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Coronavirus Pandemic

Clinical features and outcomes of COVID-19 patients admitted at a tertiary hospital in Cebu City, Philippines

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Abstract

Introduction: The World Health Organization has categorized coronavirus disease 2019 (COVID-19) into mild, moderate, severe, and critical illness severities to guide clinical decision-making. This study aimed to describe the clinical characteristics, complications, and outcomes of COVID-19 patients by illness severity, at a tertiary healthcare center in Cebu City, Philippines.

Methodology: This was a retrospective, observational cohort study that examined clinical information of patients with confirmed COVID-19 infection admitted between March and September 2020.

Results: Data from 901 admitted patients were analyzed, with 185 (20.5%) classified as mild, 429 (47.6%) as moderate, 223 (24.7%) as severe, and 64 (7.1%) as critical. The frequency of male gender, advancing age, co-morbidities (hypertension and diabetes mellitus), inflammatory marker elevation (LDH, CRP, Ferritin, Procalcitonin), and elevated mean white blood cell counts with relative neutrophilia and lymphopenia increased with COVID severity. Severe and critical cases of COVID presented with more diffuse lung involvement in chest radiographs and abnormal electrocardiographic patterns such as ischemic changes, PVCs, PACs, and sinus tachycardia. The most common complications on admission were ARDS (10.9%), AKI (10.1%), shock (6.6%), and cardiac arrest (6.3%). Mortality rates were highest in critical cases (82.8%). Severe and critical COVID-19 cases were predominant on final disposition, rising to 62.5% of the study population from 32.1% on admission.

Conclusions: This study highlights key differences in clinical characteristics, complications, and outcomes between illness severities. Risk prediction models are needed for disease progression and poor outcomes.

Key words: COVID-19; clinical features; severity; Philippines.

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Introduction

Severe Acute Respiratory Syndrome – Coronavirus 2 (SARS-CoV-2) is an enveloped positive-sense single-stranded RNA virus that emerged as the causative agent of a cluster of cases of atypical pneumonia that arose in Wuhan, China towards the end of December 2019. The World Health Organization (WHO) designated this new entity as the Coronavirus Disease 2019 (COVID-19) and declared it a global pandemic by March 2020. The Philippines reported its first case of COVID-19 on 30th January 2020. Local transmissions were later reported over the following months in the major regions of Luzon, the Visayas, and Mindanao. At present, over 2.8 million cases and 51,000 deaths have been documented in the country [1]. Chong Hua Hospital, in its capacity as a tertiary care hospital in Cebu City, served as a pillar of health in the Visayas during the pandemic in the Philippines. Our institution's experience with the disease offers a setting wherein each patient was managed by infectious disease specialists, pulmonologists, and consultants, with ready access to antivirals, immunomodulators, corticosteroids, and other adjunctive interventions outlined by both local and international guidelines, and landmark trials (i.e., the Recovery Trial), at that time [2,3].

The clinical presentation of COVID-19 ranges from asymptomatic, mild, and flu-like (i.e., coryza, sore throat, cough, fever), to severe and life-threatening, manifesting with multiorgan dysfunction and acute respiratory distress syndrome. COVID-19 is generally described by illness severities, namely as mild, moderate, severe, and critical, based on selected symptoms, vital signs, physical findings, chest radiographic findings, and laboratories particularly related to sepsis. An example of such illness severity definitions can be found in the Philippine Society for Microbiology and Infectious Diseases (PSMID)-modified and WHO Interim Clinical Guidelines of July 2020 (Supplementary Table 1). These have provided a framework by which clinical management has been

guided. Tocilizumab and Dexamethasone, for example, have been used in severe COVID-19 requiring oxygenation while antivirals like Molnupiravir have been investigated in the prevention of disease progression in mild cases [3–5]. COVID-19 is a dynamic disease, with progression to more severe illness found to be associated with higher mortality rates and certain patient characteristics (e.g., old age, male gender, co-morbidities) and laboratory parameters (e.g., lymphopenia, inflammatory marker elevation) [6–9]. Therefore, further description of the clinical features of COVID-19 by illness severities can aid in selecting the best treatment strategies and anticipating patient course and outcomes.

