Case report

Clinical outcome of bronchoalveolar lavaged COVID ARDS patients

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ABSTRACT

Introduction: One of the biggest pandemics of the human race, Coronavirus disease, has reported mortality rates as high as 80% for critically ill patients. It has killed more than 3.9 million people worldwide with no strongly proven management options to decrease its mortality. One of the options gaining interest is fiberoptic bronchoscopy and bronchoalveolar lavage. Our study was conducted to assess the clinical outcome of intubated Coronavirus disease patients that had a fiberoptic bronchoscopy and bronchoalveolar lavage done.

Methods and materials: A consecutive prospective case series of intubated patients with critical Coronavirus disease pneumonia were conducted at Bethzatha general hospital from April 20, 2021, to July 30, 2021 GC.

Results: Five patients with a median age of 55 years were included in the study. The median APACHE II1, SAPS II2, and SOFA3 scores on admission were 13, 37, and 4 respectively. The difference in the mean values of; positive end-expiratory pressure, static compliance, plateau pressure, fractional inspired oxygen, and arterial oxygen tension to fractional inspired oxygen ratio between the time of intubation and the last fiberoptic bronchoscopy and bronchoalveolar lavage were 4.4 cmH2O, 11 ml/cmH2O, 6.2 cmH2O, 45%, and 76 mmHg. All patients were liberated from mechanical ventilation.

Conclusion: – There was a numerically and clinically significant improvement in lung mechanics and oxygenation leading to a 100% ventilator liberation rate. Fiberoptic bronchoscopy and bronchoalveolar lavage in Coronavirus disease patients can improve lung mechanics, oxygenation, and rates of extubation.

Abbreviation list

AKI Acute kidney injury
APACHE-II Acute physiology and chronic health evaluation II
ARDS Acute respiratory distress syndrome
BAL Bronchoalveolar lavage

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1 Acute physiology and chronic health evaluation.
2 Simplified acute physiology score.
3 Sequential organ failure assessment.

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1. Introduction

One of the biggest pandemics of the human race, Coronavirus disease-19 (COVID-19), emerged from China in 2019. It was proven to be caused by a member of the Coronaviruses, named severe acute respiratory syndrome Coronavirus 2 (SARS COV-2). As of July 2, 2021, there have been 182,319,261 confirmed cases of COVID 19 with 3,954,324 deaths worldwide [1,2].

Among the patients that get infected, 81% become asymptomatic, 14% develop severe illness, and 4% require intensive care unit (ICU) admission [3]. The ICU admissions often require intubation and mechanical ventilation with high mortality rates. Mortality rates ranging from 40 to 80% have been reported in the literature, with lower mortalities being reported from recent studies [1,3,4].

Different management strategies to decrease the mortality of these intubated and mechanically ventilated patients have been proposed. Earlier, during the pandemic, glucocorticoids have been suggested, and later on the use of the Interleukin 6 (IL-6) inhibitor, Tocilizumab was shown to decrease mortality. These medications in addition to prone positioning, a growing experience, and meticulous ICU care have decreased the mortality of intubated COVID patients. But, despite these advances, the mortality of intubated COVID patients has remained high and further therapies are being explored in different countries [4,5].

Among the additional therapies that are being evaluated, is fiberoptic bronchoscopy with bronchoalveolar lavage (FOB-BAL). Even though the safety and utility of FOB and BAL have been demonstrated in ICU patients and specifically in patients with acute respiratory distress syndrome (ARDS), its value in COVID 19 pneumonia has been limited because of the fear of increased transmission to the health professional during the procedure. But, the need for FOB and BAL has increased for microbiologic diagnosis of the illness itself, for identification of superimposed infections, for airway management, for management of hemoptysis, for the treatment of atelectasis, and broncho aspiration [6,7].

Earlier studies had assessed the use of FOB and BAL in making the diagnosis of COVID 19 in patients with repeated negative nasal and oral swabs, thus, aiding in the isolation and management of these patients. A study that retrospectively analyzed patients who had FOB and BAL for diagnostic reasons, showed that there was an improvement in oxygenation of these patients after the procedure [6,7]. Another study in South Africa that specifically assessed the use of FOB and BAL as a treatment for intubated and mechanically ventilated COVID ARDS patients was able to show a consistent improvement in oxygenation and rates of successful extubation [3,6,7].

