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Original Article

Internal Medicine Section

Sepsis Mortality in Critical Care and Prior Statin Therapy: A Retrospective Cohort Study in Central Argentina

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ABSTRACT

Introduction: Sepsis is a major public health problem, frequent, costly, and often fatal. Despite of improvements in supportive treatments the incidence of sepsis and the number of deaths related to sepsis is increasing. Statins have been recently proposed as adjuvants in the treatment of sepsis, but its effects on mortality show conflicting results worldwide.

Aim: The purpose of this study was to describe the clinical outcome of patients diagnosed with sepsis in a university-affiliated hospital in central Argentina and to evaluate it in relation to a group of septic patients with previous use of statins before the onset of sepsis.

Materials and Methods: The present study was conducted as an observational retrospective research from April 2010 to December 2014 with patients over 18 years of age which were assigned to statins or control groups. Out of 2906 patients, 231 matched study and diagnostic criteria for sepsis and among them 33 (14.3%) belonged to the group of statins. The mean age was 64.2 ± 14.3 years.

Results: The severity of sepsis on admission was as follows: Sepsis, n=147 (63.6%), Severe sepsis, n=26 (11.3%) and Septic shock, n=58 (25.1%). The mean length of stay in Intensive Care Unit (ICU) was10.8 ± 9.6 days and 21.2 ± 17 days in general hospital ward settings, without differences between groups of statin users and controls, p=0.873 and p=0.766, respectively. The in-hospital mortality rate was 31.2% (n=72). Previous statin use did not affect in-hospital or 30-day mortality (OR 0.978; 95% CI 0.339 to 2.274; p=0.789). Creatinine levels on days 3 and 14 were substantially higher in statins group (1.80 ±1.39 vs. 1.45 ± 1.47 mg/dl) (p=0.010) and (1.42 ± 1.14 vs. 1.09 ± 1.05 mg/dl) (p=0.009), respectively.

Conclusion: Prior use of statins did not reduce in-hospital or 30-day mortality in septic patients and it may be associated with impaired renal function in this group of Argentinian participants.

Keywords: Antibiotics, Hospitalization, Microbiological analysis

INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. Commonly seen in ICU, sepsis is a major public health concern with high treatment-associated costs and poor health outcomes. The annual incidence of sepsis in the United States surpasses 1,650,000 cases with mortality rates of 50%. The universal costs estimation for the treatment of sepsis ranges from 25,000 to 50,000 dollars per patient [2]. Sepsis is the disease with the higher risk of death in ICUs and a significant proportion of cases progresses to septic shock. In Argentina, a 2003 survey estimated a 43% overall mortality due to sepsis in ICUs and every year about 10,000 demises are associated with a diagnosis of sepsis in this country [3,4]. Nevertheless, despite improvements in supportive treatments the incidence of sepsis and the number of deaths related to sepsis is increasing [2].

The need of a complementary therapy for sepsis, auxiliary to conventional treatments with antibiotics and fluid support, has motivated the search for new medicines. Statins, also known as inhibitors of the hydroxy-methyl-glutaryl-Coenzyme-A reductase, have emerged as potential candidates for the adjuvant treatment of sepsis. The role of statins in sepsis was initially observed in animal models and in-vitro research. Possible mechanisms for this drug in sepsis include a decreased synthesis of proinflammatory cytokines, a balanced immune response and reversed endothelial dysfunction [5]. Moved by the favourable findings in animal models, observational studies and clinical trials have been developed to confirm the effect of statins in septic patients. However, to date, the use of statins in sepsis is controversial with different outcomes worldwide. Some studies reported a beneficial effect while others a neutral or even a harmful effect of statins on survival of septic patients [6-9]. In Argentina, to date, there is limited information about septic patients in ICUs and very scarce research assessing the use of statins in sepsis, except for one study of patients with candidemia [10]. Therefore, the purpose of this study was to describe the clinical outcome of patients diagnosed with sepsis in a university-affiliated hospital of central Argentina and to evaluate it in relation to a group of septic patients with previous use of statins before the onset of sepsis. We also discuss our findings under the new perspective of the recently proposed third consensus definitions for sepsis and septic shock [1].

MATERIALS AND METHODS

This investigation was conducted in accordance with established ethical standards. The Research Ethics Committee from River Plate Adventist University and the Office of Academic Research at the university-affiliated hospital has approved the study protocol.

