Impact of Mechanical Ventilation on Outcomes of COVID-19 Patients in Hodeidah, Yemen

ABSTRACT

Background : Severe and critical infection of coronavirus disease 2019 (COVID -19) is characterized by Acute Respiratory Distress Syndrome (ARDS). The use of ventilators (non-invasive and mechanical), to deliver oxygen in cases of severe and critical COVID-19. Thus far, among the 10-20 % of COVID-19 patients who require treatment in an intensive care unit (ICU), about 5 % of them have been placed on mechanical ventilation (MV).
Objective : Therefore , the study aimed to estimate the impact of MV in management of COVID - 19 in Hodeidah, Yemen.
Methodology : This study was designed in a case series study that included 28 COVID-19 patients admitted to ICU, isolation department , Center of Tropical Medicine and Infectious Diseases (CTMID), AL Thawrah Public Hospital Authority, Hodeidah, Yemen an reference hospital. 28 critical ills cases were reported in first wave 2020. Data included demographics, advanced life support therapies, and MV variables. The MV variables included respiratory rate (RR); fraction of inspired oxygen (FiO2); M-V ; Tidal volume (Ti) ; positive end-expiratory pressure (PEEP) ; inspiratory to expiratory ratio (I:E) , flow rate; peak inspiratory pressure (PIP); plateau pressure; SaO_2; arterial pressure of oxygen (PaO_2) ; arterial pressure of carbon dioxide ($PaCo_2$), pH, and ventilator modes that were adjusted .
Results: The results of first wave in 2020 showed 28/505 (5.54%) patients critical illness undergo to MV. Only 6/28 patients (7,14 %) were recovered where different significant was reported (X^2 = 9.143; p = 0.0025) in comparing with severe cases with non-invasive namely 20/21 (95.23 %) that were that recovered. The main outcome for recovery was 31-day survival.
Conclusion : During the peak of the pandemic in Hodeidah ,Yemen, critically ill patients with COVID-19 often required MV and mortality was very high for critical cases in first waves, therefore the best practices of MV in COVID -19 must be improved.

***Keywords**: Impact , Mechanical Ventilator , COVID -19 , Hodeidah, Yemen.*

1. Introduction

"Mechanical ventilation (MV) is used to treat patients with severe coronavirus disease 2019 (COVID-19), little is known about the long-term health implications of this treatment" [1]. "Early observations suggested that COVID-19 pneumonia had a higher mortality rate than other causes of pneumonia" [2]. "There are large uncertainties with regard to the outcome of patients with COVID-19 and MV. High mortality (50-97%) was proposed by some groups, leading to considerable uncertainties with regard to outcomes of critically ill patients with COVID-19" [3].

"The mechanisms of COVID-19-associated ARDS include severe pulmonary infiltration/edema and inflammation, leading to impaired alveolar homeostasis, alteration of pulmonary physiology resulting in pulmonary fibrosis, endothelial inflammation and vascular thrombosis. Despite some distinct differences between COVID-19-associated Acute Respiratory Distress Syndrome (ARDS) and classical ARDS as defined by Berlin criteria, general treatment principles, such as lung-protective ventilation and rehabilitation concepts should be applied whenever possible. At the same time, ventilatory settings for COVID-19-associated ARDS require to be adapted in individual cases, depending on respiratory mechanics, recruitability and presentation timing" [4, 34-37].

"An ongoing outbreak of pneumonia associated with COVID-19 started in December, 2019, in Wuhan, China. In Hadrhmout , Yemen was reported in April, 2020 and In Hodeidah, Yemen was diagnosed in May 2020. Information about critically ill patients with COVID-19 infection is scarce" [5-7]. The study aimed to describe the clinical course and outcomes of critically ill patients with COVID-19 pneumonia.

2. Methodology

2.1. Study area, setting and designs

The study was carried out in intensive care unit (ICU) of , COVID-19 isolation department , Center of Tropical Medicine and Infectious Diseases (CTMID), AL-Thawrah Public Hospital Authority, Hodeidah, Yemen . The study was designed in a case series study (a retrospective study) from 1st June to 31st December 2020.

