sodium concentration [136.2 ± 6.5 vs. 139.6 ± 6.2, P = 0.038] as compared to survivors in a univariate analysis (Table 3).

In multiple logistic regression, the predictors of in-patient mortality were hyperglycaemia (OR = 18.5 [95% CI 2.1–165.2], P = 0.009], severe COVID-19 [OR = 31.3 (95% CI 1.5–635.5], P = 0.025), elevated white blood cell count [OR = 1.32, 95% CI 1.09–1.59, P = 0.004] and decreased lymphocyte count [OR = 0.16, 95% CI 0.03–0.81, P = 0.027], all as shown in Table 4.

**Table 1.** Baseline characteristics of COVID-19 patients and comparison by stages of acute kidney injury.

| Variable | All cases | AKI 1 (41) | AKI 2 (43) | AKI 3 (39) | P value |
|---|---|---|---|---|---|
| Age (years) μ (SD) (n = 246) | 56.3 ± 17.4 | 55.5 ± 19.9 | 57.8 ± 16.9 | 54.7 ± 18.9 | 0.597 |
| Male gender n (%) (n = 246) | 129 (52.4) | 19 (48.7) | 20 (48.8) | 18 (47.4) | 0.770 |
| Age above 60 years n (%) (n = 246) | 116 (47.2) | 18 (46.2) | 22 (53.7) | 18 (47.4) | 0.990 |
| History of diabetes n (%) (n = 245) | 93 (38.0) | 18 (46.2) | 15 (36.6) | 14 (36.8) | 0.615 |
| History of hypertension n (%) (n = 245) | 148 (60.4) | 27 (69.2) | 27 (65.9) | 22 (57.9) | 0.567 |
| Chronic kidney disease n (%) (n = 245) | 24 (9.8) | 7 (18.0) | 3 (7.3) | 3 (7.9) | 0.308 |
| Fever n (%) (n = 244) | 120 (49) | 19 (48.7) | 22 (55.0) | 21 (55.3) | 0.807 |
| Cough n (%) (n = 244) | 170 (69.7) | 30 (76.9) | 25 (62.5) | 25 (65.8 | 0.355 |
| Breathlessness n (%) (n = 244) | 162 (66.4) | 27 (69.2) | 23 (57.5) | 26 (68.4) | 0.475 |
| Random blood sugar (mmol/L) M (IQR) | 8.2 (6.2–13.8) | 9.2 (6.0–17.1) | 7.6 (6.2–12.8) | 8.3 (6.7–14.7) | 0.803 |
| Hyperglycaemia >11.1 mmol/L (n = 242) | 81 (33.5) | 13 (33.3) | 12 (30.8) | 14 (36.8) | 0.852 |
| Respiratory rate cpm μ (SD)(n = 240) | 28.9 ± 9.4 | 27.9 (10.1) | 29.2 (8.3) | 30.4 (10.0) | 0.446 |
| Systolic blood pressure (mmHg)(n = 245) | 135.0 ± 24.5 | 143.0(22.4) | 137.3 (19.0) | 135.4(24.4) | 0.309 |
| Diastolic blood pressure (mmHg)(n = 245) | 81.9 ± 15.5 | 83.3 (14.0) | 85.4 (10.4) | 82.8 (14.9) | 0.081 |
| Pulse rate (bpm) μ (SD)(n = 243) | 98.0 ± 19.8 | 94.9 (16.2) | 96.3 (20.2 | 104.1(19.7) | 0.357 |
| Hypertension n (%)(n = 245) | 111 (45.3) | 22 (56.4) | 22 (53.7) | 19 (50.0) | 0.852 |
| SPO2 (%) μ (SD)(n = 245) | 0.94 (0.88–0.97) | 91.6 (10.1) | 88.5 (14.0) | 89.9 (11.8) | 0.134` |
| Severe COVID-19 disease n (%)(n = 245) | 131 (53.5) | 17 (43.6) | 25 (61.0) | 21 (55.3) | 0.286 |
| Haemoglobin (g/dL) μ (SD) (n = 229) | 11.1 ± 2.8 | 10.5 (2.6) | 11.8 (3.0) | 11.4 (2.8) | 0.643 |
| Anaemia n (%) (n = 229) | 161 (67.9) | 28 (77.8) | 17 (47.2) | 24 (66.7) | 0.024 |
| Mean corpuscular volume (fL) μ (SD) (n = 227) | 82.3 ± 9.7 | 84.3 (10.4) | 84.2 (6.0) | 84.3 (10.4) | 0.001 |
