



ORIGINAL RESEARCH PAPER

Medicine

INVASIVE VERSUS NON INVASIVE POSITIVE PRESSURE VENTILATION IN ACUTE LUNG INJURY AND ACUTE RESPIRATORY DISTRESS SYNDROME: A COMPARATIVE COHORT STUDY

KEY WORDS: Intensive care unit (ICU), critically ill, acute respiratory failure, noninvasive positive pressure ventilation (NIPPV), noninvasive ventilation, treatment failure, mechanical ventilation, mortality, duration mechanical ventilation.

Dr. Ravi Singh	Post Graduate student, Department of General medicine, Jhalawar medical college, Jhalawar, Rajasthan – 326001.
Dr. Geetika Roat	Post Graduate student, Department of General medicine, Jhalawar medical college, Jhalawar, Rajasthan - 326001
Dr. Shailendra Kumar Bilonia*	Post Graduate student, Department of General Medicine, Jhalawar medical college, Jhalawar, Rajasthan -326001. *Corresponding Author
Dr. Madhuri Meena	Professor, Department of General Medicine, Jhalawar medical college, Jhalawar, Rajasthan - 326001

ABSTRACT

Background: Noninvasive positive pressure ventilation (NPPV) for acute respiratory failure in the intensive care unit (ICU) is associated with a marked reduction in intubation rate, complications, hospital length of stay and mortality. Multiple studies have indicated that patients failing NPPV have worse outcomes compared with patients with successful NPPV treatment; however limited data is available on risks associated with NPPV failure resulting in (delayed) intubation and outcomes compared with initial intubation. Aim of our study to determine mortality rate and length of hospital stay for ARDS AND ALI patients who received NIPPV and its comparison with ARDS patients on IMV and to determine the predicting factors for NIPPV failure and IMV use. **Method and study design:** This study was an analytical study. This was a comparative cohort study in which 68 patients were included prospectively. **Results:** Patients with age >60 years had poor outcomes as they needed IMV & NIPPV followed by IMV more than patients with age <60 years. Patients on IMV & NIPPV followed by IMV had a high mortality rate as compared to patients on NIPPV. **Conclusions:** Our study states that patients who were on NIPPV & got success they were having good outcomes in terms of mortality & those who failed NIPPV & required IMV got poorer outcomes.

INTRODUCTION

The first definition of Acute Respiratory Distress Syndrome (ARDS) dates to Ashbaugh and colleagues in 1967 when they described 12 patients with severe acute respiratory failure (1). These patients had severe hypoxemia that was refractory to supplemental oxygen, but which in some cases was responsive to the application of positive end expiratory pressure (PEEP). Widespread pulmonary inflammation, edema, and hyaline membranes were observed on autopsy.

Over the next 25 years several definitions were proposed, but there was no single definition for ARDS that was widely accepted and used. In 1994, broad consensus was achieved when the American-European Consensus Conference (AECC) published a definition (2). This group defined ARDS as the acute onset of hypoxemia (the ratio of partial pressure of arterial oxygen to fraction of inspired oxygen [PaO₂/FiO₂] ≤200 mmHg), with bilateral infiltrates on frontal chest X-ray, in the absence of left atrial hypertension. They also defined a new over-arching entity termed acute lung injury (ALI), which used the same variables but with a less stringent criterion for hypoxemia (PaO₂/FiO₂ ≤300 mmHg).

When the AECC definition criteria were strictly applied on a daily basis, the sensitivity remained reasonable at 84 %, but the specificity was significantly lower at only 51 % (3). Moreover, ALI, as defined using the AECC criteria, is under-recognized by clinicians, particularly the sub group of patients with milder hypoxemia (3-5).

The AECC definition requires that onset of respiratory failure be acute, but does not explicitly define the specific timeframe. The hypoxemia criterion has generated concerns because PaO₂/FiO₂ may vary with FiO₂, and also in response to other ventilator settings, particularly PEEP (6-11). The chest X-ray criterion has only moderate inter-observer reliability even when applied by experts, although this can be improved through use of a training set of radiographs (12-13). Finally, although the AECC definition includes a pulmonary artery wedge pressure (PAWP) 18 mm Hg, patients with hallmark

findings of ARDS often have an elevated PAWP because of elevated pleural pressures and/ or vigorous fluid resuscitation (14,15).