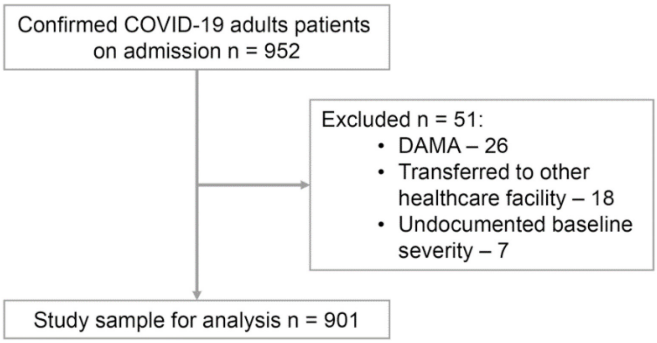
This study provides a clinical picture of COVID-19 patients admitted for care, focusing on the clinical parameters observed during admission and the complications and outcomes (in-hospital mortality, duration of admission, and illness severity) that developed during the hospital stay and upon final disposition, namely, discharge or death. In addition, this study presents its findings as a comparison between patients who presented with varying illness severities: mild, moderate, severe, and critical. It provides additional clinical findings commonly observed in each classification, particularly in more severe diseases, on top of current definitions provided by guidelines for stratifying illness severity.

Methodology

Study Design

This was a retrospective, double-center, observational cohort study that utilized existing clinical information as gleaned from the charts and hospital records of admitted patients from March to September 2020. It was conducted in two separate hospitals under the same institution, with a combined bed capacity of 998 patients. All admitted patients confirmed to have COVID-19 by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) of a nasopharyngeal or oropharyngeal swab, sputum, or bronchoalveolar lavage samples and at least 18 years of age and above, were included. The study excluded the following COVID-19 patients: 1. Discharged against medical advice (DAMA); 2. Transferred to other facilities; or 3. Had undocumented illness severity on admission, as seen in Figure 1.

Figure 1. Study population flow chart. The selection of the study sample was based on the inclusion and exclusion criteria outlined above. DAMA – discharged against medical advice.



Ethical approval

The study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Chong Hua Hospital (CHH) Institutional Review Board (IRB), with reference code no. 3320-07, before data collection. Patient data were de-identified with computer-generated participant identification codes for the electronic research database. Case record forms (CRFs) were securely stored without visible patient identifiers.

Data Collection Tool and Process

The CRF used in this study was mainly derived, with permission, from the World Health Organization. It also incorporated elements, particularly exposure history and questionnaire formatting, from the Data Collection Form (DCF) of the Philippine COVID-19 Profile study conducted by the Philippine College of Physicians (PCP) [10].

A master list of all COVID-19 patients admitted between March and September 2020 was obtained from the medical records section. Data on patient demographics, illness history and clinical presentation, past medical history, physical examination findings, laboratories, treatment maneuvers, complications, and outcomes were recorded by medical residents on the CRF. Licensed nurses also acted as research assistants to record laboratory findings and encode written data unto the electronic database.

Official chest radiograph readings by institutional licensed radiologists were semi-quantified using the scoring system for patients with severe acute respiratory syndrome, developed by the Southern Hemisphere Influenza Vaccine Effectiveness Research and Surveillance (SHIVERS) investigation team in New Zealand. Encoded chest radiograph readings were categorized as 1 - normal; 2 - patchy atelectasis and/or hyperinflation and/or bronchial wall thickening; 3 - focal consolidation; 4 - multifocal consolidation; and 5 - diffuse alveolar changes [11].

Table 1. Demographics and clinical profile.