| White blood cells (x109/L) M (IQR)(n = 229) | 8.8 (6.2–13.8) | 8.8 (7.0–12.1) | 8.7 (6.7–11.5) | 8.1 (6.5–13.8) | 0.963 |
| Neutrophil count (x109/L) M (IQR)(n = 229) | 5.6 (3.4–8.81) | 5.8 (4.9–8.9) | 6.3 (4.1–8.8) | 5.6 (3.4–7.7) | 0.287 |
| Lymphocyte count (x109/L) M (IQR) (n = 225) | 1.4 (0.95–1.95) | 1.5 (1.1–2.5) | 1.4 (1.0–2.2) | 1.3(1.0–1.9) | 0.724 |
| Lymphopenia n(%)(n = 225) | 60 (26.7) | 6 (16.7) | 12 (34.3) | 8 (22.9) | 0.217 |
| Platelet (x109/L) M(IQR) (n = 228) | 205 (136.5–260.5) | 224(169–270) | 187 (156.5–242) | 192(140–244) | 0.449 |
| ESR (mmfall/hr) M (IQR) (n = 147) | 35 (10-85) | 20(10-85) | 25 (8-105) | 32(7.5-117) | 0.672 |
| C-Reactive protein (mg/L) M (IQR) (n = 64) | 67.2 (17.0 – 137.6) | 73.8(54.0-119) | 92.3(42.2-258.5) | 20.1(0.6-164) | 0.269 |
| Ferritin (μg/L) M (IQR)(n = 42) | 996 (531.7–1745) | 1220.8 (636.5–1598.5) | 1308.5 (376–2241) | 1072(415–1951) | 0.985 |
| Total bilirubin (mmol/L) M (1QR) (n = 177) | 13.1 (8.9–21.5) | 12.1(8.4–18.4) | 18.2 (11.5–28.7) | 12.2 (7–20) | 0.032 |
| Direct bilirubin (mmol/L) M (IQR)(n = 145) | 4.3 (2.9–7.0) | 3.6 (2.6–5.6) | 5.4 (3.1–11.9) | 4.9 (2.3–7.6) | 0.262 |
| Aspartate transaminase (g/L) M (IQR) (n = 196) | 50.5 (27.6–86.1) | 53.9 (32.1–65.4) | 66.4 (39.1–101) | 47.6 925.4–73.1) | 0.191 |
| Alanine transaminase (g/L) M(IQR)(n = 190) | 34 (19.7–68.3) | 49.9 (29.3–96) | 41.7 (22–91.2) | 23.2 (14.7–36.5) | 0.003 |
| Serum Albumin (g/L) μ (SD) (n = 188) | 34.6 ± 7.8 | 37.4 (34–39.1) | 33.4(29.9–39.1) | 36.6 (27.2–41.3) | 0.004 |
| Serum Sodium (mmol/L) μ (SD) (n = 72) | 138. 4 ± 6.5 | 141.1 (7.7) | 138.1 (3.0) | 137.4 (10.2) | 0.001 |
| Hyponatraemia n (%) (n = 72) | 17 (23.6) | 1 (10) | 2 (16.7) | 7 (50) | 0.056 |
| Serum potassium (mmol/L) n(%) (n = 74) | 4.6 ±0.8 | 4.4 (0.9) | 4.9 (0.5) | 5.4 (1.0) | 0.001 |
| Serum urea (mmol/L) M (IQR) (n = 212) | 6.7 (4.2–13.9) | 8.6(5.9–14.9) | 12.7 (5.6–18.8) | 22.8 (11.5–35.90) | 0.001 |
| Serum creatinine (μmol/L) M (IQR) (n = 212) | 98 (72-–188.5) | 132 (118–132) | 198 (164–270) | 510 (136–984) | 0.001 |
| Pre-renal AKI n (%) (n = 250) | 123(49.2) | 25 (61.0) | 29 (67.4) | 11 (28.2) | 0.003 |
| Ischaemic ATN n (%) (n = 123) | 65 (52.9) | 10 (24.4) | 11 (25.6) | 16 (41.0) | 0.003 |
| Septic ATN n (%) (n = 123) | 37 (30.1) | 6 (14.6) | 3 (7.0) | 12 (30.0) | 0.003 |
| In-hospital mortality n (%) (n = 249) | 78 (31.3) | 8 (20.5) | 11 (25.6) | 16 (42.1) | 0.093 |

Abbreviations: cpm, cycles per minute; μ, mean; SD, standard deviation; bpm, beats per minute; M, median; IQR, interquartile range; SPO2, partial pressure of oxygen; AKI, acute kidney injury; ATN, acute tubular necrosis; ESR, erythrocyte sedimentation rate.

