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A Comparative Study On Sepsis Outcomes In Patients with and Without Statins at A Tertiary Care Hospital

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ABSTRACT

Sepsis is a life-threatening condition that occurs when the immune system responds to infection. Studies have shown proven results that statins control the inflammatory response associated with sepsis, which may help to minimize the disease's development and lower mortality rates. A 9-month retrospective and prospective observational study was carried out. Two groups were classified as statins and non-statins. 205 patients were included in this study, out of which 71 patients (35%) were taking a statin, while 134 patients (65%) were in non-statin group. Out of 71 patients belonging to statin group, 25 patients (35%) were prescribed with Atorvastatin, 21 patients (30%) were prescribed with a combination of Atorvastatin and Aspirin, and 4 patients (6%) were prescribed with Rosuvastatin. The incidence of multiple organ dysfunction syndrome was found to be in 28 patients (21%) of the non-statin group and 12 (17%) in the statin group and the mean multiple organ dysfunction syndrome rate among the non-statin group was 1.98 compared to 1.83 for statin group. The incidence of mortality rate among the non-statin group was found to be 72 patients (54%) compared to the statin group 29 patients (41%). The mean sequential organ failure assessment score for the non-statin group was 7.78 compared to 7.03 for the statin group and was statistically significant. Though the mortality rate was statistically insignificant in the statin group, the overall improvement in the statin group was comparatively better than in the non-statin group.

Keywords: Sepsis, Statins, Mortality Rate, Organ Dysfunction Scores.

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INTRODUCTION

Sepsis can be defined as a life-threatening condition caused by an abnormal host response to infection[1]. Sepsis causes cognitive impairment, organ dysfunction, and excessive production of inflammatory cytokines[2]. Severe sepsis develops when there is an organ failure resulting from an infection and host response, whereas septic shock occurs when there is persistent hypotension despite fluid resuscitation[3]. In the Intensive care unit, sepsis is the leading cause of death[4]. Severe sepsis is commonly seen in Indian ICUs, and it is caused primarily by gram-negative organisms [5].

Pre-existing chronic conditions are one of the major risk factors for sepsis. Recurrent hospitalizations and operations related to chronic illnesses have also been recognized as a sepsis risk factor, particularly when immunity is compromised [6].

The early detection and management of sepsis continue to be a major challenge to healthcare professionals. Several recent studies have shown the correlation between initial sepsis intervention and patient survival. Despite significant evidence demonstrating that timely administration of evidence-based, sepsis-specific therapy lowers mortality. In the initial stages of sepsis, the signs and symptoms of sepsis are nonspecific. The condition may be exacerbated by a lack of understanding of the signs and symptoms of developing sepsis [7].

Documented or suspected infections, as well as an acute elevation of two or more Sequential Organ Failure Assessment (SOFA) scores are the clinical criteria for sepsis [8]. The SOFA score is extensively used in critical care research; however, it is not commonly used clinically in the intensive care units.

The Surviving Sepsis Campaign (SSC) currently recommends that intravenous (IV) empiric broad-spectrum antimicrobials are given within 1 hour after recognition of both sepsis and septic shock [9].

The HMG-CoA reductase inhibitors, commonly known as statins are widely used in the treatment of lipid disorders [10]. There is significant evidence that statins have effects beyond lowering blood cholesterol [11]. Statins have been identified as potentially effective anti-inflammatory agents. In vitro, statins influence a number of pathways thought to be involved in sepsis development. As a result, their application in inflammatory disorders like sepsis is supported due to their pleiotropic effects [12]. Additionally, statins have been linked to anticancer and immunomodulatory properties.[13]. Statins' anti-inflammatory activities are associated with a decrease in nuclear factor kappa B and C-reactive protein.[14]. A substantial amount of data suggests that statins may have a function in the treatment of sepsis in human trials. Although the

majority of the studies are retrospective and observational, the results are encouraging. According to the findings, statins may reduce inflammatory cytokine levels, the incidence of developing sepsis, the severity of existing sepsis, and the sepsis death rate [15].

MATERIALS AND METHOD

A 9-month retrospective and prospective observational study was carried out. Patients of both gender over the age of 18 years with or without a history of statin use were included in this study. Patients with incomplete clinical and laboratory data were excluded. 205 patients were included, out of which 71 patients (35%) were taking a statin, while 134 patients (65%) were in non-statin group. All the necessary parameters, such as lab data, vital signs, length of stay, treatment plan, mortality rate, and other sepsis outcomes were monitored. All the data was pooled and analyzed using the SPSS program version 28.0.1.

