ORIGINAL ARTICLE

Evaluation of invasive ventilation rate and comorbidities, clinical signs and lab findings among COVID-19 patients

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Abstract

The severity of COVID-19 has been to be associated with comorbidities. It is defined as the presentation of severe respiratory dysfunction or failure, leading to the need for ventilation and mortality. The aim of this study is the evaluate the factors predicting the rate of invasive ventilation among these patients.

This retrospective study involved 317 COVID-19 patients referred to (XXX) Hospital in Qom, Iran. The following data were obtained for all the patients: demographic parameters, comorbidities, need for mechanical ventilation, signs and symptoms and lab findings.

The results from the demographic data of the study indicated that the need for mechanical ventilation is significantly associated with advanced age, $p = 0.001$. Additionally, hypertension, leukopenia and blood urea nitrogen to creatinine ratio $p = 0.008$. $p = 0.042$ and $p < 0.001$, respectively, are significantly associated with an increased need for mechanical ventilation. Malignancy, diabetes, asthma, chronic obstructive pulmonary disease, headache, fever, platelet count, prothrombin time, c-reactive protein, erythrocyte sedimentation rate and creatinine phosphatase were not significantly different in the two groups, $p > 0.05$.

Prediction of the extent of severity among COVID-19 patients using clinical parameters and comorbidities prepare medical practitioners and health care centres to take immediate measurements and reduce the burden of the scarcity of health supplies and care.

Keywords: Comorbidities, COVID-19, invasive ventilation

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Introduction

The novel pneumonia-causing coronavirus (2019-nCoV) leading to coronavirus disease 2019 (COIVD-19) is a single-stranded RNA virus and is known to be close to the SARS virus (severe acute respiratory syndrome virus). The first case of COVID-19 was reported in Hubei, China, where later it was considered to be an epidemic. In March 2020, the cases of COVID-19 were 13 times more in the other regions of the world and it was declared as the pandemic by the World Health Organization (WHO) [1]. According to the WHO report published on 13th December, 2020, the overall number of global cases are 70, 476, 836and 1,599,922 deaths have been reported [2].

The real-time polymerase chain reaction (RT-PCR) using a nasal throat sample is used for the diagnosis of the infection. Additionally, a chest CT (computed tomography) scan is performed to determine the extent of lung involvement [3]. The common signs and symptoms of the disease include fever, dry cough, headache, fatigue, dyspnea and vomiting [4]. Severe cases of infection can lead to organ failure and death, while ordinary respiratory distress is common in non-severe patients [5]; the presentation of respiratory distress is seen after 7 days of infection. Patients are likely to develop silent hypoxemia, as well (hypoxemia without respiratory distress) [6]. Several biomarkers can predict the severity of the disease and might be helpful in determining the need for critical care in patients [7]. Increased c-reactive protein and lymphopenia are likely to be good predictors of hypoxemia and associated mortality [8,9]. The incidence of COVID-19 among patients with comorbidities is 30–50%. Hypertension and respiratory and cardiovascular disorders can add to the severity of the disease [10]. The treatment

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of the disease using remdesivir and other antivirals is under clinical trials (NCT04252664 and NCT04257656) [8].

The aim of this study is to evaluate the incidence of comorbidities and signs and symptoms of COVID-19 in the prognosis of invasive ventilation.

Methods

This retrospective study included COVID-19 adult patients who underwent invasive ventilation at (XXX). Patients aged ≥18 years diagnosed with COVID-19 according to the WHO guideline from February 2020–March 2020 referred to our centre were included.

The information regarding demographic characteristics, clinical symptoms, lab findings, treatment and the need for invasive mechanical ventilation were collected from the record of these patients and were entered in a standardized data form. The treatment of the patients was provided according to the guideline of Infectious Diseases Society of America Guidelines on the Treatment and Management of COVID-19 Infection [11] and Iranian Expert's Consensus Statement [12]. Additionally, mild, moderate and severe cases were also determined based on these guidelines, that also determined the need for invasive mechanical ventilation in these patients. 7.0–to 8.0-mm endotracheal tube (EET) was placed between vocal cords into the trachea as per the standard procedure of invasive ventilation.