ARDS is defined by three categories based on degree of hypoxemia. These stages of mild, moderate and severe ARDS are associated with mortality risk and with duration of mechanical ventilation in survivors. (36)

SEVERITY OXYGENATION	ONSET	CHEST RADIOGRAPH	ABSENCE OF LEFT ATRIAL HYPERTENSION
Mild: 200 mmHg < PaO ₂ /FiO ₂ < 300 mmHg Moderate: 100 mmHg < PaO ₂ /FiO ₂ < 200 mmHg Severe: PaO ₂ /FiO ₂ < 100 mmHg	Acute: Within 1 week of a clinical insult or new or worsening respiratory symptoms	Bilateral opacities consistent with pulmonary edema not fully explained by effusions, lobar/segmental collapse, or nodules	Hydrostatic edema is not the primary cause of respiratory failure. If an ARDS risk factor is present, then some objective evaluation is required (e.g., echocardiography) to rule out hydrostatic edema

Etiology And Risk Factors

Of more than 50 disorders associated with the development of ARDS, sepsis, pneumonia, aspiration, trauma, and multiple blood transfusions are responsible for the majority of cases. Nearly 20% of ARDS cases have no clear risk factors. (16) Although there may be a genetic predisposition to the development and severity of ARDS, a genetic link has not been clearly established. (17-20)

The most common etiology of ARDS is sepsis, accounting for approximately 40% of cases. (21,22) Approximately 6% to 7% of patients with sepsis develop ARDS with lower rates observed among patients with non pulmonary causes and milder forms of sepsis and higher rates and worse outcomes reported among patients with septic shock. (23-26) A pulmonary source of sepsis appears to carry a higher risk of ARDS, resulting from both direct and indirect sources of ALI. (27,28) Pneumonia is also a common cause of ARDS, especially in hospitalized pneumonia patients with culture-positive microbiologic diagnosis. (29) Gram-positive and Gram-negative bacteria have similar rates of ARDS. (29) Although viral and fungal pathogens are less frequent causes of pneumonia, these pathogens are associated with a higher risk of ARDS than bacterial pneumonia; this is especially true for P. jiroveci and Blastomyces. (29) Aspiration of gastric contents is an important cause of ARDS, accounting for up to 30% of cases in some studies. (22,30) Aspiration leads to ARDS in patients more frequently and is more severe than ARDS due to other causes, with higher mortality rates (i.e., 3-fold higher). (30)

REVIEW OF LITERATURE

As per history of Acute lung injury(ALI) and Acute Respiratory distress syndrome(ARDS) described by Rubenfeld GD et al and Dowdy DW et al. Acute lung injury(ALI) and Acute respiratory distress syndrome (ARDS) are clinical syndromes of acute respiratory failure with substantial morbidity and mortality. Even in patients who survived ALI, there is evidence that their long term quality of life is adversely affected (31& 32).

Acute respiratory distress syndrome (ARDS) was first described by Ashbaugh in 1967 writing in THE LANCET. His study was based on a case series of 12 patients treated in a civilian environment in the USA. Ashbaugh states that, ARDS remains a life-threatening complication that is treated by intubation and positive pressure ventilation .When the patient's condition deteriorates resistance to mechanical ventilation increases. This reduction in lung compliance is reminiscent of the pulmonary picture in preterm neonates. Babies born before 28 weeks of gestation are unable to produce lung surfactant and develop neonatal respiratory syndrome.

ARDS has now been described as a sequelae to diverse condition such as burns, amniotic fluid embolism ,acute pancreatitis ,trauma, sepsis and damage as a result of elective surgery(1).

Patients with NIPPV failure had predominantly similar adjusted outcomes compared to patients primarily intubated without a prior trial of NIPPV. These outcomes could suggest that there are no considerable risks involved due to delayed intubation after a NIPPV trial. Length of noninvasive ventilation within 48 hours did not seem to affect mortality outcomes.

An initial trial of NIPPV therefore could be considered in patients with acute respiratory failure, since NIPPV could be potentially beneficial and does not seem to result in worse outcome in case of failure of NIPPV compared with primary intubation[33]

A study conducted by Mosier et al. in 2015 to evaluate the odds of a composite complication of intubation following failed NIPPV compared to patients intubated primarily in the medical intensive care unit (ICU). In this study a propensity-adjusted multivariate regression analysis revealed that the odds of a composite complication of intubation in patients who fail NIPPV was 2.20 (CI 1.14 to 4.25), when corrected for the presence of pneumonia or acute respiratory distress syndrome and adjusted for factors known to increase complications of intubation .When a composite complication occurred, the unadjusted odds of death in the ICU were 1.79 (95% CI 1.03 to 3.12).[34]

AIMS AND OBJECTIVE

To determine mortality rate and length of hospital stay for ARDS and ALI patients who received NIPPV and its comparison with ARDS patient on IMV .

To determine the predicting factors for NIPPV failure and IMV use.

PATIENTS AND METHODS

Study Design –

This study was a analytical study. This was a comparative cohort study in which patients were included prospectively. In this study patient of Acute Respiratory Distress Syndrome (ARDS)/Acute Lung Injury (ALI) on Non Invasive Positive Pressure Ventilation (NIPPV) were compared with patient of ARDS/ALI on Invasive Mechanical Ventilation (IMV) in terms of outcome, length of stay in hospital and predicting factors for NIPPV failure and IMV use.