The study was performed according to the Helsinki Declaration and approved by the Institutional Ethical Review Board (IERB No. SPH/Al-AM/2021/193).

RESULTS AND DISCUSSION

205 patients were included in this study, Out of which 71 patients (35%) were on statin, while 134 patients (65%) were not under statin therapy (Figure 1). Out of 71 statin patients, 25 patients (35%) were prescribed with Atorvastatin, 21 patients (30%) were with a combination of Atorvastatin and Aspirin, 8 patients (11%) were prescribed with a combination of Atorvastatin, Aspirin and Clopidogrel, and 4 patients (6%) were prescribed with Rosuvastatin.

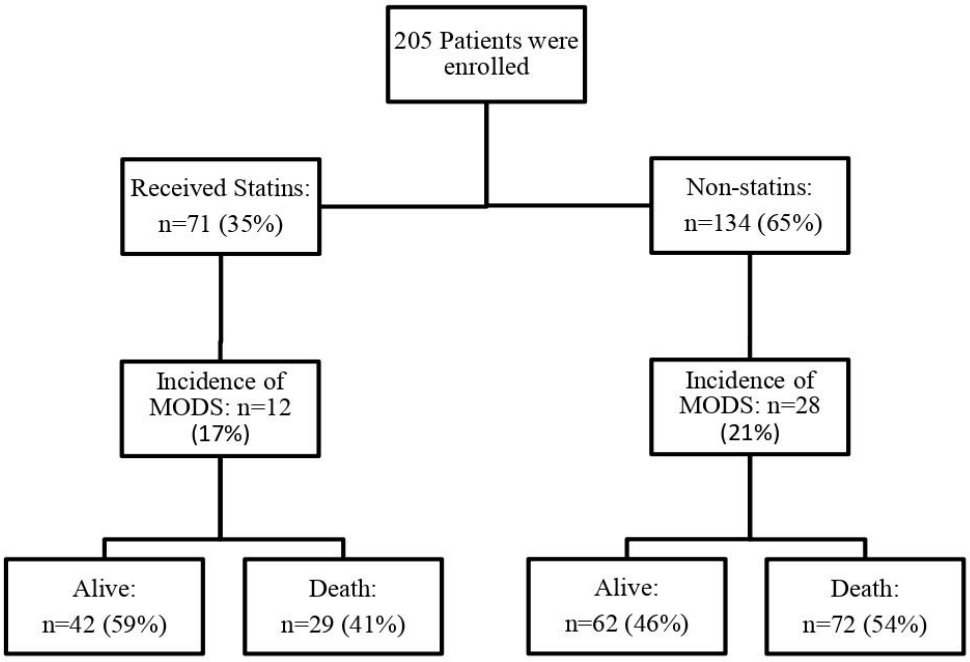

Figure 1: Summarizes the total number of sepsis patients and their outcomes during the study.

It was observed that out of 205 sepsis patients the majority 61 patients (29.8%) had pneumonia as a source of infection, 60 patients (29.3%) were having UTI as a source of infection, 37 patients (18%) were having bacteremia as the source of infection, 26 patients (12.7%) were having abscess as the source of infection, 14 patients (6.8%) were having cellulitis as a source of infection and 7 (3.4%) were having GI as a source of infection (Table 1).

Table 1: Source of infection

Source of infection	n	Percentage (%)
Pneumonia	61	29.8%
UTI	60	29.3%
Bacteremia	37	18.0%
Abscess	26	12.7%
Cellulitis	14	6.8%
GI	7	3.4%

UTI, urinary tract infection; GI, gastrointestinal infection

Intravenous fluids and vasopressors are essential for achieving and maintaining proper blood pressure and tissue perfusion, hence they must be given promptly. In our study, the most frequently prescribed vasopressor was the combination of norepinephrine and dopamine (41%) followed by norepinephrine and dobutamine combination (27%), and norepinephrine (12%).

Corticosteroids were prescribed for 171 patients (83.41%) in our study. 73% of the patients were prescribed with Budesonide, 21% of the patients received Hydrocortisone and 6% were

prescribed with Methylprednisolone. The other prescribed drugs included Anticoagulant (n= 170, 82.92%), thiamine (n= 148, 72.19%), and Antifungal drugs (n=138, 67.31%).

