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Research Article
Clinical Profile and Outcomes of Confirmed COVID 19 at Manila Doctors Hospital

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Abstract

Background and Objective: Coronavirus disease (COVID-19) is a global pandemic. The Philippines has its first confirmed case and mortality by the end of January, 2020. The aim of this paper was to define the clinical characteristics and outcomes of COVID-19 patients admitted at MDH. **Materials and Methods:** This was an observational study of all confirmed COVID-19 patients admitted at MDH between March to June 2020. The clinical profile, laboratory, imaging features and outcomes of included patients were described. **Results:** There were 124 patients included in the study. The median age on admission was at 47 years old, with male predominance. Fever and cough were the most common presenting symptoms. Hypertension was the most common co-morbid condition. Lymphocytopenia, elevated ferritin and LDH levels were the most common laboratory findings. Ground glass opacity was the most common chest CT scan finding. The most common complication was Acute Respiratory Distress Syndrome (ARDS). The mortality rate was 16.9%. **Conclusion:** This study was done during the initial salvo of COVID-19 pandemic, when symptom presentations were protean and management approaches were based on the limited knowledge available at that time. The clinical manifestations are similar to those reported in the international literature with high mortality among those with ARDS. The management of the patients through time has progressed and continues to change as more valid data become available.

Key words: COVID-19, clinical characteristic, diagnostic profile, treatment approaches, clinical complications, mortality rate

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Coronavirus disease (COVID-19) was first reported in Wuhan City, Hubei Province, China in December 2019[1] with an over-all case fatality rate of 2.3%, rendering highest mortality among the elderly (≥80-year-old) and the critical cases. Since its outbreak, other countries have quantified their own number of confirmed cases and case fatality rate. Globally, there are 67,791,491 confirmed COVID-19 cases and 1,547,645 deaths as of December 7, 2020[1] with the highest count of confirmed cases reported in America, followed by Europe[2].

A study done by Guan *et al*. done in mainland China[3] with 1,099 confirmed COVID 19, showed a median age of 47 years, of which more than half were males and a reported mortality of 1.4%. Fever, on admission (43%) and during confinement (88.7%), was the most common symptom. Other reported symptoms were cough (68%) and diarrhea (3.8%). The most common sign was ground-glass opacity (56.4%) on chest Computerized Tomography (CT).

In the Philippines, the first confirmed COVID-19 case was reported on January 30, 2020[4-6] with the first confirmed death a day later[4]. Since then, the number of cases continued to rise and curtailing measures were implemented. As of January 16, 2021, there was a total of 498,691 confirmed Covid-19 cases[5]. At the Manila Doctors Hospital (MDH), based on data from the Infection Prevention and Control Office (IPCO), the first confirmed case was seen on March 11, 2020 [personal communications, IPCO Data. 2020 Manila Doctors Hospital].

In a retrospective single-center descriptive study done by Salva *et al*.[7], 100 patients with suspected COVID-19 admitted at San Lazaro Hospital (SLH) by March 31, 2020, were described. Out of these 100 patients, 42 (40%) were confirmed COVID cases, with a median age of 56 (24 .89). Fifty five percent were male and 7% were health care workers (HCWs). The most common symptoms were cough (76%), followed by fever and coryza, both at 43%. The most common reported co-morbidities were hypertension (33%), diabetes (17%), respiratory illnesses, including asthma (17%) and cardiovascular disease (10%). The confirmed cases experienced symptoms for a median duration of 7 (0,19) days with a 21% death rate.

Since this is a new malady, there still are a few data on the clinical profiles and outcomes of these patients. Therefore, additional information will be useful in characterizing the disease. The aim of this paper was to define the clinical characteristics and outcomes of COVID-19 patients admitted at MDH with the end goal of improving medical services and patient outcomes.

Research question: Among patients with confirmed COVID-19 at Manila Doctors Hospital (MDH), what are the clinical profile and outcomes?

Objectives

General objective: To describe the clinical profile and outcomes of confirmed COVID-19 patients at MDH.

