

Epidemiology and outcome of elderly admitted to the ward for sepsis

Pyrpasopoulou A^{1,2}, Pateinakis P¹, Varouktsi A¹, Georgiou E¹, Zografou I¹, Roilides E^{2,3}, Karagiannis A¹

¹2nd Propedeutic Department of Internal Medicine

²Infectious Diseases Unit

³3rd Pediatric Department

Hippokration Hospital, Thessaloniki, Greece

Abstract

Background: The elderly represent a significant cohort of patients presenting at the emergency department, especially in the developed countries. They are characterized by impaired physical condition, comorbidities, and little immune system resources and make frequent use of the healthcare system and its facilities. This study aimed to describe the features and prognostic factors of sepsis in elderly patients (>60 years old) admitted to an internal medicine ward.

Material and Methods: Two hundred eighty eight consecutively patients aged >60 years who were admitted with sepsis during a two-year-period were retrospectively included in the study. Clinical and laboratory parameters at presentation were analyzed. Causes of sepsis and biochemical markers were compared between the healthcare facility-naïve and the healthcare facility-exposed groups. The effect of comorbidities and previous exposure to the healthcare system on clinical course and outcome of the patients was analyzed.

Results: Among the comorbidities that were recorded and included in the analysis, the presence of chronic and acute renal impairment and neurologic disabilities were associated with a worse outcome of sepsis in the elderly. In the same cohort, a previous contact with the healthcare system was found to affect the duration of hospital stay, but not the outcome per se. Sepsis-related markers, such as inflammatory markers were not found to be associated with clinical progression and outcome.

Conclusions: Timely diagnosis and accurate evaluation of the severity of sepsis is required to ensure a better outcome for the patients. Sensitive markers and accurate prognostic models are constantly pursued. The impact of living characteristics of the modern aging society is additionally addressed and their effect on sepsis outcome assessed. Hippokratia 2016, 20(4): 274-278

Keywords: Elderly, sepsis, healthcare facility, outcome, prognostic factors

Corresponding author: Athina Pyrpasopoulou, MD PhD, Consultant in Internal Medicine, 2nd Propedeutic Dept of Internal Medicine, Hippokration Hospital, 49 Konstantinoupoleos str., 54642, Thessaloniki, Greece, tel: +302310892651, fax: +302310835955, e-mail: a.pyrpasopoulou@doctors.org.uk

Introduction

The elderly are characterized by decreased endurance and physiological function^{1,2} and are additionally burdened with a high prevalence of multiple chronic conditions such as diabetes mellitus, heart failure, cerebrovascular disease, chronic respiratory failure etc³. As a direct consequence of their impaired compensatory mechanisms, they are more vulnerable and frail.

Improving healthcare has contributed to increasing life expectancy. The elderly are frequent attendants of the public/private health insurance provisions⁴. This may not always prove to their best of interest; more self-reliance has, at least in some reports, been associated with less antibiotic use, avoidance of hospitalizations, and some avoidable mortality⁵.

Sepsis is a major cause of mortality in the elderly⁶. More frequently encountered infectious syndromes in this age group include pneumonia, urinary tract infec-

tions, and soft tissue and skin infections⁷. Prevalent cause of late mortality is secondary sepsis, possibly due to the exhaustion of the patients' immune system resources⁸.

Early recognition is crucial for increased survival and reduced hospital stay⁹. For this purpose, several biomarkers have been assessed as screening and prognostic tools^{10,11}. These, however, may not be applicable in elderly patients¹².

The aim of this retrospective study was to record the presence of comorbidities in elderly patients admitted with sepsis, and investigate the clinical course and outcome, in association with clinical and laboratory markers.

Material and Methods

Patients aged >60 years, consecutively admitted to an internal medicine ward of a tertiary hospital in Northern Greece with sepsis of all-cause (between July 2013-July 2015) were retrospectively included in the study. Sepsis

was defined by fulfillment of the revised sepsis criteria¹³.