Variable	Mild (n = 185)	Moderate (n = 429)	Severe (n = 223)	Critical (n = 64)	Total (n = 901)	*p*-value
Demographics						
Male (n, %)	82 (44.3)	242 (56.2)	144 (64.2)	33 (51.5)	506(55.4)	< 0.001
Age (mean)	45.3	56.2	61.3	64.5	56	< 0.001
Co-morbidities (n, %)						
Hypertension	114 (61.6)	314 (72.8)	180 (80.3)	55 (83.3)	668(72.9)	< 0.001
Diabetes	16 (8.6)	141 (32.8)	83 (37.2)	31 (48.4)	271 (30.0)	< 0.001
Asthma	12 (16.4)	29 (6.7)	10 (4.4)	5 (7.5)	56 (6.1)	0.596
Chronic Kidney Disease	4 (2.1)	35 (8.1)	27 (12.0)	8 (12.1)	74 (8.0)	< 0.001
Coronary Artery Disease	6 (3.2)	23 (5.3)	17 (7.6)	7 (10.9)	53 (5.8)	0.117

Statistical Analysis

Categorical variables were presented as counts and percentages. Continuous variables were expressed as mean ± SD, if the data were normally distributed, or expressed as median with interquartile range (IQR) values. Proportions for categorical variables were compared using the χ^2 test, and Fisher exact test if the data were limited. Comparisons for medians of non-normal distribution data were performed using Mann–Whitney test. Comparisons between means were tested using Student's t-test and one-way ANOVA. A *p*-value < 0.05 (two-tailed) was considered statistically significant. All statistical analyses will be performed using Epi Info and STATA Intercooled version 16 software.

Results

Demographics and Clinical Profile

Table 1 shows the demographic and clinical profile of admitted patients stratified by illness severity on admission. Among the 901 patients analyzed for illness severity on admission, 185 (20.5%) were mild, 429 (47.6%) were moderate, 223 (24.7%) were severe, and 64 (7.1%) were critical. More males than females were admitted overall 506 (55.4%). Males also shared a greater percentage of moderate 242 (56.2%), severe 144 (64.2%), and critical 33 (51.5%) cases. Hypertension, diabetes mellitus, and chronic kidney disease were the most common co-morbid conditions. These were more common in moderate, severe, and critical cases when compared to mild cases.

Clinical Parameters

The mean duration from symptom onset to hospital admission was 8 days and did not vary markedly among illness severities (Table 2).

Table 2. Symptoms and vital signs.

Variable	Mild (n = 185)	Moderate (n = 429)	Severe (n = 223)	Critical (n = 64)	*p*-value
Presenting Symptoms (n, %)					
Cough	135 (21.6)	277 (64.56)	159 (71.3)	45 (70.31)	0.001
Fever	116 (73.0)	251 (58.5)	131 (58.7)	37 (57.8)	0.01
Dyspnea	78 (42.1)	208 (48.5)	105 (47.1)	29 (45.3)	0.001
Body malaise	31 (16.7)	93 (21.7)	39 (17.4)	5 (7.8)	0.052
Anosmia	15 (8.1)	8 (1.9)	1 (0.4)	0 (0.0)	0.001
Symptoms onset to admission, in days (Mean, SD)	7.4 (8.2)	8.6 (8.2)	8.3 (8.2)	8.2 (9.9)	0.053
Vital signs on admission					
Systolic blood pressure (mmHg)					
Mean, SD	122.4 (1.5)	120.7 (0.9)	124.7 (1.2)	121.6 (2.9)	0.104
Less than 90 mmHg (n, %)	1 (0.5)	4 (0.9)	3 (1.3)	3 (4.6)	0.524
Heart Rate (beats per minute)					
Mean, SD	94.0 (1.4)	96.5 (0.8)	96.1 (1.3)	96.1 (2.1)	0.464
Greater than 90 bpm (n, %)	91 (50.0)	230 (53.6)	124 (55.6)	41 (61.2)	0.536
Respiratory Rate (cycles per minute)					
Mean, SD	23.9 (0.7)	22.7 (0.27)	24.7 (0.6)	22.6 (0.6)	0.0424
Greater than 22 cpm (n, %)	31 (16.7)	105 (24.5)	117 (52.5)	41 (61.2)	0.001
Oxygen saturation					
Mean, SD	95.3 (7.8)	94.6 (5.9)	87.9 (9.6)	77.7 (18.1)	0.0490
Greater than 94% (n, %)	20 (10.8)	85 (19.8)	131 (58.7)	48 (71.6)	0.001
Temperature (°C)					
Mean, SD	36.8 (0.1)	36.8 (0.1)	37.0 (0.1)	37.0 (0.1)	0.0406
Greater than 37.8 °C (n, %)	24 (12.1)	61 (14.2)	43 (19.3)	12.0 (18.7)	0.392
Body Mass Index (BMI) (Mean, SD)	25.9 (6.1)	26.8 (5.6)	26.8 (4.5)	26.4 (5.5)	0.479

