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STUDY OF EFFECT OF EARLY PRONE POSITIONING IN MODERATE TO SEVERE COVID-19 PATIENTS ON NON-INVASIVE VENTILATION

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ABSTRACT

INTRODUCTION: Patients with COVID-19 that require invasive mechanical ventilation have a high mortality. Early prone positioning for self-ventilating patients with suspected or confirmed COVID-19 who have hypoxemia (spO2 <94%) despite HFNC or face mask oxygen via venturi (fiO2 40%) will result in improved oxygenation, reduced work of breathing and a reduced need for invasive mechanical ventilation.
METHODS: This Prospective Observational Cohort study conducted to determine the effect of early use of Prone Positioning combined with NIV or HFNC in hospitalized moderate to severe COVID-19 patients, requiring non-invasive ventilation. The study was conducted for a period of 12 months from October 2020 to September 2021.
RESULTS: The mean SpO2 among patients with NIV and Prone positioning; and with HFNC and Prone positioning were statistically significantly higher than when compared to the patients with NIV and HFNC without Prone positioning respectively (p value = 0.003 and < 0.001). The mean PaO2/FiO2 among patients with NIV and Prone position; and with HFNC and Prone position were statistically significantly higher than when compared to the patients with NIV and HFNC without Prone position.

Keywords: PRONE POSITION, COVID 19, NIV, HFNC

Background:

Since the era of the influenza pandemic of 1918, SARS-CoV-2, has had a catastrophic effect on world's demographics resulting in > 2.9 million deaths worldwide[1]. World Health Organization (WHO) declared it as global pandemic on March 11, 2020 after the first cases reported in Wuhan, Hubei Province, China, in late December 2019.
The pathogenesis of SARS-CoV-2-induced pneumonia is explained by two phases: the early phase, which is characterised by viral replication leading to direct virus-mediated tissue damage; and the late phase, which is characterised by the induction of an immune response by infected host cells through the recruitment of T lymphocytes, monocytes, and neutrophils and the release of cytokines such as tumour necrosis factor (TNF), granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-1 (IL-1), interleukin-6 (IL-6),), IL-1β, IL- 8, IL-12 and interferon (IFN)-γ.
The National Institutes of Health (NIH) classifies COVID-19 into 5 distinct types.
Presymptomatic or asymptomatic Infection: SARS-CoV-2 test results that are positive but do not exhibit any COVID-19-like clinical symptoms.
Mild illness: Symptoms including fever, coughing, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of smell, or dysgeusia, but no abnormal chest imaging or shortness of breath.
Moderate illness: Clinical symptoms or radiologic evidence of lower respiratory tract disease.
Severe illness: SpO2 ≤ 94% on room air; a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen, (PaO2/FiO2) < 300; marked tachypnoea with respiratory frequency > 30 breaths/min or lung infiltrates > 50%.
Critical illness: Acute respiratory failure, septic shock, and/or multiple organ dysfunctions. Patients may become critically ill with the development of acute respiratory distress syndrome (ARDS).

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ARDS is characterized by a severe new-onset respiratory failure or worsening of an already identified respiratory picture. The Berlin definition classifies ARDS into three types based on the degree of hypoxia, with the reference parameter being PaO2/FiO2 or P/F ratio.[2]

Mild ARDS: 200 mmHg < PaO2/FiO2 ≤ 300 mmHg in patients not receiving mechanical ventilation or in those managed through non-invasive ventilation (NIV) by using positive end-expiratory pressure (PEEP) or a continuous positive airway pressure (CPAP) ≥ 5 cmH2O.

Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg

Severe ARDS: PaO2/FiO2 ≤ 100 mmHg.

PRONE POSITION VENTILATION IN COVID-19

AHRF and ARDS, leading to mechanical ventilation are common manifestations of COVID- 19 disease process and are found with a higher morbidity and mortality rate[3]. The fragile and under resourced health care systems of developing countries are facing severe limitations in managing patients during the pandemic, especially in constrained capacity and resource shortages[4]. While there is an urgent need of non-invasive and invasive ventilators in low- to-middle-income countries (LMIC) like our setting, there is definite need for cost-effective, scalable modalities to manage acute hypoxemia which, if left untreated, can progress to ARDS and AHRF[5,6].

Oxygen therapy, HFNC, and NIV may reduce necessity for endotracheal intubation and decrease ventilator-associated complications and mortality. Although NIV may help patients in a safe way, it can cause risks to the health care staff due to presence of infected aerosol. Hence, NIV may be employed as an early intervention for selected patients who are infected by COVID-19 with milder AHRF[7].

Prone Positioning improves gas exchange via several mechanisms that improve ventilation perfusion ratio. It involves more equal distribution of ventilation with redistribution of perfusion, recruitment of dorsal alveoli and increased lung volume[9,10]. It also promotes enhanced clearance of secretions from the lungs which improves ventilation perfusion ratio [11].

MATERIALS AND METHODS:

STUDY DESIGN:

This study was conducted at the hospital level as a Prospective Observational Cohort study to determine the effect of early use of Prone Positioning combined with NIV or HFNC in hospitalized moderate to severe COVID-19 patients, requiring ventilatory assist.

STUDY PERIOD, PLACE OF STUDY AND DURATION:

The study was conducted in the Department of Anaesthesia, Dr Pinnamaneni Siddhartha Institute of Medical Sciences & Research Foundation, a tertiary care centre teaching hospital for a period of 12 months from October 2020 to September 2021.

