Clinical characteristics of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV2) patients in Hospital Tengku Ampuan Afzan

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ABSTRACT

Background: The COVID-19 is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This study aims to describe the clinical characteristics of COVID-19 patients admitted to Hospital Tengku Ampuan Afzan (HTAA), Pahang, Malaysia and to identify the clinical and laboratory markers for severe disease, complications and virologic clearance according to clinical staging.

Methods: This was a single-centre, retrospective, descriptive study. All COVID-19 patients admitted to HTAA from March 9 to April 15, 2020, were included in the study. Patients were categorised according to clinical staging. Data obtained from the medical report includes baseline characteristics of patients, comorbidities, presenting symptoms, laboratory findings, treatments, complications, and outcomes.

Results: Of the total of 247 patients hospitalised, the majority consisted at clinical-stage 1 (43%) and stage 2 (39%) disease. Older patients, diabetes mellitus, hypertension, cardiovascular diseases, and chronic kidney disease were found more common among patients with severe disease. Fever was uncommon and the majority had normal haemoglobin levels, white cell counts, and platelet counts. C-reactive protein (CRP) was found statistically significant to predict pneumonia or hypoxia at a cut-off value of 14mg/L (sensitivity 73.8%, specificity 91.3%) and 50mg/L (sensitivity 100%, specificity 96.4%) respectively. Pneumonia was mostly diagnosed radiologically using chest radiography, especially among clinical stage 3. Acute kidney injury (AKI) was a significant complication, with 31% of clinical stage 3 and above developed AKI and 44% of them requiring haemodialysis. Median virologic clearance time was 15 days from onset of illness, and asymptomatic patients had longer clearance time.

Conclusion: COVID-19 presented with a wide spectrum of clinical patterns. CRP was a valuable predictor of severe disease. In this study risk and severity of acute kidney injury were found to be higher. A longer duration of virologic clearance was observed among the asymptomatic patients.

KEYWORDS:
Clinical characteristics, COVID-19, clinical staging, C-reactive protein

INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemic had reached Malaysia since late January 2020 and had subsequently caused the national outbreak. Hospital Tengku Ampuan Afzan (HTAA), being a tertiary hospital, had become the treatment centre for the state Pahang, Malaysia.

The published data mostly originates from overseas, including mainland China, South Korea, and Italy, among others.[1-4,7,8] The study by Guan et al., found that only 43.8% of patients had fever on admission.[1] Zhou et al., identified older age groups, higher Sequential Organ Failure Assessment (SOFA) score, and positive d-dimer on admission as predictors for mortality.[2] Both studies found that patients with comorbidities of diabetes, hypertension, chronic obstructive lung disease, and coronary heart disease were at higher risk for severe form of the disease and mortality. Malaysia is a multiracial country with a tropical climate, and thus COVID-19 might demonstrate a different clinical characteristics compared to other countries. To the best of our knowledge, this is the first publication of clinical characteristics study among the Malaysian population. The availability of local data may assist clinicians in disease management.

We managed COVID-19 according to the Ministry of Health (MoH) guideline.[5] All patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were required to be hospitalised irrespective of symptoms. Patients were categorised into five clinical stages, from asymptomatic to critically ill. Our study intended to provide robust data comparing clinical stages across different severity.

The primary objective of this study was to describe the clinical characteristics of COVID-19 patients admitted to HTAA. Secondary objectives were to identify clinical and laboratory markers for severe disease, complications among COVID-19 patients, and virologic clearance according to clinical staging.

MATERIALS AND METHODS

Methodology

This study was a single-centre, retrospective, observational study. The study population included all laboratory-confirmed SARS-CoV-2 infected patients admitted to HTAA from March 9 to April 15, 2020. They were diagnosed via either sputum sample or nasopharyngeal and oropharyngeal

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swab using real-time reverse transcription-polymerase chain reaction (rRT-PCR) test. The list of the subjects was obtained from the HTAA registry and extracted from the medical records. The data cutoff for the study was April 15, 2020. Informed consent was not required, and no subjects were excluded from the study. Data collected were baseline characteristics, comorbidities, presenting symptoms, laboratory findings, treatments, complications, and outcomes. The ethics review for this study was conducted and approved by the Ministry of Health Medical Research Ethics Committee (NMRR-20-811-54513).