Table 3. Selected laboratory parameters.

Laboratory Parameters	Normal Range	Mild (n = 185)	Moderate (n = 429)	Severe (n = 223)	Critical (n = 64)	*p*-value
Hemogram (Mean, SD)						
White blood cells (10^3/uL)	4.8 – 10.8	8.5 (5.6)	8.21 (4.3)	9.6 (4.9)	15.7 (11.8)	0.001
Red Blood Cell Distribution Width (RDW) (%)	11.0 – 16.0	14.9 (3.1)	14.8 (2.1)	14.9 (2.0)	15.1 (2.3)	0.823
Platelets (10^3/uL)	130 – 400	228.2 (120.7)	207.8 (85.7)	205.2 (89.9)	228.0 (110.0)	0.089
Neutrophils, relative differential count (%)	40 – 74	68.3 (13.2)	70.8 (13.1)	77.6 (12.4)	83.5 (9.6)	0.001
Lymphocytes, relative differential count (%)	19 – 48	22.1 (11.4)	19.4 (10.3)	14.3 (9.3)	10.1 (7.7)	0.001
Absolute lymphocyte count (ALC)	0.9 – 5.2	1.61 (0.8)	1.69 (4.5)	1.78 (5.3)	1.25 (0.8)	0.855
Inflammatory Markers						
Ferritin (ng/mL)	300 – 400					
Mean, SD		1879.9 (358.8)	1974.9 (170.93)	1667.4 (173.9)	1736 .9 (272.2)	0.168
> 150 (n, %)		103 (55.6)	335 (78.0)	170 (76.0)	53 (82.0)	0.001
Lactate Dehydrogenase (U/L)	150 – 250					
Mean, SD		401.1 (31.14)	425.3 (14.9)	418.8 (22.7)	357.4 (22.3)	0.104
> 250 (n, %)		69 (37.3)	258 (60.1)	174 (78.0)	60 (93.8)	0.001
C-Reactive Protein (CRP) (mg/L)	0 – 5					
Mean, SD		87.1 (9.8)	82.5 (6.6)	77.1 (9.5)	68.4 (13.9)	0.765
> 5 (n, %)		62 (33.5)	249 (58.0)	165 (74.0)	48 (75.0)	0.001
Procalcitonin (ng/mL)	< 0. 3					
Mean, SD		6.1 (3.2)	2.5 (0.8)	4.9 (2.3)	1.92 (1.3)	0.411
> 0.3 (n, %)		24 (12.9)	86 (38.5)	97 (43.4)	45 (70.3)	0.001

Table 4. Chest radiographic and electrocardiographic findings.