The diagnosis of COVID-19 in symptomatic patients was made using RT-PCR using a throat-swab specimen. The routine lab tests included complete blood count, renal and liver function tests, coagulation profile and c-reactive protein (CRP). The CT scan was also performed in all the patients.

The data obtained was digitized and statistically analysed using SPSSv22. The mean and variance indices were used to describe the concentration and distribution of quantitative data and relative frequency and frequency indices for qualitative variables. Fisher's Chi-square and precision tests were used to compare the rate of invasive ventilation in qualitative variables. P value < 0.05 was considered to be statistically significant.

Results

A total of 317 patients were included in the study where 167 were male and 139 were female. The average age of patients was 59.71 ± 16.46 years. Advanced age was significantly associated with the need for invasive ventilation, p = 0.001 (Fig. 1). The need for invasive ventilation was not different among the two genders, p = 0.44.

The rate of arthralgia was 30.2% for patients with invasive ventilation and 39.1% for patients without invasive ventilation. The Chi-square test showed no significant relationship between arthralgia and invasive ventilation, p = 0.193.

Among asthmatic COVID-19 patients, the rate of invasive ventilation was 3.2%, and non-asthmatic patients was 4.6%. Fisher's exact test showed no significant relationship between asthma and invasive ventilation, p = 0.465.

The rate invasive ventilation among patients with malignancy was 4.8% and among the patients without malignancy was 2.1%. The results from Fisher's exact test showed that there was no significant relationship between malignancy and invasive ventilation, p = 0.371.

The rate of invasive ventilation among patients with BUN to creatinine ratio greater than 20:1 was 42.9% and 11.8% for patients without invasive ventilation. The Chi-square test showed a significant association between BUN to creatinine ratio and invasive ventilation, p < 0.001 (Fig. 2).

The COPD rate was 4.8% among patients needing invasive ventilation and 1.7% in patients without invasive ventilation. Fisher's exact test showed that there was no significant relationship between the incidence of COPD and the need for invasive ventilation, p = 0.162.

The CPK level was high in 3.2% of patients with invasive ventilation and 2.5% of patients without invasive ventilation. Fischer's exact test showed that the levels of CPK were not significantly associated with the need for invasive ventilation, p = 0.675.

The need for invasive ventilation among patients with CRP >3.0 mg/L was 46% and 52.9% for patients without invasive ventilation. The findings from the Chi-square test showed that the levels of CRP were not significantly different among patients with or without invasive ventilation p = 0.675.

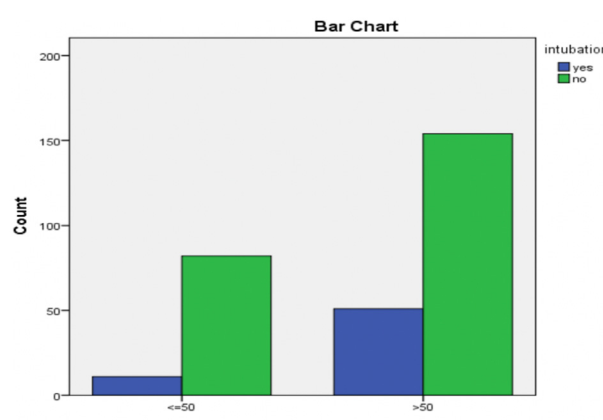

FIG. 1. The relationship between invasive ventilation and age.