Definitions

Clinical staging was defined as the worst clinical stage according to the fifth edition of Malaysia COVID-19 management guideline[5] from MoH. Stage 1: was asymptomatic, stage 2: was symptomatic without pneumonia, stage 3: was pneumonia without hypoxia, stage 4: was pneumonia requiring oxygen supplement, and stage 5: was critically ill with multiorgan involvement. Severe disease in this article includes both clinical stages 4 and 5. Cardiovascular disease reported in records were: cardiomyopathies, valvular heart disease, ischemic heart disease, and heart failure. Obesity was defined as body mass index (BMI) ≥30. Malignancy included any neoplasms, active or in remission. Last contact was defined as the last day of a positive contact according to the history of the patients. Fever was defined as surface temperature more or equal to 37.5°C, measured by an infrared thermometer. Other presenting symptoms were obtained by history taking without specific assessment tools. Pneumonia was diagnosed either clinically by the judgement of the physicians or radiologically based on chest radiography. All chest radiographs were reported by certified radiologists. Acute kidney injury was defined according to Kidney Disease Improving Global Outcomes (KDIGO) 2012 criteria, with either increase in serum creatinine by 26.5µmol/l within 48 hours, increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the previous seven days, or urine volume <0.5ml/kg/h for six hours. Haemodialysis reported included both acute and end-stage kidney disease indications. Virologic clearance was defined as a first negative result without a subsequent positive test, using rRT-PCR.

Statistical Analysis

Subjects were categorised according to clinical staging.[5] Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 23. Categorical data were analysed using Fisher's exact test. Numerical data were expressed as median and interquartile range (IQR). Numerical data were analysed using the Kruskal-Wallis test. Logistic regression analysis was performed to describe the relationship between pneumonia (stage 3 to 5) or hypoxia (stage 4 to 5) with fever, lowest lymphocyte count, and peak c-reactive protein (CRP) levels. A receiver operating characteristic (ROC) curve analysis was done to identify the best cutoff value for the variables with significant predictive value.

RESULTS

Clinical Characteristics

A total of 247 patients with COVID-19 were hospitalised at HTAA as of April 15, 2020. This represents the majority (96.5%) of cases in Pahang state, with the rest hospitalised at the district hospital. The clinical characteristics of the patients are shown in Table I. The majority of patients were in clinical stage 1 (43%) and stage 2 (39%) of the disease. The older patients were more common to have the severe form of the disease. 73.3% of patients were above 50 years old and in stages 4 and 5. This was in comparison with, having 82.8%of patients in stage 3 and below being younger than 50 years old. Males were predominant (69.6%) but not significantly different across the five stages of the disease. Malays were predominant in our study population due to an outbreak of religious gathering, consisting of 93% of the study population, with remaining being Chinese (1%), Indian (1%), and foreigners students (5%). Healthcare workers consisted of 4% of the study population. Only (22.7%) of the studied patients had any coexisting illnesses. Diabetes mellitus, hypertension, cardiovascular diseases, and chronic kidney disease (CKD) were found more common among patients with severe disease. Median time from the last positive contact till the onset of illness was three days with an interquartile range of 1 to 7 days. The most common presenting symptom reported was cough (32.4%). Fever, however, was uncommon in our study population even in severe disease, with only 28.6% and 37.5% found in stages 4 and 5, respectively. Diarrhoea occurred in 9.7% of the study population. Anosmia was reported more commonly among patients with milder disease. Majority of the patients had normal haemoglobin levels, white cell counts, and platelet counts. Lymphocytopenia and raised CRP on presentation were found significantly more among those with severe disease. Symptomatic patients were commonly given chloroquine or hydroxychloroquine (27.5%). Most patients with severe disease were co-administered with antibiotics (85.7% of stage 4 and 100% of stage 5).