Age, sex, nursing home residence, referral from a hospice/chronic care facility, healthcare facility exposure for a period longer than 48 hours within the preceding six months, and comorbidities were recorded. Cause of sepsis was categorized as pneumonia (lower respiratory tract infection, defined as such by the presence of infiltrates in lung imaging or respiratory failure of abrupt onset not attributable to other causes), urinary tract infection (defined as such by a positive urinary culture or the presence of microorganisms and leucocytes in urine analysis), and other sources of sepsis (skin/soft tissue infections, abdominal infections, bacteremia). Duration of symptoms before presentation and prescription of antibiotics on an outpatient basis were also recorded.

Vital signs and laboratory parameters were recorded and included in the analysis. In a sub-analysis, demographics and laboratory parameters were compared among the group of patients who were admitted from home and did not mention any contact with a healthcare facility for longer than 48 hours within the preceding six months (Group I), and the group that were either admitted from another healthcare facility/nursing home or mentioned contact with a healthcare facility for longer than 48 hours within the preceding six months (Group II).

Outcome (death or survival) and length of stay were analyzed in association with the presence of comorbidities, previous healthcare system exposure, and different clinical and laboratory parameters.

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) statistical software, version 13.0 (SPSS Inc., Chicago, IL, USA). Correlations between variables were tested with the χ^2 -test, the independent samples – t-test and Pearson's and Spearman's correlation, depending on continuity or normality of values of tested variables. A p value <0.05 was considered statistically significant. The study was approved by the Institution's Review Board (Clinical Studies' Review and Ethical Committee Board, Hippokraton Hospital, 19/10/2016).

Results

Two hundred eighty-eight patients were included in total (42.7 % male). The median age of the patients was 82 years (range: 60-97 years). The frequencies of comorbidities were: diabetes mellitus 31.9 %, heart failure 53.4 %, respiratory failure 19.5 %, neurologic disability 33.8 %, and chronic kidney disease (stages III-IV) 57.7 %. Pneumonia was diagnosed in 54.4 %, urinary tract infection in 42.5 %, and other infections in 27 % of the patients. Two hundred forty-four patients (84.7 %) were admitted directly from home, 21 patients (7.3 %) were admitted to the hospital from a nursing home, and 23 patients (8.0 %) were referred from a chronic care facility/ hospice.

One hundred eighty-one (62.8 %) patients were healthcare facility - naïve (Group I), compared to 107 (37.2 %) healthcare facility - previously exposed patients (Group II). No significant differences between these two groups were recorded regarding patients' age and gender as well as their comorbidities. Pneumonia was more frequently recorded in Group I (58.7 % vs 49.1 %, $p=0.058$). Bacteremia (22.4 % vs 11.1 %, $p=0.009$) and urinary tract infection (56.8 % vs 33.9 %, $p<0.001$) were significantly more prevalent among patients of Group II.

Among all laboratory parameters tested, the patients in Group II had significantly lower hemoglobin levels (10.55 g/L vs 11.34 g/L, $p<0.001$) and lower albumin (2.94 g/dL vs 3.34 g/dL, $p<0.001$), than patients in Group I.

Mortality positively correlated with age [$p=0.041$, 95 %CI (-4.6 - -0.1)]. Chronic kidney disease (73.3 % vs 53.4 %, $p=0.006$) and the presence of acute kidney injury at presentation or during the admission for sepsis (69.5 % vs 27.9 %, $p<0.001$) were the most significant prognostic factors for death. A previous admission within the preceding six months did not favor a worse outcome (32.3 % vs 30.1 %, $p=0.743$; Table 1). The duration of symptomatology before presentation correlated negatively with the outcome ($p=0.041$), probably indicating that severe sepsis causing alarming symptomatology usually ran a fulminant course. Among the other parameters

Table 1: Demographics, comorbidities and source of infection in the whole sample, and comparison of the variables in Group I (patients with no contact with a healthcare facility for more than 48 hours within the preceding six months) and Group II (patients admitted from another healthcare facility/nursing home or mentioned contact with a healthcare facility for more than 48 hours within the preceding six months).

