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Clinical profile and outcome in critically ill patients with respiratory failure on invasive mechanical ventilator

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Abstract
Background: Mechanical ventilation plays an important role in the management of critically ill patients with respiratory failure. However, survival among ventilated patients depends on the primary disease and its management.
Aims: To study the clinical profile, outcome and complications in critically ill patients on invasive mechanical ventilators admitted in the MICU.
Methods: A prospective study was carried out in SSG Hospital, Vadodara from 2nd July 2011 to 5th December 2012 and 155 adult patients aged >12 years requiring IMV >48hours were enrolled. Detailed history, clinical examination, and Investigations were carried out and patients were followed up until discharge or death. Pre-intubation Sequential Organ Failure Assessment (SOFA) score and Arterial Blood Gas analysis (ABGA) were done and repeated on follow-up.
Results: According to this study, 67% of the patients (104/155) belonged to the most productive age (15-44) group. However, the least mortality (17.86%) was noted in 15-29 age group. Mortality rates were higher in older age groups (50% in both 40-59years and 65+ years). Organophosphorus (OP) poisoning was the major indication for IMV (105/155 patients) but was associated with lower mortality rates (26.67%). A higher mortality rate of 41.17% was noted in ARDS group. Pre-ventilation SOFA scores had high sensitivity in predicting mortality in OP cases. Score >7 had a poor prognosis. However, there was no role of SOFA score in Malarial ARDS as thrombocytopenia was observed. Higher complications were seen in patients requiring IMV >7days (39.6% had Vocal cord edema and 28.30% has VAP).
Conclusion: Early diagnosis and management of primary disorders leading to respiratory failure prevents the complications and improves the outcome of the patient. The goal of IVM therapy is to overcome the crisis and once it is resolved, early weaning prevents further complications.

Keywords: mechanical ventilation, SOFA scores, ventilation associated complications

1. Introduction
Invasive mechanical ventilation (IMV) has become an essential tool in resuscitation and comprehensive treatment of critically ill patients who cannot breathe spontaneously or in case of compromised respiration due to severe illness or trauma. IMV tides over the crisis, eliminate the need of unplanned intubation, emergency tracheostomy and associated post tracheostomy care and nursing issues. IMV is employed in acute respiratory failure resulting from varied etiologies. Once the crisis is resolved, IMV has to be weaned off as prolonged IMV is associated with complications like ventilator associated pneumonia, Barotrauma, etc. ICU clinicians work towards the goal of successfully weaning patients on a daily basis while aiding spontaneous breathing trial if patient is hemodynamically stable and complications are resolved. This study's purpose is to determine outcome of patient on invasive mechanical ventilation in medical intensive Care unit at S.S.G.H, Baroda.

2. Materials and Method
This study was carried out in Medicine Department of SSG Hospital which is a tertiary care hospital, Vadodara from 2nd July 2011- 5th December 2012. 155 patients of various etiologies like Organophosphate poisoning (OP), Guillain–Barre Syndrome (GBS), Tetanus, Chronic Obstructive Pulmonary Disease(COPD), Acute Respiratory Distress Syndrome (ARDS), Eclampsia, Snakebite, Viral Encephalitis (VE), Cerebral malaria (CM), Cerebrovascular stroke (CV), Dilated Cardiomyopathy (DCM) requiring invasive ventilator >48 hours were included in study.
Informed written consent was taken from the patients or their relatives requiring Invasive Mechanical Ventilation (IMV). Patients less than 12 years of age, those on Non –Invasive Ventilation (NIV), and those requiring mechanical ventilation for less than 48 hours were not included in our study. In all the patients, a diagnosis was made on basis of history, clinical examination, and investigations. Pulse rate (PR), respiratory rate (RR), mean arterial blood pressure (MBP), Glasgow coma scale (GCS, pre-intubation), daily urine output were recorded. Arterial Blood Gas Analysis (ABGA), Sequential Organ Failure Assessment Score (SOFA), serum electrolytes were done before the initiation of ventilation and were repeated post-ventilation (30mins to 2 hours). Daily ABGA, S. creatinine, S. urea, S. Bilirubin, S. transaminases, complete blood counts (CBC) were done for 3 days. Percutaneous Dilatation technique for tracheostomy was used when

required. ABG analysis was done using an AVL -995S Auto-analyser.