2.2. COVID-19 confirmation

The cases were confirmed with COVID-19 using on Real Time - Ploymerase Chain Reaction (RT-PCR) in biological molecular unit of CTMES - Authority of Public Al Thawara Hospital, Hodeidah, Yemen [8,9]

2.3. Critical cases diagnosis

The case definition of critical cases depended on Yemeni national guideline that was extracted on World Health Organization (WHO) guideline [10-11] . Different clinical investigations were used to assess the critical cases namely radiological features, hematological features and biochemical features [12-14]

2.4. Critical cases management

2.4.1. Pharmacological approach

The pharmacological approach of COVID-19 critical illness was summarized in Table (1) [15]

Table 1. National guideline of COVID-19 Critical Illness , Hodeidah, Yemen

Medicines Used	Critical
Paracetamol 1000 mg IV	three times a day (10-14 days)
Azithromycin 500 mg Tablet	once a day (6 days)
Ondansetron 8 mg IV	If necessairy
Enoxaparin 60 mg Subq.	once a day (14 days)
Pantoprazole 40 mg IV	once a day (14 days)
Acetylcysteine IV 300 mg	three times a day (14 days)
Oseltamivir 75 mg Tablet	once dose (14 days)
Dexamethasone 10 – 20 mg IV	twice a day (10 days)
Piperacillin and Tazobactam 4.5 g IV	three times a day (10-14 days)
Moxifloxacin 400 mg IV	once a day (10 -14 days)
Meropenam 1 g IV	three times a day (10-14 days)
Vitamin D 50000 IU Tablet	once weekly (two weeks)
Vitamin C 1g IV	once a day (14 days)
Zink 300 mg Tablet	once dose (14 days)

Note :

1) Dose of dexamethasone was prescribed 20 mg in first five days and reduced into 10 mg in other five (first wave of COVID-19)
2) The doses of antibiotics were adjusted according to creatinine clearance . Antibiotic used to prevent the secondary infection and most cases had leukocytosis.
3) *Critical cases (acute respiratory distress syndrome "ARDS: , respiratory failure, shock, or multi-organ system dysfunction).*

2.4.2. Non – pharmacological approach (Mechanical ventilation)

The MV parameters for treatment of COVID-19 critical illness was summarized in Table 2 [16,17] .

Table 2: Mechanical Ventilator (if needing) adjustment the parameters according the case

Variable	Setting
Ventilator mode	Volume assist – control
Tidal volume (ml kg^{-1})	6 (adjusted according to plateau pressure)
Plateau pressure (cm H_2O)	< 30
Rate (bpm)	6-35
I:E ratio	1:1 – 1:3
Oxygenation target	
- PaO_2	7.3 – 10.7
- SpO_2	88-95
PEEP and FIO_2	Set according to predetermined combinations (PEEP range 5-24 cm H_2O)
[16,17]	

Table 3: Mechanical ventilator variables for recovered case

Mechanical Ventilator Parameters	**COVID-19 Patients**
• RR	22
• Vt	380
• M-V	8.3 L
• FiO2	100
• PEEP	8
• I:E	1.2
• Flow rate ,	50
• PIP	30
• Ti	1.3
• Ventilator mode	Simv_V

The MV variables included Respiratory rate (RR); Tidal volume (Vt) ; Fraction of inspired oxygen (FiO2) ; Minute volume (M-V) ; Time inspiration (Ti) ; Positive end-expiratory pressure (PEEP) ; inspiratory to expiratory ratio (I:E) , Flow rate , Peak inspiratory pressure (PIP) , Plateau pressure (Pplat) , SaO_2, PaO_2,$PaCo_2$,pH, and ventilator modes that were adjusted .

Medications with MV :

- Midazolam 0.01-0.1 mg/kg
- Ketamine 2.5 – 15 mcg/kg/min
- Propofol 25-100 mcg/kg/min
- Atracurium 0.005-0.01 mg/kg/min
- Fentanyl 1-2 mcg/kg/h
- Morphine 0.05-0.2 mg/kg
- Pethadine 0.25 mg [18,21]

4.5. Data collection and analysis

The independent variables studied namely age, gender, clinical signs , risk factors, co-morbidity, co-infection, pharmacological medication , non – pharmacological medication (MV parameters) that were collected. Data were checked and entered in Statistical Package for Social Science (SPSS) and Microsoft Excel. The data were subsequently visualized using tables, graphs and text. Data were described through calculations , mean and percentages. Comparisons between qualitative variables were analyzed using Chi-squared test.

