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Clinical Profile and Outcome of Sepsis Patients on Mechanical Ventilation in A Tertiary Care Medical Intensive Care Unit

Rajnish Kaushik, Devyani Thakur**, Rohit Saini***, Himanshu Sikri****, MPS Chawla******

Abstract

Background: In a hospital, the highest-risk patients are managed in Intensive Care Unit (ICU). Of these, the subgroup of patients with sepsis and on mechanical ventilation has a high mortality rate. And yet, research exclusive to this cohort is sparse.

Method: In this study, the data of 309 consecutive patients was analysed retrospectively, who were admitted throughout one year in a non COVID, medical ICU of a tertiary care hospital in central Delhi. Out of these 309, our study group was of 223 sepsis patients on mechanical ventilation who were analysed for their clinical profile and outcome.

Results: We found that the mean age of the sample was 46.5years which ranged from 18 years to 97 years. There were 93 (41.7%) females and 130 (58.3%) males and 67.7% of our participants had no co-morbidities at baseline. 39.01% (n = 87) of patients had septic shock and 48.88% (n = 109) had MODS at admission to the ICU. 13.5% (n = 30) developed Ventilator Associated Pneumonia and Acinetobacter baumanii was the most common isolate. 128 patients (57.4%) survived whereas 95 (42.6%) succumbed to their illness.

Conclusion: The deadly combination of sepsis and mechanical ventilation is fairly common but grossly under-researched in Indian ICUs. They lead to a high mortality and the factors affecting mortality need to be further researched and reported.

Key words: Sepsis, mechanical ventilation, ICU, mortality rate.

Introduction

Sepsis, classically defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection, is an important cause of hospitalisation and a major cause of death in the Intensive Care Units (ICUs) worldwide[1]. Additionally, it has been found that patients on mechanical ventilation form a major subgroup among those admitted to the ICU with a very high mortality. Thus, this intersecting group of patients with sepsis on mechanical ventilation has been associated with a high mortality rate by several studies[2,3].

Most epidemiological data that is available is from Western literature, which is drawn from their central registries and national healthcare database. Indian data is sparse and there is a glaring lacuna in information from Indian Intensive Care Units. One of the reasons is due to heterogeneous policies regarding admission to ICUs in the public sector, private hospitals and smaller nursing homes, leading to non uniform trends in admission, management and mortality[4]. It is undeniable that patients with sepsis and mechanical ventilation put a large burden on the intensive care resources and individually as well as collectively influence the outcomes of survival and mortality. Therefore there is an imperative need to study them and the factors which influence the outcomes.

Ours is a tertiary care public sector hospital with very pressing requirements for rapid turnover of beds. Through this study we aim to analyze one of the most dreaded combinations that we face in our ICU – sepsis and mechanical ventilation.

Objective

To study the clinical profile and outcome of patients on mechanical ventilation complicated by sepsis, in a Non-Covid Medical ICU of a tertiary care hospital in Delhi.

Material and Methods

It was a retrospective, observational, cross-sectional descriptive study conducted by reviewing the data of 309 consecutive patients admitted in a tertiary care medical ICU throughout a one-year duration from Jan 2020 to Dec

Assistant Professor, Department of Pulmonary Medicine, VMMC and Safdarjung Hospital, New Delhi - 110 029, **Medical Specialist, Department of Internal Medicine, 171 Military Hospital, Samba - 184 121, J & K, ***Senior Resident, *****Professor and Head, Department of Medicine, ****Senior Medical Officer, Department of Emergency Medicine, ABVIMS and Dr Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001.

Corresponding Author: Dr Himanshu Sikri, Senior Medical Officer, Department of Emergency Medicine, ABVIMS and Dr Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001. Tel: 8285506075, E-mail: drhimanshu.sikri@gmail.com.

2020. Of these, our study group was of 223 sepsis patients on mechanical ventilation, in a non Covid, medical ICU of a tertiary care hospital in central Delhi.

Patients included in the study were: 1) > 18 years of age, 2) On mechanical ventilation, 3) COVID-19 negative, 4) Fulfilling the criteria of sepsis wherein Sepsis was defined as systemic inflammatory response syndrome (SIRS) with suspected or proven microbial aetiology. SIRS includes the presence of at least two of the following: (1) Body temperature >38° C or <36° C, (2) Heart rate >90/min, (3) Respiratory rate >20 breaths/min or hyperventilation with a PaCO2 <32 mmHg, (4) White blood cell count >12,000/mm^3 or <4,000/mm^3, or with >10% immature neutrophils[5].