SOFA score is used to determine the rate and the extent of organ failure in patients admitted to the Intensive Care Units in the first 24-48 hours. It includes following components:

Table 1: SOFA scores

System	Determinants	SOFA score 0	SOFA score 1	SOFA score 2	SOFA score 3	SOFA score4
Respiratory System	PaO_2/FiO_2 (mmHg)	≥ 400	<400	<300	<200 & mechanically ventilated	<100& mechanically ventilated
Central Nervous System	Glasgow Coma Scale	15	13-14	10-12	6-9	<6
Cardiovascular System	Mean Arterial Pressure (MAP) or Vasopressors administered	MAP ≥ 70mm Hg	MAP<70 mm Hg	Dopamine ≤ 5 µg/kg/min orDobutamine (any dose)	Dopamine > 5 µg/kg/min or Epinephrine ≤ 0.1 µg/kg/min or Norepinephrine ≤ 0.1 µg/kg/min	Dopamine > 15 µg/kg/min or Epinephrine > 0.1 µg/kg/min or Norepinephrine > 0.1 µg/kg/min
Liver	Bilirubin levels (mg/dl)	< 1.2	1.2–1.9	2.0–5.9	6.0–11.9	> 12.0
Coagulation Profile	Platelet Count (platelet $*10^3$ / µl)	≥ 150	< 150	< 100	< 50	< 20
Renal System	Creatinine (mg/dl)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0

Standard treatment policies as per hospital protocol were followed. For the purpose of the study, following data were recorded:

1) Total number of days on ventilator
2) Duration of hospital stay

The endpoint of our study was discharge from the hospital or death.

Out of all patients admitted to the Medical Intensive Care Unit (MICU), 155 patients fulfilled the inclusion criteria and were enrolled in the study.

Patients were divided into two groups based on the duration of IMV:

- Group 1- IMV required for <7 days.
- Group 2- IMV required for > 7 days.

Group 1 and 2 were further classified based on the outcome as survivors and non-survivors.

Various parameters like age, SOFA score, heart rate (B.HR) were recorded for all the cases of OP, ARDS, snake bite, GBS, tetanus, and COPD. Long-term follow-up of patients was not a part of our study design.

3. Statistical Analysis

Data collected was analyzed using SPSS 10.0 statistical software. Data was described in form of mean plus SD (standard deviation). Clinical and laboratory parameters and outcomes were compared in two groups using Mann Whitney U test. A similar test was applied between survivors and non-survivors to define mortality predictors. Confidence limit for significance was kept at $p<0.005$ i.e. 95% confidence interval.

4. Results

110 out of 155(70.96%) patients survived and eventually discharged. None of the survivors had any residual disability at the time of discharge.

Table 2: Data of Survivors and Non survivors in the study groups

Groups	Total no. of patients in subgroup	Subgroups	No. of Patients
Group 1: IMV<7 days	95	Survivors	57
		Non-survivors	38
Group 2: IMV>7 days	60	Survivors	53
		Non-survivors	7
Total	155		155

In group1 out of 95 patients, 57patients (60%) survived while in group 2 out of 60 patients, 53 (88%) survived.