Except for the study done in South Africa, all other studies assessed the utility of FOB and BAL as a diagnostic tool [3,6,7]. The South African study also limited the intervention to patients that had failed to be extubated after seven days of ventilation, in addition, the protocol and procedures for the FOB and BAL were not explicitly explained. Even though there have been 276,250 confirmed cases with 4325 deaths in Ethiopia, we have found no literature regarding the clinical outcome of intubated COVID patients that had FOB and BAL [3,6-8].

Our study was conducted to assess whether FOB and BAL would affect lung mechanics, oxygenation, and extubation rates in intubated patients with COVID 19. We hope that our observation will stimulate others in the country and abroad, working in tertiary centers, to replicate and confirm our findings and thus aid in the further decline of mortality.

2. Methods and materials

The study was conducted in Bethzatha general hospital COVID ICU located in Addis Ababa, Ethiopia. A privately owned hospital with a capacity of 10 ICU beds with in-house dialysis service and 50 medical ward beds. The study was conducted from April 20, 2021,
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... to July 30, 2021 GC.

All COVID-positive patients who required intubation and mechanical ventilation and all COVID positive patients intubated and stable at day four post-intubation were used as the sampled and study population respectively.

A consecutive prospective case series was used to answer the question “Do FOB and BAL affect lung mechanics, oxygenation, and extubation rates of intubated COVID patients?”

2.1. Inclusion criteria

➢ Age above 18 years
➢ Reverse transcriptase-polymerase chain reaction (RT PCR) positive for SARS-COV-2 virus
➢ Severe ARDS based on the Berlin criteria
➢ Intubated and mechanically ventilated for at least 3 days
➢ Hemodynamically stable after the third day
➢ Not on chest tube for iatrogenic pneumothorax
➢ No requirement for other organ support

2.2. Primary outcome

Clinically significant improvement in lung mechanics, oxygenation, and rates of extubation.

2.3. Secondary outcome

Observed adverse outcomes related to FOB and BAL.
Rates of symptomatic nosocomial COVID 19 staff infections.

2.4. Procedure

All patients were made to have a 7.5 French Gauge (FG) endotracheal or tracheostomy tube in place before their FOB and BAL. The procedure was done by a trained pulmonologist and ICU internist in either a supine or prone position. Change in position was not allowed during the procedure. Starting from day four of intubation, the patients got FOB and BAL done until they were able to be successfully extubated or died. After the bronchoscopy was successfully inserted, it was advanced to segmental and subsegmental bronchi, normal saline was instilled in aliquots of 5–10 ml, based on the bronchoscopists evaluation of the thickness of the secretion, and then it was sucked out. A maximum of 200ml of normal saline was used per session. The positive end-expiratory pressure (PEEP) and tidal volume were titrated up, to compensate for leaks that occur around the bronchoscopy insertion port by the bronchoscopy assistant. The bronchoscope was withdrawn and the patient’s oxygen status stabilized if the oxygen saturation fell below 85%. The procedure was aborted if the patient either became hemodynamically or rhythmically unstable. Arterial blood gas sampling and documentation of lung parameters were taken 24 hours after FOB and BAL were done, as all of the patients had transient elevation (the longest lasting up to 24 hours) in the amount of FIO₂, PEEP, and sedation they required, especially after the first session of FOB and BAL.

Serial laboratory surveillance of staff members was not allowed, unless they were symptomatic, as there was a shortage of staff members, and a positive result would, by the hospital policy, preclude active involvement in the care of patients.

2.5. Ethical clearance

Informed verbal consent was taken from immediate caretakers. Further ethical clearance was also taken from the Addis Ababa health bureau as part of a large ICU registry being run in the hospital’s ICU (BIRD project) (A/A/H/2464/227)

Data collection and Statistical analysis - The history, physical exam, investigations, and mechanical ventilator parameters were collected during the management of the patients in the ICU. The collected data regarding lung mechanics, oxygenation, and successful extubation, was entered into SPSS V25. The median, range, and standard deviations were calculated.

2.6. Operational definition

Successful extubation- A patient maintaining oxygenation (Spo₂ >90%) with low work of breathing, 48 hours after extubation, or being taken off mechanical ventilation if on Tracheostomy.

3. Results

Thirty-three patients were admitted to the ICU during the study period. 20 patients were excluded because they were not intubated. Out of the 13 intubated patients, eight were excluded. Three for hemodynamic instability, one for the requirement of dialysis, one for a high arterial oxygen tension to fractional inspired oxygen (P/F) ratio for inclusion, another one, for being transferred to our hospital after prolonged intubation at another hospital, and the other two had died before day four of intubation.