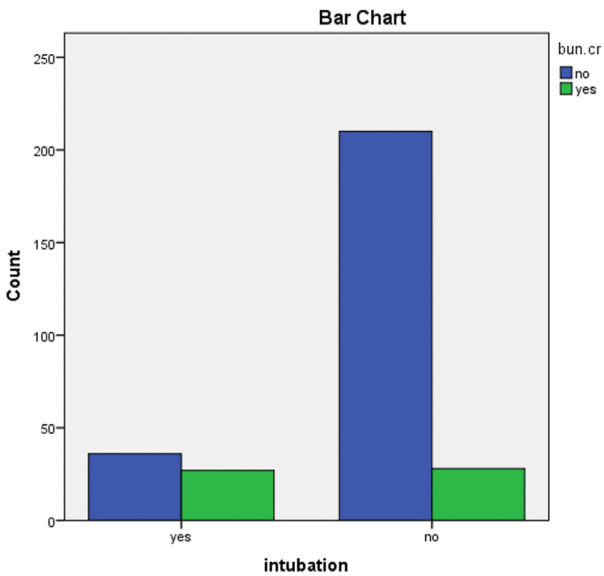

FIG. 2. The relationship between invasive ventilation and blood urea nitrogen (BUN) to creatinine ratio.

The need for invasive ventilation among DM patients was 23.8%, and 26.1% of DM patients did not need invasive ventilation. The Chi-square test showed no significant relationship between the prevalence of DM and the need for invasive ventilation, p = 0.717.

The incidence of olfactory dysfunction was 4.8% in patients with invasive ventilation and 3.4% in patients without invasive ventilation. Fisher's exact test showed that no significant relationship between olfactory dysfunction and invasive ventilation, p = 0.704.

The incidence of anorexia nervosa was 6.3% among patients with invasive ventilation and 5.9% in patients without invasive ventilation. Fisher's accurate test showed no significant relationship between anorexia nervosa and invasive ventilation, p = 1.

The invasive ventilation was provided to 1.6% of patients with diarrhoea and 0.8% non-diarrhoea patients. The results from Fisher's exact tests did not show any significant relationship between the incidence of diarrhoea and the need for mechanical ventilation, p = 0.507.

The incidence of increased ESR (1–13 mm/hr for males and 1–20 mm/hr for females) was 28.6% for patients with invasive ventilation and 26.1% for patients without invasive ventilation. Fisher's exact test showed that ESR was not correlated with the need for invasive ventilation among COVID-19 patients, p = 0.678.

The incidence of hypertension was 37.7% among patients with invasive ventilation and 23.1% in patients without invasive ventilation. The Chi-square test showed a significant association between the incidence of hypertension and invasive ventilation, p = 0.008. The need for mechanical ventilation was 55% higher among hypertensive patients (Fig. 3).

The incidence of fatigue was 12.7% among patients receiving invasive ventilation and 12.6% in patients without invasive ventilation. The Chi-square test showed no significant relationship between fatigue and invasive ventilation, p = 1.

The incidence of IDH was 23.2% among invasive ventilation patients and 16.4% in patients without invasive ventilation. The Chi-square test showed no significant relationship between IDH and invasive ventilation, p = 0.172.

The incidence of lymphopenia was 42.9% in patients with invasive ventilation and 29.4% in patients without invasive ventilation. The results from the Chi-square test showed that the incidence of lymphopenia was significantly greater among patients needing invasive ventilation, p = 0.042 (Fig. 4). The risk of COVID-19 patients with lymphopenia needing invasive ventilation was 1.79 times higher than patients without lymphopenia.

The incidence of leukopenia was 7.9% in patients receiving invasive ventilation and 17.4% in patients without invasive ventilation. The Chi-square test showed no significant relationship between leukopenia and invasive ventilation, p = 0.068.

The rate of invasive ventilation among transplant recipients and non-recipient was 3.2% and 0.8%, respectively. The Chi-square showed no significant difference in the need to ventilation among these two groups p = 0.194.