Specific objectives:

- To describe the clinical profiles of confirmed COVID-19 patients at Manila Doctors Hospital
- To describe the laboratory parameters and imaging results of confirmed COVID-19 patients at Manila Doctors Hospital
- To enumerate the treatment measures administered to confirmed COVID-19 patients at Manila Doctors Hospital
- To describe the clinical complications and outcomes of confirmed COVID-19 patients at Manila Doctors Hospital

MATERIAL AND METHODS

Study design, participants and source of data: This is an observational descriptive study of all confirmed COVID-19 patients admitted at MDH between March to June, 2020. All patients, 18 years old and above, admitted with confirmed COVID-19 infection using the government-approved RT-PCR kit, were reviewed. Confirmed COVID-19 patients seen at the Emergency Room (ER) of MDH but were discharged and advised home quarantine were excluded.

Using medical charts, two trained physicians collected and analyzed relevant data, namely: Demographics, clinical characteristics, treatment measures, laboratory data and imaging studies. During the period of collection, diagnostic examination and management were mostly based on the Philippine Society of Microbiology and Infectious Disease (PSMID) Interim Guidelines on COVID-19 infection released on 31 March, 2020[6] and review of related literature[3,8,9]. Clinical complications and outcomes such as ARDS, Acute Renal Injury (AKI), Acute Cardiac Injury (ACI), arrhythmia, septic shock and in-hospital all-cause mortality were determined. A standardized data collection form with no individual patient identifier was used to document the variables. Cardiologists in the study group (WAG and CGT) independently read the ECG tracings. If the reading/s had any discrepancies, they were sent to another cardiologist (NSP) for collation and adjudication. Final adjudicated readings were sent to the primary investigator (FERP) and the data manager for encoding. All data collected were given to the data encoder who entered all variables in the study database used for analysis.

Definition of terms:

- Acute Respiratory Distress Syndrome (ARDS) using the Berlin criteria[10] is defined by the PaO2 to FiO2 Ratio (PFR) classified as mild (≤300 and >200), moderate (100-200) and severe (<100)
- Acute renal injury based on KDIGO definition, is any of the following:[11] "absolute increase in serum creatinine (sCr), of at least 0.3 mg dL^{-1} (26.5 µmol L^{-1}) within 48 hrs or by a 50% increase in sCr from baseline within 7 days or a urine volume of less than 0.5 mL/kg/hr for at least 6 hrs
- Acute cardiac injury is defined as (1) significant elevation of cardiac troponin I above 99th percentile upper reference limit or (2) new abnormalities seen in electrocardiography and/or echocardiography[12-15]. The new abnormalities would be based on serial ECGs done during admission and comparison with previous echoes of identified patients when available
- Arrhythmia is the presence of any tachyarrhythmia and/or bradyarrhythmia[12] that necessitates an intervention or leads to sudden cardiac death either documented by ECG tracing or as written in the chart or as part of the final diagnosis
- Septic shock based on the third International Consensus Definitions for Sepsis and Septic shock (Sepsis-3)[16,17] is a score of ≥2 on qSOFA (which stands for quick Sequential (Sepsis-Related) Organ Failure Assessment Score) plus presence and use of vasopressors to maintain MAP ≥65 mm Hg despite adequate fluid resuscitation and serum lactate level ≥2 m mol L^{-1}. qSOFA consists of the following parameters: respiratory rate ≥22 min^{-1}, altered mentation (Glasgow Coma Scale score of 13 or less) and systolic blood pressure of ≤100 mm Hg
- Mortality is in-hospital death from any cause
- Discharged with improved status has the following criteria: "patients who have clinically recovered (with resolution of symptoms, namely: the body temperature returns to normal >3 days, respiratory symptoms have improved significantly or chest radiograph shows significant improvement) with two consecutive negative tests for SARS-CoV-2 24 hrs apart or if a repeat test is not possible, patients can be discharged upon the discretion of the healthcare team"[6]
- Duration of hospitalization is the length of hospitalization from the date of admission to the date of discharge or last contact with the patient

Study duration: The data collection started in April and ended in mid-June, 2020.

