Small hospitals in battle against COVID-19: A single-center cohort study

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ABSTRACT

INTRODUCTION In Greece, higher morbidity and mortality due to COVID-19 pandemic were recorded during the third pandemic wave. Only a small percentage of the population was fully vaccinated at the beginning of the third pandemic wave. Our effort was multi-level, from the emergency room department to the ward. The aim of this article is to communicate a single secondary center's experience during the third pandemic wave in Greece.

METHODS A retrospective cohort study was conducted at the regional Agios Andreas General Hospital of Patra, Greece, including 360 hospitalized COVID-19 patients. A standard of care protocol was applied in all cases and its outcomes are examined.

RESULTS The median age of the patients was 64.2 years (IQR: 18–100) and the median duration of hospitalization was 8 days. The overall case fatality rate was 8.1%. Of the 360 patients, 12 (3.3%) needed to be intubated. Most of the hospitalized patients (n=316; 87.8%) were treated with nasal canula or Venturi mask. Twenty-six patients (7.2%) were supported with HFNC and 18 (5%) received any available type of non-invasive mechanical ventilation.

CONCLUSIONS An articulate protocol and coordinated collaboration among specialists were the cornerstone of proper, immediate, and individualized treatment. The international recommendations in force at that time proved to be efficient in reducing progress to SRF and intubation. Full vaccination of the medical staff ensured long and dedicated presence in the patients' rooms.

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INTRODUCTION

The novel SARS-CoV-2 pandemic that was firstly identified as the cause of pneumonia in Wuhan, at the end of 2019, rapidly spread worldwide[1]. More than 190 million people have been diagnosed with COVID-19 and more than four million deaths have been confirmed[2]. Every healthcare system had to contribute to the management of the pandemic. In Greece, higher morbidity and mortality were recorded during the third pandemic wave. That was the result of a greater spread of the virus and higher pressure on the country's healthcare system. Our effort was multi-level; beginning from the emergency room department where the patients who needed to be hospitalized were properly chosen and extending even to the ICU care with the challenges that occurred from the mechanical ventilation and the complications of the new virus. Unfortunately, only a small percentage of the population was fully vaccinated at the beginning of the third pandemic wave, probably less than 1%[3]. Our aim was to describe a single center experience during the third pandemic wave in Greece and describe the outcomes of the patients admitted during the aforementioned period.

METHODS

Study design and setting

This is a retrospective observational cohort study carried out in Agios Andreas General Hospital of Patras, a regional 450-bed hospital in Greece, which included 360 hospitalized COVID-19 patients with pneumonia admitted between 13 February 2021 and 31 May 2021. This period was consistent with the third pandemic wave in Greece. We collected data on patients' characteristics, comorbidities, clinical symptoms, laboratory and radiological exams, from their medical records. All COVID-19 patients were admitted to wards with ICU potential, since the medical staff had integrated the use of high flow nasal cannula and non-invasive ventilation (NIV) devices.

Study definitions

ARDS was defined as per the Berlin definition. Severity of illness was evaluated using Sequential Organ Failure Assessment (SOFA). Severe Respiratory Failure (SRF) was defined as severe decrease of the respiratory ratio demanding intubation or mechanical ventilation. Sepsis and septic shock were defined as per the 2016 Third International Consensus Definition for Sepsis and Septic Shock. For management and therapy of critically ill patients with COVID-19, national and international established recommendations were followed[4-7].

Inclusion and exclusion criteria

All patients included in this study were adults who were

admitted for at least 24 hours in the ICU ward until death, intubation, or discharge. Diagnosis of COVID-19 infection was defined as at least one positive result of reverse transcriptase polymerase chain reaction obtained from nasopharyngeal swabs.