SAMPLE SIZE:

The sample size of 120 patients divided into four groups. Each group had 30 patients each as follows:

- Group A: 30 patients with NIV (BIPAP) in Prone position
- Group B: 30 patients with NIV (BIPAP) in supine
- Group C: 30 patients with HFNC in Prone position
- Group D: 30 patients with HFNC in supine

INCLUSION CRITERIA:

1. Patients admitted in Dr Pinnamaneni Siddhartha Institute of Medical Sciences & Research Foundation, tertiary care centre teaching hospital with moderate to severe COVID-19 patients who met the Berlin definition criteria[12].
2. COVID-19 patients with PaO2/FiO2 less than 200mmHg on this level of support.

EXCLUSION CRITERIA:

1. Signs of Respiratory Fatigue (RR>40/min, PaCO2>50mmHg/ PH< 7.30 and obvious accessory respiratory muscle use)

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2. Immediate need for intubation (PaO2/FiO2<50mmHg, unable to protect airway or change of mental status)
3. Unstable hemodynamic status
4. Inability to collaborate with PP with agitation or refusal.
5. patients with pre-existing severe systemic comorbidities

APPROACH:

Subjects who have been admitted in the ICU with moderate to severe COVID-19 patients who met the Berlin definition criteria in the study period October 2020 to September 2021 were selected for the study were recruited after getting approval from the Institutional Ethics Committee.

The efficacy in improving oxygenation was evaluated by Blood Gas Analysis, SpO2, FiO2 and the final outcome was evaluated by PaO2/FiO2 ratio. Therefore, we determined whether Prone positioning can increase the PaO2/FiO2ratio and decrease mortality in moderate to severe ARDS patients with COVID-19.

STATISTICAL ANALYSIS:

The collected data was entered into a MS excel sheet and analysis was done using the Statistical Package for Social Sciences software version 18. Descriptive statistics were employed to summarize the quantitative variables of demographic and clinical data. Standard deviation was calculated as a measure of variation. Qualitative variables were expressed as percentages with 95% confidence interval. Differences in the mean values were tested for statistical significance employing student's t test/ Mann Whitney test in case of non-normal distribution. Similarly to test for differences in the two proportions, Chi-square test/ Fisher's exact test was employed. Odd's ratio along with 95% confidence interval was estimated for various factors after dichotomizing the data. The level of significance [P-Value] was set at P<0.05.

OBSERVATIONS & RESULTS

Table 1: Distribution of subjects according to age

Age	Group A	Group B	Group C	Group D	Total
< 40 years	1 (3.3%)	0 (0%)	0 (0%)	1 (3.3%)	2 (1.7%)
40 - 59 years	9 (30%)	11 (36.7%)	9 (30%)	10 (33.3%)	39 (32.5%)
60- 79 years	16 (53.4%)	15 (50%)	19 (63.3%)	17 (56.7%)	67 (55.8%)
≥ 80 years	4 (13.3%)	4 (13.3%)	2 (6.7%)	2 (6.7%)	12 (10%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
Mean (years)	62.1 ± 12.72	63.5 ± 12.03	63.8 ± 11.07	61.7 ±11.92	62.8 ± 11.83
p-value	0.745		0.762		

Chart 1: Column diagram showing age distribution among subjects

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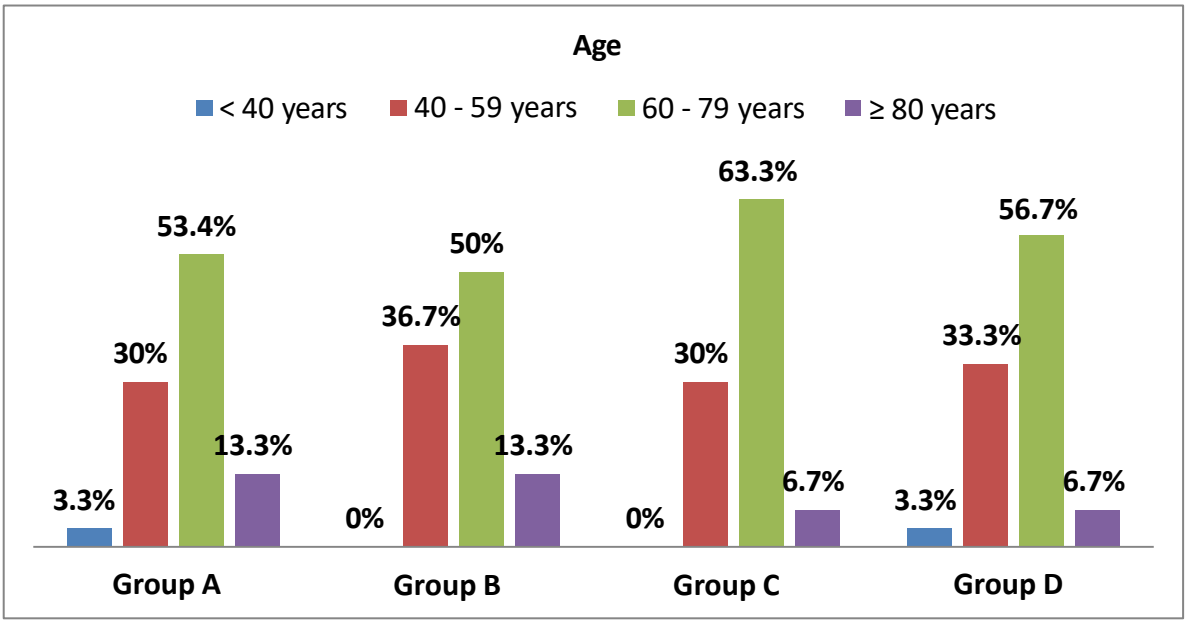

Table 1 shows the age distribution of the subjects.Out of 120, 2 were aged < 40 years, 39 between 40and 59 years, 67 between 60- 79 years and 12 were aged ≥ 80 years. The mean age in the present study was 62.8 ± 11.83years. Majority were aged between 60- 79 years (55.8%). There was no significant difference of age between the subjects of Group A and B; and that between Group C and D (p-values > 0.05).