Study Population-

This study was conducted at Jhalawar Medical College,

Jhalawar.

Study Duration –

This study was conducted from March 2022 to Nov 2022.

Criteria For Selection:-

Inclusion Criteria:-

All patients presented with ARDS/ALI to RICU/MICU of Jhalawar medical college, Jhalawar of age group 18yrs and above, who required MV with full resuscitation code, were included in the study.

Exclusion Criteria:-

- 1) Age < 18 years
- 2) Patients with no consent for mechanical ventilation (MV)
- 3) Acute cardiogenic pulmonary edema
- 4) Mechanical ventilation (MV) not required

METHODOLOGY:-

The present study was conducted in a rural medical college located in Jhalawar, Rajasthan. All the patients presented in Out Patient Department & emergency department were evaluated by residents of Internal Medicine under supervision of Internal Medicine faculty & admitted in RICU/MICU as per need.

The patients included in this study were divided into three groups.

Patients On:

Non invasive mechanical ventilation (NIV): patients who presented with increased respiratory rate and developed oxygen desaturation despite increasing oxygen concentration were given NIV.

Invasive Mechanical Ventilation (IMV):

Patients who presented with altered consciousness, irregular respiration, hemodynamic instability, increased secretion, high risk of aspiration, inability to protect airways, or revived after cardiac arrest, were kept on invasive mechanical ventilation.

Non invasive ventilation followed by invasive mechanical ventilation: Patients who deteriorated while on NIV, and developed complications such as cardiac arrest, encephalopathy, GIT bleed, aspiration, hemodynamic instability due to MODS etc. were shifted to IMV.

Ventilator Settings:

Non invasive mechanical ventilation: For NIV, We kept the patients on CPAP, PS, PV modes depending on the patient's requirement. Initial settings were done by the trained and experienced doctor in the intensive care unit (ICU) so that the patient can be observed closely and immediate action can be taken as and when needed. We used bi-level devices for patients who needed few hours of day time and overnight ventilation. Those patients who needed longer hours of ventilation (more than 18 hours per day), and bi-level devices were observed to be inadequate for them, we used volume targeted or hybrid devices.

Invasive Mechanical Ventilation:

Those patients who presented to the emergency department with increased secretions and poor sensorium were put on invasive mechanical ventilation. For invasive ventilation an expert doctor intubated patient with a cuffed endotracheal tube and initiated volume or pressure limited ventilation as per need. We kept tidal volume low ($\leq 6\text{ml/kg PBW}$), plateau pressure $\leq 30\text{cmH}_2\text{O}$, and respiratory rate $\leq 35\text{bpm}$. Proper oxygenation was taken care of to keep $\text{FiO}_2 \leq 0.6$ and SpO_2 88-95%.

Statistical Analysis:

All the data was analyzed through SPSS 23.0 (trial version).

Categorical variables were calculated as number and percentage. All applicable tests including chi-square were used for data analysis. Difference between groups was analyzed by chi-square test and p-value <0.05 was considered as significant in univariate analysis to identify independent risk factors for NIV failure.

RESULTS AND INTERPRETATION:

Table 1: Distribution Of Cases According To Age

	PT. ON			Total	Chi sq	P value
	NIPPV	IMV	NIPPV followed by IMV			
<60 Years	38 88.4%	0 0.0%	5 11.6%	43 100.0%	7.396	0.025*
>60 Years	18 72.0%	4 16.0%	3 12.0%	25 100.0%		
Total	56 82.4%	4 5.9%	8 11.8%	68 100.0%		

In above bar diagram, we compared distribution of cases according to age.i.e. above 60years and less than 60years in patients who were in NIPPV,IMV and NIPPV followed by IMV. Patients on IMV were 4 and all 4(100%) were having age > 60 years, Patients on NIPPV followed by IMV were 8 and out of which 5(62.5%) were having age <60 years and 3(37.5%) were having age > 60 years.

Patients on NIPPV were 56 out of which 38(67.85%) were having age <60 years and 18(32.14%). were having age > 60 year.

Patients who were >60 years of age had poor outcome as they were the once who needed IMV & NIPPV followed by IMV. All 4 patients were of >60 years who required IMV & 3 out of 8 were >60 years who required IMV after NIPPV failure.

Table 2: Distribution Of Cases According To Gender

Gen der		PT. ON			Total	Chi sq	P value
		NIPPV	IMV	NIPPV followed by IMV			
Male		32 78.0%	4 9.8%	5 12.2%	41 100.0%	2.883	0.237
	Female	24 88.9%	0 0.0%	3 11.1%			
Total		56 82.4%	4 5.9%	8 11.8%	68 100.0%		

In above bar diagram, we compared distribution of cases according to gender in patients who were in NIPPV, IMV and NIPPV followed by IMV.