Risk stratification and treatment strategies

Disease severity upon admission was classified as moderate, severe, or critically ill, based on the National Institutes of Health criteria. Moderate infection was defined as presence of lower respiratory disease and oxygen saturation (SpO_2) ≥94% on room air. Severe disease was defined as infection with SpO_2 <94% on room air, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, respiratory frequency >30 breaths/min, or lung infiltrates >50% of the lung parenchyma. Critically ill were those patients who presented with respiratory failure, septic shock, and/or multiple organ dysfunction[7]. All patients were treated according to the recommendations and guidelines in force at that time, namely remdesivir 200 mg IV once upon admission, then 100 mg IV qd, prophylactic dose low molecular weight heparin (LMWH) SC qd, dexamethasone 6 mg IV qd, inhaled budesonide, and antibiotic agents[8-11]. Our standard of care also included orally administered 600 mg bd of N-acetylcysteine (NAC) until hospital discharge, based on the results of Assimakopoulos et al.[12]. The dose of LMWH was intensified (nearly therapeutic, weight adjusted dose) in high-risk patients, and patients started on non-invasive ventilation (NIV) or high flow nasal cannula (HFNC) that developed severe respiratory failure (SRF). In the latter group, a single dose of IL-6 inhibitor (tocilizumab) was administered (800 mg if weight >90 kg; 600 mg for >65 and ≤90 kg; 400 mg if weight >40 and ≤65 kg), provided there were no contraindications. Patients who presented clinical deterioration or bilateral opacities in the chest X-ray or had PaO_2/FiO_2 between 100 and 200 mmHg (either upon admission or if respiratory failure developed during their hospitalization), underwent a thorax computed tomography (CT) in order to estimate accurately the extent of the disease and to determine if onset of fibrosis was present. In case of prolonged fever, rise of inflammation laboratory markers or overweight patients, we intensified the dose of dexamethasone (6 mg or 8 mg IV bd) after clinical assessment. The thorax CT was also combined with a CTPA in patients who showed little or no response to NIV (no de-escalation after 5 days) in order to exclude pulmonary embolism.

Patient monitoring and clinical assessment

Standard protocol also included daily chest physiotherapy, chest x-ray repeats in case of clinical deterioration, constant monitoring of vital signs and pulse oximetry depending on disease status. Patients with lung infiltrates >20% where assisted to frequently change bed positions during the day in order to achieve maximal SpO_2 and at least 94%. Prone positioning was encouraged in several awake non-intubated patients.

All the patients' condition and vital signs were easily, closely and constantly monitored, since the COVID-19 wards consisted of rooms with doors with glass.

Patients on HFNC or NIV were assessed by intensive care doctors and/or pulmonologists on a daily basis and underwent regular alterations between HFNC and NIV devices to ensure maximal ventilation. A wait-and-see strategy was implemented instead of early intubation. 'Early intubation' was defined as the occurrence of intubation within 24 hours from the onset of acute respiratory distress syndrome. Our medical staff were fully vaccinated against COVID-19 and all ward rooms had a negative pressure environment.

RESULTS

Details of the characteristics, clinical state and outcomes of the patients are given in Table 1. Of the patients, 194 were men (53.9%), and the median age of the patients was 64.2 years (IQR: 18–100). The median duration of hospitalization was 8 days. The overall case fatality was 29 (8.1%); and 12 (3.3%) needed to be intubated. Thus, 41 patients (11.4%) had progressed to SRF.

Based on the criteria of the National Public Health

Table 1. Characteristics, clinical state and outcomes of the patients (N=360)

Characteristics	n (%)
Gender	
Male	194 (53.9)
Female	166 (46.1)
Primary outcomes	
Overall case fatality rate	29 (8.1)
Progress to severe respiratory failure rate	41 (11.4)
Intubation rate	12 (3.3)
Disease severity upon admission	
Moderate	214 (59.4)
Severe	137 (38.1)
Critically ill	9 (2.5)
Oxygenation and ventilation during hospitalization	
Nasal canula/venturi mask	316 (87.8)
HFNC	26 (7.2)
NIV	18 (5.0)
Comorbidities of patients	
Hypertension	171 (47.5)
Dyslipidemia	99 (27.5)
Diabetes	90 (25.0)
Coronary heart disease/heart failure	81 (22.5)