Markers for Severe Disease

Logistic regression analysis, shown in Table II, was done to identify variables that predict the development of pneumonia or hypoxia. In the multivariable logistic regression model, only peak CRP level was found associated with the development of pneumonia or hypoxia. Peak CRP level further analysed using ROC curve analysis demonstrated that area under the curve (AUC) for predicting pneumonia was 0.868 ($p<0.001$) at 14mg/L cutoff with sensitivity 73.8% and specificity 91.3%. For predicting of hypoxia, AUC was 0.992 ($p<0.001$) at 50mg/L cutoff with sensitivity 100% and specificity 96.4%.

Complications

The complications of COVID-19 were shown in Table III. 17% of the study population developed pneumonia. Among stage 3 disease, 96.3% of pneumonia were diagnosed based on chest radiograph, whereas only 3.7% were diagnosed clinically. The majority of the chest radiography reported as having interstitial or ground-glass opacities. 75% of stage 5 patients required ICU admission and mechanical ventilation. Raised total bilirubin and aspartate aminotransferase were found more commonly in those with severe disease. There were no acute liver injury or failure reported, and liver complications were managed conservatively. 6.5% of total patients developed acute kidney injury (AKI) with 44% of them requiring haemodialysis. Among clinical stage 3 and above, up to 31% developed AKI. Characteristics of COVID-19 patients with acute kidney injury were described in Table