3. RESULTS
3.1. Sex – age and outcome

A total of 28 patients were confirmed undergo to MV . Males were significantly overrepresented in this group compared with females (X^2 = 7; p = 0.00815). The results showed a statistically significant of COVID1-9 infection with increasing with age , where higher frequency of COVID–19 infection in older patients namely between 50 and 80 years old. The case fatality rate (CFR) was very high in critical cases that received MV namely 22/28 cases (78.57 %) (Table 4).

Table 4 : Sex – age and outcome of critical illness with COVID-19 infection undergo MV

Sex/Age	**Mortality**			**Recovery**			**Total (n)**		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
<15	1	0	1	0	1	1	1	1	2
15-29	2	0	2	1	0	1	3	0	3
30 -49	0	0	0	1	0	1	1	0	1
50-59	6	2	8	2	1	3	8	3	11
60+	8	3	11	0	0	0	8	3	11
	17	5	22	4	2	6	21	7	28
Total		22			6			28	

3.2. Risk factors associated with MV

The mortality rate namely case fatality rate (CFR %) was high overall, with 22/28 cases (78.57%) with critical COVID-19 dying. Of these, the majority (53.57 %, n=15) were afflicted with underlying co-morbidities, including 3 cases (10.71 %) each of diabetes mellitus or cardiovascular disorders as single co-morbidities, and 4 cases (14.28 %) with both diabetes mellitus and cardiovascular disorders together. 3 cases (10.71 %) had bronchial asthma, including 1 case (3.57%) with cardiovascular disorders as an additional co-morbidity, and 1 case (3.57 %) had acute renal failure. Of 1 patients (3.57%) with underlying infections, the patient with HCV succumbed to COVID-19. On the other hand, 7 cases (28%) died without having any chronic diseases or co-infections (Fig. 1).