We excluded the following patients: 1) <18-year-old, 2) Not on mechanical ventilation, 3) With diagnoses other than sepsis at presentation such as acute left ventricular failure, myocardial infarction, stroke, etc., and 3) Had incomplete or missing data.

Other definitions that were used were: 1) *Septic shock*- sepsis with persisting hypotension requiring vasopressors to maintain Mean Arterial Pressure ≥ 65 mmHg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation[6], and, 2) *Multiple organ dysfunction syndrome (MODS)* - critical illness characterised by simultaneous dysfunction of two or more organs. This organ dysfunction was assessed using the sequential organ failure assessment (SOFA) score which includes scores from 0 - 4 for six major organ systems (pulmonary, haematologic, hepatic, cardiovascular, central nervous, and renal)[7].

Statistics

The data entry was done in Microsoft EXCEL spreadsheet and final analysis was done using Statistical Package for Social Sciences (SPSS) software, ver 25.0. The association of qualitative variables was analysed using Chi-Square test with Fisher's exact test, where necessary. A p-value of less than 0.05was considered statistically significant.

Results

Data of 309 patients consecutive patients admitted to the ICU was analysed; of these 223 patients were included in our analysis. They were divided into two major groups as per the outcome-survivors and non survivors (Fig. 1). And then further divided into subgroups for analysis as per age defined in the APACHEII scoring system, gender, number of co-morbidities, duration of ICU stay and prevalence of Ventilator-associated pneumonia (VAP).

We found that most of our patients (47.53%) were young

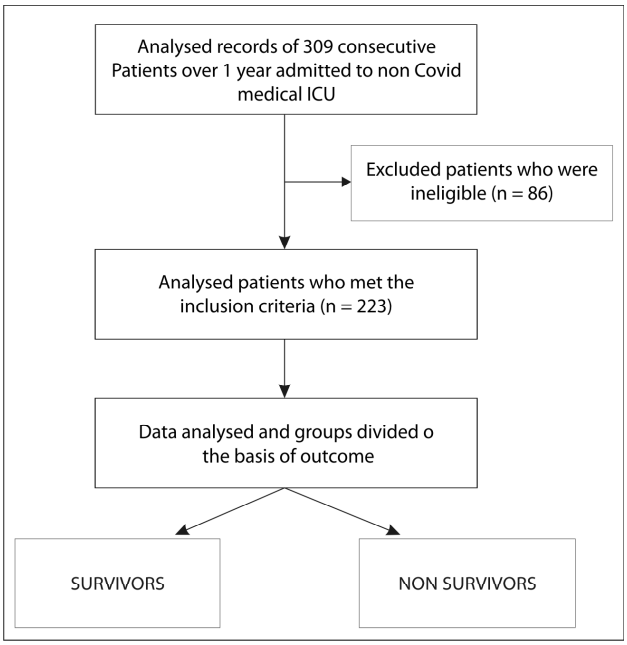

Fig. 1: *Line diagram of research method.*

and in the <44 yrs age group. Mean age of the study population was 46.5 years which ranged from 18 years to 97 years and median 45 years. There were 93 (41.7%) females and 130 (58.3%) males. 67.7% of our participants had no comorbidities whereas, 22.8% had a single, 8% had two, 1% had three and 0.5% of our sample had more than three comorbidities as per Charlson Comorbidity Index[8]. Diabetes mellitus was the most common comorbid condition we encountered. 87 (39.01%) patients had septic shock and 109 (48.88%) patients had MODS at the time of admission to the ICU. 89 patients (39.91%) had an ICU stay of a week or less and 134 (60.09%) stayed on for more than 7 days. This ranged from the shortest stay of 1 day to the longest of 93 days with a median stay of 10 days (5 - 16 days).

When we broadly divided the focus of sepsis into six groups, we found that 59% (n = 132) of our patients had a pulmonary aetiology. This was followed by 14.8% in whom no focus could be identified and 12% who were admitted with CNS infections (Fig. 2).

Although, all our patients were on invasive mechanical ventilation and admitted with sepsis, 13.5% (n = 30) developed VAP diagnosed as per the Clinical pulmonary infection score (CPIS)[9]. *Acinetobacter baumanii* was the most common isolate in the culture of secretions sent. The overall survival rate was 57.4% such that 128 patients survived and were transferred out to the wards in a stable condition and 95 patients, i.e., 42.6% succumbed to their illness in the ICU (Table I).