Table I: Clinical characteristic of COVID-19 patients

	Total N=247	Stage 1 N=108	Stage 2 N=97	Stage 3 N=27	Stage 4 N=7	Stage 5 N=8	p-value
Baseline Characteristic							
Age-years							
Median (IQR)	28 (20-45)	24 (18-35)	27 (20-35)	41 (31-55)	59 (49-60)	58 (51-66)	<0.001
Distribution							
0-18	48 (19.4)	29 (26.9)	17 (15.5)	2 (7.4)	0 (0)	0 (0)	.
19-49	148 (59.9)	63 (58.3)	69 (71.1)	12 (44.4)	2 (28.6)	2 (25.0)	.
50-64	46 (18.6)	16 (14.8)	9 (9.3)	12 (44.4)	5 (71.4)	4 (50.0)	.
≥65	5 (2.0)	0 (0)	2 (2.1)	1 (3.7)	0 (0)	2 (25.0)	.
Male sex	172 (69.6)	77 (71.3)	60 (61.9)	20 (74.1)	7 (100)	8 (100)	0.131
Comorbidity							
COPD	5 (2.0)	0 (0)	2 (2.1)	1 (3.7)	2 (28.6)	0 (0)	.
Bronchial asthma	9 (3.6)	3 (2.8)	6 (6.2)	0 (0)	0 (0)	0 (0)	.
Diabetes mellitus	18 (7.3)	5 (4.6)	3 (3.1)	0 (0)	5 (71.4)	5 (62.5)	<0.001
Hypertension	28 (11.3)	9 (8.3)	8 (8.2)	4 (14.8)	4 (57.1)	3 (37.5)	0.001
Cardiovascular disease	8 (3.2)	3 (2.8)	1 (1.0)	0 (0)	2 (28.6)	2 (25.0)	0.001
Chronic kidney disease	9 (3.6)	2 (1.9)	1 (1.0)	0 (0)	3 (42.9)	3 (37.5)	<0.001
Obese	4 (1.6)	1 (0.9)	1(1.0)	1 (3.7)	1 (14.3)	0 (0)	.
Malignancy	6 (2.4)	2 (1.9)	1 (1.0)	0 (0)	0 (0)	3 (37.5)	.
Pregnant	1 (0.4)	0 (0)	1 (1.0)	0 (0)	0 (0)	0 (0)	.
Elderly ≥65 years	5 (2.0)	0 (0)	2 (2.1)	1 (3.7)	0 (0)	2(25.0)	.
Last Contact to Illness Onset							
Median (IQR)-days	3 (-1-7)	.	3 (-2-7)	2 (0-5)	3 (3-5)	4 (0-14)	.
Presenting Symptom							
Fever ≥37.5°C	14 (5.7)	0 (0)	6 (6.2)	3 (11.1)	2 (28.6)	3 (37.5)	0.012
Myalgia	14 (5.7)	0 (0)	9 (9.3)	4 (14.8)	0 (0)	1 (12.5)	0.604
Headache	7 (2.8)	0 (0)	4 (4.1)	1 (3.7)	1 (14.3)	1 (12.5)	0.230
Rhinorrhoea	34 (13.8)	0 (0)	25 (25.8)	7 (25.9)	2 (28.6)	0 (0)	0.465
Sore throat	33 (13.4)	0 (0)	27 (27.8)	4 (14.8)	1 (14.3)	1 (12.5)	0.514
Dyspnoea	14 (5.7)	0 (0)	4 (4.1)	0 (0)	4 (57.1)	6 (75.0)	<0.001
Cough	80 (32.4)	0 (0)	55 (56.7)	14 (51.9)	5 (71.4)	6 (75.0)	0.626
Sputum	34 (13.8)	0 (0)	23 (23.7)	6 (22.2)	1 (14.3)	4 (50.0)	0.384
Nausea and vomiting	7 (2.8)	0 (0)	2 (2.1)	2 (7.4)	1 (14.3)	2 (25.0)	0.015
Diarrhoea	24 (9.7)	0 (0)	12 (12.4)	6 (22.2)	3 (42.9)	3 (37.5)	0.035
Anosmia-no/total no (%)	34/193 (17.6)	0/99 (0)	32/74 (43.2)	2/11 (18.2)	0/4 (0)	0/5 (0)	.
Presenting Laboratory Findings							
Haemoglobin							
Median (IQR)-g/dL	14 (13-15)	14 (13-15)	14 (13-15)	15 (13-15)	13 (8-15)	7 (7-12)	<0.001
White-cell count							
Median (IQR)-per mm^3	7490 (6130-9200)	7580 (6650-8960)	7340 (5910-9350)	7400 (5400-9660)	7510 (5300-11700)	6890 (2440-11380)	0.922
>11,000 per mm^3-n/N (%)	27/246 (10.9)	12/107 (11.2)	10/97 (10.3)	1/27 (3.7)	2/7 (28.6)	2/8 (25.0)	0.189
<4,000 per mm^3-n/N (%)	6/246 (2.4)	3/107 (2.8)	1/97 (1.0)	0/27 (0)	0/7 (0)	2/8 (25.0)	0.037
Lymphocyte count							
Median (IQR)-per mm^3	2320 (1880-2980)	2500 (2000-3090)	2330 (1950-2950)	2150 (1610-2930)	2000 (1120-2640)	780 (340-1800)	0.001
<1500 per mm^3-n/N (%)	30/246 (12.1)	8/107 (7.5)	7/97 (7.2)	6/27 (22.2)	3/7 (42.9)	6/8 (75.0)	<0.001
Platelet count							
Median (IQR)-per 1000mm^3	284.5 (222-335)	296 (241-343)	287 (222-330)	252 (190-346)	228 (192-455)	171 (28-213)	0.010
<150,000 per mm^3-n/N (%)	9/246 (3.6)	1/107 (0.9)	3/97 (3.1)	2/27 (7.4)	0/7 (0)	3/8 (37.5)	0.002
C-reactive protein							
Median (IQR)-mg/L	2.0 (0.8-6.4)	1.1 (0.6-2.8)	2.6 (1.0-6.1)	7.9 (1.3-15.9)	75.7 (57.6-83.7)	139.2 (93.3-199.0)	<0.001
≥10mg/L-n/N (%)	44/242 (17.8)	6/105 (5.7)	12/95 (12.6)	11/27 (40.7)	7/7 (100)	8/8 (100)	<0.001
Distribution of other findings-n/N (%)							
Lactate dehydrogenase ≥250U/L	88/241 (35.6)	37/105 (35.2)	30/95 (31.6)	10/27 (37.0)	5/7 (71.4)	6/7 (85.7)	0.018
Total bilirubin >17.1µmol/L	23/245 (9.3)	14/107 (13.1)	5/96 (5.2)	1/27 (3.7)	0/7 (0)	3/8 (37.5)	0.026
Aspartate aminotransferase >40U/L	39/245 (15.8)	15/107 (14.0)	11/96 (11.5)	4/27 (14.8)	3/7 (42.9)	6/8 (75.0)	<0.001
Alanine aminotransferase >40U/L	49/245 (19.8)	20/107 (18.7)	21/96 (21.9)	6/27 (22.2)	1/7 (14.3)	1/8 (12.5)	0.972
Creatinine ≥133µmol/l	11/245 (4.5)	2/107 (1.9)	1/96 (1.0)	0/27 (0)	3/7 (42.9)	5/8 (62.5)	<0.001
Treatment							
Osetamivir[a]	11 (4.5)	1 (0.9)	3 (3.1)	3 (11.1)	3 (42.9)	1 (12.5)	.
Duration-median (days)	2	10	4	1	2	1	.
Antibiotics[b]	26 (10.5)	2 (1.9)	8 (8.2)	2 (7.4)	6 (85.7)	8 (100)	.
Duration-median (days)	6.5	7	4	7	7	7	.