Continued

Table 1. Continued

Characteristics	n (%)
Obesity	54 (15.0)
Chronic obstructive pulmonary disease	45 (12.5)
Atrial fibrillation	45 (12.5)
Malignancy	18 (5.0)
No comorbidities	8 (2.2)
N/A	1 (0.3)
Complications	**n**
UTI	18
Sepsis/septic shock	13
Acute kidney injury	10
Aspiration pneumonia	9
Arrhythmia	6
N-STEMI	6
Gastrointestinal bleeding	5
Ischemic stroke	4
Acute pulmonary edema	3
Organic psycho syndrome	3
Myocarditis	1
Rhabdomyolysis	1
Massive pulmonary embolism	1
Immune thrombocytic purpura	1
Rectus sheath hematoma	1

Organization, upon admission, 214 patients had moderate disease (59.4%), 137 severe disease (38.1%), and only 9 (2.5%) patients were characterized as critically ill.

The majority of the hospitalized patients (n=316; 87.8%) were treated with nasal canula or venturi mask. Twenty-six patients (7.2%) required the use of HFNC and 18 (5%) needed to receive any available type of NIV during their hospitalization.

The main co-morbidities among the 360 patients were hypertension (47.5%), dyslipidemia (27.5%), diabetes (25%), coronary heart disease or heart failure (22.5%), obesity (15%), COPD (12.5%), atrial fibrillation (12.5%), malignancy (5%); 8 patients had no co morbidities, and 1 patient the medical history was not available.

Most complications were identified in elderly patients with several co-morbidities. Complications included: UTI (18 cases), sepsis or septic shock (13 cases), acute kidney injury (10 cases), aspiration pneumonia (9 cases), arrhythmia (6 cases), non-STEMI (6 cases), gastrointestinal bleeding (5 cases), ischemic stroke (4 cases), acute pulmonary oedema (3 cases), organic psycho syndrome (3 cases), myocarditis (1 case), rhabdomyolysis (1 case), massive pulmonary embolism (1 case), immune thrombocytopenic purpura (1 case) and a single case of rectus sheath hematoma.

DISCUSSION

During the third pandemic wave in Greece, our region exhibited high viral burden while vaccination had just been nationally implemented. Our institution had to confront an unprecedented pressure on the healthcare system with minimum staff. At the beginning of that period, the vaccination campaign targeted the elderly, and only a few percent of the population were fully vaccinated until the middle of the recorded period[3].

Careful planning was essential in order to cope with the novel virus and provide optimal healthcare to the patients. Starting from the Emergency Room Department, a specially formed area was used to examine the general population. The decision to admit them was based on the National Public Health Organization criteria[7]. The areas through which COVID-19 patients would pass were always free of visitors, medical staff, or other patients, hence virus spread to non-infected population was prevented. Once the admitted patients reached the ward, they were reexamined by the on-call doctor in order to adjust the treatment and correct any oversights due to the heavy workload in the ER. Thus, every admitted patient received the standard of care immediately and any alterations were made in accordance with their medical history.

According to the literature, there is disagreement whether routine LMWH therapy is essential in cases other than severe or critically ill patients[13]. As mentioned in our treatment strategy, we applied early routine LMWH therapy, irrespective of disease severity. Based on the proposed algorithm by Carfora et al.[13] for anticoagulation strategy, we recorded only one case related to COVID-19 coagulopathy (massive pulmonary embolism).

Position changes, and especially prone positioning, are documented to benefit patients presenting ARDS. Although prone positioning is widely used in intubated patients, we also implemented this strategy in awake non-intubated COVID-19 patients, with optimal clinical outcomes. Gürün et al.[14] support that prone positioning could be a standard of care, when applicable, in non-intubated COVID-19 patients to ameliorate oxygenation and delay the need for intubation.