Male patients on NIPPV are 32(78%), on IMV 4(9.8%) and on NIPPV followed by IMV 5(12.2%)., total of 41.

Female patients on NIPPV are 24, on IMV 0, and NIPPV followed by IMV 3, total of 27.

Gender had no significance on outcome as both male and female required NIPPV & IMV in equal amount.

Table 3: Distribution Of Cases According To Hospital Stay

Hospital Stay		PT. ON			Total	Chi sq	P value
		NIPPV	IMV	NIPPV followed by IMV			
<=5 days		29 51.8%	4 100.0%	7 87.5%	40 58.8%	6.661	0.036*
	>5 days	27 48.2%	0 0.0%	1 12.5%			
Total		56 100.0%	4 100.0%	8 100.0%	68 100.0%		

In above bar diagram, we compared distribution of cases according to hospital stay (hospital stay <=5 days />5 days) in patients who were in NIPPV,IMV and NIPPV followed by IMV. Patients on IMV were 4 out of which all 4 (100%) hospital stay was < 5 days.

Patients on NIPPV followed by IMV were 8 out of which 7 (87.50%) stayed for <5 days in hospital and 1 (12.5%) stayed for > 5 days.

Patients on NIPPV were 56 out of which 29(51.78%) stayed for < 5days in hospital and 27(48.21%) stayed for > 5 days.

Patients on IMV were 4 and all 4(100%) were stayed in hospital for less than or equal to 5 days in hospital, patients on NIPPV followed by IMV were 8 out of these 7(87.5%) were stayed for less than or equal to 5 days in hospital and only 1(12.5%) stayed for more than 5 days. These results were due to the death of patients in <=5 days.

Table 4: Distribution Of Cases According To Outcome

Status		PT. ON			Total	Chi sq	P value	
		NIPPV	IMV	NIPPV followed by IMV				
Relieved & Discharged		54 96.4%	1 25.0%	1 12.5%	56 82.4%	48.782	<0.0001*	
	Referred	1 1.8%	0 0.0%	0 0.0%				1 1.5%
	Expired	1 1.8%	3 75.0%	7 87.5%				11 16.2%
Total		56 100.0%	4 100.0%	8 100.0%	68 100.0%			

In above bar diagram ,we compared distribution of cases according to status (relieved & discharged, referred and expired) in patients who were in NIPPV,IMV and NIPPV followed by IMV.

Total 56 patients were on NIPPV out of which 54 were relieved and discharged, 1 patient referred and 1 expired.

Total of 4 patients were on IMV out of which 1 relieved and discharged and 3 expired.

Total of 8 patients were on NIPPV followed by IMV out of which 1 relieved and discharged and 7 expired.

There Chi sq value was 48.782 and P value was <0.0001

Patients on NIPPV were 56 out of which 1 got expired & 1 got referred & rest 54 got relieved and discharged. Patients on IMV were 4 and all got expired and patients on NIPPV followed by IMV were 8 and 7 got expired and 1 got referred. It clearly suggests that NIPPV was better modality than IMV.

Table 5: Distribution Of Cases According To Pulse Rate, SBP And DBP

		N	Mean	Std. Deviation	F value	P value
Pulse Rate	NIPPV	56	89.5000	12.04990	5.069	0.009*
	IMV	4	104.0000	5.16398		
	NIPPV followed by IMV	8	98.8750	4.88255		
	Total	68	91.4559	11.91817		
SBP	NIPPV	56	112.0357	14.77340	1.159	0.320
	IMV	4	101.5000	22.88376		
	NIPPV followed by IMV	8	107.5000	11.64965		

	Total	68	110.8824	14.98410		
DBP	NIPPV	56	74.0054	8.37799		
	IMV	4	65.5000	17.54043	2.004	0.143
	NIPPV followed by IMV	8	70.7500	7.77817		
	Total	68	73.1221	9.08343		

In above bar diagram , we compared distribution of cases according to pulse rate, SBP(systolic blood pressure) and DBP (diastolic blood pressure) in patients who were in NIPPV, IMV and NIPPV followed by IMV.

Total 4 patients were on IMV and there mean pulse rate was 104 i.e. tachycardia and total 8 patients were on NIPPV followed by IMV and there mean pulse rate was 98.87.

Total 56 patients were on NIPPV their mean pulse rate were 89.500, standard deviation 12.0499 , their mean Systolic B.P. were 112.03, standard deviation 14.77, their mean Diastolic B.P.were 74.00 and standard deviation 8.377.

Patients on IMV and NIPPV failure tachycardia was an important sign.