Data analysis: Data were encoded and tabulated using the Microsoft Excel™ 2016. The categorical variables were summarized using frequencies, rates and proportions. Continuous variables with a normal distribution were summarized as mean and standard deviation or when needed, median value and interquartile range (IQR).

Ethical consideration: The protocol was approved by the MDH Institutional Review Board (IRB) last April 13, 2020, with MDH IRB Code 2020-002. All the pieces of information were kept confidential in compliance with the Data Privacy Act of 2017. All data collected and analysis were kept secure in a password-protected computer. There were no conflicts of interest between the investigators and the study. Patient benefits were indirect since knowledge generated from this study will help improve quality of care.

RESULTS

Clinical profile and characteristics: The study included 124 patients with confirmed COVID-19 infection. As shown in Table 1, the patients were mostly male (55%) with median age of 47 years old, ranging from 19 to 83 years. Around one third of our admissions were health care workers (39.5%). Only 2.4% have a documented travel history to places with sustained community transmission while 30% recalled that they had exposure to a confirmed COVID-19. The table also shows comorbidities with hypertension as the most common. Included in the other conditions were dyslipidemia (6.5%), hyperuricemia (3.2%), benign prostatic hyperplasia (2.4%), hypothyroidism (1.6%), peripheral arterial disease (0.8%) and myasthenia gravis (0.8%).

Fever and cough were the most common symptoms (Table 2). The median time to hospital admission was on the 6th (3,8) day of illness.

Table 1: Demographic profile (n = 124)

Characteristics	n (%)
Age in years, median (Q1, Q3), (range)	47 (29,63), (19-83)
Male	68 (55)
History of travel	3 (2.4)
Exposure to known COVID positive case	38 (30.6)
Healthcare worker	49 (39.5)
Comorbidities	
Hypertension	53 (42.7)
Diabetes mellitus	31 (25)
Bronchial asthma	12 (9.7)
CKD	11 (8.9))
CAD	10 (8.1)
CVD	4 (3.2)
Malignancy	3 (2.4)
Autoimmune disease CVD	1 (0.8)
Others	19 (15.3)

Table 2: Most common clinical signs and symptoms (n = 124)

Clinical parameters	n (%)
Symptoms	
Cough	63 (51)
Fever	60 (48)
Shortness of breath	24 (19)
Nasal congestion	21 (17)
Diarrhea	20 (16)
Weakness/fatigue	20 (16)
Signs	
Temperature on admission in °C, mean (SD)	37.0 (±0.73)
With fever on consult (≥ to 38°C)	18 (14.5)
With crackles on auscultation	28 (22.6)

Table 3: Baseline hematologic workups

Diagnostic parameters	Median (Q1, Q3)
Complete blood count (n = 116)	
Hemoglobin (g L^{-1})	141.4 (129,152.8)
White blood cell ($\times 10^9$ L^{-1})	7.6 (5.7,9.1)
Platelet count ($\times 10^9$ L^{-1})	263.5 (196.5, 317.5)
Lymphocytes, mean (SD)	0.22 (±0.09)
With lymphocytopenia (<0.24), n (%)	67 (57.8)
Blood chemistry	
Creatinine (µmol L^{-1}), n = 97	78 (60, 105)
eGFR (mL/min/1.73 m^2)	88 (65, 113)
hs-CRP (mg L^{-1}), n = 66	18.2 (1.8,67.4)
With high hs-CRP (>3.00 mg L^{-1}), n (%)	19 (28.8)
LDH (U L^{-1}), n = 90	219.5 (161.7, 286)
With high LDH (>245.00 µ L^{-1}), n (%)	36 (40)
Ferritin (ng L^{-1}), n = 81	437.92 (232.4, 863.7)
With high ferritin (>300 ng mL^{-1}), n (%), (range)	37 (45.7), (301.3-987.1)
D-dimer (ng mL^{-1}), n = 9	838 (332.5,1767)
hs-troponin I (ng mL^{-1}), n = 11	0.027 (0.019,0.124)
With elevated hs-troponin I (0.034 ng mL^{-1}), n (%), (range)	5 (45.5), (0.074-0.431)

Diagnostics

Laboratory parameters: The tests and number of patients who had the exams done were shown in Table 3. *Lymphocytopenia* was present in 58%. The most requested biomarkers were LDH, ferritin and HS CRP. Almost half of those who had LDH and ferritin tests had elevated levels, while elevated HS CRP was noted in one third of those who had the test.