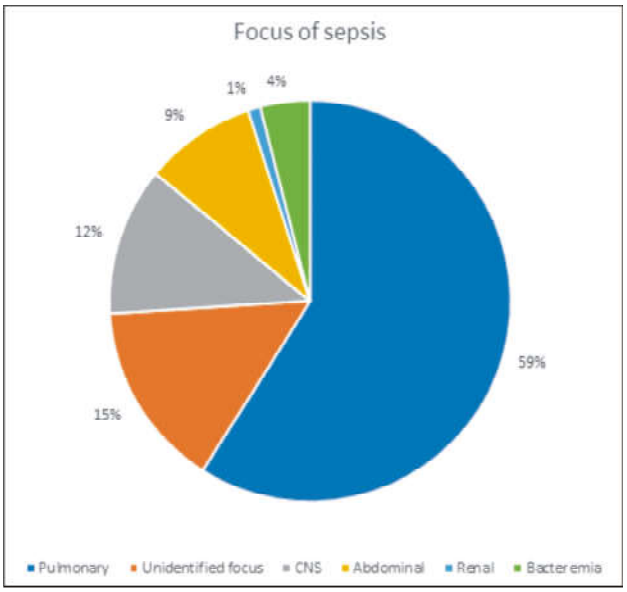

Fig. 2: *Pie chart showing distribution of foci of sepsis.*

Table I: Demographic profile and clinical outcome of studied patients.

Parameters	Frequency	Percentage
Age (years)		
< = 44 years	106	47.53%
45 - 54 years	36	16.14%
55 - 64 years	35	15.70%
65 - 74 years	27	12.11%
> = 75 years	19	8.52%
Mean ± SD	46.54 ± 18.8	
Median (25th - 75th percentile)	45 (30 - 60)	
Range	18 - 97	
Gender		
Female	93	41.70%
Male	130	58.30%
Number of co-morbidities		
0	151	67.71%
1	51	22.87%
2	18	8.07%
3	2	0.90%
4	1	0.45%
Duration of stay (days)		
< = 7 days	89	39.91%
> 7 days	134	60.09%
Mean ± SD	12.45 ± 11.85	
Median (25th - 75th percentile)	10 (5 - 16)	
Range	1 - 93	
VAP		
Not present	193	86.55%
Present	30	13.45%
Outcome		
Non Survivors	95	42.60%
Survivors	128	57.40%

In the final analysis, it was found that advancing age was associated with co-morbidities ($p < 0.0001$) and increasing age was also associated with higher frequency of VAP (p - 0.034).

Though most patients had an ICU stay of greater than a week, yet it was found that increasing age was associated with a prolonged ICU stay of over a week (p - 0.041). However, we did not find any significant relation between advancing age and the outcome of survival and demise (p - 0.883) or between gender and outcome (p - 0.704) or number of co-morbidities and outcome (p - 0.188). The presence of septic shock or MODS, also did not correlate with the outcome (p - 0.697 and p - 0.395 respectively). Similarly, there was no relation between frequency of VAP and duration of ICU stay (p - 0.111). It was found with statistical significance that those with an ICU stay of one week or less (56%) succumbed, whereas most of those who survived beyond one week, i.e., 66%, were transferred out of the ICU (p - 0.0008) (Table II).

Table II: Correlation between clinical parameters and outcome.

Parameter	Survivors	Non-survivors	p-value
Gender			0.704
Male	76	54	
Female	52	41	
Number of co-morbidities			0.188
0	81	70	
1	32	19	
2	13	5	
3	2	0	
4	0	1	
Age			0.883
< 44 years	61	45	
45 - 54 years	23	13	
55 - 64 years	18	17	
65 - 74 years	15	12	

> 75 years	11	8	
Days in ICU			**0.0008**
< 7 days	39	50	
>7 days	89	45	
Septic shock			0.395
Present at admission	53	34	
Absent at admission	75	61	
MODS			0.697
Present at admission	64	45	
Absent at admission	64	50	
Site of infection			0.376
Pulmonary	79	53	
Abdomen	9	10	
Renal	3	0	
CNS	12	15	
Bacteremia	5	4	
Unidentified focus	20	13	

Discussion

A hospital's highest risk patients are managed in the ICU. Sepsis patients on mechanical ventilation are one such high risk group. We found several studies on patients with sepsis and patients on mechanical ventilation, however, sparse literature was found which exclusively studied patients with both sepsis and mechanical ventilation.