	Total	Group I	Group II	p
Number of patients (%)	288 (100.0)	181 (62.8)	107 (37.2)	
Age (years)	82 [60-97]	80.4	80.3	0.885
Sex (male) (%)	42.7	43.1	42.0	0.863
Diabetes Mellitus (%)	31.9	30.9	33.7	0.634
Heart Failure (%)	53.4	51.7	56.1	0.478
Respiratory Failure (%)	19.5	19.9	18.9	0.833
Neurologic Deficits (%)	33.8	30.4	39.6	0.110
Chronic Kidney Disease (%)	57.7	57.5	55.8	0.625
Acute Kidney Injury (%)	36.9	35.7	38.8	0.599
Pneumonia (%)	54.4	58.7	49.1	0.058
Urinary Tract Infection (%)	42.5	33.9	56.8	<0.001
Other (infection) (%)	27.0	23.4	33.0	0.082
Bacteremia (%)	15.3	11.1	22.4	0.009
Outcome (Death) (%)	21.5	18.2	27.1	0.077
Duration of stay (survivors) (days)	8.6 [1-38]	8	9.7	0.050

tested, low mean arterial blood pressure (MAP), low bicarbonate levels, high lactate, hypernatremia, anemia, increased leucocyte counts, and hypoalbuminemia were all significantly associated with a worse outcome (Table 2). In the patients who survived, duration of hospital stay was not related to age, sex or present comorbidities, but was longer in the patients who had previously been healthcare facility exposed (9.7 vs 8.0 days, $p = 0.050$). Prolongation of hospital stay was recorded in relation to increased serum creatinine ($p = 0.011$) at presentation.

Discussion

The actual global burden of sepsis can only be estimat-

ed upon, as population-level epidemiologic data for sepsis is scarce, particularly for low- and middle-income countries¹⁴. The biggest part of the available research has dealt with the epidemiology of sepsis in specific high-risk populations, such as surgical patients postoperatively, patients in burn units, maternal and neonatal sepsis etc¹⁵. Recent studies have suggested that the global incidence of sepsis has been rising in the last decades¹⁶. However, carefully designed global population-based studies to assess the real burden of sepsis and its mortality are scarce.

This study is one of only few providing data about sepsis incidence and outcome on general medical wards¹⁷. Moreover, it addresses the elderly, an age group with sev-

Table 2. Correlation of the outcome (death) with epidemiological, clinical and laboratory variables.

Variable (Units)	Death	Recovery	p	95% CI
Age (years)	82.2	79.8	0.041	-4.6 - -0.1
Sex (male) (%)	41.9	42.9	0.890	NA
Duration of symptoms (days)	2.5	3.8	0.041	+0.1 - +2.5
Prior treatment with ABx (%)	60.0	50.5	0.570	NA
Previous Admission (%)	32.3	30.1	0.743	NA
Community-only (%)	53.2	65.5	0.077	NA
Diabetes Mellitus (%)	38.7	30.1	0.197	NA
Heart Failure (%)	50.1	54.1	0.650	NA
Respiratory Failure (%)	16.4	20.4	0.489	NA
Neurologic Disabilities (%)	44.3	31.0	0.052	NA
Chronic Kidney Disease (%)	73.3	53.4	0.006	NA
Acute Kidney Injury (%)	69.5	27.9	<0.001	NA
Pneumonia (%)	54.1	54.5	0.951	NA
Urinary Tract Infection (%)	49.1	40.7	0.255	NA
Bacteremia (%)	24.2	12.8	0.028	NA
Mean Arterial Blood Pressure (mmHg)	76.4	86.0	<0.001	+4.9 - +14.4
Leucocytes (/uL)	15,418	12,038	0.001	-5440 - -1319
Hemoglobin (g/L)	10.8	11.4	0.040	+0.0 - +1.2
Albumin (g/dL)	2.7	3.3	<0.001	+0.4 - +0.8
Potassium (K) mEq/L	4.4	4.2	0.132	-0.4 - +0.1
Sodium (Na) mEq/L	139.7	137.1	0.005	-4.5 - -0.8
Lactate (mg/dL)	31.1	12.9	<0.001	-24.4 - -11.9
HCO₃⁻ (mmol/L)	20.5	22.8	0.040	-0.1 - +4.4
Prothrombin time (sec)	15.5	13.1	0.009	-4.2 - -0.6
Partial thromboplastin time (sec)	39.6	32.6	<0.001	-10.1 - +4.0
Fibrinogen (mg/dL)	488.4	518.5	0.373	-36.4 - +96.8
Erythrocyte Sedimentation Rate (mm/hr)	57.2	66.7	0.411	-13.3 - +32.4
C-Reactive Protein (mg/L)	121.7	101.9	0.224	-51.8 - +12.2