Pulmonary workup: ABG was done on admission in 92 patients with median PaO2 of 90.4. Seventeen (18.5%) patients had ARDS on admission, of which 10 were classified as mild, 4 as moderate and 3 as severe.

At baseline, 51% had in filtrates on CXR. The most common finding on Chest CT scan done on 70 patients were ground glass opacities and infiltrates (Table 4).

Cardiovascular Workup: ECG was done in 96 patients. The most common rhythm (97%) was sinus. The most common abnormality was non-specific ST-T wave changes in 35.4% of patients. *Echocardiography* was performed in 37 patients with 11% having abnormal Left Ventricular (LV) systolic function with mean ejection fraction of 43.5% (SD 6.8). None had RV dilatation or dysfunction.

Table 4: Baseline pulmonary workups

Diagnostic parameters	n (%)
Arterial blood gas, n = 92	
PaO2, median (Q1, Q3)	90.4 (72.6, 105.5)
PaO2 to FiO2 ratio (PFR), median (Q1, Q3)	403 (318.6, 469.8)
With ARDS based on PFR	17 (18.5)
Chest X-ray, n = 123	
Normal findings	60 (48.8)
Unilateral infiltrates	27 (22.0)
Bilateral infiltrates	36 (29.3)
Chest CT scan, n = 70	
Ground-glass opacity	53 (75.7)
Bilateral infiltrates	52 (74.3)
Unilateral infiltrates	7 (10.0)

Table 5: Treatments initiated (n = 124)

Interventions	n (%)
Antimicrobial therapy	92 (74.2)
Chloroquine/hydroxychloroquine	75 (60)
Hcq+azithromycin	56 (45)
Lopinavir+ritonavir	28 (22.6)
Cq+azithromycin	19 (15.3)
Remdesivir	2 (1.6)
Tocilizumab	20 (16.1)
Systemic glucocorticoids+tocilizumab	14 (11.3)

Treatment: Majority of patients received at least one antimicrobial dose as shown in Table 5. Many also received hydrochloroquine/chloroquine (HCQ/CQ) during the study period. Systemic glucocorticoids, tocilizumab and remdesivir were given in 11.3, 16.1 and 1.6%, respectively. Only one patient received both convalescent plasma therapy and stem cell infusion.

Vitamin C with Zinc was given to 106 (85.5%) while melatonin was given to 36 (29.0%) of patients. Hemoperfusion with or without hemodialysis was performed in 18 patients (14.51%). Hemoperfusion alone was done in nine patients (7.30%). Fifty seven patients (46%) had non-mechanical oxygen supplementation. VTE prophylaxis was given in 13.7%.

Clinical complications and outcomes during admission: The most common complication was ARDS, followed by septic shock, Acute Kidney Injury (AKI), Acute Cardiac Injury (ACI) and arrhythmias in descending frequency.

Another 23 patients (18%) developed ARDS during hospitalization. Overall, there were 40 (32.3%) patients with ARDS in the study population. 47.5% of those with ARDS expired.

Twenty (16.1%) patients developed septic shock, acute kidney injury occurred in 13.7% and acute cardiac injury in 7.2%. Arrhythmias were present in 8 patients (6.5%). These included new onset atrial fibrillation (3 patients), ventricular tachycardia (1 patient), non-sustained ventricular tachycardia (1 patient), sustained ventricular tachycardia to PEA (1 patient), supraventricular tachycardia (1 patient) and another which was unspecified.

The mortality rate was 16.9%, predominantly in the older age group. The median age at death was 67 (IQR 61,73) years while the median age of the survivors was 38 (IQR 29,60) years. The median duration of hospitalization was around 12 days (IQR 9,19).

DISCUSSION

Clinical profile: This cohort included 124 confirmed COVID-19 infected patients ranging from asymptomatic to the critically ill. The median age was 45 years old, mostly male. The reported median age of other studies was between 42-61 years old[3,7,18] with males consistently the more affected as well with a 56.5-69.1% reported incidence[3,7,18].