Table 2: Distribution of subjects according to gender

Gender	Group A	Group B	Group C	Group D	Total
Male	22 (73.3%)	19 (63.3%)	21 (70%)	20 (66.7%)	82 (68.3%)
Female	8 (26.7%)	11 (36.7%)	9 (30%)	10 (33.3%)	38 (31.7%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
p-value	0.405		0.781		

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Chart 2: Column diagram showing gender distribution among subjects

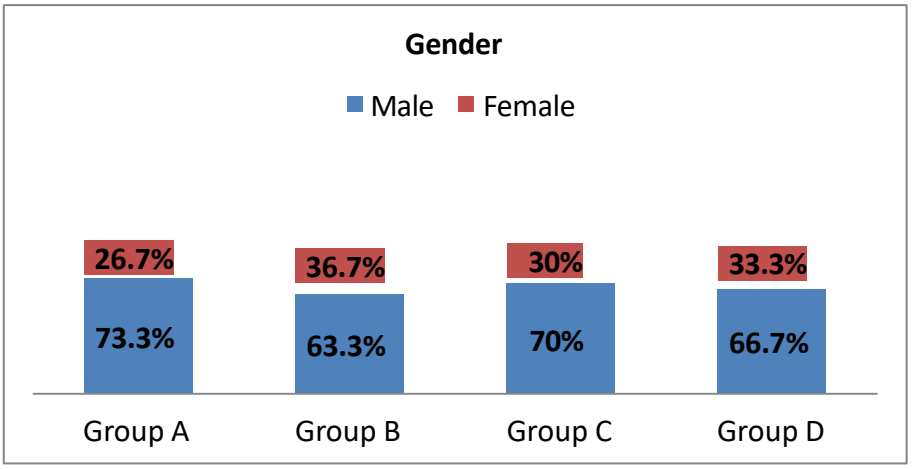

Table 2 shows the gender distribution of the subjects which consisted of 82 males and only 38 females. There was no significant difference of gender between the subjects of Group A and B; and that between Group C and D (p-values > 0.05).

Table 3: Distribution of subjects according to their imaging features

Imaging Features	Group A	Group B	Group C	Group D	Total
Unilateral Infiltrates	5 (16.7%)	4 (13.3%)	6 (20%)	5 (16.7%)	20 (16.7%)
Bilateral Infiltrates	25 (83.3%)	26 (86.7%)	24 (80%)	25 (83.3%)	100 (83.3%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
p-value	0.718		0.739		
Consolidation	7 (23.3%)	5 (16.7%)	8 (26.7%)	6 (20%)	26 (21.7%)
Interstitial Infiltrates	23 (76.7%)	25 (83.3%)	22 (73.3%)	24 (80%)	94 (78.3%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
p-value	0.519		0.542		

Chart 3: Pie chart showing distribution of subjects according to their imaging features

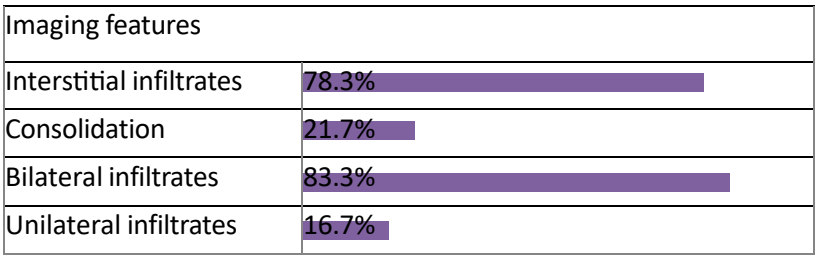

Table 3 shows the distribution of subjects according to their imaging features. The infiltrates were unilateral in only 20 subjects. The rest 80 subjects had bilateral infiltrates. Interstitial infiltrates were documented in majority (94 subjects) and consolidation in rest 26 subjects. There was no significant difference of imaging features between the subjects of Group A and B; and that between Group C and D (p-values > 0.05).

Table 4: Distribution of subjects according to Severity of disease

Severity of disease	Group A	Group B	Group C	Group D	Total
Moderate	10 (33.3%)	9 (30%)	11 (36.7%)	12 (40%)	42 (35%)
Severe	20 (66.7%)	21 (70%)	19 (63.3%)	18 (60%)	78 (65%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
p-value	0.781		0.791		

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Chart 4: Column diagram showing distribution of subjects according to Severity of disease

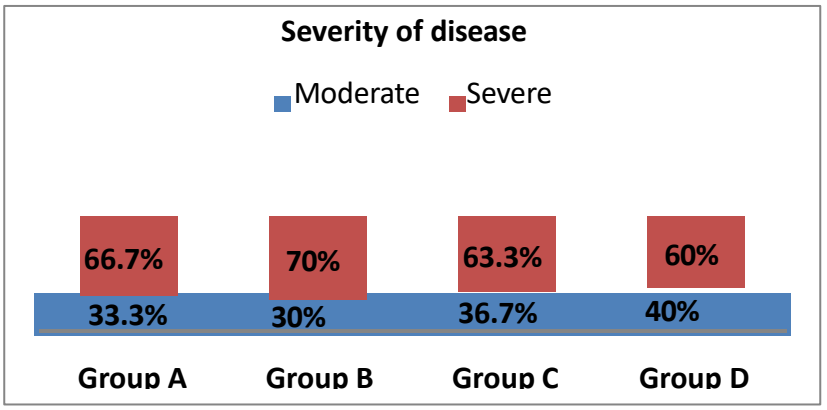

Table 4 shows the distribution of subjects according to the severity of disease. The subjects included in the current study were those with COVID-19. Majority of the subjects had severe ARDS (78 subjects). The rest 42 subjects had moderate ARDS. There was no significant difference of severity of disease between the subjects of Group A and B; and that between Group C and D (p-values > 0.05).