To determine the appropriate antibiotic therapy, a deep understanding of the causative organisms is required. The most common causative microorganism observed in our study was E. coli in blood, urine, and pus-positive cultures. The other isolated organisms were found to be K. pneumoniae, S. Aureus, E. Faecalis, and P. Aeruginosa. In patients with positive blood cultures, the most common causative organism was found to be E. coli (37%)

The statin group had a statistically significant longer length of stay in the hospital than the non-statin group. Despite the difference being statistically insignificant, patients on statin therapy spent less time in the ICU than those who did not take a statin. Patients taking statin had lower temperatures after initiation of treatment, compared to non-statin patients, which was statistically significant. (Table 2).

Table 2: Statistical data

	Mean		**SD**		**P-value**
	Statin n = 71	**Non Statin n = 134**	**Statin**	**Non Statin**	
Length of hospital stay	9.82	8.04	7.695	6.289	0.039
Length of ICU stay	4.83	6.31	3.854	8.418	0.081
Temperature	98.69	99.18	1.103	1.387	0.005
Heart rate	94.69	107.89	20.560	21.186	< 0.001
Respiratory rate	23.80	26.06	7.266	7.949	0.024
GRBS level	187.37	212.01	102.971	130.028	0.084
WBC count	15,550	15,424	7248.52	8218.05	0.457
Creatinine level	1.83	1.98	1.285	1.466	0.225
Albumin level	2.92	2.80	0.789	0.654	0.135
Lactate level	1.12	1.92	0.527	1.052	< 0.001
MODS	1.83	1.98	1.285	1.466	0.247
Mortality rate	0.42	0.52	0.497	0.501	0.088
SOFA Score	7.03	7.78	2.342	3.357	0.046

ICU, intensive care unit; MODS, multiple organ dysfunction syndromes; SOFA, sequential organ failure assessment

Compared with the non-statin group, patients who took statins had a statistically significant lower respiratory rate. The difference between both the groups was statistically insignificant, and the statin group had lower GRBS levels.

It was statistically observed that the statin group had lower creatinine levels than the non-statin group. In comparison to the non-statin group, the statin group had decreased WBC value, which was statistically insignificant. The statin group showed higher albumin values compared to the non-statin group, however, it was statistically insignificant.

The other parameter was the lactate level, in which the statin group showed a statistically significant lower level than the non-statin group.

The difference in the incidence of multiple organ dysfunction syndrome (MODS) between the two groups was statistically insignificant. Similarly, the mortality rate was comparatively lesser in the statin group but was statistically insignificant.

The Sequential Organ Failure Assessment, commonly known as SOFA score, is used to evaluate the function of different organ systems in the body. The higher the SOFA score, the greater the chance of death.

According to the SOFA score, 107 patients (52%) fall under the scale of 5-9 followed by 85 patients (41%) under 10-14 and 13 patients (6%) were 15-19. It was found that the SOFA score was low and statistically significant in the statin group.

CONCLUSION

During the study period of nine months, a total of 205 patients from the inpatient wards were enrolled. In our study, male patients were higher in number (52.2%) than female patients (47.8%), and the majority of the patients were geriatrics and adolescents. Atorvastatin was commonly prescribed (35%), followed by a combination of Atorvastatin and Aspirin (30%),

The statin group had a statistically significant longer length of stay in the hospital than the non-statin group. Patients on statin therapy spent less time in the ICU than those who did not take a statin, regardless of the difference being statistically insignificant. The lower temperature in the statin group was statistically significant. Statin patients had a lower respiratory rate which was statistically significant. Both groups had statistically insignificant differences; however, the statin group had lower GRBS levels. It was statistically observed that the statin group had lower creatinine levels than the other group. In comparison to the non-statin group, the statin group had decreased WBC numbers, which was statistically insignificant. The statin group showed higher albumin values compared to the non-statin group, however, it was statistically insignificant. The other parameter was the lactate level, in which the statin group showed a statistically significant lower level than the non-statin group. The difference in the incidence of MODS between the two groups was statistically insignificant. Similarly, the mortality rate was comparatively lesser in the statin group but was statistically insignificant. It was found that the SOFA score was low and statistically significant in the statin group. Rosuvastatin was found to be the most effective among other statins used. We conclude the study by stating that though the mortality rate was statistically insignificant in the statin group, the overall improvement was comparatively better in the statin group than in non-statin.

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