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Lopinavir/Ritonavir[c]	37 (15.0)	0 (0)	7 (7.2)	17 (63.0)	6 (85.7)	7 (87.5)	.
Duration-median (days)	7	.	2	8	10	7	.
Chloroquine or Hydroxychloroquined	68 (27.5)	2 (1.9)	34 (35.1)	23 (85.2)	4 (57.1)	5 (62.5)	.
Duration-median (days)	5	3	5	5	5	5	.
Interferon beta 1a[e]	11 (4.5)	0 (0)	0 (0)	0 (0)	4 (57.1)	7 (87.5)	.
Duration-median (days)	6	.	.	.	6	6	.
Ribavirinf	4 (1.6)	0 (0)	0 (0)	1 (3.7)	1 (14.3)	2 (25.0)	.
Duration-median (days)	6.5	.	.	5	10	5	.

Data reported as n (%) unless otherwise stated.
Abbreviations: n= number, N=total number, IQR= interquartile range, COPD= chronic obstructive pulmonary disease.
[a]Oseltamivir oral, various dose. [b]Any antibiotics, oral or intravenous. [c]Lopinavir/Ritonavir, oral 400mg/100mg twice daily (BD). [d]Chloroquine, oral 500mg BD; hydroxychloroquine, oral 400mg BD day 1, then 200mg BD. eInterferon beta 1a, subcutaneous, 44mcg 3 times per week. fRibavirin, oral 2.4g load and 1.2g BD.

Table II: Logistic regression analysis to predict pneumonia and hypoxia

	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Comparing no pneumonia (stage 1 and 2) and pneumonia (stage 3, 4 and 5)				
Peak C-reactive protein	1.028 (1.017-1.039)	<0.001	1.024 (1.013-1.036)	<0.001
Lowest lymphocyte count	0.287 (0.168-0.490)	<0.001	.	.
Fever ≥37.5°C	7.804 (2.548-23.900)	<0.001	.	.
Comparing no hypoxia (stage 1, 2 and 3) and hypoxia (stage 4 and 5)				
Peak C-reactive protein	1.047 (1.028-1.067)	<0.001	1.047 (1.027-1.068)	<0.001
Lowest lymphocyte count	0.081 (0.028-0.233)	<0.001	.	.
Fever ≥37.5°C	12.39 (3.50-43.83)	<0.001	.	.

Variable selection was done using forward likelihood ratio test and model fitness had been checked with Hosmer-Lemeshow goodness-of-fit test.
Abbreviations: OR= odd ratio, CI: confidence level.