Table 5 : Mean PaO2/FiO2(mmHg) among study subjects

PaO2/FiO2(mmHg)	Group A	Group B	Group C	Group D	Total
Mean	168.5	145.4	140.5	107.8	140.6
SD	6.34	27.99	20.39	15.21	28.82
p-value	< 0.001		< 0.001		

CHART 5:

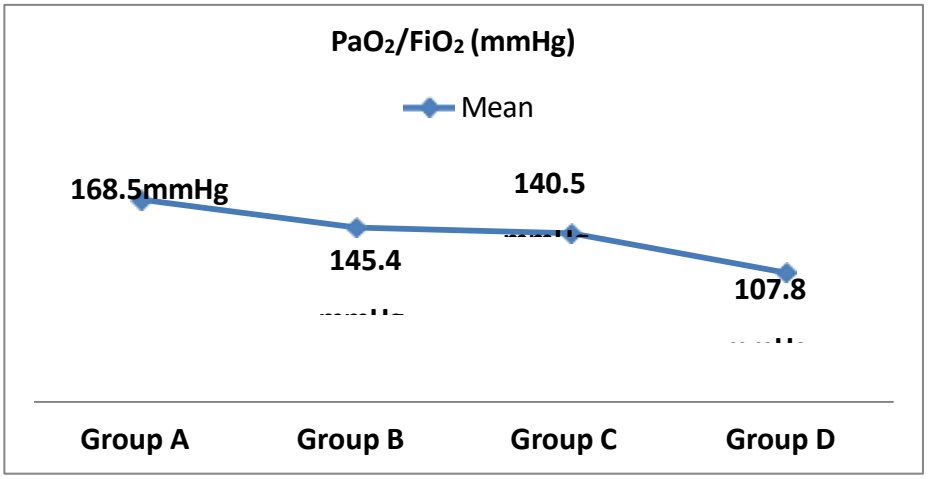

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Table 5 shows the mean values of PaO_2/FiO_2 (mmHg) among study subjects. On comparing the mean values of PaO_2/FiO_2between Group A and B subjects, the mean PaO_2/FiO_2among Group A subjects was higher (168.5 ± 6.34 mmHg) than when compared to the Group B subjects (145.4 ± 27.99mmHg) with a p value < 0.001 and was found to be statistically significant. On comparing the mean values of PaO_2/FiO_2between Group C and D subjects, the mean PaO_2/FiO_2among Group C subjects was higher (140.5 ± 20.39 mmHg) than when compared to the Group B subjects (107.8 ± 15.21 mmHg) with a p value < 0.001 and was also found to be statistically significant.

Table 6: Distribution of subjects according to intubation

Intubation	Group A	Group B	Group C	Group D	Total
Yes	0 (0%)	3 (10%)	0 (0%)	0 (0%)	3 (2.5%)
No	30 (100%)	27 (90%)	30 (100%)	30 (100%)	117 (97.5%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
p-value	0.046		-		

Chart 6: Pie chart showing the distribution of subjects according to intubation

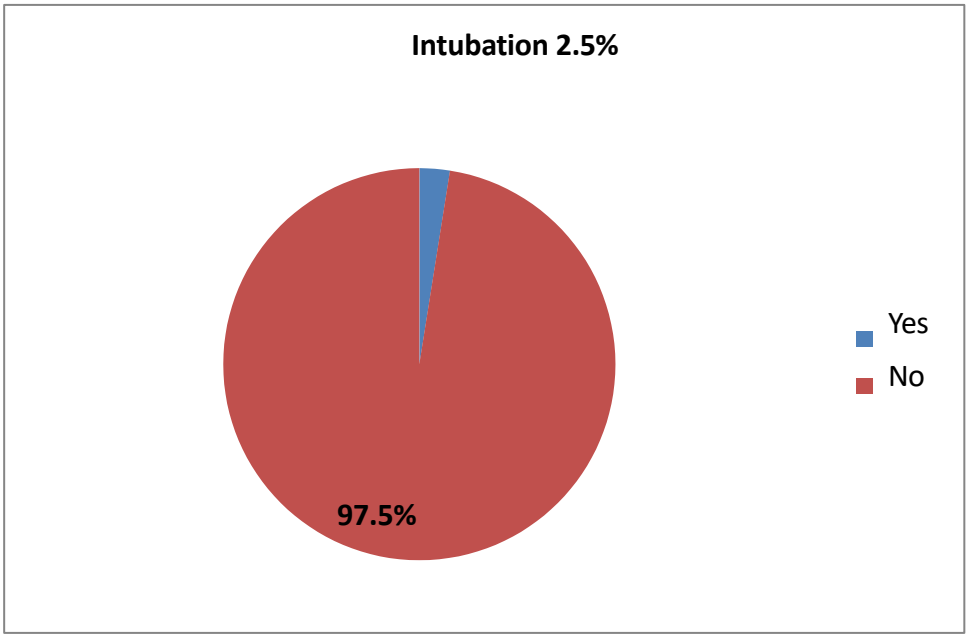

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Table 6 shows the distribution of subjects according to intubation. Among the Group B subjects, 3 subjects need intubation, while none among those from Group A in whom PP was followed needed any intubation and this found to be statistically significant with a p value of 0.046. But there was no difference observed between Group C and D subjects as none of them needed intubation.