Chest radiograph findings (n, %)	**n = 172**	**n = 412**	**n = 213**	**n = 57**	***p*-value**
Normal	61 (35.1)	33 (7.9)	4 (1.8)	1 (1.6)	< 0.001
Patchy atelectasis, bronchial wall thickening, hyperinflation	19 (10.9)	23 (5.5)	4 (1.8)	1 (1.6)	0.001
Focal consolidation or pneumonia	41 (23.6)	115 (27.5)	35 (16.0)	7 (11.6)	0.01
Multifocal consolidation or pneumonia	32 (18.3)	140 (33.5)	62 (28.8)	17 (28.3)	0.02
Diffuse alveolar consolidation or pneumonia	19 (10.9)	101 (24.2)	108 (50.2)	31 (51.7)	< 0.001
12-Lead electrocardiography (n, %)	**n = 78**	**n = 216**	**n = 109**	**n = 39**	
Normal ECG	27 (34.6)	66 (30.6)	16 (14.7)	5 (12.8)	0.001
Sinus tachycardia	14 (17.9)	36 (16.7)	32 (29.4)	16 (41.0)	0.050
Sinus bradycardia	3 (3.8)	7 (3.2)	0.0 (0.0)	0.0 (0.0)	0.126
Ischemia	7 (9.0)	17 (7.9)	20 (18.3)	13.0 (33.3)	0.003
Arrhythmia	5 (6.4)	14 (6.5)	5 (4.6)	1.0 (2.6)	0.597
Atrial Fibrillation	4 (5.1)	12 (5.6)	3 (2.8)	1 (2.6)	0.533
Ventricular chamber enlargement	5 (6.4)	12 (5.6)	5 (4.6)	3 (7.7)	0.931
Bundle branch blocks	8 (10.3)	25 (11.6)	15 (13.8)	4 (10.3)	0.823
Premature Ventricular Contraction/ Premature Atrial Contraction	1 (1.3)	7 (3.2)	11 (10.1)	6 (15.4)	0.007
Non-specific ST segment and T-wave changes	17 (21.8)	69 (31.9)	30 (27.5)	12 (30.8)	0.541

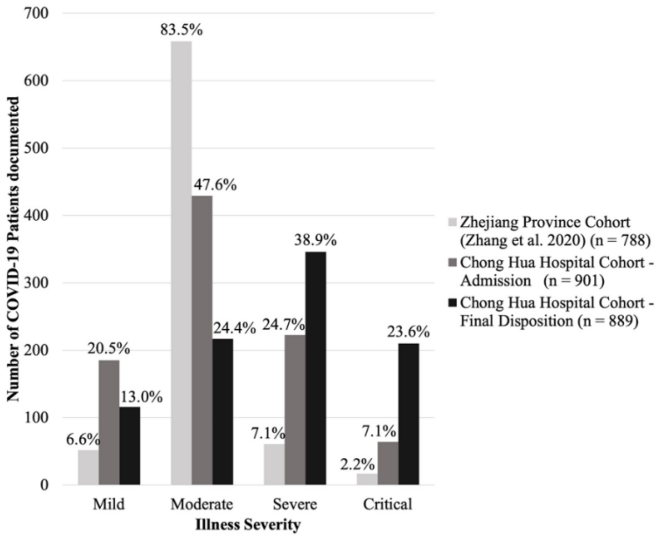
Table 5. Complications and outcomes.

Variable	**Mild (n = 185)**	**Moderate (n = 429)**	**Severe (n = 223)**	**Critical (n = 64)**	**Total (n = 901)**	***p*-value**
Complication (n, %)						
Acute respiratory distress syndrome (ARDS)	6 (3.2)	22 (5.1)	39 (17.5)	31 (48.4)	98 (10.9)	< 0.001
Acute kidney injury (AKI)	7 (3.8)	26 (6.1)	32 (14.4)	26 (40.6)	91 (10.1)	< 0.001
Shock	3 (1.6)	12 (2.8)	20 (8.9)	25 (39.1)	60 (6.6)	< 0.001
Cardiac arrest	2 (1.1)	11 (2.56)	23 (10.3)	21 (32.8)	57 (6.3)	< 0.001
Anemia	3 (1.6)	13 (3.0)	8 (3.59)	8 (12.5)	32 (3.6)	< 0.001
Arrhythmia	1 (0.5)	7 (1.6)	14 (6.3)	9 (14.1)	31 (3.4)	< 0.001
Bacteremia	3 (1.6)	8 (1.9)	8 (3.6)	8 (12.5)	27 (3.0)	< 0.001
Bleeding	1 (0.5)	11 (2.6)	5 (2.2)	1 (1.6)	18 (2.0)	0.41
Liver Injury	3 (1.6)	6 (1.4)	6 (2.7)	1 (1.6)	16 (1.8)	0.65
Pulmonary Embolism	4 (2.2)	3 (0.6)	3 (1.4)	5 (7.8)	15 (1.7)	< 0.001
Acute cerebrovascular disease infarct	1 (0.5)	4 (0.9)	3 (1.4)	1 (1.6)	9 (1.0)	0.84
Deep venous thrombosis	1 (0.5)	0 (0)	0 (0)	0 (0)	1 (0.1)	0.27
Pancreatitis	1 (0.5)	0 (0)	2 (0.9)	0 (0)	3 (0.3)	0.24
Myocarditis	0 (0)	1 (0.2)	0 (0)	0 (0)	1 (0.1)	-
Endocarditis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Outcomes In-Hospital Mortality (n, %)	9 (5.4)	35 (8.1)	54 (27.0)	53 (82.8)	151 (18.2)	< 0.001
Duration of admission, in days (Mean)	12.2	12.3	12.5	10.7	12.2	0.647
Illness severities on final disposition (n, %)	116 (13.0)	217 (24.4)	346 (38.9)	210 (23.6)	889	-