IV. Cardiac complications were rare in our population and invariably present in those with severe disease. Two subjects developed atrial fibrillation and three subjects were clinically diagnosed as acute heart failure. However, the diagnosis was limited by lack of echocardiogram and natriuretic peptide test. No neurological complications were reported.

Outcomes

The outcome of COVID-19 was shown in Table V. Our population recorded a median virologic clearance time of 15 days from illness onset and 19 days from the last positive contact. Asymptomatic patients required a longer time for clearance with a median of 24 days from the last positive contact. Upon the date of data collection, 121 patients had been discharged, 125 patients still hospitalised, and one patient died. The average median time to discharge was 18 days from illness onset and 22 days from last positive contact.

DISCUSSION

Our study population, in general, had similar clinical characteristics compared to other studies with few exceptions.[1,2] Similarly, the older age groups had a higher risk for severe disease, and COVID-19 patients were predominantly males. Our study population was generally younger with fewer coexisting illnesses. This explained a higher number of stage 1 and 2 diseases with a low mortality rate in our patients. Chronic kidney disease was more common, especially in severe disease (stage four 42.9%, stage five 37.5%). This was in comparison with studies from China having CKD in 1.7% of severe disease and 9% of non-survival.[1,2] We use the time of last positive contact until the onset of illness to reflect the incubation period. Median of three days (interquartile range -1 to 7 days) in our study was almost similar to a study in China, with an incubation period of four days (interquartile range 2 to 7 days). In terms of presenting symptoms, our population recorded more patients having diarrhoea (9.7% in total), compared with studies in China having 3.8% and 5%, respectively.[1,2] Anosmia was reported at a rate of 33.9% in one study.[6] Our patients reported more anosmia at the milder stage, with a frequency of 43.2% among stage two. However, no formal assessment tools were used in the assessment of anosmia. Anosmia symptom might be masked in more symptomatic patients. Treatment of COVID-19 was based on MoH guideline with chloroquine or hydroxychloroquine being used as the first-line agent.[5]

Malaysia COVID-19 management guideline[5] emphasised on using fever as the warning signs, dropping levels of lymphocytes count, raised CRP, and tachycardia to identify patients with risk for severe disease.[5] Multiple descriptive studies did not indicate fever associated with severe disease.[1,2,7,8] The association of lymphocytopenia with severe disease was described in a study China.[9] There was a predictive study[10] on CRP, which found an association with severity of computer tomography (CT) scan findings. Multivariable logistic regression study on our population indicated that only CRP was predictive of severe disease. It was accurate to predict the development of pneumonia and the requirement of oxygen at a cutoff value of 14mg/L and 50mg/L, respectively. Our study showed CRP peaked at a mean of 12.8 days from illness onset (95% CI 11.6 to 14.0 days). Patients with CRP value of <14mg/L may be used as a selection criterion for outpatient management. On the contrary, patients with CRP value of >50mg/L should be monitored closely, especially those without other explainable inflammatory cause. Unfortunately, data on tachycardia was not collected. Literature search on PubMed did not find any study on tachycardia in COVID-19. Our experience did not