It is well established that advancing age is an independent risk factor for severe sepsis and co-morbidities. Most studies also found an average age of 60 years but a younger cohort was reported in certain ICU studies with a mean age of 53.8 years. Contrary to the majority, our study had a much younger mean age group of 46.5 years which ranged between 18 to 97 years.

A few arguments could be made to explain this younger patient subset. Research suggests that given the poor prognosis, physicians do not readily admit older individuals > 80 years to ICUs, and those admitted to the ICU often do not receive mechanical ventilation[10,11]. And more importantly, India has one of the youngest demographic dividends in an ageing world.

In gender distribution, our findings of 41.7% females and 58.3% males, were similar to most reports but quite different from Mohamed *et al* who studied 71.25% males and 28.75% females in their ICU[2].

Only 32.3% of our participants had co-morbidities at baseline, whereas most ICU studies report a much higher prevalence, even as much as 79%[12]. This could be because of the younger mean age of admitted patients or possibly as the Charlson Comorbidity Index is itself criticised to be insufficiently discriminative[13].

In our study, patients had a median ICU stay of 10 days (5 - 16 days). Comparable figures of ICU patients with severe sepsis were 8 (4 - 12) days, as reported by Chatterjee *et al* and 10 (5 - 15) days in another study[14,15].

Septic shock and MODS, both are reportedly associated with a high mortality rate in several studies. Our data revealed a mortality rate of 39% (n - 34) among patients with septic shock, which was slightly less than studies reporting mortality in excess of 40%[6]. Similarly, there are studies from various medical and surgical ICUs that report a higher mortality rate among patients with MODS ranging from 27 to 100%. Our mortality rate was 41.3% (n - 45), even though the setting of septic shock and MODS was with the additional factor of mechanical ventilation[7]. Although this mortality rate of patients with septic shock and MODS was comparable with others, there was no statistically significant association between mortality and the presence of septic shock or MODS in our studied population.This could be due to mechanical ventilation itself compounding the calculated mortality rate.

All patients in our study were on mechanical ventilation, of which 30 (13.5 %) developed VAP. This falls within the known range of VAP incidence of 5 - 40% reported by previous studies[16]. It is much lower than 57.14%, reported from an Indian research. However, similar to us, they also found *Acinetobacter* as the most common pathogen in their ICU[17]. There are large variations in incidence rates depending upon the country, ICU type and clinical criteria used to define VAP in studies[16].

There is extensive data reporting high mortality rates in ICU patients and patients with sepsis. A mortality rate of 35% was found in the INDICAPS II and 26.5% in the multicentric ANZICS. Other studies show that mortality rate in patients given Mechanical Ventilation in the ICU ranges from 23% to 51%[18-21]. The mortality rate in our study was also a comparable 42.6%. The only similar study group was a subset of mechanically ventilated patients in severe sepsis (n = 56) studied by Vincent *et al* who have reported a mortality rate of 85.72% (n = 48)[22].

We found no significant association between age, female gender, number of co-morbidities and mortality. This was in agreement with the results of Mohamed *et al*, Liang *et al* and Prabhdev *et al*[2,23-24]. Contrary to these, are Koleef *et al*, who have found in their ICU setting that female gender had a higher mortality on mechanical ventilation[25].

The most common focus of infection we found was pulmonary, in as high as 59% of the admitted patients. This is much like the results of Patel *et al* (49.3%) , Artero *et al* (24.1%) and Watanbe *et al*, who found most of their studied patients to have pulmonary focus of infection. Jain *et al* have reported their prevalence of 70% pulmonary infections from a primarily Respiratory ICU. In congruence with our results, all of them have reported no association of the outcome with source of infection[26-29].

There are several limitations of our study and larger quantum of data is required to make any definitive generalisations. This is a single centre study over the period of one year, analysed in retrospect and the patients transferred out could not be followed up. As this is a very high volume centre, no uniform policy of admission to the medical ICU could be practiced to channel the influx of patients in sepsis alone and no step down unit with intensive monitoring was available for faster transit of patients.

The strength of this study is in the large sample size of a relatively under-reported subgroup. Patients with sepsis and mechanical ventilation usually form just a subset of study groups and due to their high mortality rates, remain an under reported cohort. The lack of such a comparative group in literature makes drawing conclusions from results difficult and we hope that more such studies are reported to trace further patterns for reducing mortality benefit in such patients.

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