Symptoms and vital signs on admission are shown in Table 2. Cough (70%), fever (60.6%), dyspnea (42.1%), and body malaise (47.1%) were the most common symptoms reported. Cough was less frequent in mild cases (21.6% vs 64.56%, 71.3%, 70.31%). Hypotension with systolic blood pressure (SBP) less than 90 mmHg was rare. Severe and critical cases more commonly presented with tachypnea (> 22 cycles per minute) and oxygen saturation of less than 94%. Selected laboratory parameters, namely the hemogram and inflammatory markers, are shown in Table 3. The mean white blood cell count (WBC) and neutrophil differential count were higher in critical cases, 15.7 and 83.5%, as compared to other illness severities. The mean absolute lymphocyte count was comparably lower in critical cases at 1.25 but this was not statistically significant. In general, inflammatory markers were higher in moderate to critical cases when compared to mild cases, with values ranging from 95.0 to 212.0 for serum ferritin, 1.2 to 4.2 for serum procalcitonin, and 4.6 to 18.7 for serum C-reactive protein (CRP). The mean difference between serum lactate dehydrogenase (LDH) in mild to critical cases was 44.0. However, the number of patients presenting with inflammatory markers above the normal limit increased with higher illness severity. Table 4 shows chest radiographic and electrocardiographic findings in our patients. On admission chest radiography, greater lung involvement was present in moderate to critical cases as compared to mild cases, with mean differences in frequencies ranging from 8.7% to 14.7% for multifocal lung consolidation, and 13.3% to 38.2% for diffuse alveolar consolidation. Electrocardiographic (ECG) findings on admission were documented in only 442 patients. These showed ischemic changes, tachycardia, premature ventricular contractions (PVCs), and premature atrial contractions (PACs) to be more common in severe and critical cases. Likewise, normal ECG tracings were observed more frequently in mild and moderate cases.

Table 5 shows the complications and outcomes (in-hospital mortality, duration of admission, and illness severity) of patients on final disposition. Primary outcome data were available for 827 of the 901 patients. Critical cases had an all-cause in-hospital mortality rate of 82.7%, followed by severe cases with 27.0%. Illness severities on final disposition (death or discharge) were obtained from 889 of the 901 patients since 12 patients had no documented illness severity on final disposition. A decrease in mild and moderate cases with a corresponding increase in severe and critical cases is noted on final disposition.

Figure 2. Comparison between frequencies of illness severities on admission between the cohort of Zhang *et al.* 2020 across multiple hospitals in Zhejiang Province (light gray bars, n = 788) [12], and Chong Hua Hospital cohort on admission (dark gray bars, n = 901) and upon final disposition (black bars, n = 889). Frequencies of documented illness severities are indicated as percentages (%) above each bar.