Table 7: Mean duration of hospital stays (days)

Duration of hospital stay (days)	Group A	Group B	Group C	Group D	Total
Mean	8.9	9.2	9.0	9.3	9.2
SD	1.51	1.26	1.24	1.29	1.31
p-value	0.781		0.919		

Chart 7: Line graph showing distribution of subjects according to the mean duration of hospital stay (days)

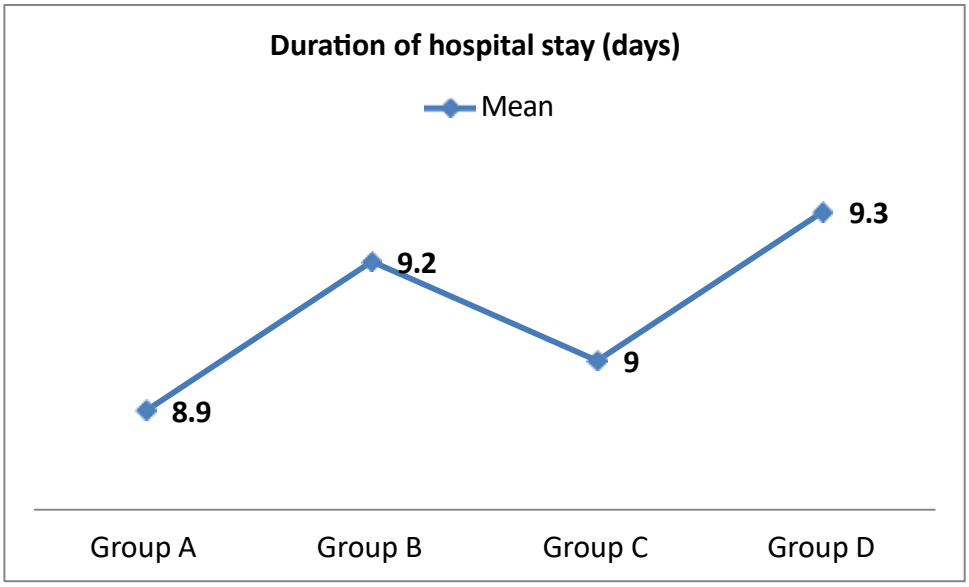

Table 7 shows the mean duration of hospital stay (days) among the study subjects. There was no statistically significant difference between the mean duration of hospital stay between the 4 groups even though the mean duration of hospital stay (9.3 ± 1.29 days) among Group D subjects was higher than that found in the other 3 groups (p value > 0.05). There was no significant difference of duration of hospital stay between the subjects of Group A and B; and that between Group C and D (p-values > 0.05)

Table 8: Distribution of subjects according to Outcome

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Outcome	Group A	Group B	Group C	Group D	Total
Death	0 (0%)	3 (10%)	0 (0%)	0 (0%)	3 (2.5%)
Discharged	30 (100%)	27 (90%)	30 (100%)	30 (100%)	117 (97.5%)
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)	120 (100%)
p-value	0.046		-		

Chart 14: Pie chart showing the distribution of subjects according to Outcome

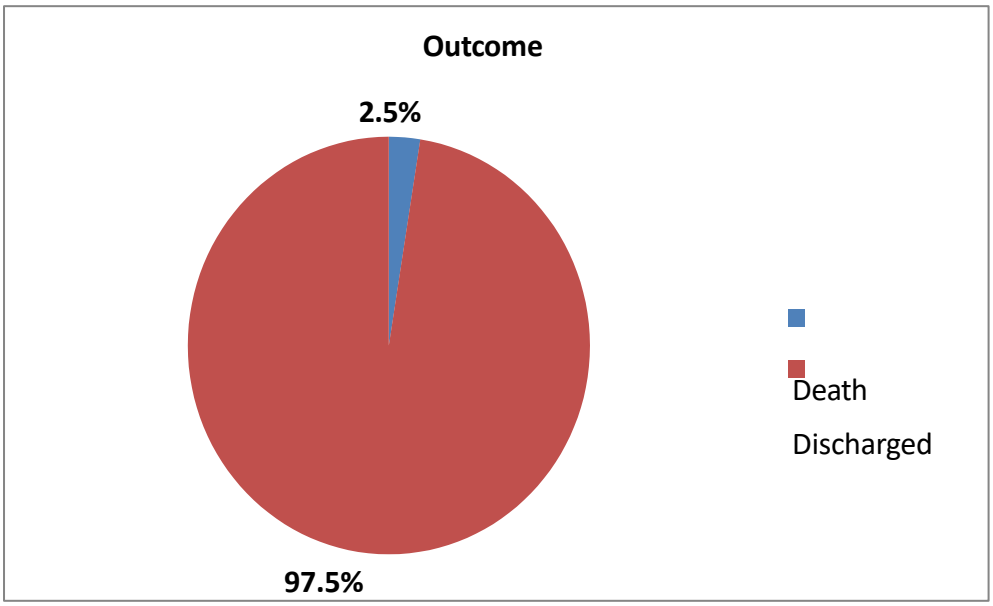

Table 14 shows the distribution of subjects according to outcome. Among the group B subjects, 3 subjects had mortality, while none among those from Group A in whom PP was followed had any mortality and were discharged and this found to be statistically significant with a p value of 0.046. But there was no difference
observed between Group C and D subjects as none of them had any mortality and all were discharged.