Study design: Retrospective review of adult ICU admissions from April 2010 until December 2014, including patients from both sexes, older than 18 years with the diagnosis of sepsis, severe sepsis or septic shock according to the definition of the "American College of Chest Physicians" and the “Society of Critical Care Medicine" [11]. These diagnostic criteria had to be present at the time of admission, or during hospitalization. Exclusion criteria were: pregnancy, decompensated heart failure, terminal disease, systemic inflammatory response not associated with infection, and prior treatment with statins less than 30 days. Initial information of patients was obtained using the SATI-Q database for critical care services. Preliminary searches included the keywords "sepsis"

or "septic shock", then a more detailed search was completed including any infection and infectious process for the period of ICU stay. Paper medical records were then reviewed, selecting those patients who matched the study criteria. Baseline data was collected including demographic information, admission diagnosis and sites of infection, sepsis severity, APACHE II and SOFA scores, comorbidities measured by the Charlson score and medications. Patient´s clinical and laboratory information for the days 1, 3 and 14 of hospitalization were collected including microbiological analysis and antibiotic treatments. The ICU, the in-hospital and the 30-day mortality were recorded. The medication classified as statins included simvastatin, atorvastatin and rosuvastatin, with daily doses for lipid control within conventional range (10-40 mg/day). All information was recorded in an individual pre-printed database sheet, then computerized and twice revised by two different researches.

Admitted patients were divided into two subgroups on the basis of statins use. Statin user group were defined as those receiving statins for at least 30 days before the beginning of the study and the control group included those who were not users of statins. The primary endpoint was 30-day mortality and secondary outcomes included the in-hospital mortality.

STATISTICAL ANALYSIS

Univariate analysis for absolute frequencies and percentages, mean and standard deviation were calculated. For bivariate analysis, the chi-square test, the t-test and the Mann-Whitney U test was used according to the distribution of variables, with a confidence level of 95%. Multiple logistic regression analysis was performed to determine Odds Ratio (OR) and 95% confidence interval for risk factors and protective factors associated with the 14-day and the 30-day mortality. SPSS Inc., (Chicago, IL, USA) version 17 software was used for statistical analysis. A p-value <0.05 was considered statistically significant.

RESULTS

During the time of the study, 2906 patients were hospitalized in the ICU and among them, 231 patients met inclusion criteria, and 33 (14.3%) of those patients were assigned to the group of statins and the other 198 (85.7%) patients to the group of controls. The mean (±SD) age of patients was 64.2 ±14.3 years, with the group of statins presenting a higher age than controls, 71.58± 10.51 years vs. 63.02 ± 14.51 years, respectively (p<0.001). The medication used by the majority of the patients in the group of statins was atorvastatin (81.8%). The most prevalent site of infection was the respiratory tract 134 (58%), followed by the genitourinary tract 45 (19.5%). There were 60 positive blood cultures (25.9%), of which Gram-negative bacteria were isolated in 31 cases (51.6% of the positive blood cultures) [Table/Fig-1].

Comorbidities, assessed by the Charlson score, were elevated in both groups but higher in the statin group than in the controls (6.97 ± 2.32 vs. 5.35 ± 2.98; p=0.002). Statin users showed a higher prevalence of antecedents associated with hypertension (p=0.003), coronary artery disease (p=0.049), acute myocardial infarction (p <0.001), heart failure (p=0.016) and obesity (p=0.028). The score of the APACHE II was similar in both groups.

The mean (± SD) duration of hospitalization in ICU was 10.84 ± 9.65 days and 21.2 ± 17.0 days in general hospital ward settings. No statistical differences were found regarding the duration of hospitalization comparing statin users and controls. The average in-hospital mortality was 31.2% and the 30-day mortality was 38.5% [Table/Fig-1].

Logistic regression analysis showed that higher scores in the Charlson comorbidity scale was associated with a higher risk of 14-day and 30-day mortality, OR 1.46 (1.24-1.73) p<0.001 and OR 1.20 (95% CI, 1.06 to 1.36) p=0.003, respectively; and leukocytosis at day 14 was associated with a lower risk of 14-day and 30-day mortality, OR 0.26 (0.10-0.63) p=0.003 and OR 0.41 (95% CI, 0.19-0.86) p=0.018, respectively. Higher scores in the APACHE II, qSOFA and the use of ciprofloxacin were also associated with a higher mortality risk at day 14. The prior use of statins did not affect the 14-day or the 30-day mortality risk, OR 1.00 (95% CI, 0.31-3.16), p=1.000, OR 0.978 (95% CI, 0.339- 2.274), p=0.789, respectively [Table/Fig-2].