**Table 2.** Comparison of COVID-19 patients with severe and mild–moderate AKI (n = 123).

| Variable | Severe AKI (n = 39) | Mild–moderate AKI (n = 84) | P value |
|---|---|---|---|
| Age (years) μ (SD) | 54.7 ± 18.9 | 56.7 ± 18.3 | 0.596 |
| Male gender n (%) | 18 (47.4) | 40 (50.0) | 0.789 |
| Age above 60 years n (%) | 18 (47.4) | 39 (48.8) | 0.888 |
| History of diabetes n (%) | 14 (36.8) | 33 (41.3) | 0.648 |
| History of hypertension n (%) | 22 (64.4) | 54 (67.5) | 0.309 |
| Chronic kidney disease n (%) | 3 (7.9) | 10 (12.5) | 0.545 |
| Random blood sugar (mmol/L) M (IQR) | 8.3 (6.7–14.5) | 7.9 (6.2–13.8) | 0.717 |
| Hyperglycaemia (RBS>11.1) n (%) | 14 (36.8) | 25 (32.1) | 0.608 |
| Pulse rate (bpm) μ (SD) | 104.1 ± 19.7 | 95.6 ± 18.2 | 0.026 |
| Respiratory rate (cpm) μ (SD) | 30.4 ± 10.0 | 28.6 ± 9.2 | 0.346 |
| Systolic BP (mmHg) μ (SD) | 135.4 ± 24.4 | 140.1 ± 20.8 | 0.288 |
| Diastolic BP (mmHg) μ (SD) | 82.8 ± 14.9 | 84.4 ± 12.3 | 0.529 |
| Hypertension n (%) | 19(50) | 44 (55.0) | 0.611 |
| Partial pressure of oxygen (%) μ (SD) | 89.9 ± 11.8 | 90.0 ± 12.3 | 0.978 |
| Severe COVID-19 disease n (%) | 21 (55.3) | 42 (52.5) | 0.779 |
| Haemoglobin (g/dL) μ (SD) | 11.3 ± 2.8 | 11.1 ± 2.8 | 0.698 |
| Anaemia n (%) | 24 (66.7) | 45 (62.5) | 0.671 |
| Mean corpuscular volume (fL) μ (SD) | 84.3 ± 10.4 | 81.7 ± 9.4 | 0.195 |
| Platelets (x109/L) M (IQR) | 192 (140–244) | 208.5 (159.5–253) | 0.463 |
| White blood cell count (x109/L) M (IQR) | 8.1 (6.5–13.8) | 8.8 (6.9–11.6) | 0.915 |
| Lymphocyte count (x109/L) | 1.3 (1.0–1.85) | 1.5 (1.0–1.85) | 0.195 |
| Lymphopenia n (%) | 8 (22.9) | 18 (25) | 0.779 |
| Neutrophil count (x109/L) M (IQR) | 5.6 (3.3–7.7) | 5.8 (4.1–8.9) | 0.428 |
| ESR (mmfall/hr) M (IQR) | 32 (7.5–117) | 25 (9–89.5) | 0.446 |
| C-Reactive protein (mg/L) M (IQR) | 20.1 (0.6–164) | 80.6 (54.0–119) | 0.105 |
| Ferritin (μg/L) M (IQR) | 1072.9 (415.2–1951) | 1220.8 (625–1808) | 0.914 |
| Total bilirubin (mmol/L) M (IQR) | 12.2 (7.0–20.0) | 14.2 (9.9–22.8) | 0.159 |
| Aspatate transaminase (U/L) M (IQR) | 47.6(25.4–73.1) | 54.6 (34–94.6) | 0.089 |
| Alanine transaminase (U/L) M (IQR) | 23.2 (14.7–36.5) | 49.6 (24.1–96.0) | 0.001 |
| Albumin (g/L) μ (SD) | 34.1 ± 9.7 | 34.8 ± 6.5 | 0.700 |
| Serum sodium (mmol/L) μ (SD) | 137.4 ± 10.2 | 139.5 ± 5.7 | 0.431 |
| Potassium (mmol/L) μ (SD) | 5.4 ± 1.0 | 4.7 ± 0.7 | 0.014 |
| Hyponatraemia n (%) | 7 (50) | 3 (13.6) | 0.026 |
| Urea (mmol/L) M (IQR) | 22.8 (11.5–35.8) | 10.1 (5.9–18.1) | <0.001 |
| Serum creatinine (μmol/L) M (IQR) | 510 (136–984) | 159 (125–213) | <0.001 |
| In-hospital mortality | 16 (42.1) | 19 (23.2) | 0.034 |

Abbreviations: cpm, cycles per minute; μ, mean; SD, standard deviation; bpm, beats per minute; M, median; IQR, interquartile range; AKI, acute kidney injury; ATN, acute tubular necrosis; ESR, erythrocyte sedimentation rate.