CI: Confidence Interval, ABx: antibiotics, NA: not applicable.

eral ominous features: high prevalence of comorbidities and a high frailty score¹⁸. Chronic neurologic disability has been associated with increased severity of sepsis in patients with other concomitant comorbidities¹⁹. In our setting, neurologic disability tended to negatively affect the outcome of sepsis in this cohort; however, chronic and acute deterioration of renal function were the strongest prognostic factors of death among the comorbidities included in the analysis²⁰.

As the world population continues to age, frequent utilization of healthcare system will become increasingly more common in the elderly. Readmission for a secondary sepsis alone is common and has been associated with an unfavorable prognosis²¹. Hospitalizations for other causes have also been linked to a predisposition for a late (within 90 days) development of sepsis²². Regular users of different healthcare services may, as suggested by the results of this study, carry distinct clinical (worse nutritional status-anemia, hypoalbuminemia) and sepsis-associated features (higher incidence of bacteremia/urinary tract infection) compared to their community-derived counterparts. The previous hospitalization did not predict a worse clinical outcome. However, users of the healthcare system tended to have a worse prognosis. This could also partly be attributed to the fact that specific forms of sepsis, such as bacteremia, which associates with increased severity of sepsis and a higher incidence of death, was more frequently encountered in this group. The impact of previous healthcare facility exposure was more prominent on the duration of hospital stay, probably because of the higher frailty score of these particular patients. Established prognostic factors for the outcome of sepsis such as hypoalbuminemia, abnormal clotting tests, acidosis, severe anemia were capable to predict death/survival; as no significant difference in terms of outcome between the two groups could be proven, this effect was probably related to the severity of sepsis per se rather than a reflection of worsening physical condition. Other markers like C-reactive protein or fibrinogen did not, probably indicating an impaired systemic inflammatory response syndrome potentially masking the underlying clinical condition of the affected individuals²³.

The elderly who are characterized by impaired physiological responses and little immune system resources represent a particular group for which general population guidelines and practices may not be directly applicable.

This study has several drawbacks. The patients that were included were not rated according to their sepsis severity. It was conducted in a large hospital covering for a densely-populated urban area. Well-designed multi-centered studies with larger numbers of enrolled patients are expected to provide a more concrete reflection of the size of the problem and the special features of this infectious syndrome in this cohort. Nevertheless, it describes a significant clinical problem of this particular age group and its components and addresses the impact of living characteristics of modern society on a continuously aging population.

Conflict of interest

Authors declare no conflict of interest related to this study. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgement

We wish to thank Dr Iordanis Romiopoulou, Prof. Konstantinos Petidis and Prof. Charalampos Antachopoulos for their valuable consultations on the patients' diagnostic evaluation and medical care.