Table 6: Distribution Of Cases According To PaO2/FiO2

	PT. ON NIPPV			Total	Chi sq	P value	
	NIPPV	IMV	NIPPV followed by IMV				
PaO2/ FiO2	<100	4	2	4	14.735	0.005*	
		7.1%	50.0%	50.0%			14.7%
	100-200	19	1	2			22
		33.9%	25.0%	25.0%			32.4%
	201-300	33	1	2			36
	58.9%	25.0%	25.0%	52.9%			
Total	56	4	8	68			
	100.0%	100.0%	100.0%	100.0%			

In above bar diagram, we compared distribution of cases according to PaO2/FiO2 in patients who were in NIPPV, IMV and NIPPV followed by IMV.

Patients on IMV were 4 out of which 2 had PaO2/FiO2 ratio <100, 1 had 100-200 and 1 had 201-300. Patients on NIPPV followed by IMV were 8 out of which 4 had <100 PaO2/FiO2 ratio, 2 had 100-200 PaO2/FiO2 ratio and 2 had PaO2/FiO2 ratio 201-300. Patients on NIPPV were 56 out of which 4 had <100 PaO2/FiO2 ratio, 19 had 100-200 PaO2/FiO2 ratio and 33 were having 201-300 PaO2/FiO2 ratio.

There p value was 0.005 Patients with PaO2/FiO2 ratio <100 were having severe ARDS and patients in IMV & NIPPV followed by IMV were having 50% of patients whereas NIPPV had only 7.1% patients with PaO2/FiO2 ratio <100 .Thus, patients with severe ARDS had poor outcome.

Table 7: Distribution Of Cases According To WBC Counts

	PT. ON NIPPV			Total	Chi sq.	P value
	NIPPV	IMV	NIPPV followed by IMV			
WBC < 4 K	5	0	1	6	9.745	0.046*
	8.9%	0.0%	12.5%			
WBC 4- 11 K	33	0	2	35		
	58.9%	0.0%	25.0%			
WBC ≥ 11 K	18	4	5	27		
	32.1%	100.0%	62.5%			
Total	56	4	8	68		
	100.0%	100.0%	100.0%	100.0%		

In above bar diagram, we compared distribution of cases according to WBC Counts in patients who were in NIPPV, IMV and NIPPV followed by IMV

Total of 56 patients were on NIPPV out of which 5 patients having WBC counts <4 k, 33 were having WBC counts 4-11K and 18 patients having ≥11K.

Total 4 patients were on IMV out of which all 4 were having WBC counts ≥11K.

Total 8 patients were on NIPPV followed by IMV out of which 1 having WBC counts ≤4K, 2 having WBC counts 4-11K and 5 having WBC counts ≥11K.

Sepsis and septic shock was strongly associated with NIV failure and poor outcome.

Table 8: Distribution Of Cases According To Blood Urea, S. Creatinine And LDH

		N	Mean	Std. Deviation	F value	P value
Blood Urea (mg/dl)	NIPPV	56	48.2679	21.83782	9.741	<0.0001*
	IMV	4	100.2500	32.58195		
	NIPPV followed by IMV	8	77.6250	53.49750		
	Total	68	54.7794	30.97127		
S. Creatinine (mg/dl)	NIPPV	56	1.3321	.76250	3.761	0.028*
	IMV	4	2.3500	.17321		
	NIPPV followed by IMV	8	1.4900	.51403		
	Total	68	1.4106	.75154		
LDH (IU/L)	NIPPV	56	449.1250	261.18771	0.034	0.967
	IMV	4	474.7500	244.85557		
	NIPPV followed by IMV	8	471.0000	408.48046		
	Total	68	453.2059	276.03875		

In above bar diagram, we compared distribution of cases according to Blood urea, Serum Creatinine, LDH in patients who were in NIPPV, IMV and NIPPV followed by IMV.

Patients on IMV were 4 and their mean blood urea value were 100.25 mg/dl, patients on NIPPV followed by IMV were 8 and their mean blood urea value 77.625 mg/dl and patients on NIPPV were 56 there mean blood urea value 48.26mg/dl and P value of these data was <0.0001.

Patients on IMV were 4, their mean serum creatinine level were 2.35mg/dl ,patients on NIPPV followed by IMV were 8 , their mean serum creatinine level were 1.49mg/dl and patients on NIPPV were 56 there mean serum creatinine level were 1.33mg/dl and P value is 0.028.

Patients on IMV were 4 their mean LDH vale were 474.75 IU/L , patients on NIPPV followed by IMV were 8 ,their mean LDH value were 471IU/L and patients on NIPPV were 56 ,their mean LDH value were 449.125IU/L and P value is 0.967.

Mean blood urea was 100mg/dl of patients on IMV; mean blood urea was 77mg/dl of patients on NIPPV followed by IMV and mean blood urea was 48mg/dl of patients on NIPPV. This suggests that higher the blood urea level poorer the outcome. Mean serum creatinine was 2.3mg/dl of patients on IMV , mean serum creatinine was 1.49mg/dl of patients on NIPPV followed by IMV and mean serum creatinine was 1.33mg/dl of patients on NIPPV. This suggests that higher the serum creatinine level poorer the outcome.