Of the patients, 1.6% with platelet count lesser than 150,000 received invasive ventilation and 7.6% did not receive invasive ventilation. Fisher's exact test showed no significant

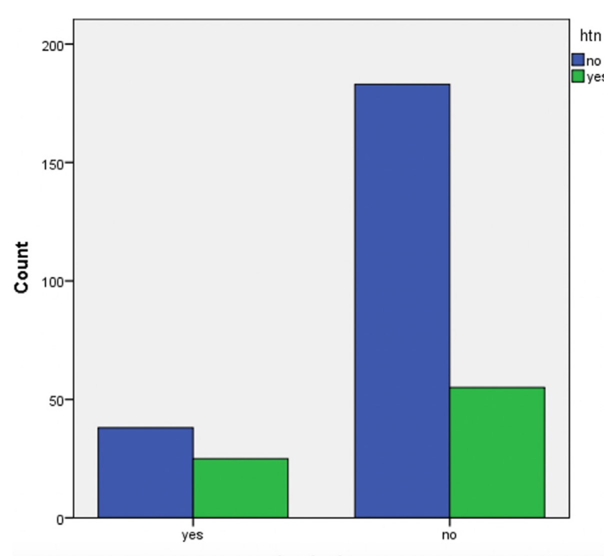

FIG. 3. The relationship between invasive ventilation and hypertension.

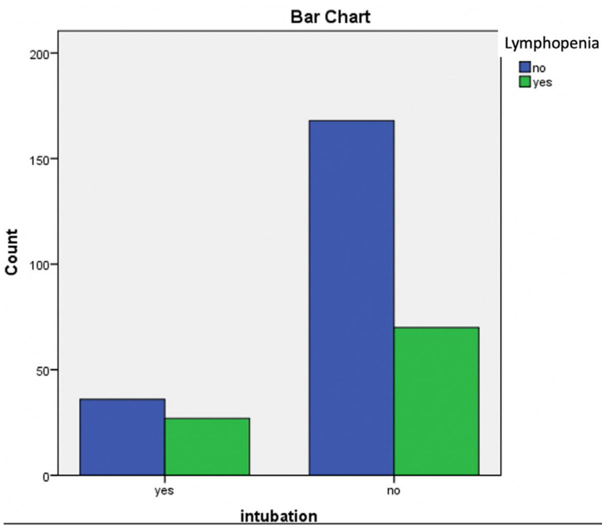

FIG. 4. The association of invasive ventilation and lymphopenia.

relationship between platelet count and the need for ventilation p = 0.14.

For 1.6% with prothrombin time ≤16 seconds, invasive ventilation was provided whereas, 1.3% of these patients did not receive invasive ventilation. Fisher's exact test showed no significant difference between the two groups, p = 1.

The incidence of headache among patients needing and not needing invasive ventilation was 4.8% and 9.2%, respectively. The Chi-square did not show any significant difference among the two groups, p = 0.252.

The rate of cough among patients needing and those not needing mechanical ventilation was 60.3% and 58.4%, respectively. The Chi-square test did not show any significant difference among the two groups, p = 0.784.

The rate of productive cough was 9.5% in patients with invasive ventilation and 7.1% among patients without invasive ventilation. Fisher's exact test showed that there was no significant relationship between productive cough and invasive ventilation, p = 0.953.

The need for mechanical ventilation among patients with fever was 71.4%. 69.3% of pyretic patients did not need mechanical ventilation The Chi-square test showed no significant association between fever and invasive ventilation, p = 0.747.

The rate of nausea was 12.7% in patients with invasive ventilation and 10.5% among patients without invasive ventilation. The Chi-square test showed no significant relationship between nausea and invasive ventilation, p = 0.620.

Respiratory distress was 87.3% among patients with invasive ventilation and 87.8% in patients without invasive ventilation. The Chi-square test showed no significant relationship between shortness of breath and invasive ventilation, p = 0.860.

Discussion

Acute hypoxemic respiratory insufficiency/failure is one of the common presentations of COVID-19, needing ventilation and intubation [13,14]. The severity of the disease is defined as tachypnoea ≥30 breaths per min, oxygen saturation ≤93% at rest, or PaO2/FiO2 ratio <300 mm Hg and respiratory failure requiring mechanical ventilation, septic shock, or other organ dysfunction or failure, requiring intensive care [15]. Our study evaluated the relationship between the need for mechanical ventilation with commodities and clinical and lab presentation.