Discussion

Demographics and Clinical Profile

The majority of the patients admitted to our institution were moderate to critical cases, comprising 79.4% of the total admissions. A similar study was conducted by Zhang *et al.*, that assessed the differences in clinical characteristics between patients with varied illness severities in a cohort of 788 Chinese patients admitted between 17th January and 12th February 2020 to hospitals in the Zhejiang Province of China. Comparably more patients admitted to our institution were mild, severe, and critical cases, however, the most common severity group was moderate (Figure 2) [12]. The cohort of patients admitted to our institution was predominantly male (55.4%), with a mean age of 56.0 years, a similar trend observed in other meta-analyses [12,13]. In contrast, a meta-analysis by Li *et al.* reported a relatively younger mean age of 46.7 years. The majority of the patients (79.5%) in this meta-analysis were from the United States of America, followed by China, Italy, and South Korea [13]. A large Chinese study reported a median age of 47 [14]. However, in all studies, mean or median age increases with higher illness severities [12–15]. The increasing frequencies of male gender and age, and the prevalence of co-morbidities such as hypertension, diabetes, and chronic

disease as illness severity scaled upwards were also seen in other studies [12,14–16]. Our findings support existing evidence of male gender, advanced age, and co-morbidities as risk factors for more severe COVID-19 illness requiring admission. Body mass indices (BMI) were not statistically different across illness severities, a finding that contrasts the notion that elevated BMI is a risk factor for poorer composite outcomes [17]. This is in concordance with a study by Soria *et al.*, which showed no significant differences in BMI between COVID-19 patients who recovered and died [10].

Clinical Parameters

The most common presenting symptoms were cough, fever, dyspnea, and body malaise. The incidence of cough was markedly lesser in mild cases. Expectedly, with increasing illness severity greater lung involvement was observed on chest radiography, with diffuse lung disease observed in half of the severe and critical cases on admission (Table 4). The incidence of hypoxemia on arterial blood gases and peripheral saturations also increased with worsening illness severities. In contrast to other studies, self-reported fever was more common among mild than more severe cases [12,16]. Documented fever upon admission was also not significantly different among illness severities. In severe and critical cases, tachypnea and hypoxemia by peripheral saturations were more frequent. As illness severity increased, more patients had elevated inflammatory markers and leukocytosis with a neutrophilic predominance and relative lymphopenia. This pattern has also been described in other studies [6,18,19]. No significant differences existed in platelet counts between illness severities. In contrast, a meta-analysis done by Lippi *et al.* found that platelet counts were lower in patients with more severe COVID-19 [20]. Severe and critical cases of COVID more often presented with abnormal ECG patterns, ischemic changes, PVCs, PACs, and sinus tachycardia on admission in our study. These findings have been observed in COVID-related myocarditis, defined as myocardial injury and inflammation in the absence of an ischemic cause, as described in literature [21]. A study done by Bergamaschi *et al.* found that ischemic alterations with primary ST-T segment and T-wave changes and signs of left ventricular hypertrophy on admitting ECGs were associated with a severe prognosis. The prevalence of abnormal ECGs was higher in severe COVID cases [22]. Additionally, a New York study found that right bundle branch blocks and localized T-wave inversions, and non-specific repolarization abnormalities increased the odds of death in a 2-week follow-up period [21]. A systematic review cited sinus tachycardia as the most common abnormality in COVID patients while atrial fibrillation, non-specific ST-T segment and T-wave changes, and ventricular arrhythmias were associated with poorer outcomes [23]. These latter findings were not found to be significantly different among illness severities in our study.

Complications

The most common complications occurring among admitted patients were acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), shock of any cause, and cardiac arrest (Table 5). ARDS, AKI, and shock are also the most common complications listed in large studies and a meta-analysis done [14,15,24]. Cardiac complications had a frequency of 9.7%. in our population. In comparison, an international patient registry called CAPACITY-COVID looked into the role of cardiovascular disease in the COVID-19 and reported that 11.6% of its cohort had cardiac complications [25]. The registry also reported that pulmonary embolism occurred in 6.6% of patients. Our study reported a lesser frequency at 1.7% but, as with CAPACITY COVID, pulmonary embolism occurred mostly in critical cases. Some studies in China have noted higher frequencies of cardiac complications, with arrhythmias occurring in 16.7% of patients in one study and acute cardiac injury occurring in 44% of patients in another [26,27]. Notably, the frequencies of these complications and others listed (i.e., anemia, bacteremia, arrhythmia) increased significantly with higher illness severities, an observation seen in other studies, especially in patients that died [13–15].