Characteristics	Total (N= 231)	Statins (N= 33)	Controls (N= 198)	p-value for Chi-square test
Age (Mean ± SD)	64.2 ± 14.3	71.5 ± 10.5	63.0 ± 14.5	<0.001*
Male	150 (64.9%)	26 (78.8%)	124 (62.6%)	NS(0.072)
Charlson Index	5.5 ± 2.3	6.9 ± 2.3	5.3 ± 2.9	0.002†
APACHE II	17.1 ± 7.2	17.0 ± 6.4	17.1 ± 7.4	NS(0.810)†
Cardiovascular Diseases				
Arterial hypertension	150 (64.9%)	29 (87.9%)	121 (61.1%)	0.003
Coronary artery disease	31 (13.4%)	8 (24.2%)	23 (11.6%)	0.049
Myocardial infarction	12 (5.2%)	6 (18.2%)	6 (3.0%)	<0.001
Cerebrovascular disease	24 (10.4%)	4 (12.1%)	20 (10.1%)	NS(0.758)
Heart failure	37 (16.0%)	10 (30.3%)	27 (13.6%)	0.016
Diabetes	67 (29.0%)	13 (39.4%)	54 (27.3%)	NS(0.155)
Chronic kidney disease	32 (13.9%)	6 (18.2%)	26 (13.1%)	NS(0.431)
Cancer	35 (15.2%)	3 (9.1%)	32 (16.2%)	NS(0.294)
COPD	36 (15.6%)	7 (21.2%)	29 (14.6%)	NS(0.336)
Obesity	34 (14.7%)	9 (27.3%)	25(12.6%)	0.028
Sites of Infection				
Respiratory	134 (58.0%)	20 (60.6%)	114 (57.6%)	NS(0.744)
Genitourinary	45 (19.55%)	7 (21.2%)	38 (19.2%)	NS(0.786)
Gastrointestinal	41 (17.7%)	3 (9.1%)	38 (19.2%)	NS (0.160)
Central nervous system	9 (3.9%)	2 (6.1%)	7 (3.5%)	NS (0.488)
Other‡	61(51.1%)	8(18.7%)	53(32.4%)	NS (0.670)
Blood Culture				
Gram-negative bacteria	31 (13.4%)	5 (15.2%)	26 (13.1%)	NS(0.753)
Gram-positive bacteria	27 (11.7%)	1 (3.0%)	26 (13.1%)	NS(0.095)
Yeasts	2 (0.9%)	0 (0%)	2 (1.0%)	NS (0.561)
Types of Statins				
Atorvastatin	27 (11.7%)	27 (81.8%)	-	
Simvastatin	2 (0.9%)	2 (6.1%)	-	
Rosuvastatin	4 (1.7%)	4 (12.1%)	-	
Days in ICU	10.8 ± 9.6	12.0 ± 14.0	10.6 ± 8.7	NS(0.873)†
Days of hospitalization	21.2 ± 17.0	23.0 ± 19.9	20.8 ± 16.5	NS (0.766)†
Sepsis Severity				
Sepsis	147 (63.6%)	24 (72.7%)	123 (62.1%)	NS (0.241)
Severe sepsis	26 (11.3%)	1(3.0%)	25 (12.6%)	NS (0.106)
Septic shock	58 (25.1%)	8 (24.2%)	50 (25.3%)	NS (0.901)
ICU mortality	58 (25.1%)	6 (18.2%)	52 (26.3%)	NS (0.322)
In-hospital mortality	72 (31.2%)	11 (33.3%)	61 (30.8%)	NS (0.772)
30-day mortality	89 (38.5%)	16 (48.5%)	73 (36.9%)	NS (0.204)

[Table/Fig-1]: Baseline characteristics, sepsis severity and sepsis mortality in statin users and controls.
COPD: Chronic obstructive pulmonary disease. ICU: Intensive Care Unit. NS: Non-significant.* p-value for t-test; † p-value for Mann-Whitney U test; ‡Other: skin, soft-tissues, surgical wounds, osteo-articular; bloodstream and unknown sites.