Table 9: Distribution Of Cases According To Reason For IMV

REASON FOR IMV	Frequency	Percent
Severe Encephalopathy	4	5.9
Increase Secretion	6	8.8

Hemodynamic Instability due to MODS	2	2.9
NA	56	82.4
Total	68	100.0

In above bar diagram, we compared distribution of cases according to reason for IMV i.e. Invasive Mechanical Ventilation in patients who were in NIPPV, IMV and NIPPV followed by IMV.

Out of total 68 patients 12 needed IMV and out of these 12 , 4 were intubated because of severe encephalopathy, 6 were intubated because of increased secretions and 2 were intubated because of hemodynamic instability due to shock.

Out of 68 patients there were no patients of facial injury (n=0),burn(n=0), GI Bleed (n=0) ,upper airway obstruction (n=0).

Total 68 patients were studied of which 12(17.64%) were intubated. In these 12(17.64%), 6 (8.8%) were having increased secretions, 4(5.8%) were having severe encephalopathy and 2(2.9%) were hemodynamically unstable due to MODS.

DISCUSSION

In our study ARDS/ALI patients who were >60 years of age had poor outcome as they were the ones who needed IMV & NIPPV followed by IMV. All 4 patients were of >60 years who required IMV & 3 out of 8 were >60 years who required IMV after NIPPV failure. The study conducted by Laura R A Schouten et al. in ARDS patients; they investigated the association between age and mortality. Ninety day mortality rates were 30 % (63/209) in young, 37% (78/213) in middle aged and 43% (84/196) in elderly patients. Middle aged and elderly patients had a higher risk of death compared to young patients . (35) Similar prospective cohort study conducted by M R Suchyta et al in 1987 , 256 ARDS patients were included in this study. Seventy two of 112 patients older than 55 years (64%) died vs. 65 of 144 patients 55years and younger (45%) (P=0.002). Mortality rate significantly higher for patients with ARDS patients older than 55 years. (36) These studies supports our study.

In our study the patients who required IMV, there hospital stay was <5days .This was due to the fact that all the patients who ultimately required IMV were 12 and out of which 11 got expired in <5days. The similar study conducted by Meeder et al states that NIPPV success results in better survival & shorter ICU stay as in their study patients who put on IMV were having poor outcome & longer ICU stay. (27)

Our study states that patients who were on NIPPV & got success they were having good outcome in terms of mortality & who failed NIPPV & required IMV got poorer outcome. The study conducted by Chandra Stamm, Taylor et al during 1998-2000 on COPD patients demonstrates similar results. (28)

In our study patients having tachycardia i.e. heart rate >100b/m were on IMV and patients having respiratory rate >30 breath/min were mainly on IMV and NIPPV followed by IMV thus having worst outcome. Study conducted in USA in 2011 validated a model, the Lung Injury prediction score (LIPS) to identify high risk for ARDS/ALI .LIPS included tachypnea i.e.>30 breath/min as poor prognostic marker.

Another study conducted by Jun Duan, Xiaoli Han, Linfu Bai, Lingtong Zhan & Shicang Huang in 2016 to develop and validate a scale using variables easily obtained at the bedside for prediction of failure of noninvasive ventilation (NIV) in hypoxemic patients.

Patients with PaO2/FiO2 ratio <100 were having severe ARDS and patients in IMV & NIPPV followed by IMV were having 50% of patients whereas NIPPV had only 7.1% patients with PaO2/FiO2 ratio <100 .Thus, patients with severe ARDS had

poor outcome..A large observational study to Understand the global impact of Severe Acute respiratory Failure (LUNG SAFE) Study, here 2,813 patients that were diagnosed with ARDS criteria within 2 days of developing AHRF enrolled into the LUNG SAFE study, 436 (15.5%) were managed with NIV on Days 1 and 2 of ARDS, success rates of NIV in mild ARDS were 78%, this decreased to 58% in moderate and 53% in severe ARDS.

In our study patients who required IMV developed acute kidney injury (mean blood urea of 100mg/dl & mean serum creatinine 2.3mg/dl) very often with poor outcome. The similar study conducted by Johannes P C van den Akker, MahamudEgal, A B Johan Groeneveld, they included 31 studies on invasive mechanical ventilation. The pooled odd ratio for the overall effect of IMV on AKI was 3.16 (95% CI 2.32 TO 4.28, p<0.001). Nearly all subgroups showed that IMV increases risk of AKI. This study concluded that IMV is associated with a threefold increase in the odds of developing AKI. (37)

CONCLUSION

Patients with age >60 years had poor outcome as they needed IMV & NIPPV followed by IMV more than patients with age <60 years.