## DISCUSSION

This is the first study to describe acute kidney injury and mortality in patients with RT-PCR-proven COVID-19 in Ghana, to the best of our knowledge. AKI occurred in almost half of the admitted patients and was mostly due to pre-renal AKI and acute tubular necrosis. Mortality was significantly higher among those with severe AKI as compared to those with mild–moderate AKI. Half of the patients requiring intermittent haemodialysis died on admission. The in-hospital mortality of all patients with COVID-19 was 31% and was associated significantly with

**Table 3.** In-hospital mortality of patients with COVID-19 at the Komfo Anokye Teaching Hospital.

| Variable | Mortality (n = 78) | Survival (n = 171) | P value |
|---|---|---|---|
| Age (yrs) μ (SD) | 58.7 ± 17.8 | 55.2 ± 17.1 | 0.141 |
| Age greater than 60 n (%) | 42 (55.3) | 72 (43.4) | 0.085 |
| Male gender n (%) | 37(50.7) | 88 (52.4) | 0.809 |
| History of diabetes n (%) | 27 (37.0) | 65 (38.9) | 0.777 |
| History of hypertension n (%) | 44 (60.3) | 103 (61.7) | 0.837 |
| History of chronic kidney disease n (%) | 5 (6.9) | 19 (11.4) | 0.282 |
| History of sickle cell disease n (%) | 0 (0) | 7 (3.7) | 0.076 |
| Human immunodeficiency virus n (%) | 7(9.6) | 7 (4.4) | 0.142 |
| Malignancy n (%) | 10 (13.0) | 2 (1.2) | 0.001 |
| Respiratory rate (cpm) | 32.2 ± 11.0 | 27.4 ± 8.2 | 0.0002 |
| Systolic BP (mmHg) μ (SD) | 135.9 ± 25.6 | 134.5 ± 24.1 | 0.678 |
| Diastolic BP (mmHg) μ (SD) | 83.6 ± 17.7 | 81.2 ± 14.4 | 0.257 |
| Hypertension n (%) | 38 (49.4) | 73 (43.7) | 0.411 |
| Random blood sugar (mmol/L) M (IQR) | 9.3 (6.4–15.5) | 7.9 (6.2–12.8) | 0.184 |
| Hyperglycaemia (RBS >11.1mmol/L) n (%) | 33 (44.0) | 48 (28.9) | 0.022 |
| Pulse rate (bpm) μ (SD) | 104.2 ± 19.1 | 95.2 ± 19.5 | 0.001 |
| Partial pressure of oxygen (%) n (%) | 88.4 ± 13.2 | 91.7 ± 8.8 | 0.022 |
| Severe COVID-19 disease n (%) | 57 (74.0) | 73 (43.7) | <0.001 |
| Haemoglobin (g/dL) μ (SD) | 11.2 ± 2.8 | 10.9 ± 2.8 | 0.225 |
| Platelet (x109/L) M (IQR) | 188.5 (105–245) | 206 (149–272) | 0.053 |
| White blood cell count (x109/L) M (IQR) | 12.6 (7.2–15.0) | 7.9 (6.1–11.7) | 0.004 |
| Lymphopenia n (%) | 28 (40.6) | 32 (20.7) | 0.002 |
| Lymphoctyte count (x109/L) M (IQR) | 1.2 (0.7–1.6) | 1.5 (1.1–2.1) | <0.001 |
| Neutrophil count (x109/L) M (IQR) | 5.4 (3.0–8.8) | 5.8 ( 3.7–8.9) | 0.573 |
| ESR (mmfall/hr) M (IQR) | 25 (10–70) | 40 (12.0–90) | 0.304 |
| C-reactive protein (mg/L) M (IQR) | 33.2 (11.6–110.1) | 67 (17.1–130.6) | 0.551 |
| Ferritin (μg/L) M (IQR) | 913.5 (415.2–1421) | 921 (531.7–1808) | 0.201 |
| Total bilirubin (mmol/L) M (IQR) | 13.8 (8.6–25.6) | 13.1 (9.3¬¬-¬¬-19.6) | 0.696 |
| Aspartate transaminase (U/L) M (IQR) | 49.7 (34.1–106.5) | 51.1 (23.9–76.4) | 0.112 |
| Alanine Transaminase (U/L) M (IQR) | 34 (17.7–95.8) | 35.2 (20–63.4) | 0.758 |
| Albumin (g/L) μ (SD) | 32.6 ± 9.8 | 35.6 ± 6.7 | 0.006 |
| Sodium (mmol/L) | 136.2 ± 6.8 | 139.6 ± 6.1 | 0.038 |
| Potassium (mmol/)L μ (SD) | 4.6 ± 0.8 | 4.6 ± 0.9 | 0.903 |
| Urea (mmol/L) M (IQR) | 6.1 ( 3.7–11.5) | 6.8 (4.5–15.5) | 0.201 |
| Serum creatinine (μmol/L) M (IQR) | 97 (68–178) | 98 (74–191.5) | 0.792 |
| Acute kidney injury n (%) | 35 (44.9) | 84 (50.0) | 0.454 |
| Stage 3 AKI n (%) | 16 (20.5) | 22 (13.2) | 0.139 |