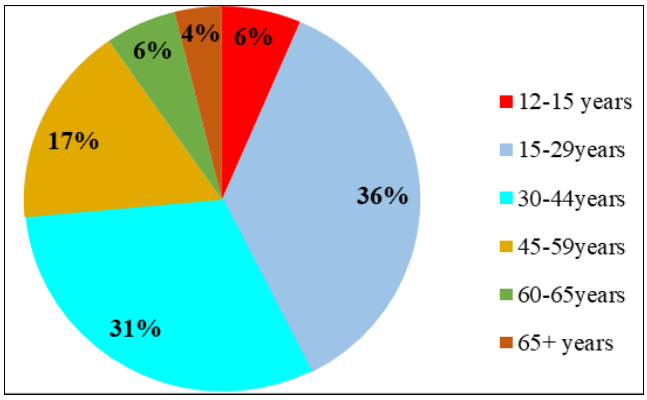

Fig 1: Age distribution

4.1 Age distribution

- The highest number of patients belonged to 15-29 years of age i.e. 36% of the entire sample.
- 31% patients (30-44years) constitute the second highest cluster in which IMV was indicated.
- Only 4% patients in >65+ years required IMV. (This can be attributed to less number of cases and not significant.) This figure (3.1) implies that IMV support was required in the most productive age group (15-44 years).

4.2 Age distribution and mortality

Table 3: Mortality and Survival rates in different Age groups

Age groups	No. of Pts (N=155)	Deaths (N=45)	Mortality rate (%)	Survivors (N=110)	Survival Rate (%)
12-15years	10	6	60	4	40
15-29 years	56	10	17.86	46	82.14
30-44 years	48	10	20.84	38	79.16
45-59 years	26	13	50	13	50
60-65years	9	3	33.33	6	66.67
65+	6	3	50	3	50

As shown in the table, 6 out of 10 patients died in 12-15 years of age group. Although the highest number of patients requiring IMV belonged to 15-29 years of age, the mortality rates were lowest (17.86%).50% mortality rates were noted in both 40-59 years and 65+ year age group.

4.3 Distribution of patients according to various etiologies

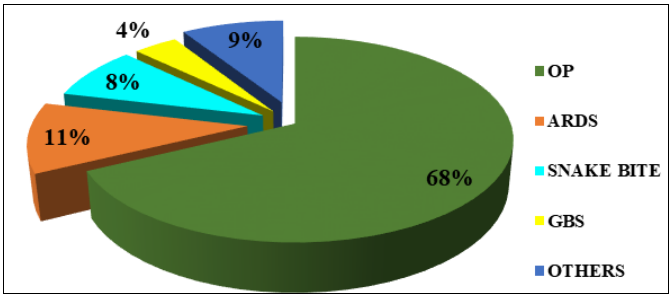

Fig 2: Patient distribution based on Etiologies

Majority of patients with OP poisoning, i.e. 105/155 patients, required IMV in our study. In our setting, malaria was the most common cause of ARDS (17 patients) which constitutes the second largest group requiring IMV >48hours. 13 patients of snake bite and 6 patients of GBS were the 3rd and 4th common causes requiring IMV in our study group. Others group consists of: Tetanus (4patients), COPD (3patients), Eclampsia (2 patients), VE (1 patient), cerebral malaria (2), DCM (1), CV stroke (1).

4.4 Relationship between diagnostic group and mortality rates

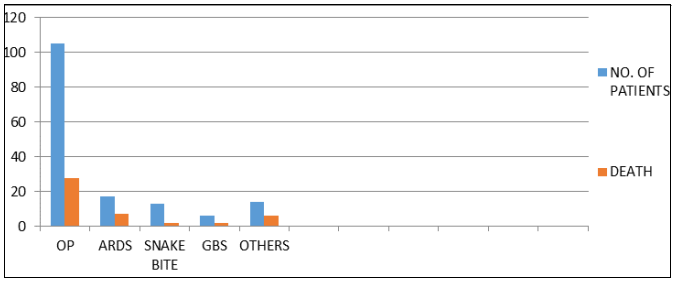

Fig 3: Mortality rates in different etiologies

Patients with OP poisoning constitute the largest diagnostic group which required IMV for >48hours but with a mortality rate of 26.66% suggesting the beneficial outcome of IMV.
ARDS was the 2nd *most* prevalent cause with a high mortality rate of 41.17%.
Patients with snake bite were highly benefitted with IMV as 11 out of 13 patients survived with the *least* mortality rate of 15.38%.
2 out of 4 patients of Tetanus and 1 out of 3 COPD cases died.
No mortality was recorded in CM, VE, DCM cases.