Patients on IMV & NIPPV followed by IMV had hospital stay of <5 days.

Patients on IMV & NIPPV followed by IMV had high mortality rate as compared to patients on NIPPV.

Patients on IMV and NIPPV failure had mean pulse rate of >100 beat/min. Tachycardia is associated with poor outcome in IMV and NIPPV failure.

Total 4 patients were on IMV out of which all 4 were having WBC counts ≥11K. Total 8 patients were on NIPPV followed by IMV out of which 1 having WBC counts ≤4K, 2 having WBC counts 4-11K and 5 having WBC counts ≥11K. Sepsis and septic shock was strongly associated with NIV failure and poor outcome.

Patients on IMV & NIPPV followed by IMV were having 50% of patients with PaO2/FiO2 ratio <100 i.e. severe ARDS, whereas NIPPV had only 7.1% patients with PaO2/FiO2 <100.

Patients on IMV mean blood urea was 100mg/dl, patients on NIPPV followed by IMV mean blood urea was 77mg/dl and patients on NIPPV mean blood urea was 48mg/dl.

Patients on IMV mean serum creatinine 2.3mg/dl, patients on NIPPV followed by IMV mean serum creatinine 1.49mg/dl and patients on NIPPV mean serum creatinine 1.33mg/dl.

Total 12(17.64%) patients were intubated out of which 6 (8.8%) were having increased secretions, 4(5.8%) were having severe encephalopathy and 2(2.9%) were hemodynamically unstable due to MODS.

REFERENCES

1. Ashbaugh D.G., Bigelow D.B., Petty I.L. et al. Acute respiratory distress in adults Lancet 1967.
2. G.R. Bernard, A. Artigas, KL Brigham, J. Carlet-K. Folke et al American European Consensus Conference 1994
3. Ferguson ND, Frutos-Vivar F, Esteban A, Fernandez-Segoviano P, Aramburu JA, Na'jera L, Stewart TE (2005) Acute respiratory distress syndrome: under recognition by clinicians and diagnostic accuracy of three clinical definitions. Crit Care Med 33:2228-2234
4. Kalhan R, Mikkelsen M, Dedhiya P, Christie J, Gaughan C, Lancken PN, Finkel B, Gallop R, Fuchs BD (2006) Underuse of lung protective ventilation: analysis of potential factors to explain physician behavior. Crit Care Med 34:300-306.
5. Rubenfeld GD, Cooper C, Carter G, Thompson BT, Hudson LD (2004) Barriers to providing lung-protective ventilation to patients with acute lung injury. Crit Care Med 32:1289-1293
6. Villar J, Perez-Mendez L, Kacmarek RM (1999) Current definitions of acute lung injury and the acute respiratory distress syndrome do not reflect their true severity and outcome. Intensive Care Med 25:930-9357.