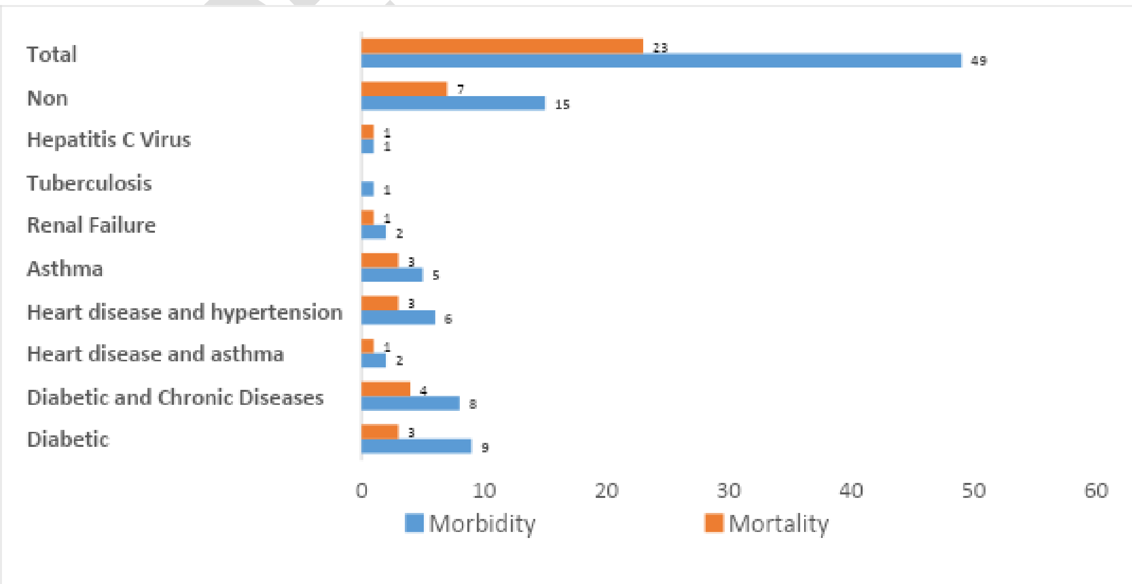

Fig. 1. Risk factors of COVID-19 in first wave 2020 for patients undergo MV

4. DISCUSSION

"Severe respiratory failure from COVID-19 pneumonia not responding to non-invasive respiratory support requires MV. Although ventilation can be a life-saving therapy, it can cause further lung injury if airway pressure and flow and their timing are not tailored to the respiratory system mechanics of the individual patient. The pathophysiology of COVID-19 infection can lead to a pattern of lung injury in patients with severe COVID-19 pneumonia typically associated with two distinct phenotypes, along a temporal and pathophysiological continuum, characterized by different levels of elastance, ventilation-to-perfusion ratio, right-to-left shunt, lung weight and recruitability. Understanding the underlying pathophysiology, duration of symptoms, radiological characteristics and lung mechanics at the individual patient level is crucial for the appropriate choice of MV settings to optimize gas exchange and prevent further lung injury. Previous study propose fundamental physiological and mechanical criteria for the selection of ventilation settings for COVID-19 patients in ICU. In particular, the choice of tidal volume should be based on obtaining a driving pressure < 14 cmH_2O, ensuring the avoidance of hypoventilation in patients with preserved compliance and of excessive strain in patients with smaller lung volumes and lower lung compliance. The level of PEEP should be informed by the measurement of the potential for lung recruitability, where patients with greater recruitability potential may benefit from higher PEEP levels. Prone positioning is often beneficial and should be considered early. The rationale for the proposed mechanical ventilation settings criteria is presented and discussed" [22].

"Early after establishment of MV, COVID-19 patients follow ARDS physiology, with compliance reduction related to the degree of hypoxemia, and inter-individually variable respiratory mechanics and recruitability" [23]. "COVID-19-ARDS is a subset of ARDS characterized overall by higher compliance and lung gas volume for a given PaO_2/FiO_2, at least when considered within the timeframe of our study" [24].

"The most commonly used analgesics and sedatives for all patients admitted to the ICU were pethidine (26.14%) and midazolam (32.18%), respectively. Sedatives and analgesics were more commonly used in mechanically ventilated patients. Among analgesics, the usage rate of pethidine and morphine decreased, whereas the usage rate of fentanyl and remifentanil increased. Among sedatives, the usage rate of benzodiazepine decreased, whereas the usage rate of propofol increased [20]. There was discordance between current usage of analgesics and sedatives and the recommended usage stipulated by ICU guidelines. However, the trend of drug usage is changing to match the guidelines, which recommend maintenance of light sedation using an analgesia-based regimen and usage of short-acting drugs for routine monitoring of pain, agitation, and delirium in ICU care" [21].

"For a similar initial oxygenation, COVID-19 ARDS initially differs from classical ARDS by a higher CRS, dissociated from oxygenation. CRS become similar for patients remaining on mechanical ventilation during the first week of evolution, but oxygenation becomes lower in COVID-19 patients" [25]. "The compliance of the respiratory system is similar between COVID ARDS and non-COVID ARDS when calculated at the same PEEP level and while taking into account patients' anthropometric characteristics" [26].

"Old age and co-morbidity with chronic diseases namely diabetes, hypertension, cardiac disorder, and asthma that may be contributing factors to excess deaths among COVID-19 patients [5-6]. On the other hand , the co-infections with other infections like vector – borne diseases dengue , malaria, and west – Nile virus is of high concern in Hodeidah, Yemen" [27-31].

On the other hand , study in Yemen reported that 9.7 % of COVID-19 patients needed ICU admission (severe and critical illness) [6] that is similar with previous study that reported range of ICU admission with COVID-19 infection from 9.4 to 45.9% [32]. In addition, the finding reported that the CFR (%) of admitted patients (critical illness) to ICU was 23/49 cases (46.9%). On the other mean, 28/49 cases (57.14 %) in isolation department who had received MV and 22/28 cases (78.57 %) of those died and this result agreed with other countries. “In China , Wuhan, mortality rates among those admitted to ICUs ranged from 52 to 62% and increased to 86–97% among those requiring invasive MV. In United Kingdom, 67 % of those who had received MV died. In the United States, indicated that 50–67% of patients admitted to the ICU and 71–75% of those receiving invasive MV died” [33].

5. CONCLUSION

The impact of MV on mortality outcome was very high in Hodeidah, Yemen. Also, the COVID-19 has complications that increases the mortality rate . In addition , the old age, chronic diseases and co-infection may be contributing factors to excess mortality among COVID-19 patients. On the other hand , a greater emphasis toward training in best practice of MV and ICU medicine namely respiration therapy, are needed to help overcome these challenges.

CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the authors. The raw data are secured in the Center of Tropical Medicine and Infectious Diseases (CTMID), Al-Thawara Public Hospital Authority, Hodeidah, Yemen.

ETHICAL APPROVAL

The studies involving human participants were reviewed and approved by the Ethics Committee of the Center for Tropical Medicine and Epidemiology Studies, Hodeidah University (CTMES – HU), Hodeidah, Yemen.

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Details of the AI usage are given below:

1.

2.

3.

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