Table 4: Cause Specific Mortality Rates

Indication for IMV	No. of Patients	Death	Cause-specific mortality Rate (%)
OP	105	28	26.67
ARDS	17	7	41.17
Snakebite	13	2	15.38
GBS	6	2	33.33
Others	14	6	-

4.5 Mean and standard deviation of different parameters in OP, ARDS, GBS, SB based on their outcome from IMV

Table 5: Mean and SD values of different parameters amongst survivors and nonsurvivors

Diagnostic group	No. of patients	SURVIVORS[mean+/-SD]				No survivors [mean+/-SD]			
		AGE(years)	SOFA	B. HR	S.CH	AGE	SOFA	B.HR	S.CH
Organophosphate poisoning	105	31.97+-12.98	6.16+-1.20	68.50+-18.95	1690+-2061.95	39.32+-14.06	8.5+-1.37	66.16+-11.63	1670+-1928.22
ARDS	17	39.70+-20.05	9.30+-3.23	98.85+-20.74	--	38.00+-23.40	9.28+-2.13	105.9+-17.00	--
Snakebite.	13	26.72+-11.22	5.27+-0.78	79.45+-3.35	--	37.50+-17.67	11.00+-5.65	84.00+-5.65	--
GBS	6	30.50+-15.95	5.5+-0.57	103+-19.48	--	14.50+-0.70	7.5+-0.70	94.00+-22.62	--

105 patients of OP poisoning admitted in MICU were included in our study. Frequent clinical signs in these patients were miosis, excessive sweating, hyper salivation, vomiting, bradycardia, and neuromuscular weakness. By comparing the two groups, we infer that pre-ventilation SOFA score had high sensitivity in predicting the probability of mortality in OP cases. Score >7 was a predictor for worse outcome. Stepwise logistic regression analysis showed that SOFA score is the most powerful predictor of the outcome of IMV and an increase in score by 1 significantly increases mortality. This is also supported by Spearman's ranked correlations. Other variables, when compared in both groups, didn't show any statistical significance.
Similarly, in 17 patients with ARDS, age and B. HR compared

in two groups showed no significance. SOFA scores were decreased in group 2 as compared to group 1. Platelet count was a part of the SOFA score. In our study, malaria was the common condition leading to ARDS. Moreover, thrombocytopenia is seen in malaria. And so the SOFA scores are low in severe malaria. So, this is statistically insignificant. Therefore, it should not be used as a prognostic indicator in malarial ARDS.

Majority of patients of snake bite were males (12 out of 13) who belonged to 13-50 years of age. There was no statistically significant effect of age on outcome of IMV. B. HR was increased in group 2 as compared to group 1 but was insignificant. *SOFA scores are* highly increased in group 2 as compared to group 1.

Out of 6 patients with GBS, mean age comparison in both groups showed no significance. B. HR on admission time was decreased in group 2 as compared to group 1 but was found insignificant. SOFA scores were highly increased in group 2.

4.6 Monitored variables and modes of ventilation in patients

Table 6: Mean and SD of various parameters monitored on different modes of ventilation