7. Gowda MS, Klocke RA (1997) Variability of indices of hypoxemia in adult respiratory distress syndrome. *Crit Care Med* 25:41-4
8. Ferguson ND, Kacmarek RM, Chiche J-D, Singh JM, Hallett DC, Mehta S, Stewart TE (2004) Screening of ARDS patients using standardized ventilator settings: influence on enrollment in a clinical trial. *Intensive Care Med* 30:1111-1116.
9. Villar J, Perez-Mendez L, Lopez J, Belda J, Blanco J, Saralegui I, Suarez-Sipmann F, Lopez J, Lubillo S, Kacmarek RM (2007) An Early PEEP/ FIO2 trial identifies different degrees of lung injury in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 176:795-80423.
10. Aboab J, Louis B, Jonson B, Brochard L (2006) Relation between PaO₂/FIO₂ ratio and FIO₂: a mathematical description. *Intensive Care Med*
11. Britos M, Smoot E, Liu KD, Thompson BT, Checkley W, Brower RG, National Institutes of Health Acute Respiratory Distress Syndrome Network Investigators (2011) The value of positive end-expiratory pressure and Fio₂ criteria in the definition of the acute respiratory distress syndrome. *Crit Care Med* 39:2025-2030
12. Rubenfeld GD, Caldwell E, Granton JT, Hudson LD, Matthay MA (1999) Interobserver variability in applying a radiographic definition for ARDS. *Chest* 116:1347-1353
13. Meade MO, Cook RJ, Guyatt GH, Groll RJ, Kachura JR, Bedard M, Cook DJ, Slutsky AS, Stewart TE (2000) Interobserver variation in interpreting chest radiographs for the diagnosis of acute respiratory distress syndrome. *Am J Respir Crit Care Med* 161:85-90
14. Ferguson ND, Meade MO, Hallett DC, Stewart TE (2002) High values of the pulmonary artery wedge pressure in patients with acute lung injury and acute respiratory distress syndrome. *Intensive Care Med* 28:1073-1073
15. National Heart Lung and Blood Institute Acute Respiratory Distress Syndrome ARDS Clinical Trials Network, Wheeler AP, Bernard GR, Thompson BT, Schoenfeld D, Wiedemann HP, deBoisblanc B, Connors AF, Hite RD, Harabin AL (2006) Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med* 354:2213-2224
16. Eworuke E, Major JM, Gilbert McClain LI. National incidence rates for acute respiratory distress syndrome (ARDS) and ARDS cause-specific factors in the United States (2006-2014). *J Crit Care*. 2018;47:192-197.
17. Marshall RP, Webb S, Hill MR, Humphries SE, Laurent GJ. Genetic polymorphisms associated with susceptibility and outcome in ARDS. *Chest*. 2002;121(3 suppl):68S-69S.
18. Marshall RP, Webb S, Bellingan GJ, et al. Angiotensin converting enzyme insertion/deletion polymorphism is associated with susceptibility and outcome in acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2002;166(5):646-650.
19. Copland IB, Kavanagh BP, Engelberts D, McKerlie C, Belik J, Post M. Early changes in lung gene expression due to high tidal volume. *Am J Respir Crit Care Med*. 2003;168(9):1051-1059.
20. Grigoryev DN, Finigan JH, Hassoun P, Garcia JGN. Science review: searching for gene candidates in acute lung injury. *Crit Care*. 2004;8(6):440.
21. Hudson LD, Milberg JA, Anardi D, Maunder RJ. Clinical risks for development of the acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 1995;151(2 pt 1):293-301.
22. Pepe PE, Potkin RT, Reus DH, Hudson LD, Carrico CJ. Clinical predictors of the adult respiratory distress syndrome. *Am J Surg*. 1982;144(1):124-130.
23. Mikkelsen ME, Shah CV, Meyer NJ, et al. The epidemiology of acute respiratory distress syndrome in patients presenting to the emergency department with severe sepsis. *Shock*. 2013;40(5):375-381.
24. Gajic O, Dabbagh O, Park PK, et al. Early identification of patients at risk of acute lung injury: evaluation of lung injury prediction score in a multicenter cohort study. *Am J Respir Crit Care Med*. 2011;183(4):462-470.
25. Ferguson ND, Frutos-Vivar F, Esteban A, et al. Clinical risk conditions for acute lung injury in the intensive care unit and hospital ward: a prospective observational study. *Crit Care*. 2007;11(5):R96.
26. Fein AM, Calalang-Colucci MG. Acute lung injury and acute respiratory distress syndrome in sepsis and septic shock. *Crit Care Clin*. 2000;16(2):289-317.
27. Pelosi P, D'Onofrio D, Chiumello D, et al. Pulmonary and extrapulmonary acute respiratory distress syndrome are different. *Eur Respir J Suppl*. 2003;42:48s-56s.
28. Sheu CC, Gong MN, Zhai R, et al. The influence of infection sites on development and mortality of ARDS. *Intensive Care Med*. 2010;36(6):963-970.
29. Kojacic M, Li G, Hanson AC, et al. Risk factors for the development of acute lung injury in patients with infectious pneumonia. *Crit Care*. 2012;16(2):R46.
30. Lee A, Festic E, Park PK, et al. Characteristics and outcomes of patients hospitalized following pulmonary aspiration. *Chest*. 2014;146(4):899-907.
31. Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, Stern EJ, Hudson LD. Incidence and outcomes of acute lung injury. *N Engl J Med*. 2005;353:1685-169
32. Dowdy DW, Eid MP, Dennison CR, Mendez-Tellez PA, Herridge MS, Guallar E, Pronovost PJ, Needham DM. Quality of life after acute respiratory distress syndrome: a meta-analysis. *Intensive Care Med*. 2006;32:1115-1124.)
33. Meeder et al. Noninvasive ventilation for acute respiratory failure. *Journal of Thoracic Disease*, Vol 8, No 5 May 2016
34. Mosier et al. *Annals of Intensive Care* (2015) Failed noninvasive positive-pressure ventilation is associated with an increased risk of intubation-related complications Jarrod M DOI 10.1186/s13613-015-00441
35. Harrison's principles of internal medicine 21st edition.
36. Schouten LRA, Bos LDJ, SerpaNeto A, van Vught LA, Wiewel MA, Hoogendijk AJ, et al. Increased mortality in elderly patients with acute respiratory distress syndrome is not explained by host response. *Intensive Care Med Exp*. 2019;7:58. doi:10.1186/s40635-019-0270-1..
37. Suchyta MR, Clemmer TP, Elliott CG, Orme JF, Morris AH, Jacobson J, et al. Increased mortality of older patients with acute respiratory distress syndrome. *Chest*. 1997;111(5):1334-1339. doi:10.1378/chest.111.5.1334.