Abbreviations: cpm, cycles per minute; μ, mean; SD, standard deviation; bpm, beats per minute; M, median; IQR, interquartile range; AKI, acute kidney injury; ATN, acute tubular necrosis; ESR, erythrocyte sedimentation rate.

severe COVID-19, hyperglycaemia, high white cell count, and low lymphocyte counts.

The proportion of COVID-19 patients with AKI was 49.% higher than a similar study in two tertiary-level hospitals in South Africa, where AKI occurred in 33.9% of cases [20] and even lower than 5.1% in China in 2020 [5]. Our high prevalence of AKI could also be attributed to the fact the HIIU is a referral site for severe cases including patients

**Table 4.** Predictors of in-hospital mortality of patients with COVID-19 by multiple logistic regression.

| Variable | Standard error | Z value | Odds ratio | 95% CI | P value |
|---|---|---|---|---|---|
| Malignancy | 13.58 | 1.28 | 8.26 | 0.33–207.30 | 0.199 |
| Respiratory rate | 0.058 | –1.63 | 0.90 | 0.79–1.02 | 0.104 |
| Hyperglycaemia | 20.65 | 2.61 | 18.48 | 2.07–165.2 | 0.009 |
| Pulse rate | 0.03 | 1.12 | 1.03 | 0.98–1.07 | 0.262 |
| Admission SPO2 | 1.42 | 1.95 | 1.19 | 0.86–1.64 | 0.051 |
| Severe COVID-19 | 48.16 | 2.24 | 31.3 | 1.53–638.53 | 0.025 |
| White cell count | 0.125 | 2.91 | 1.32 | 1.09–1.59 | 0.004 |
| Lymphocyte count | 0.132 | –2.21 | 0.16 | 0.03–0.81 | 0.027 |
| Serum sodium | 0.073 | –1.37 | 0.89 | 0.76–1.05 | 0.171 |

Abbreviations: cpm, cycles per minute; μ, mean; SD, standard deviation; bpm, beats per minute; M, median; IQR, interquartile range; AKI, acute kidney injury; ATN, acute tubular necrosis; ESR, erythrocyte sedimentation rate.

who require ICU care with severe and critical COVID-19 disease and that may account for the similar prevalence of AKI in our study as compared to other studies conducted in ICU settings [21].

AKI has been attributed directly or indirectly to the SARS-COV-2 infections [1]. Pre-renal AKI was the most common cause of AKI in our cohort. This could be attributed to the low intravascular depletion due to anorexia, dehydration and hypovolaemia associated with the infection. Septic and ischaemic ATN may have resulted also from the infection, poorly managed pre-renal AKI due to late reporting of cases to the hospital as recorded in other studies [5, 11].

It is still debatable to what extent the virus directly affects the kidneys in patients with COVID-19 but it has been suggested that the AKI is mainly indirect as a result of the cytokine storm syndrome, which has been shown to be the principal contributing factor of disease severity in patients with COVID-19 [22]. A postmortem report of COVID-19 patients showed found no evidence of SARS-COV-2 in biopsied kidneys [10]. A recent study implicating collapsing glomerulopathy as a cause of kidney disease has been published in sub-Saharan Africa [8], highlighting the importance of COVID-19-associated nephropathy (COVAN) in some patients with increased risk of progression to CKD [9].