Discussion:

Prone positioning (PP) was first suggested as a way to enhance gas exchange in ARDS in the 1970s. Hypoxemia, bilateral lung infiltrates, and microvascular thrombosis within the pulmonary vasculature are characteristics of COVID-19 pneumonia, all of which contribute to a severe ventilation-perfusion mismatch. Therefore, COVID-19 has the same pathophysiologic traits that are pathognomonic of ARDS in its most severe form.
Patients with hypoxemic respiratory failure and COVID- 19 who are not yet intubated may benefit from Prone positioning because it can delay intubation and enhance outcomes. In moderate and severe COVID-19 ARDS, prone positioning was reported to increase lung recruitment when associated with non-invasive ventilation (NIV) and to improve oxygenation when combined with HFNC.

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COVID-19 Characteristics among the study participants:

In the current study, the infiltrates were unilateral in only 16.7% of the subjects. The rest 83.3% of the subjects had bilateral infiltrates. Interstitial infiltrates were documented in majority (78.3% subjects) and consolidation in rest 21.7% of the subjects. Majority of the subjects had severe ARDS (65% of the subjects). The rest 35% of the subjects had moderate ARDS. There was no significant difference of imaging features and severity of the disease between the subjects of 4 groups (p-values > 0.05).

There was no statistically significant difference between the mean duration from onset of illness to hospitalization between the 4 groups even though the mean duration from onset of illness to hospitalization (9.5 ± 1.68 days) among the Group C subjects was higher than that found in the other 3 groups (p values > 0.05).

The study by Iffat Khanum, et al., showed that fever (91.3%) and cough (82.6%) were the most frequent presenting symptoms, followed by shortness of breath (69.6%) and myalgia (30.4%). From the start of symptoms to hospitalisation, it took an average of 5 (4–10) days. 82.6% of patients had bilateral lung involvement with interstitial infiltrates, and 91.3% of patients (60.9%) had severe illness. All patients received normal medical care linked to COVID-19 in accordance with national recommendations, with careful consideration of any drug-specific contraindications[13]. These characteristics of the participants regarding imaging features and severity of the disease of this study were similar to those of the current study participants.[14]

Study by Davide Chiumello, et al., showed that majority of the subjects had moderate ARDS (55% of the subjects). The rest 35% and 10% of the subjects had mild and severe ARDS respectively. Six [5-10] days after the commencement of the symptoms, they were admitted to the hospital[15]. These characteristics regarding were not similar to that of the current study participants due to difference in sample size and inclusion criteria. This study included all cases of COVID-19 (mild, moderate and severe) unlike which the current study included only moderate and severe cases.

Study by Mahendra Damarla, et al., reported that median time from onset of symptoms to ICU consultation/ admission was 8.5 days (range, 5–11 d), and median time from ICU admission to PP was 5 hours (interquartile range [IQR], 2.25–13.25 h). 8 patients had bilateral lower-lobe infiltrate on chest imaging, 2 with an alveolar pattern, 3 with an interstitial pattern, and 3 with both alveolar and interstitial pattern [16].

The nationwide cohort study by Lars Engerström et al., showed that the median duration of symptoms before ICU admission was 10 (IQR 7–13) days[17].

Management of COVID-19 and duration of hospital stay among the study participants:

The current study showed that the mean durations of hospital stay among those with prone positioning (Groups A and C: 8.9 ± 1.51 days and 9.0 ± 1.24 days respectively) were higher than those without prone positioning (Groups B and D: 9.2 ± 1.26 days and 9.3 ± 1.29 days respectively) even though there was no significant difference in duration of hospital stay between the subjects of 4 groups (p-values > 0.05).

This can be justified because in the study participants who were included in the groups A and C in whom prone positioning was included in the management of COVID-19, the recovery which was aided by the physiological mechanism of prone positioning was evidently fast than when compared to the study participants who were included in the groups B and D in whom prone positioning was not included in the management of COVID-19 and hence the duration of hospital stay was lower among the groups A and C study participants than when compared to those in groups B and D study participants.

The study by Iffat Khanum, et al., showed that all the patients received COVID-19 related standard medical treatment according to National guidelines with careful evaluation of contraindications to

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any particular drug. The median length of hospital stay was 10 (5-35) days while the median length of special care stay was of 6 (4-8) days. After shifting out of special care units, patients spent a median of 4 (3-6) days in the ward before being discharged home. All patients except one were discharged in stable condition, on room air or on a minimal oxygen requirement of 1-2 litres[13].

Gad S. Gad reported that the mean duration of ICU stay was 8 ± 3 days in the PP group and 7 ± 2 days in the NIV group and the difference in the mean duration of ICU stay among the groups was not found to be statistically significant. The mean duration of hospital stay was 28 ± 5 days in the PP group and 26 ± 5 days in the NIV group and the difference in the mean duration of hospital stay among the groups was not found to be statistically significant[14]. These results were in accordance with the results of the current study.

Chiara Sartini, et al., in their cross-sectional survey showed that at the 14-day follow-up, 9 patients were discharged home, 1 improved and stopped pronation, 3 continued pronation, 1 patient was intubated and admitted to ICU, and 1 patient died[18].

Study by Mahendra Damarla, et al., reported that at 28 days of follow-up, all patients had been discharged from the hospital to their homes[16].