Cough and fever represent the most common presenting symptoms in this study consistent with international reports[3,9,19-22]. Myalgia or fatigue, which was present in 35.8% in the study of Li[23], was seen only in 2% of our population. Diarrhea, another common symptom described to be between 4.8-23.7% in Li's study[23] in China and Goyal's study[19] in New York respectively, was present in 16% of our patients. Recent published data though showed an increase in reporting of diarrhea as an associated or presenting symptom of COVID-19[24,25]. This may reflect an increase in reporting of the symptom as knowledge on the different presentations of the disease increases.

The risk of mortality is known to increase with the presence of comorbidities. Hypertension (HPN) was present in 42.7% and diabetes mellitus (DM) in 25% in our study population. These prevalences were markedly higher in comparison to the studies by Guan *et al.*[3] showing 15 and 7.4% for HPN and DM and Goel[26] reporting 20.8 and 12.39% respectively. This may be a reason behind the 1.4% mortality rate in Guan's study compared to our 16.9%.

The patients in this study came to the hospital for admission on a median of 6 days of illness. This was almost comparable to the Italian study of Giocomelli[18] with overall median of 7 days (IQR 4-9) but shorter than the Salva's local study[7] which showed that confirmed cases experienced symptoms for a median duration of 11.5 (IQR 8,18).

Diagnostics: The diagnostic tests requested were based on the attending physicians' decision and clinical indications but generally in accordance with the recommendations from PSMID guidelines[7]. Based on the PSMID guideline dated 31 March 2020[6] and review of related literature[3,8,9], the following laboratory exams were identified as important prognostic factors, namely: WBC count, lymphocyte count, LDH, ferritin, CRP, procalcitonin, D-dimer and hs-Trop I. Some tests (like D-dimer and hs trop I) were infrequently done perhaps due clinical indication and cost.

More than half of the patients in this cohort had lymphocytopenia frequently seen in the other studies as well: Guan 83.2[3], Du 77.6[8], Li 64.5[23], Goyal 90[19] and Wu 64%[20].

The most common markers done in our study are ferritin, LDH and HS CRP. Ferritin level of >1000 ng mL^{-1} can be a marker for cytokine storm[6]. Around sixty-five percent of our patients who had this test had ferritin level >300 ng mL^{-1} (45.7% had level >300 ng mL^{-1} and 19.8% had levels >1000 ng mL^{-1}). In a study of Wu[20], 78.5% had elevated ferritin with a median value of 594.0 (IQR 315.69-1266.16) and mortality rate of 21.9%. In a study by Zhou[9], which involved COVID patients with different severity, 80% had a level of >300 µg L^{-1} and on multivariate analysis, it showed HR 9.1 (2.04-40.58, p-value = 0.0038) and mortality rate of 28.3. A high hs-CRP was a measure to monitor mortality risk[6]. Twenty eight percent (28.8%) of our patients who had a hs-CRP have levels >3.0 mg L^{-1}.

Forty percent of our patients had LDH levels >245.00 µ L^{-1}, which is a marker of poor prognosis[6]. Du[8] and Zhou[9] reported increases such as 82.4 and 67%, respectively. In a univariate analysis done by Zhou[9], LDH level >245 µ L^{-1} showed an increased odd of in-hospital death (OR of 45.43 (6.10-338.44, p = 0.0002).

Pulmonic infiltrates were seen on chest X-ray in more than half of this cohort which is similar to the study of Guan[3] and Shi[21]. Ground-glass opacity with bilateral infiltrates were noted in two-thirds of our patients with CT scan which were also found in the study of Du[8]. More than half of our patients had CXR and CT scan findings but only 19% had shortness of breath (SOB) on admission. Similarly, Guan and Shi reported SOB in 18.7 and 28.1%, respectively but on chest CT scan, ground glass opacities were 56.4%[3] and on Chest X-ray, bilateral pneumonia was seen in 74.8%[21]. The symptoms, particularly SOB, which ranged from 18.7 to 28.1% may not reflect the pulmonary status on admission (75.7% of our patients had ground-glass opacity on chest CT scan).