Outcomes

The overall mortality rate was 18.2%. This is comparable to the national study by Soria *et al.*, which reported a mortality rate of 18.5%. Pooled mortality rates reported by meta-analyses ranged from only 5 to 6% [13,15]. In a large study based in a New York hospital system, the mortality rate was reported at 21% [16]. 83.1% of deaths occurred during the months of June and July 2020, when the pandemic was at its peak in the region. The in-hospital mortality rates of mild, moderate, severe, and critical cases were 5.4%, 8.1%, 27.0%, and 80.3%, respectively. Severe and critical COVID-19 cases were predominant on final disposition, rising to 62.5% of the study population from 32.1% on admission, with a concomitant decrease in mild and moderate cases (Table 5). Hence,

progression in illness severity is evident in our study population. The lack of known evidence-based treatment modalities combined with the novelty of COVID-19 at this time may have been contributory to this observation and the high mortality rates in June and July 2021. There were no significant differences in duration of admission among varying illness severities.

Study Limitations

The retrospective nature of this study imposes several limitations. Firstly, the comprehensiveness of patient data, particularly exposure histories and symptoms, is affected by variability in chart documentation among medical personnel. Second, the generalizability of data is affected by admission bias since a majority of patients hail from the Visayas region. In addition, the examination of patient data collected upon admission provides a limited picture of COVID. The disease course was not included, which may provide a more comprehensive description of our study population.

Conclusions

This study showed that with worsening illness severity the frequencies of the following clinical observations on admission increased as well: older age (more than 50 years old), male gender, co-morbidities such as hypertension and diabetes mellitus, diffuse lung involvement, tachypnea, hypoxemia on peripheral oxygen saturations and ABG, increase in inflammatory markers, leukocytosis with relative neutrophilia and lymphopenia, and abnormal ECG patterns (particularly ischemic changes, PVCs, PACs, and sinus tachycardia). Complications occurred more frequently in patients admitted with worse illness severities, with ARDS, AKI, shock of any cause, and cardiac arrest being the most common. Mortality rates were highest in severe and critical cases. Hence, closer monitoring and appropriate management are warranted in these cases. Progression in illness severity was evident. Risk prediction models are needed for disease progression and poor outcomes.

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Authors' Contributions

All authors contributed to the conception and design of the work. DMG and CMT conducted the data collection process, with the set-up of the database and subsequent data analysis done. All authors participated in drafting, critical revision, and final approval of the version to be submitted for publication.

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Annex – Supplementary Items

Supplementary Table 1. Disease severity classification of adult patients with probable or confirmed COVID-19 (modified from WHO interim clinical guidance May 2020).

Classification	Signs and Symptoms
Mild	Fever, cough, fatigue, anorexia, myalgias. Other non-specific symptoms such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, loss of smell (anosmia) or loss of taste (ageusia) preceding the onset of respiratory symptoms No signs of pneumonia or hypoxia
Moderate	With signs of non-severe pneumonia (e.g., fever, cough, dyspnea or difficulty of breathing, RR 21-30/minute, SpO_2 > 92% on room air)
Severe	Severe pneumonia or severe acute respiratory infection, as follows: Fever, cough, dyspnea. RR > 30 breaths/minute, severe respiratory distress or SpO_2 < 92% on room air
Critical	Onset within 1 week of known clinical insult (pneumonia) or new or worsening respiratory symptoms, progressing infiltrates on CXR or chest CT, with respiratory failure not fully explained by cardiac failure or fluid overload (COVID-ARDS). Sepsis: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, Signs of organ dysfunction: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia. Septic shock: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L