Five patients with a median age of 55 years (42–70) were included in the study. All of the included patients had at least one co-morbidity, the commonest one being diabetes. The median APACHE II, SAPS II, and SOFA scores on admission were 13 (9–19), 37 (28–49), and 4 (3–8) respectively. While all patients were tried on noninvasive ventilation (NIV) before intubation (median number of days on NIV 2 (1–11)), three patients started from High flow nasal oxygen therapy (HFNOT) and were later switched to NIV (median number of days on HFNOT 1 (1–7)) (Table-1)
A total of ten FOB and BAL procedures were done for five patients. Two patients had three sessions, one patient had two sessions, and two patients had one session. For the two patients that had only one session, the first patient was extubated before the second session was due, and the second patient was transferred out to another hospital without FOB and BAL capacity for financial reasons but was followed up and extubated five days after the procedure.

All pre- and post-FOB and BAL PEEP parameters were optimized to achieve the lowest driving pressure in all patients. Despite the improvement of oxygenation and lung parameters in patients 1 and 4, FOB and BAL were continued because they failed a trial of spontaneous breathing, and as the prespecified treatment target was successful extubation. Patients 2 and 5 were allowed the same FIO\textsubscript{2} pre and post FOB and BAL because their PEEP and ΔP were decreased after the procedure (Table 2).

All patients had a varying amount of thick gelatinous mucus in the airways (Figure 1). The mean; baseline PEEP (mmHg), static compliance (Cstat) (ml/cmH\textsubscript{2}O), plateau pressure (Pplat) (mmHg), fractional inspired oxygen (F\textsubscript{IO}\textsubscript{2}) (%) and P/F ratios (mmHg) for the patients were 11.2 (8–16) SD-3.3, 20.6 (17–25) SD-3.3, 25.6 (22–28) SD-2.3, 90 (60–100) SD - 17.3, and 87.8 (65–112) SD-21.2 respectively. The same parameters after the last session of FOB and BAL were 6.8 (5–10) SD-2.2, 31.6 (24–38) SD-5.5, 19.4 (15–25) SD-4.0, 45 (35–60) SD-9.4, and 163.8 (117–211) SD-34.9 respectively. The difference in the mean values of; PEEP, Cstat, Pplat, F\textsubscript{IO}\textsubscript{2}, and P/F ratio between the time of intubation and after the last FOB and BAL were 4.4 (1.2–7.5) SD-2.5, 11 (1.2–20.7) SD-7.8, 6.2 (1.4–10.9) SD-3.8, 45% (13.6–76.3%) SD-25, and 76 (13.9–138.0) SD-49.9 (Table 2).

All patients were extubated, and were free from mechanical ventilation, for more than 48 hours. Two patients were reintubated for Type II respiratory failure caused by critical illness myopathy. One of the patients, while on tracheostomy, was successfully taken off mechanical ventilation, the other one was decannulated eight days later. The median duration of intubation was 15 days (12–27), with the median time spent on a ventilator, from the time of the first session of FOB and BAL, being eight days (2–22).

There were no symptomatic infections in staff members, procedural hemodynamic instabilities, arrests, or deaths. There were two episodes of atrial fibrillation, two episodes of significant desaturation events requiring procedural pause among the 10 sessions performed (Table 3).

### 4. Discussion

We have demonstrated in our case series that FOB and BAL may have a place in the management of intubated COVID patients by improving lung mechanics, oxygenation, and rates of successful extubation. This was seen in patients that were stable and that were not requiring any other organ support after the fourth day of intubation. These results have come, with no harm to the patient during the procedure, and to the staff members performing or supporting during the procedure.

Different studies have shown that for intubated COVID patients the median age was 70 years (60–81), the median APACHE, and SOFA scores were 18.0 (14.0–24.5), and 7.0 (5.0–9.0), while the median duration of mechanical ventilation was 8.6 days. These findings are different from the ones we have presented. The disparity between our result and these findings may have arisen from the small size of the patients included in our study and the relatively older population in western countries with multiple comorbidities, as