Baseline left ventricular systolic function was mostly preserved with only 10.8% had abnormal systolic function in our study population. This finding was comparable to that of

the study done by Szekely[27] which performed echo in 100 consecutive COVID patients within 24 hrs of admission (March 21-April 16, 2020) in Tel Aviv Medical Center, Israel. The LV systolic dysfunction was noted in 10%. The most common echo finding was RV dilatation with or without dysfunction (39%) which was not seen in current study.

Treatment modalities: At the time when this study was conducted, the interim PSMID Guidelines (March, 2020) in the management of suspected or confirmed COVID-19 infection were limited. The drugs were used as off-label for compassionate use[6]. For most cases, usually the mild ones, supportive treatment could be provided, namely: Hydration, antipyretics and self-quarantine[28]. During the initial months of the COVID infection, chloroquine and hydroxychloroquine with or without azithromycin were seen as potential therapies.

In this study, many patients received chloroquine/ hydroxychloroquine +/-Azithromycin while a fifth received lopinavir and ritonavir. During this study's observational period from March to June 15, 2020, these drugs were being given for "compassionate" use while awaiting definite evidence.

Since then, several trials were initiated. One such trial was Recovery trial[29]. It was a randomized, controlled, open-label trial comparing 1561 hospitalized patients to hydroxychloroquine plus usual standard of care and 3155 patients on usual standard of care. The mean age of patients was 65.4+/-15.3 years and Asians were included. At the time of randomization, only 17% were on invasive mechanical ventilation, 60% were on oxygen only and 24% received neither. Results showed no difference in the mortality rate. Moreover, patients on hydroxychloroquine had longer duration of hospitalization and higher risk of invasive mechanical ventilation or death.

A randomized, controlled, open-label trial done by Wang *et al.*[30], which enrolled 199 confirmed SARS-CoV-2 seriously ill patients, at Hubei Province, China, compared lopinavir-ritonavir (400 and 100 mg, respectively) twice a day given for 14 days plus standard of care versus standard of care alone. Results showed that there was no difference in the time to clinical improvement. Mortality at 28 days, a secondary outcome of the study, showed no difference between the two treatment arms.

With the release of these results, on 4 July 2020, the World Health Organization (WHO) abided by the recommendation from the Solidarity Trial's International Steering Committee to discontinue the trial's hydroxychloroquine and lopinavir/ritonavir arms[31]. In this regard, the Antimicrobial Stewardship Committee of Manila Doctors Hospital last July 9, 2020 recommended against the continuous off-label use of chloroquine/hydroxychloroquine and lopinavir/ritonavir among COVID-19 patients at MDH.

There is increasing evidence that in COVID patients with ARDS, virally induced pro-inflammatory cytokines lead to both hyperinflammatory and procoagulatory states at the late stage of the disease[32]. In this study, there were 20 patients (16.1%) who received tocilizumab based on the initial trials mentioned. In an international trial named REMAP-CAP[33], critically ill adult patients with Covid-19 admitted to Intensive Care Unit (ICU) were randomized to three treatment arms, namely, 353 patients to tocilizumab, 48 to sarilumab and 402 to control. Results showed that treatment with the interleukin-6 receptor antagonists tocilizumab and sarilumab improved in-hospital mortality (27% in the pooled interleukin-6 receptor antagonist groups and 36% in the control group). The median number of organ support-free days was 10, 11 and 0 in the tocilizumab, sarilumab and control group, respectively.

In this study, 14 patients (11.3%) received systemic glucocorticoids. The preliminary report done by the Recovery collaborative group[34] was an open-label trial comparing oral or intravenous dexamethasone (at a dose of 6 mg once daily) given for 10 days versus usual care alone in Hospitalized Patients with COVID-19, only 16% of these patients at randomization received invasive mechanical ventilation or extra-corporeal membrane oxygenation. Results showed reduction in the 28-day mortality with a risk ratio of 0.83 (0.75-0.93). Moreover, among patients receiving invasive mechanical ventilation, the use of dexamethasone resulted in lower incidence of death (rate ratio, 0.64, 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (rate ratio, 0.82, 95% CI 0.72 to 0.94). The trial result was released in July 2020 and the data were not initially available which explains the low rate of usage in our study. At present, the use of dexamethasone among COVID-19 patients requiring oxygen has been currently implemented.