Adding orally administered N-acetyl-cysteine in the therapeutic protocol was decided after having considered the significant results from the study carried out in the neighboring University Hospital of Patras[12]. Even though the administration of N-acetyl-cysteine was not further evaluated in the present study, it was found to be catalytic in our struggle to delay or prevent progress to SRF, increase survival rates, and lower the intubation risk in combination with the rest of our therapeutic protocol.

In order to maintain a balance between admissions and discharges we sought to function in a way to accelerate recovery and to avoid complications *ab initio*. The combination of functional ward configuration, and close collaboration with pulmonologists and intensive care physicians, offered efficient and individualized treatment

for the more critically ill patients and contributed to a well-coordinated 'wait-and-see' strategy with a result of low intubation rates. Besides, as suggested in the literature a 'wait-and-see' strategy instead of early intubation had already gained ground among physicians internationally and could be just as beneficial, while avoiding the complications of invasive ventilation[15,16]. Except for the daily rounds, additional meetings were held among the specialists to evaluate the everyday clinical status of each patient and decisions for further interventions or alterations on the treatment were implemented, within thirty minutes at most. Prompt interventions following the clinical examination and ABGs evaluation played a pivotal role in ensuring high effectiveness of our treatment and reducing the risk of progress to SRF and intubation.

Of crucial significance was the fact that all physicians were fully vaccinated, which led to risk-free and meticulous handling of the patients, so as to ensure ventilation was unproblematic and to prevent any complications regarding both to the hospitalization and the disease. Our non-intubated patients in prone position particularly benefited from this protocol.

Based on clinical trials, among our patients who developed SRF, our standard of care included the administration of a single weight-adjusted dose of tocilizumab. The statistical analysis of clinical outcomes indicated a satisfactory result in the majority of our patients. We strongly recommend the use of the monoclonal antibody, although it is not yet clear in the literature what the exact dosage and timing are for this agent in COVID-19 patients[9].

Comparing our results with previously published studies, our results on mortality rates stand out. The meta-analysis of Macedo et al.[17] reported an overall 17% mortality rate for admitted COVID-19 patients. In addition, Asch et al.[18] reported 8.25% overall mortality while in a retrospective single-center study, van Halem et al.[19] reported an overall case fatality rate of 25%. According to our data, all-cause mortality in our institution was 8.1%.

The aforementioned studies recorded fatality rates for the period January to June 2020. Evidently the therapeutic algorithms were different at that time, which highlights the high effectiveness of the care protocol that we followed against COVID-19 infection one year later[8-12]. Based on the study's outcomes, we believe that our protocol might be practical and efficient for similar institutions that are required to treat COVID-19 patients during the current pandemic.

Limitations

Although the present cohort study indicates that the protocol of a small regional hospital against COVID-19 provides satisfactory outcomes, several limitations exist in our study. There is a potentiality of bias, since we excluded from the mortality rates all patients that were intubated and transferred into the ICU. Another potential limitation is the fact that parameters such as smoking and prior influenza or pneumococcal vaccination, were not investigated. Despite the statistically significant study population, we performed only simple statistical analysis. Finally, further investigation is essential for the documentation of the optimal standard of care for COVID-19 patients proceeding to regional hospitals worldwide.

CONCLUSIONS

The challenges that the novel coronavirus poses during hospitalization demand both careful and decisive actions. Management of COVID-19 patients with a well-defined therapeutic protocol and the coordinated collaboration among specialists were the cornerstones of proper and individualized treatment without delay, and in our experience 'time equaled treatment'. Treatment using the current standard of care was efficient in reducing patient progress to SRF and intubation rates. Full vaccination of the medical staff ensured long and dedicated presence in the patients' rooms.

CONFLICTS OF INTEREST

The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

ETHICAL APPROVAL AND INFORMED CONSENT

This study was conducted according to the World Medical Association Declaration of Helsinki recommendations. All participants provided verbal informed consent.

DATA AVAILABILITY

The data supporting this research cannot be made available for privacy reasons.

PROVENANCE AND PEER REVIEW

Not commissioned; externally peer reviewed.

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