Diagnostic groups	SIMV (Synchronized Intermittent Mechanical Ventilation)			IPPV (Intermittent positive pressure ventilation)			RR (Mean, SD)	FIO2 Mean, SD)	PEEP (Mean, SD)	P_{IP} (CmH$_2$O)	MV (L/M)	PIF (L/M)
	Survivors IMV <days	Survivors IMV> 7days	Non survivors	Survivors IMV< 7days	Survivors IMV > 7days	Non survivors						
OP	38	39	28	--	--	--	14.01 (0.19)	46.34(15.07)	5(0.0)	10-30	6-10	40-60
ARDS	07	03	06	--	--	01	20.23(2.22)	97.64(9.70)	8.94(1.02)	12-20	6-10	44-60
Snakebite	08	03	02	--	--	--	14	44.61(16.64)	5	11-24	6-10	44-55
GBS	01	03	02	--	--	--	14.0(0.00)	43.33(8.16)	5(0.0)	13-17	6-8.3	40-60
*Tetanus	--	--	--	00	02	02	14(0.0)	45(10.00)	5(0.0)	12-16	7-10	50-55
COPD	--	--	--	01	--	02	16(2.82)	80(28.28)	8(0.0)	14-24	6-10	50-56
Eclampsia	00	--	01	--	--	01	14	60	5	13-16	7-10	48-60
V E	--	--	--	00	01	00	14	60	5	12-14	8-10	50-52
C M	--	--	--	01	01	00	14	40	5	14-16	7-7.5	50-60
D C M	01	00	00	--	--	--	18	100	8	12-14	8-8.5	45-50
C V Stroke	00	00	01	--	--	--	16	40	5	14-16	9-10	50-52

*It is evident from the data that the tetanus patients were the only group which required IPPV with higher FiO2, PEEP, PIP, IMV, and PIF.
[FiO_2: Fraction of inspired oxygen; PEEP: Positive end-expiratory pressure; P_{IP}: Peak Inspiratory pressure; MV: Minute Ventilation; PIF: Peak Inspiratory Flow].

4.7 Complications of patients based on the duration of mechanical ventilation

Table 6: Various complications observed in both groups on IMV

Complications	Group1(57)	Group2 (53)
Vocal cord edema	0	21
VAP (Ventilator associated pneumonia)	6	15
Barotraumas	0	2
DVT(Deep Vein Thrombosis)	1	3
Thrombophlebitis	0	12
Other systemic complications.	0	1

As per above data representation, 30% patients suffered from major complications. Group 1 had lesser complications (VAP, deep vein thrombosis) than Group B [vocal cord edema, VAP, Barotraumas, DVT, Thrombophlebitis and Other systemic complications]. Amongst group B, vocal cord edema had the highest prevalence & occurred in 39.62% patients, followed by VAP which prevailed in 28.30% patients.

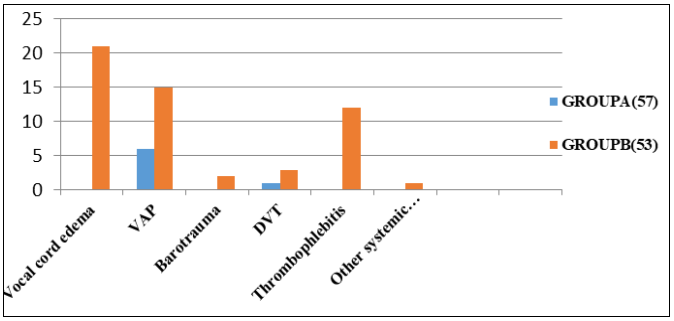

Fig 4: Comparison of incidence of complications in both groups represented by bar diagram

Table 7: Causative microbes in VAP in both group

Organisms	Group 1	Group2
Klebsiella pneumoniae	04	04
Pseudomonas	02	04
Staphylococcus Aureus	00	07

Polymicrobial organisms are known to cause VAP. In group 1 Klebsiella *Pneumoniae* was the most common organism; whereas, in group 2 Staphylococcus *Aureus* was commonest organism.

5. Discussion

Out of 6 prospective cohort studies [1, 2, 4, 6, 21, 22] which evaluate the effect of age on the outcome of patients treated with mechanical ventilation, 5 [2, 4, 6, 21, 22] found that age was independently associated with mortality. Ely *et al.* [1] studied 300 mechanically ventilated patients admitted to ICU and found 38.1% mortality rate in age >75 years and 38.8% among younger patients. However, in our study, younger age group mortality was 17.88% and older age group was 50%. 6 out of 10 patients in 12-15 years age group died. This explains the effect of age as an independent factor on the outcome of mechanical ventilation in the extremes of age (very young and very old).