Remdesivir was used in this study in only two patients (1.6%). Remdesivir for the Treatment of Covid-19 (ACCT-1) was a double-blind, randomized, placebo-controlled trial study done by Beigel *et al.*[35] which compared intravenous Remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) with placebo for a total of 10 days. The primary outcome was the time to recovery. Result showed that patients in the Remdesivir group had a shorter time to recovery than patients in the placebo group (median, 10 days as compared with 15 days, rate ratio for recovery, 1.29, 95% confidence interval, 1.12 to

1.49). The usage of Remdesivir in this study was low since results of ACCT-1 was not yet available when the study was conducted.

Melatonin was considered as a sleep-aid supplement, with anti-inflammation, anti-oxidation and immune enhancing properties[36,37]. Notably, there were 36 patients (29.0%) who received melatonin in this study. A case series[38] involving 10 patients with findings suggestive of COVID 19 infection was published with patients given melatonin 36-72 mg day^{-1} by mouth in four divided doses. In the ten included patients given high dose melatonin (hdM), all survived and clinical improvement was noted within 4-5 days after the start of treatment. In this light, a randomized, double-blind, placebo-controlled trial has been conceptualized to address the benefit of melatonin as an adjuvant treatment against COVID-19.

Lastly, the interim WHO SOLIDARITY TRIAL[39] results showed that repurposed antiviral drugs for COVID-19, namely, Remdesivir, Hydroxychloroquine, Lopinavir and Interferon-β1a done in 30 countries did not show reduction in overall mortality. All drugs did not reduce the initiation of ventilation and duration of hospital stay.

Only 13.7% of our patients received venous thromboembolism (VTE) prophylaxis. In July 2020, the Philippine Society of Vascular Medicine (PSVM) released an interim guideline[40] on the use of anticoagulation among Covid-19 patients. In the absence of contraindications, all hospitalized Covid-19 patients at risk for VTE, including those with high ($\geq$4) Padua score and with D-dimer of $\geq$1500 ng mL^{-1} must receive prophylactic anticoagulation. Awareness of these guidelines can help the managing team increase the utilization of VTE prophylaxis.

The Antimicrobial Stewardship Committee of MDH and the multidisciplinary team of physicians continue to tailor the management of the COVID-19 patients according to the evidence as the results of the different trials are released.

Outcomes and mortality rate among those with complications: Mortality at Manila Doctors hospital was at 16.9% lower than the reported in-hospital mortality rates of 20.6 to 30% by the other authors[7,18,20,26,41]. Guan et al reported a much lower mortality rate of 1.4%[3] perhaps because 84% of the patients had nonsevere infection and less comorbidities.

Acute respiratory distress syndrome: ARDS is one of the major complications if not the dominant finding in critically ill COVID-19 patients. In this study, 32.25% had ARDS and this carried a 47.5% mortality rate in this group. Compared to a study of Wu[20] comprising a cohort of 201 patients admitted for COVID-19 pneumonia, 41.8% developed ARDS and of these, 52.4% died. Risk factors seen to be associated with the development of ARDS and its progression to death include older age, presence of comorbidities such as hypertension, cardiovascular disease and diabetes mellitus, neutrophilia, lymphocytopenia and organ and coagulation dysfunction (e.g., higher lactate dehydrogenase and D-dimer).

Cardiovascular complications: The frequency of myocardial injury in admitted Covid-19 patients varies from study to study. It can be as low as 7% to as high as 27.8%[13,42]. In current study, nine patients were labelled with acute cardiac injury. Five of them were noted to have wall motion abnormalities on echocardiogram. Hs-troponin was requested in 11 patients, five (45.5%) of them had elevated levels. Myocardial injury was seen to be related to a higher mortality rate (51.2%) in the study by Shi[22] highlighting its importance. The postulated mechanisms by which COVID-19 leads to cardiovascular morbidity include direct myocardial injury as a result of the inflammatory cascade or cytokine release, microvascular damage due to disseminated intravascular coagulation and thrombosis[43,44]. In this study, a total of 37 patients had baseline echocardiograms. Only 13.5% (5) of the patients had abnormal wall motion abnormalities on baseline.