Characteristics	Day 14		Day 30	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Charlson index	1.46 [1.24-1.73]	<0.001	1.20 [1.06-1.36]	0.003
APACHE II score	1.08 [1.00-1.15]	0.028	1.05 [0.99-1.11]	NS (0.068)
SOFA day 3	1.06 [0.92-1.22]	NS (0.397)	1.10 [0.98-1.23]	NS (0.105)
qSOFA day 3	1.85 [1.03-3.32]	0.038	1.12 [0.70-1.77]	NS (0.631)
Days of hospitalization	0.95 [0.91-1.00]	NS (0.055)	0.98 [0.96-1.01]	NS (0.413)
Days of ICU	1.02 [0.95-1.08]	NS (0.560)	0.99 [0.94-1.04]	NS (0.792)
Female	2.41 [0.99-5.85]	NS (0.051)	1.18 [0.57-2.46]	NS (0.643)
Septic shock at admission	0.49[0.19-1.28]	NS (0.146)	0.51 [0.23-1.16]	NS (0.111)
Ciprofloxacin use	2.87[1.02-8.09]	0.046	1.95 [0.86-4.43]	NS (0.107)
Leukocytosis day 3	0.71[0.30-1.64]	NS (0.430)	0.71 [0.35-1.43]	NS (0.341)
Leukocytosis day 14	0.26[0.10-0.63]	0.003	0.41 [0.19-0.86]	0.018
Prior statin use	1.00[0.31-3.16]	NS (1.000)	0.97 [0.33-2.27]	NS (0.789)

[Table/Fig-2]: Risk factors and protective factors associated with sepsis mortality. NS: Non-significant; OR: Odds-Ratio; CI: Confidence-interval; p-value for multiple logistic regression analysis.

During the course of sepsis, several clinical and laboratory parameters were assessed and the scores of APACHE II, SOFA, qSOFA, and sepsis severity on days 1, 3 and 14 were not shown to be statistically different in both group of statin users and controls. However, some aspects, such as the blood creatinine levels on days 3 and 14 were significantly higher in the statin group than in controls, 1.80 ± 1.39 vs. 1.45 ± 1.47 mg/dl (p=0.010), and 1.42 ± 1.14 vs 1.09 ± 1.05 mg/dl (p=0.009), respectively [Table/Fig-3].

DISCUSSION

The present study did not find a clinical benefit associated with the prior use of statins on 30-day mortality in septic patients. There were no significant differences between statin users and controls with reference to the severity of sepsis during the course of time and days of hospitalization in ICU or in the general hospital ward settings.

Previous observational studies, included in reviews and meta-analysis, suggest a favourable outcome with the use of statins on sepsis [6-8,12]. One of these meta-analysis from Janda S et al., found a protective overall effect of statins on the reduction of sepsis mortality, OR 0.49 (95% CI, 0.37-0.61) [8]. Out of the 20 studies included in this meta-analysis, 15 showed a protective effect for statins with an OR ranging from 0.06 to 0.75, and four studies reported no benefits for the use of statins and in one of the studies the use of statins was associated with an increased mortality in septic patients. Nevertheless, this meta-analysis presented a funnel plot asymmetry suggesting the existence of publication bias.

In the last years; however, the enthusiasm for the discovery of a drug as an adjuvant for the treatment of sepsis appears to be declining due to the advent of new evidences found in recent clinical trials [13-15], which suggests a limited benefit from the use of statins in sepsis. This included two large clinical trials that were prematurely interrupted due to the ineffectiveness of statins as an adjuvant in the treatment of sepsis [14-15]. The main findings of these clinical trials are consistent with the global results of our study.

In a recent meta-analysis, including 1720 patients from seven randomized double-blinded clinical trials by Deshpande A et al., the obtained Jadad score was high [16]. This scale is used to authenticate the quality of the methodology used in a clinical trial.