Table III: Complications of COVID-19 patients

	Total N=247	Stage 1 N=108	Stage 2 N=97	Stage 3 N=27	Stage 4 N=7	Stage 5 N=8	p-value
Lung Complication							
Clinically diagnosed pneumonia	11 (4.5)	0 (0)	0 (0)	1 (3.7)	4 (57.1)	6 (75.0)	.
Radiologically diagnosed pneumonia	41 (16.6)	0 (0)	0 (0)	26 (96.3)	7 (100)	8 (100)	.
Ground glass opacities-n/N (%)	14/37 (37.8)	.	.	9/24 (37.5)	1/5 (20.0)	4/8 (50.0)	.
Consolidation-n/N (%)	11/37 (29.7)	.	.	5/24 (20.8)	3/5 (60.0)	3/8 (37.5)	.
Interstitial opacities-n/N (%)	24/37 (64.9)	.	.	15/24 (62.5)	3/5 (60.0)	6/8 (75.0)	.
Nodular opacities-n/N (%)	3/37 (8.1)	.	.	0/24 (0)	1/5 (20.0)	2/8 (25.0)	.
Oxygen therapy	14 (5.7)	0 (0)	0 (0)	0 (0)	7 (100)	7 (87.5)	.
ICU Admission	6 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	6 (75.0)	.
Mechanical Ventilation	6 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	6 (75.0)	.
Haematological Complication							
Peak white-cell count >11,000 per mm^3	40 (16.2)	12 (11.1)	11 (11.3)	7 (25.9)	4 (57.1)	6 (75.0)	<0.001
Time from illness onset-median (days)	12	.	10	13	14.5	13	
Lowest white-cell count <4,000 per mm^3	11 (4.5)	3 (2.8)	4 (4.1)	1 (3.7)	0 (0)	3 (37.5)	0.019
Time from illness onset-median (days)	9	.	9	.	.	14	
Lowest lymphocyte count <1,500 per mm^3	47 (19.0)	12 (11.1)	12 (12.4)	10 (37.0)	6 (85.7)	7 (87.5)	<0.001
Time from illness onset-median (days)	11	.	12.5	6	14.5	14	
Lowest platelet count <150,000 per mm^3	20 (8.1)	2 (1.9)	8 (8.2)	3 (11.1)	2 (28.6)	5 (62.5)	<0.001
Time from illness onset-median (days)	8	.	7	6	19	1	
Peak C-reactive protein, median (IQR)-mg/L	2.4 (1.0-10.0)	1.3 (0.7-2.5)	2.8 (1.2-9.5)	15.9 (4.8-22.9)	139.9 (122.0-144.0)	251.9 (131.3-307.8)	<0.001
Time from illness onset-median (days)	12	.	12	11	14	13	
Liver Complication							
Peak total bilirubin >17.1µmol/L-n/N (%)	75/238 (30.4)	25/102 (24.5)	19/94 (20.2)	19/27 (70.4)	5/7 (71.4)	7/8 (87.5)	<0.001
Time from illness onset-median (days)	13	.	13	12	14	15.5	.
Peak AST >40 U/L-n/N (%)	58/239 (23.5)	15/103 (14.6)	19/94 (20.2)	11/27 (40.7)	5/7 (71.4)	8/8 (100)	<0.001
Time from illness onset-median (days)	13	.	13	12	14	13.5	.
Peak ALT >40 U/L-n/N (%)	71/239 (28.7)	24/103 (23.3)	29/94 (30.9)	10/27 (37.0)	5/7 (71.4)	3/8 (37.5)	0.063
Peak AST and ALT >40 U/L-n/N (%)	47/239 (19.0)	12/103 (11.7)	18/94 (19.1)	9/27 (33.3)	5/7 (71.4)	3/8 (37.5)	0.001
Renal Complication							
Acute Kidney Injury	16 (6.5)	0 (0)	3 (3.1)	4 (14.8)	3 (42.9)	6 (75.0)	<0.001
Haemodialysis	8 (3.2)	0 (0)	0 (0)	0 (0)	2 (28.6)	6 (75.0)	.
Cardiac Complication							
Inotropic support	6 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	6 (75.0)	.
Duration-median (IQR) (days)	4 (3-7)	.	.	.	.	4 (3-7)	
New-onset arrhythmia	2 (0.8)	0 (0)	0 (0)	0 (0)	0 (0)	2 (25.0)	.
Myocardial ischemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	.
Myocarditis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	.

Data reported as n (%) unless otherwise stated.
Abbreviations: n= number, N=total number, IQR= interquartile range, ICU= intensive care unit, AST= aspartate aminotransferase, ALT= alanine aminotransferase.