Eight patients (6.5%) had arrhythmias, three of whom had ventricular tachycardia. In a study done by Wang[42], the incidence of arrhythmias was 17% and was independently associated with an increased risk of in-hospital death. In a study done by Guo[13], involving 187 COVID-19 confirmed patients, ventricular tachycardia and ventricular fibrillation had an incidence of 5.9% and significantly more common in patients with elevated TnT level.

Acute kidney injury: Acute Kidney Injury (AKI) foreshadows a higher risk of mortality[45]. In our patients, the incidence of AKI was 13.7 and 82.4% of those patients died. In a cohort study of 701 Covid-19 patients done by Cheng[46], AKI occurred in 5.1% and the in-hospital death was 33.7%. In the US cohort of 5449 covid-19 patients, AKI was diagnosed in 37% and among patients with AKI, 35% died[47]. Hirsch reported the following as independent predictors: older age, black race, diabetes, hypertension, cardiovascular disease, mechanical ventilation and use of vasopressor medications[47]. Su *et al.*[48] in their postmortem studies of COVID patients observed significant acute tubular injury, the occlusion of microvascular lumens mainly by erythrocytes with ensuing endothelial damage as well as glomerular and vascular changes indicative of underlying diabetic or

hypertensive disease. Rate of deterioration necessitating renal replacement therapy in Manila Doctors Hospital was 14.51% (18 patients). This was consistent with the findings of Hirsch *et al.*[47] were 15% of patients who had AKI required hemodialysis.

Septic shock: Septic shock (at 16.1%) was the third most common complication seen and carried a mortality rate of 80%. The study of Guan[3] which included severe and nonsevere cases), showed a lower incidence of shock (1.1%) but Du[8] and Zhou[9] reported incidences of septic shock at 32.9 and 20%, respectively. Du[8] included 85 fatal cases with older median age 65.8 years (IQR 14,82) and higher inflammatory markers (LDH, Hs-CRP and D-dimer). The higher incidence in the study of Zhou[9] could be attributed to higher disease severity (35% were severe and 28% were critical cases).

CONCLUSION

When this study was started, it was the time of the initial salvo of COVID-19 pandemic, when symptom presentations were protean and management approaches were based on the limited knowledge available at that time. The clinical manifestations were similar to those reported in the international literature. The mortality rate was not far from those reported in other studies. This was especially magnified when there were ARDS, AKI, septic shock, arrhythmia and ACI. The management of the patients, through time, has progressed and continues to change as more valid data become available.

Limitations of the study: The cohort of patient included in the study was a mixture of asymptomatic to critical symptomatic COVID-19 cases and did not include characteristics and outcomes of other confirmed COVID-19 cases who were advised home quarantine. Some clinical presentations in relation to the complications (e.g. ACI) during hospitalization were not systematically gathered. Certain diagnostic data were not done as the laboratory examinations were guided by indications based on clinical presentation. The guidelines on diagnosis and treatment continue to evolve and the findings in this study may not fully reflect the current up-to-date evidence-based management.

Implications to research: The data presented were the first 124 cases admitted at MDH. Since then, more patients have been admitted, and presentations as well the treatment options continue to evolve through time. Continuing data collection may be warranted. Further analytic studies on our data set will shed light on whether these outcomes are truly associated with higher mortality. Sub-studies on particular aspect/s of COVID -19 infection, like cardiac manifestations and treatment modalities in confirmed COVID-19 patients, can be presented more comprehensively.

Implications to clinical practice: The data presented showed the initial epidemiology of the infection at MDH and the course of the illness among those admitted. Medical management during this time when evidences for effective treatment modalities were few and inconclusive, helped the health care providers to learn from one case to another. Descriptive studies such as these also give us an insight into the high-risk population who may benefit from early access to novel therapies and vaccines when they become available.

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