Characteristics	Day 1		Day 3		Day 14		p-value
	Statins	Controls	Statins	Controls	Statins	Controls	
	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)	
Temperature	36.52±1.49 (33)	36.64±1.42 (198)	36.20±0.98 (32)	36.53±1.07 (194)	36.51±1.00 (26)	36.45±0.90(146)	NS
HR	94.39±19.19 (33)	103.61±23.93 (198)	90.94±16.11 (32)	94.20±19.01 (194)	87.54±17.76 (26)	90.10±17.55(146)	**0.037***
MAP	77.67±20.78 (33)	78.39±19.23 (197)	81.09±14.27 (32)	83.71±16.80 (194)	82.42±15.94 (26)	83.96±18.72 (147)	NS
RR	23.94±6.98 (33)	24.19±6.52 (197)	20.47±3.82 (32)	20.54±4.72 (193)	22.65±6.31 (26)	21.02±4.59(147)	NS
PCO_2 mmHg	39.54±7.80 (33)	37.35±10.43 (196)	39.54±7.80 (33)	39.73±9.69 (196)	40.00±6.66 (24)	40.96±12.81(124)	NS
PO_2 mmHg	97.63±31.52 (33)	86.04±35.62 (195)	86.18±23.81 (32)	91.26±27.95 (191)	84.19±21.86 (24)	86.17±27.92 (124)	**0.013†**
Haematocrit	33.36±5.74 (33)	32.68±6.29 (198)	32.63±4.39 (32)	32.20±5.54 (194)	32.08±4.81 (26)	31.32±5.20 (146)	NS
Haemoglobin	10.98±2.00 (33)	10.83±2.21 (198)	10.72±1.56 (32)	10.56±1.94 (194)	10.18±1.51 (26)	10.05±1.68 (146)	NS
WBC	13122±5818 (33)	14725±8072 (197)	12920±6361 (32)	14183±7340(194)	12428±6866 (26)	12277±6350 (146)	NS
Serum creatinin	1.76±1.41 (33)	1.54±1.50 (194)	**1.80±1.39 (32)**	**1.45±1.47 (191)**	**1.42±1.14 (25)**	**1.09±1.05 (141)**	**0.010 0.009**
Blood glucose	153.42±85.60 (31)	133.86±54.60 (191)	138.66±42.42 (32)	126.14±41.15 (186)	114.52±24.70 (25)	118.41±32.51 (136)	NS
CRP	174.27±130.44 (28)	171.75±116.65 (160)	142.35±90.81 (23)	150.82±113.04 (127)	100.16±85.97 (20)	89.34±85.13 (84)	NS
Total bilirrubin	1.93±3.78 (18)	1.63±3.38 (126)	1.85±4.57 (18)	1.44±1.95 (107)	1.24±2.15 (11)	1.81±3.63 (64)	NS
Platelets	195038±95203 (26)	246184±170489(146)	189700±91751 (20)	226333±156354(123)	288833±167060(12)	287114±199004(68)	**0.033***
Sepsis severity	n (%)	n(%)	n (%)	n (%)	n (%)	n (%)	NS‡
Sepsis	18 (54.5)	108 (54.5)	16 (50.0)	102 (52.3)	12 (42.9)	64 (40.0)	
Severe sepsis	8 (24.2)	32 (16.2)	8 (25.0)	31 (15.9)	6 (21.4)	19 (11.9)	
Septic shock	6 (18.2)	54 (27.3)	7 (21.9)	44 (22.6)	2 (7.1)	28 (17.5)	
SOFA	7.13±3.284 (31)	7.29±3.552 (190)	7.93±4.059 (30)	6.90±3.727 (181)	5.48±2.442 (21)	6.10±4.077 (141)	NS
qSOFA	1.55±0.959 (33)	1.64±0.812 (197)	1.16±0.808 (32)	1.23±0.844 (192)	1.38±0.941 (26)	1.19±0.905 (146)	NS

[Table/Fig-3]: Vital signs, laboratory and clinical parameters at days 1, 3 and 14 of sepsis. HR: heart rate; MAP: Mean arterial blood pressure; RR: Respiratory rate; WBC: White blood cells; CRP: C-reactive protein; NS: Non- significant, * p-value for t-test, † p-value for Mann-Whitney U test, ‡ p-value for Chi-square test.

The assessed risk of bias was low, according to the analysis carried out with the Cochrane Collaboration´s tool. The in-hospital mortality, available in six clinical trials of this meta-analysis (representing 1620 patients), did not show any benefit associated with the use of statins on the reduction of sepsis mortality, RR 1.04 (95% CI, 0.87-1.24) and the 28-day mortality, available in three clinical trials (representing 634 patients), did not show either any positive effect indicating the use of statins on sepsis, RR 0.93 (95% CI, 0.46-1.89). Also, the different doses or types of statins considered in these clinical trials did not affect the 28-day mortality. To assess the robustness of the findings of this meta-analysis, each clinical trial was excluded, one by one, and such approach failed to alter the overall outcome of the study. This meta-analysis concluded that statins did not significantly reduce mortality of patients with sepsis compared to placebo controls. As a limitation of this meta-analysis, few clinical trials were available which prevented the completion of the examination to assess the funnel plot publication bias and one of the clinical trials had a dominant weight in the investigation.