Table IV: Characteristics of 16 COVID-19 patients with acute kidney injury

	n (%)
AKI Severity	
KDIGO stage 1	8 (50.0)
KDIGO stage 2	1 (6.3)
KDIGO stage 3	7 (43.8)
Oliguria or anuria	6 (37.5)
Requiring haemodialysis	7 (43.8)
Risk Factors	
Any comorbidities	10 (62.5)
CKD stage 3	2 (12.5)
CKD stage 4	0 (0)
CKD stage 5, predialysis	3 (18.8)
Hypertension	5 (31.3)
Diabetes Mellitus	6 (37.5)
Elderly age ≥65 years	3 (18.8)
COVID-19 Severity	
Clinical stage 4	3 (18.8)
Clinical stage 5	6 (37.5)
ICU admission	5 (31.3)
Inotropic support	5 (31.3)
Mechanical ventilated	5 (31.3)

Abbreviations: n= number, AKI= acute kidney injury, AKIGO= Kidney Disease Improving Global Outcomes, CKD= chronic kidney disease, ICU= intensive care unit.

Table V: Outcome for COVID-19 patients

	Total N=247	Stage 1 N=108	Stage 2 N=97	Stage 3 N=27	Stage 4 N=7	Stage 5 N=8	p-value
Virologic Clearance							
From last contact-median (IQR)-days	20 (15-26)	24 (16-27)	20 (15-27)	15 (12-21)	20 (16-33)	14	0.020
From illness onset-median (IQR)-days	15 (13-20)	.	15 (13-19)	13 (10-20)	19 (15-25)	18 (12-24)	0.391
Discharge							
From last contact-median (IQR)-days	22 (19-28)	24 (19-28)	23 (17-31)	22 (19-23)	26 (21-36)	.	0.355
From illness onset-median (IQR)-days	18 (15-23)	.	18 (15-22)	19 (16-21)	24 (21-29)	.	0.178

Abbreviations: n= number, N=total number, IQR= interquartile range, ICU= intensive care unit.

suggest unexplainable tachycardia as a common finding in patirnts with severe disease. A study by Zhou et al.,[2] suggests presence of d-dimer as a predictor for mortality. However, d-dimer was not routinely done in our patients to allow meaningful analysis.

Our study demonstrated the importance of radiographic imaging in the diagnosis of pneumonia as the majority of stage 3 patients were clinically silent. A small study done in Korea suggested CT scan was superior to chest radiograph.[11]

A study from China by Wang et al., presented with a bold title of "COVID-19 infection does not result in acute kidney injury".[12] Their study consisted of 116 subjects of at least stage three diseases with half of the subjects (49.2%) having either severe pneumonia or acute respiratory distress syndrome (ARDS). None of their study population developed acute kidney injury or aggravated existing chronic kidney disease. Another observational study of 1099 subjects described AKI complication of a mere 0.5%. However, our study demonstrated differently.[1] Thirty one percent of patients with clinical diseases stage 3 and above developed AKI. Out of those developed AKI, 44% required haemodialysis. This may be partially explained by a higher number of CKD patients in our patients. Dedicated nephrology expertise with adequate dialysis equipment should be made available in all COVID-19 treating centre.

Our study showed that a median time for sustained virologic clearance was 15 days from onset of illness (interquartile range of 13 to 20 days). This was shorter in comparison with a study from China, which showed a median duration of 20 days (interquartile range of 16 to 23 days).[2] However, this was a retrospective study, and results might be affected by a different testing policy. A longer duration of virologic clearance was observed in our asymptomatic groups. A small study in China has shown that asymptomatic patients were having a lower risk of transmission compared to symptomatic patients.[13]

LIMITATIONS

This study was limited by its study design, being retrospective and single centred. HTAA is a public hospital with budget constraints that limit the choices of laboratory and imaging testing. As the disease had become widely spread, identification of the time of positive contact was difficult.

CONCLUSION

COVID-19 presented with a wide spectrum of clinical patterns. CRP was a valuable predictor of severe disease. Risk and severity of acute kidney injury were found higher in this study. A longer duration of virologic clearance was observed among the asymptomatic patients.

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