The mortality of patients with COVID-19 in our study was higher than in another study showing a mortality of 16.1% [5] but lower than 68.9% in one conducted in an ICU setting [21]. A high mortality of 58.9% has been recorded in patients on dialysis in South Africa, where the predictors of mortality were found to be a requirement for renal replacement therapy, the use of inotropes and the presence of shock. The authors did not find any association with gender, hypertension and diabetes mellitus [23] as also noted in our study.

Mortality in our subjects was predicted by clinical hyperglycaemia and not a history of diabetes mellitus. Hyperglycaemia has been shown to be significantly associated with mortality in COVID-19 patients [24]. Glycaemic control is essential to improve the survival of patients with COVID-19. Hyperglycaemia results in an impaired immune response, thereby increasing susceptibility to SARS-CoV-2 infection [24]. The decreased immunity has also been shown by other researchers to predict the death of patients, as found also in our study [25]. There is also growing evidence to suggest new onset diabetes in patients with COVID-19 causes ketoacidosis requiring high doses of insulin in their management [26].

Mortality in our study was predicted by the severity of COVID-19 as also shown in other studies [2, 11]. The severity of COVID-19 may be associated with cytokine storm, which has been demonstrated to be associated with increased risk of AKI. Severe COVID-19 disease increases the risk of ICU admission, AKI, requirement for renal replacement therapy and mortality [21].

Mortality was also predicted significantly by lower lymphocyte count, which has also been documented as a poor prognostic factor in COVID-19 patients in a meta-analysis [27]. Lymphopenia impairs the adaptive antiviral response and renders the host susceptible to severe systemic inflammatory response and a cytokine storm [22]. This may have also resulted in the development of AKI and a rise in serum creatinine in our study.

Mortality was further predicted by an increased white cell count as was reported in a meta-analysis by Henry et al. [27]. This may have been due to superimposed bacterial infections, which may increase the severity of disease and contributed significantly to mortality as shown in our study.

Dysregulation of neutrophils has been postulated to contribute to widespread immune thrombogenesis leading to end organ damage [28].

Our study did not show an association between AKI in general and mortality as shown in other studies [1, 5] but indicated a high mortality rate in those with severe (stage 3) AKI as compared to those with mild–moderate AKI as also shown by a large study in South Africa [20] and the Democratic Republic of Congo [29]. They showed that severe AKI was associated with increased use of ICU care, prolonged hospital stays and mortality.

Our study had some limitations. First, it was retrospective and data were missing in some cases. Second, it was a single-centre study and the findings may not be generalisable. In addition, some patients were also not able to afford some laboratory investigations due to cost and the risks associated with drawing frequent blood samples while observing strict safety protocols in full personal protective equipment by staff. Furthermore, urine output was not routinely monitored in most cases and the diagnosis of the cause of AKI was based on clinical judgement of the attending physician, which may have been subjective. The causes of mortality were not stated in patients' records and hence could not be reported. We recommend a prospective study to look more into the mortality associated with AKI in poorly resourced settings such as Ghana.

## CONCLUSIONS

AKI is relatively common among patients with COVID-19. Generally, the condition was not significantly associated with increased mortality. Severe AKI was, however, associated with increased mortality as compared to mild–moderate AKI. In-hospital mortality occurred in a third of COVID-19 patients and was significantly associated with hyperglycaemia, severe COVID-19, increased white blood cell count and low lymphocyte count.

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### Availability of data and material

All data supporting our conclusions are included within the article.

### Ethical approval

Ethical approval was obtained by the institutional review of the Komfo Anokye Teaching Hospital before the start of the study (IRB number KATH IRB/AP/132/20). Informed consent was waived by the institutional review board as this was a retrospective study and did not involve direct interaction with patients but clinical notes of patients admitted to the medical ward of the hospital.

### Authors' contribution

EKT initiated the study and wrote the proposal and the first version of the manuscript. EO, KHM, MA and FAA collected the data. Cleaning the data for analysis was performed by EO and EKT. EKT analysed the data and wrote the first draft. All authors were involved in critically revising the manuscript and approved the manuscript before submission. EKT and EO had full access to all the data in the study and take responsibility for its integrity and the accuracy.

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### Conflict of interest

The authors declare that they have no conflict of interest.

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