### Table 1
Background demographic and clinical characteristics of treated patients.

| Patient | 1 | 2 | 3 | 4 | 5 |
|---------|---|---|---|---|---|
| Age (years) | 42 | 70 | 48 | 70 | 55 |
| Sex | M | F | M | F | M |
| Comorbidities | Diabetes | Diabetes | Diabetes | Diabetes | Diabetes |
| | Dyslipidemia | Hypertension | Dyslipidemia | |
| Remdesivir * | 5 days | 5 days | 5 days | 5 days | 5 days |
| Tocilizumab | 8mg/kg stat. | 8mg/kg stat. | NO | 8mg/kg stat. | 8mg/kg stat. |
| Analgo-sedation | Ketamine | Ketamine | Propofol | Diazepam | Ketamine |
| Propofol | Diazepam | Ketamine | Propofol | Ketamine | Ketamine |
| Dexametomidine | Morphine | Dexametomidine | Morphine/Fentanyl | Diazepam | Morphine/Fentanyl |
| Dexametomidine | Morphine/Fentanyl | Diazepam | Morphine/Fentanyl | Diazepam | Morphine/Fentanyl |
| Paralytics | Vecuronium | Vecuronium | Vecuronium | Vecuronium | Vecuronium |
| Proneing | Done | Done | Done | Done | Done |
| Bromhexine ‡ | YES | YES | YES | YES | YES |
| APACHE II | 13 | 11 | 9 | 18 | 19 |
| SOFA | 4 | 4 | 3 | 5 | 8 |
| SAPS II | 37 | 36 | 28 | 45 | 49 |
| Organ failures | 1 | 1 | 1 | 1 | 2 |
| NIV (Days)§ | 1 | 2 | 11 | 1 | 10 |
| HFNOT (Days) ¶ | 0 | 1 | 0 | 1 | 7 |

HD: ischemic heart disease, AKI: Acute kidney injury, NIV: Non-invasive ventilation, HFNOT: High flow nasal oxygen therapy *Duration of standard-dose remdesivir treatment, †Mixture of analgesic and sedative drugs used, ‡Type of Paralytic administered, §Early (within 24 hours) initiation of bromhexine, ¶Number of organ failures on admission to the ICU, §Number of days spent on non-invasive ventilation before intubation, ¶¶Number of days spent on high flow nasal oxygen therapy before intubation.
well as a lower threshold for intubation [4,9,10].

A retrospective analysis of bronchoscopies done for intubated COVID patients had shown the pre bronchoscopy median lung parameter values to be, FiO2 0.8 (IQR, 0.4 – 1), PEEP 8 (IQR, 5 – 10), and P/F ratio 122 (IQR,74 – 148). While a single-center experience from Spain showed the pre bronchoscopy lung parameter results to be as follows; FiO2 0.8 ([IQR], 0.67 – 0.82), PEEP 10 cm H2O (IQR, 9 – 11), and P/F ratio 111 ([IQR],103 – 125). When our patients are contrasted with these findings, it is visible that they required a higher level of FiO2 and PEEP with a worse P/F ratio, this might be because we selected only the patients with severe ARDS [6,7].

The same study cited above had also reported that the post bronchoscopy median value for P/F was 150 (IQR 61 to 174). our result is similar to their finding even though the objective of their study was only to perform mini-BAL for microbiologic diagnosis [6].

Table-2
Pre and post bronchoscopy changes in lung mechanics, oxygenation, and arterial blood gas of treated patients.

| Patient | 1 | 2 | 3 | 4 | 5 |
|---------|---|---|---|---|---|
| Pre BAL | 16 | 12 | 12 | 8 | 12 |
| 1st* BAL | 6 | 12 | 12 | 10 | 8 |
| 2nd† BAL | 6 | 5 | 8 | 5 | 5 |
| 3rd‡ BAL | 5 | 5 | 5 | 5 | 5 |

ΔP (cmH2O)

| Patient | 1 | 2 | 3 | 4 | 5 |
|---------|---|---|---|---|---|
| Pre BAL | 6 | 8 | 8 | 12 | 15 |
| 1st* BAL | 15 | 16 | 15 | 18 | 10 |
| 2nd† BAL | 10 | 10 | 17 | 16 | 13 |
| 3rd‡ BAL | 11 | | | | |

Cstat (ml/cmH2O)

| Patient | 20 | 26 | 26 | 25 | 30 |
|---------|---|---|---|---|---|
| Pre BAL | 23 | 24 | 17 | 28 | 30 |
| 1st* BAL | 18 | 21 | 25 | 21 | 18 |
| 2nd† BAL | 16 | 11 | 20 | 21 | 17 |
| 3rd‡ BAL | 20 | 17 | 18 | 20 | 16 |

P/F ratio (mmHg)

| Patient | 7.39 | 7.51 | 7.45 | 7.43 | 7.47 |
|---------|---|---|---|---|---|
| Pre BAL | 7.47 | 7.47 | 7.52 | 7.45 | 7.48 |
| 1st* BAL | 7.43 | 7.47 | 7.52 | 7.45 | 7.48 |
| 2nd† BAL | 7.43 | 7.47 | 7.52 | 7.45 | 7.48 |
| 3rd‡ BAL | 7.43 | 7.47 | 7.52 | 7.45 | 7.48 |