In our study, more than 61% males received mechanical ventilation. Similar results were reported in other studies like Behrendt *et al.* [2] and Esteban *et al.* [3] However, in other multivariate analyses in patients with similar severity of illness and a similar number of organ derangements before IMV, a greater mortality rate was found in females (Kollef *et al.* [4]). Studies by Epstein and Vyoung *et al.* [5] and Luhr *et al.* [6] reported that sex was not independently associated with mortality. In our study, considering all the baseline parameters and time-dependent factors, we conclude that there is no association of sex with mortality.

Etiology determines the prognosis in many cases like OP poisoning where prognosis is known to be good as per many studies. Various studies have addressed the outcome of IMV for a specific etiology. Very few multivariate cohorts have been undertaken to study outcomes of IMV from various etiology [6, 7]. The mortality rate in these studies was found to be 30-40%. The mortality rate in our study was 29.03% after receiving IMV for >48hours. This is similar to Jimenez *et al.* [8] (28%). This necessitates the availability of prediction scores before performing IMV to predict the outcome of IMV. So SOFA scores should be used in such cases. Lower the score, better the outcome on weaning, and vice versa.

OP poisoning was the major indication (105/155) for IMV in our study and it was evident that 66% victims were younger or adult aged (13-29 years). This is comparable to 83% reported by Chaudhary *et al.* [9], Thomas *et al.* [10] and Dickson *et al.* [11] Easy availability of pesticides and socioeconomic factors may be the cause. Younger population is relatively more affected and this can be due to occupation (farming), rural population, joint family pressure as compared to elderly, lesser maturity, etc.(Roberts *et al.* Eddleston *et al.*) [12, 13]. Our study shows a mortality rate of 26.66%, which is in agreement with case series reported on OP poisoning and ICU management by Rauf *et al.* [14] Also, the survival rate of 73.33% is comparable with that of Shaikh *et al.* [15] The most frequent signs reported in our study were miosis, excessive salivation, respiratory muscle weakness, proximal and distal muscle weakness and bradycardia. To conclude, Pre-ventilation SOFA score is the single most important factor which predicts prognosis in OP cases.

ARDS was the 2nd most common indication for IMV. Hypoxemia severity and its progression are factors deciding prognosis. In our study, the mortality rate was 41.17% which is much lower than Hudson *et al.* [16] where the most important cause was sepsis. This is because of the fact that malaria is the common cause of ARDS in our area. Early diagnosis and prompt management of underlying etiology result in quick resolution of ARDS and early weaning from IMV and hence lesser mortality. Platelet count is a component of the SOFA score. SOFA scores are not reliable predictors because of thrombocytopenia in malarial ARDS which yields low scores.

Snakebite was the third most common indication requiring IMV in our setup. It showed 92% male preponderance which can be attributed to low socioeconomic status, working in fields, sleeping on floors and staying in huts. The mortality rate was the least at 15.38% among the indications studied. This data is similar to that of Kulkarni *et al.* [17] but higher than Ahmed *et al.* [18] (5.1%) and may be attributed to the small sample size.

Our study shows that out of 6 patients of GBS, 4 survived and 2 expired. It is in agreement to Fletcher *et al.* **(19)** which showed IMV was required in 81% and mortality of 20% in patients ventilated for GBS.

Group 2 had more complications like vocal cord edema (39.62%), VAP (28.30%), barotraumas (3.77%), DVT (5.66%), Thrombophlebitis (22.64%), and systemic complications (1.88%) as compared to group 1 which was similar to Masroor A. *et al.* [20]. Other studies have stated that post-extubation complication rates at 1-year follow-up are higher when IMV >7days but long term follow-up was not part of our study.

6. Clinical implications

The aim should be to promptly diagnose and treat the underlying disorders leading to respiratory failure and use mechanical ventilation therapy to tide over the crisis. Limiting the duration of mechanical ventilation is likely to be associated with lesser complications.

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