Effect of Prone Positioning on SpO2 and PaO2/FiO2 ratio among the study participants:

The postulated multifaceted processes for the improvement in oxygenation caused by the prone position were known from the previous literature. As well as increasing tidal and end- expiratory lung volumes, decreasing alveolar shunting, and improving ventilation-perfusion (V/Q) ratio through a more uniform distribution of ventilation, PP has been shown to assist the recruitment of alveoli in dorsal lung areas.
As better oxygenation has not been linked in previous studies to survival in ARDS, it seems doubtful that this is the only factor underlying the possible benefits of prone positioning in non-intubated patients. Reduced respiratory effort and a lower frequency of intubation could arise from homogenous lung aeration and prone positioning.
In the current study, the mean SpO2 among patients with NIV and Prone Positioning was statistically significantly higher (97.9 ± 1.02 %) than when compared to the patients with NIV without Prone Positioning (92.1 ± 10.19 %) (p value = 0.003). Also, the mean SpO2 among patients with HFNC and Prone Positioning was statistically significantly higher (96.6 ± 1.01 %) than when compared to the patients with HFNC without Prone Positioning (94.5 ± 0.90 %) (p value < 0.001). 57
This can be justified because in the study participants who were included in the groups A and C in whom prone positioning was included in the management of COVID-19, the gain in the oxygen saturation which was aided by the physiological mechanism of prone positioning was evidently at a fast pace than when compared to the study participants who were included in the groups B and D in whom prone positioning was not included in the management of COVID-19 and hence the mean SpO2 was higher among the groups A and C study participants than when compared to those in groups B and D study participants.
The mean PaO2/FiO2among patients with NIV and Prone Positioning was statistically significantly higher (168.5 ± 6.34 mmHg) than when compared to the patients with NIV without Prone Positioning (145.4 ± 27.99 mmHg) (p value < 0.001). Also, the mean PaO2/FiO2among patients with HFNC and Prone Positioning was statistically significantly higher (140.5 ± 20.39 mmHg) than when compared to the patients with HFNC without Prone Positioning (107.8 ± 15.21 mmHg) (p value < 0.001).
This can be justified because in the study participants who were included in the groups A and C in whom prone positioning was included in the management of COVID-19, the ratio of arterial oxygen partial pressure to fractional inspired oxygen which was aided by the physiological mechanism of prone positioning was evidently at a fast pace than when compared to the study participants who

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were included in the groups B and D in whom prone positioning was not included in the management of COVID-19 and hence the mean PaO2/FiO2 was higher among the groups A and C study participants than when compared to those in groups B and D study participants. Among the patients with NIV without Prone Positioning, 3 subjects needed intubation and 3 subjects had mortality, while none among those with NIV and Prone Positioning needed any intubation or had any mortality and this found to be statistically significant with a p value of 0.046. But there was no difference observed between patients with HFNC with and without Prone Positioning as none of them needed intubation nor had any mortality.

The study by Iffat Khanum, et al., showed that one patient needed to be moved to ICU for mechanical ventilation before passing away from severe ARDS. The remaining 22 patients improved gradually in terms of their oxygen needs and PF ratio, but responses varied due to the patients' varying initial levels of sickness severity. After 3-5 days of prone positioning, the majorities of patients demonstrated improvement in their PF ratio and were effectively weaned off of NIV. Patients with both mild (P=0.008) and severe illness (P<0.001) showed an improvement in the PF ratio before and after prone positioning. Those receiving PP and oxygen therapy alone, without the use of NIV, were contrasted with patients receiving PP and oxygen therapy in combination. With the exception of day 1 of PP (P=0.03), there was no evidence of statistically significant improvement in PF ratio between the two groups[13].

The study by Lin Ding, et al., showed that 12 patients were treated on HFNC+Prone position, and 7 of them needed to be escalated to NIV; 2 of those patients were given NIV+PP for further assistance. 7 patients who got NIV+Prone position afterwards could not be given HFNC. When HFNC alone failed, 1 patient needed NIV+Prone position without trying PP on HFNC. 9 patients were intubated whereas 11 patients avoided intubation. Extracorporeal membrane oxygenation (ECMO) assistance was required for 3 of the 9 intubated patients. In the entire group, only 1 patient passed away. When Prone position was added to NIV, PaO2/FiO2 was only lower in two cases, and in those two instances, HFNC+Prone position had a greater PaO2/FiO2 than NIV[19].

In study by Gad S. Gad ,the mean SaO_2 at admission 79 ± 8.47% in PP, 82 ± 7.05% in NIV, after PP or NIV applying the mean saO_2 and paO_2 was significantly increased (mean SaO_2 93 ± 5.9%, mean PaO_2 107 ± 12 mmHg)PP, (mean sao_2 95 ± 4.2%, mean PaO_2 129 ± 11 mmHg) NIV, the mean $pacO_2$ was decreased significantly in NIV (39.34 ± 5.12 mmHg) compare to PP (43.41 ± 3.2 mmHg) p value <0.001. ICU mortality is 20% in each group that requires intubation, with no real difference in length of stay in the ICU or hospital. In COVID-19 patients, awake prone positioning and non-invasive ventilation significantly reduced intubation rates while improving clinical symptoms and SaO2 and PaO2 values. NIV also performed better in patients who were hypercapnic. Regarding the outcome, among the 40 enrolled patients, 7 (18%) required endotracheal intubation and invasive mechanical ventilation, and 4 of these (53%) died within the 28 days .[14]

Study by Davide Chiumello, et al., showed that in comparison to supine, the PaO2/FiO2 was greater in PP (314 [232-398] mmHg vs. 166 [136-224] mmHg, p<0.001). In ARDS caused by COVID-19, the awake PP combined with helmet CPAP allows for a decrease in work of breathing and an increase in oxygenation[15].