Differences of outcomes found in recent clinical trials, compared with previous observational studies, may be related with the inclusion of different bias. The meta-analysis of Janda S et al., [8] and of Wan YD et al., [17], suggested the presence of publication bias, the latter with a predominance of asymmetry in the middle and lower segments of the funnel plot analysis, indicating that small studies with negative results are not being published. However, publication bias is not the unique explanation for differences found in studies assessing the use of statins in sepsis. Truwit JD et al., hypothesized that patients receiving statins might belong to a higher socioeconomic status and, therefore, would have better access to health care services and would receive antibiotic therapy earlier for sepsis than those who did not use statins [15]. In this case, reduction of sepsis mortality would not be associated solely with the use of statins. Also, the so-called "healthy user bias" is conceivable. Patients who adhere to preventive therapies are more likely to adopt a broad spectrum of healthy behaviours connected with the lifestyle. In a study by Brookhart MA et al., [18], statin users had a higher rate of influenza vaccination, HR 1.21 (95% CI, 1.12-1.31), and also *Streptococcus pneumonia* vaccination, HR 1.46 (95% CI, 1.17-1.83), which prompts the immune responses to these microorganisms.

In addition to the primary end point of our study, the statin group was about eight years older in average and showed more comorbidities than those in the control group, at the expense of cardiovascular conditions and obesity. This is expected since the main indication for statins is associated with the treatment of atherosclerosis. Similarly, septic patients with prehospital use of statins were an average of 10 years older than patients in the control group of the study of Martin CP et al., [19].

The rate of sepsis mortality at our center (31.2%) was a little below the global average of the ICUs in Argentina (43%), according to a sepsis census at the year 2003 [4]. However, it is known that sepsis outcome is associated with severity at hospital admission. In our study, the APACHE II score averaged 17.1 points while in other Argentinian ICUs with less than 25 points in that score the sepsis mortality was around 36%, similar to ours.

The serum creatinine concentration in the statin group was higher on days 3 and 14, compared to the control group of our study. This finding warrants further investigations but suggests that prior use of statins in septic patients may have a negative effect on renal function. Truwit JD et al., [15] also found that patients with sepsis consuming rosuvastatin had fewer days free of renal failure assessed at day 14 of admission (10.1 ± 5.3 vs. 11.0 ± 4.7, p=0.01). Recent evidence suggests that statins may both protect or harm the kidney depending on a variety of conditions such as dose, type of statins [20] and associated comorbidities.

In our study, previous known predictors of mortality as the Charlson comorbidity index and the APACHE II scores were confirmed. The leukocytosis, in contrast with the leucopenia that may portend poor prognosis, was associated with a lower risk of mortality in sepsis. The use of ciprofloxacin was associated with a higher risk of mortality in septic patients which warrants additional research for proper interpretation. A recent study reported a harmful interaction between the use of statins and ciprofloxacin during urinary tract infection [21].

LIMITATION

As limitations of the present study, we do not have sufficient information of the comparative basal cholesterol levels between both groups, since it is not a routine practice to request lipid profiles to septic patients in this center and the lactate level was not daily requested for all patients. The third international consensus definitions for sepsis (sepsis-3) have proposed differentiating sepsis from septic shock when mean arterial blood pressure is low (≤65 mmHg) and lactate level is increased (≥18mg/dl). It was also recommended that the SOFA score for organ dysfunction should be systematically used in the course of sepsis and that the concept of severe sepsis is redundant [1]. In our study, the average of SOFA score was calculated throughout the evolution of sepsis and no significant differences were found comparing statin users and controls. Forthcoming observational studies about sepsis from Low- and Middle-Income Countries (LMIC) will be challenged with the new classifications due to the lack of systematic lactate determination. A recent publication revised the new sepsis definitions, which is based on data from hospitals in highly developed countries, emphasizing the need for a different paradigm for LMIC where disparities in health services access abound. It also highlights the urgent need of studies of sepsis in LMIC and requests information on sepsis mortality in those contexts [22].

CONCLUSION

To conclude, the findings of the present study indicate that previous use of statins in septic patients admitted in this Argentinian ICU did not reduce in-hospital mortality or 30-day mortality from any cause and also that the use of statins in these patients may be associated with renal impairment.

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