Goyal P *et al.,* [16] reported that obesity, male gender, elevated liver function test, inflammatory markers are predictors of invasive ventilation in COVID-19 patients. Our study did not report any significant difference among the levels of inflammatory markers like CRP and ESR in invasive ventilation and non-invasive ventilation group. The patients presented with hypertension, cardiovascular disease and diabetes mellitus are at a greater risk of the infection. 2019-nCoV binds to the angiotensin-converting enzyme-2, which is widely expressed in lung epithelium. Its expression is elevated in diabetic and hypertensive patients, which can increase the risk of infection in these patients. The result of our retrospective study revealed that the need for invasive mechanical ventilation is significantly greater in hypertensive patients; however, it was untrue for diabetic patients. These outcomes indicate that hypertension is likely to be associated with the severity of the disease marked with severe respiratory distress [17].

Eosinophilia and early onset of shortness of breath are also associated with an increased risk of mortality [18]. A single centre retrospective study by Chen Q *et al.,* [19] on 145 patients reported that the severity of the disease is significantly associated with advanced age, diabetes mellitus, anorexia, chest tightness, greater body mass index and dyspnea. The outcomes of our study indicated that these parameters do not identify the potential candidates for invasive ventilation.

COVID-19 severity (defined by ICU admission, the need for mechanical ventilation or mortality) is significantly associated with a low platelet count (thrombocytopenia). Morphological change in the capillary bed of the lung epithelial can affect platelet defragmentation. It is also hypothesized that coronavirus can affect bone marrow leading to abnormal hematopoiesis [20]. Furthermore, coagulopathy and prothrombin time ≥16 is also significantly associated with in-hospital death [21]. Nonetheless, platelet count and prothrombin time were not significantly associated with the need for invasive ventilation in our patient group.

Zhang L *et al.,* [22] reported that the severity of the disease among cancer patients infected with coronavirus 2019 is associated with a greater need for invasive mechanical ventilation. The need for mechanical ventilation among these patients was recorded to be 35.7%. In our study group, the requirement of invasive mechanical ventilation was not associated with the presence of malignancy. The outcomes are likely to be dependent on the stage of cancer and the usage of immunosuppressant drugs.

The outcomes from a very limited number of renal and heart transplant patients have suggested that transplant recipients are likely to present similar mild COVID-19 symptoms as non-transplant patients due to the modulation of the inflammatory response [23,24]. The findings of our study also indicated that the need for invasive ventilation does not differ significantly among transplant and nontransplant recipients.

A meta-analysis and systematic review by Zhao *et a.l,* [25] concluded that the incidence of COPD is significantly associated with an increased risk of severe COVID-19 and the need for mechanical ventilation. The results of our study are not in parallel with these findings.

Elevated creatine and BUN in kidney disease COVID-19 patients are independent risk factors of in-hospital mortality [26]. A study from Cao [27] stated that BUN and creatinine might not be involved in the prognosis of the disease. The results of our study report a significant difference in BUN to creatinine ratio among patients who received invasive ventilation and those who did not.

Conclusion

The continuous increase in the number of COVID-19 cases has led to extensive demand for medical supplies and facilities. Critically ill patients require ICU care and ventilation. Predictors of the need for mechanical ventilation can prepare health care workers and hospitals to provide a strategic plan to meet the demands. Further studies involving outcomes from multi centres and a greater number of patients are therefore required.

Transparency declaration

The authors deny any conflict of interest in any terms or by any means during the study.

Ethical approval and consent to participate

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication

Not applicable.

Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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Authors contributions

Dr. Nina Farzan: Planned the study, wrote the protocol, collected the data and drafted the manuscript and accepted the final draft.

Dr. Sepideh Vahabi: Planned and designed the study, collected the data.

Dr. Behrooz Farzan: analysed the data and critically revised the draft and finally approved the manuscript.

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