Chiara Sartini, et al., in their cross-sectional survey showed that all patients experienced a decrease in respiratory rate during and after pronation (P<0.001 for both); all patients experienced an improvement in SpO2 and PaO2:FiO2 after pronation (P<0.001 for both); 12 patients (80%) experienced the same improvement in SpO2 and PaO2:FiO2; and 1 patient (6.7%) experienced a worsening. 13 patients (86.7%) had improved comfort after pronation, and 2 (13.3%) had the same value as baseline, while 11 patients (73.3%) had improved comfort during pronation and 4 (26.7%) had the same value. At the 14-day checkup, 9 patients were sent home, 1 got better and stopped

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pronating, 3 kept pronating, 1 needed an intubation and was admitted to the intensive care unit, and 1 passed away[18].

Study by Mahendra Damarla, et al., reported that the oxygenation rapidly improved after PP, and at 1 hour after assuming a PP, median oxygen saturations had increased from 94% (IQR, 91–95%) to 98% (IQR, 97–99%). After PP, work of breathing had improved, as evidenced by reduced median respiratory rate from 31 (IQR, 28–39) to 22 (IQR, 18–25) breaths/min. Patients endorsed improved dyspnoea with PP. 7 of 10 patients did not require escalation of respiratory care. 8 of 10 patients did not require intubation. The 2 patients who required intubation were intubated within 24 hours after the initial prone positioning. These two patients also had the highest respiratory support on admission to the ICU, with an FIO2 of 0.50 and 0.60 on HFNC [16].

In a nationwide cohort study by Lars Engerström et al., mortality at 30 days was 24.3%. The use of early prone increased from 8.5% in March 2020 to 48.1% in April 2021 in the study population of 1714 patients with lower admission oxygenation (PaO2/FiO2 ratio ≤ 20 kPa). Crude 30-day mortality in patients who did not receive early prone positioning was 27.2% as opposed to 30.2%. Early prone posture utilisation was not significantly associated with survival. In patients on mechanical ventilation who had severe hypoxemia at the time of ICU admission, there was no correlation between early prone placement and survival [17].

The huge percentage of COVID-19 patients who have severe hypoxemia may find great clinical benefit from prone positioning. In order to apply this procedure safely and effectively, emergency physicians should be aware of the appropriate inclusion and exclusion criteria.
Many questions remain, even if the data given here were consistent with the conclusion that prone positioning is helpful as an adjuvant therapy in COVID-19 patients with moderate to severe ARDS. How long does pronating have an effect? Does pronation continue to have a positive effect following supination? Does pronation eliminate the necessity for intubation or does it only postpone it? Could prone positioning speed up recovery? Hence, further research is needed to take up to answer these questions.

Limitations of the study

- Only one data source from a single centre made up the sample size. As a result, generalising the study's findings would be impossible.
- Convenient and limited sample size was chosen due to the feasibility considerations. Hence generalisability of the study's findings is questionable.
- Selection bias in choosing to prone position patients.
- Standardized Prone position protocol was not used, which may have led to variability in duration and frequency.
- Tolerability to Prone position was not assessed.

CONCLUSION

In some COVID-19 patients who require oxygen supplementation by NIV/HFNC, awake prone positioning seems to be safe and may prevent respiratory deterioration and maintained better SPO2 and PaO2/FiO2 ratios.
Those who are in Prone position had lesser duration of hospital stay. In turn, this might lower the demand for Invasive mechanical ventilation, reducing the pressure on ICU services globally. This straightforward, inexpensive solution may help raise the ceiling of care for patients who might otherwise have no alternative options in situations with limited resources.

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There are currently a lot of questions about how well awake prone positioning in ARDS and COVID-19 works. To determine extent to which awake prone positioning may be helpful and to identify those who may benefit from it most, high-quality research is necessary.
With such a simple intervention, there might be a temptation to act out of compassion; nevertheless, in the absence of data, it will be challenging to determine the genuine usefulness of prone positioning for upcoming pandemics.

SUMMARY

There was no significant difference of the following conditions between subjects of 4 groups (p-values > 0.05).

The mean age in the present study was 62.8 ± 11.83 years. Majority aged between 60 - 79 years (55.8%). Male preponderance was present (68.3%). Majority of the subjects were overweight (54.1% of the subjects). 26.7%were obese,17.5% of subjects had normal BMI and the rest were underweight. The infiltrates were unilateral in only 16.7% of the subjects. The rest 83.3% of the subjects had bilateral infiltrates. Interstitial infiltrates were documented in majority (78.3% subjects) and consolidation in rest 21.7% of the subjects. Majority of the subjects had severe ARDS (65% of the subjects). The rest 35% of the subjects had moderate ARDS. The mean duration from onset of illness to hospitalization was 9.3 ± 1.73 days. The mean SpO2 among patients with NIV and PP; and with HFNC and PP were statistically significantly higher than when compared to the patients with NIV without PP; and with HFNC withoutPP (p value = 0.003 and < 0.001). The mean PaO2/FiO2among patients with NIV and PP; and with HFNC and PP were statistically significantly higher than when compared to the patients with NIV without PP; and with HFNC withoutPP (p values < 0.001).

Among the patients with NIV without PP, 3 subjects needed intubation and 3 subjects had mortality, while none among those with NIV and PP needed any intubation or had any mortality and this found to be statistically significant with a p value of 0.046. But there was no difference observed between patients with HFNC with and without PP as none of them needed intubation nor had any mortality.

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