PCO2 (mmHg)

| Patient | 38.3 | 43.8 | 51.8 | 38.1 | 42.5 |
|---------|---|---|---|---|---|
| Pre BAL | 38.5 | 67.3 | 36.1 | 49.5 | 49.9 |
| 1st* BAL | 38.5 | 67.3 | 36.1 | 49.5 | 49.9 |
| 2nd† BAL | 38.5 | 67.3 | 36.1 | 49.5 | 49.9 |
| 3rd‡ BAL | 38.5 | 67.3 | 36.1 | 49.5 | 49.9 |

PH

| Patient | 7.34 | 7.38 | 7.38 | 7.34 | 7.38 |
|---------|---|---|---|---|---|
| Pre BAL | 7.38 | 7.34 | 7.38 | 7.34 | 7.38 |
| 1st* BAL | 7.38 | 7.34 | 7.38 | 7.34 | 7.38 |
| 2nd† BAL | 7.38 | 7.34 | 7.38 | 7.34 | 7.38 |
| 3rd‡ BAL | 7.38 | 7.34 | 7.38 | 7.34 | 7.38 |

well as a lower threshold for intubation [4,9,10].

Fig. 1. Thick gelatinous secretion (Arrows) in the segmental bronchi (A) and main bronchus (B) of patient 5.

Table-3
Number of FOB and BALs performed, circumstances around extubation, and tracheostomy along with BAL culture reports.

| Patient | 1 | 2 | 3 | 4 | 5 |
|---------|---|---|---|---|---|
| FOB and BAL* | 3 | 1 | 1 | 2 | 3 |
| Extubation attempts| | | | | |
| YES | 1 | 1 | 1 | 1 | 0 |
| Successful extubation | YES | YES | YES | YES | YES |
| Tracheostomy| | | | | |
| YES | NO | NO | YES | YES | YES |
| Reintubation| | | | | |
| CIM|| | NO | CIM|| | NO | Type IV RP| |
| Days on ventilator** | 6 | 10 | 2 | 8 | 22 |
| Days on tracheostomy| | | | | |
| 8 | 0 | 0 | 0 | 15 |
| Duration of intubation| | | | | |
| 16 days | 13 | 12 | 15 | 27 |
| BAL culture | A.baumannii | K.pneumoniae | No Growth | No Growth | K.pneumoniae |

*Total number of FOB and BALs performed, |Number of extubation attempts, |Need for tracheostomy, |§ reason for reintubation, || Critical illness myopathy, ¶ Type IV respiratory failure, ** total number of days spent on a ventilator from the first session of FOB and BAL, || total number of days spent on a tracheostomy, | Total number of days spent with either an endotracheal tube or tracheostomy.

A South African study that was done to evaluate the impact of bronchoscopy and BAL as a treatment for severe COVID pneumonia, in patients that fail to respond to standard of care after the 7th day of intubation, found out that the mean pre and post bronchoscopy P/F ratios were 80.9 (33–160) SD-33.5 and 119.5(60–233) SD-49.3. Even though the baseline parameter is the same as ours we were able to achieve better post-BAL results. This might be explained by the fact that we did our BALs early in the course of the disease and repeated the procedures until we had improvements [3].
see whether the lung mechanics and oxygenation variable changes are indeed significant. Moreover, the number of patients included has also limited our ability to assess the impact of the intervention on mortality.

Given the low risk to the health professional seen in our series, and the clinically significant improvement in lung mechanics, oxygenation, and successful extubation rates, which probably occurs due to atelectasis improvement from better mucus removal, and removal of active inflammatory mediators from the bronchial lumen, we would recommend the procedure to subsequent patients that we manage. We believe, our study, if replicated, in different tertiary centers, would produce robust data to place FOB and BAL as one of the management strategies for patients with severe COVID pneumonia that get intubated.

Guarantor

Dr.Zablon Mesfin Anbessie is responsible for all the contents of this manuscript.

Author contributions

Dr.Zablon Mesfin-Diagnosis, Management, assisting FOB and BAL, follow-up, proposal submission, data collection, data analysis, manuscript write up, revision of the manuscript, Corresponding author.

Dr.Dawit Kebede Huluka-Diagnosis, management, performing FOB BAL, follow-up, revision of the manuscript.

Dr.Zelalem Abdlsa Kenea-Diagnosis, Management, Followup Data collection, Data analysis.

Names of collaborators

None.

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Other contributors

None.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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