References

1. Fabricio-Wehbe SC, Rodrigues RA, Haas VJ, Fhon JR, Diniz MA. Association of frailty in hospitalized and institutionalized elderly in the community-dwelling. *Rev Bras Enferm.* 2016; 69: 691-696.
2. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc.* 2013; 14: 392-397.
3. Ward BW, Black LI. State and Regional Prevalence of Diagnosed Multiple Chronic Conditions Among Adults Aged ≥18 Years - United States, 2014. *MMWR Morb Mortal Wkly Rep.* 2016; 65: 735-738.
4. van den Busche H, Kaduszkiewicz H, Schäfer I, Koller D, Hansen H, Scherer M, et al. Overutilization of ambulatory medical care in the elderly German population?--An empirical study based on national insurance claims data and a review of foreign studies. *BMC Health Serv Res.* 2016; 16: 129.
5. Kroneman M, Boerma W, van den Berg M, Groenewegen P, de Jong J, van Ginneken E. Netherlands: Health System Review. *Health Syst Transit.* 2016; 18: 1-240.
6. Liang SY. Sepsis and Other Infectious Disease Emergencies in the Elderly. *Emerg Med Clin North Am.* 2016; 34: 501-522.
7. Liang SY, Mackowiak PA. Infections in the elderly. *Clin Geriatr Med.* 2007; 23: 441-456, viii.
8. Suzuki K, Inoue S, Kametani Y, Komori Y, Chiba S, Sato T, et al. Reduced Immunocompetent B Cells and Increased Secondary Infection in Elderly Patients With Severe Sepsis. *Shock.* 2016; 46: 270-278.
9. Smyth MA, Brace-McDonnell SJ, Perkins GD. Identification of adults with sepsis in the prehospital environment: a systematic review. *BMJ Open.* 2016; 6: e011218.
10. Ryu JA, Yang JH, Lee D, Park CM, Suh GY, Jeon K, et al. Clinical Usefulness of Procalcitonin and C-Reactive Protein as Outcome Predictors in Critically Ill Patients with Severe Sepsis and Septic Shock. *PLoS One.* 2015; 10: e0138150.
11. Hwang YJ, Chung SP, Park YS, Chung HS, Lee HS, Park JW, et al. Newly designed delta neutrophil index-to-serum albumin ratio prognosis of early mortality in severe sepsis. *Am J Emerg Med.* 2015; 33: 1577-1582.
12. Yilmaz H, Duran L, Yanik K, Altuntaş M, Sünbül M. Differences in the effectiveness of serum biomarkers for the diagnosis of bacterial infections in adult and elderly patients admitted to the emergency department. *Turk J Med Sci.* 2015; 45: 553-557.
13. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med.* 2003; 31: 1250-1256.
14. Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P, et al; International Forum of Acute Care Trialists. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. *Am J Respir Crit Care Med.* 2016; 193: 259-272.
15. Jawad I, Lukšić I, Rafnsson SB. Assessing available information on the burden of sepsis: global estimates of incidence, prevalence and mortality. *J Glob Health.* 2012; 2: 010404.
16. Gobatto AL, Besen BA, Azevedo LC. How Can We Estimate

- Sepsis Incidence and Mortality? *Shock*. 2017; 47: 6-11.
17. Mazzone A, Dentali F, La Regina M, Foglia E, Gambacorta M, Garagiola E, et al. Clinical Features, Short-Term Mortality, and Prognostic Risk Factors of Septic Patients Admitted to Internal Medicine Units: Results of an Italian Multicenter Prospective Study. *Medicine (Baltimore)*. 2016; 95: e2124.
 18. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age Ageing*. 2006; 35: 526-529.
 19. Liao KM, Lin TC, Li CY, Yang YH. Dementia Increases Severe Sepsis and Mortality in Hospitalized Patients With Chronic Obstructive Pulmonary Disease. *Medicine (Baltimore)*. 2015; 94: e967.
 20. Tang Y, Choi J, Kim D, Tuddud-Hans L, Li J, Michel A, et al. Clinical predictors of adverse outcome in severe sepsis patients with lactate 2-4 mM admitted to the hospital. *QJM*. 2015; 108: 279-287.
 21. Sun A, Netzer G, Small DS, Hanish A, Fuchs BD, Gaieski DF, et al. Association Between Index Hospitalization and Hospital Readmission in Sepsis Survivors. *Crit Care Med*. 2016; 44: 478-487.
 22. Prescott HC, Dickson RP, Rogers MA, Langa KM, Iwashyna TJ. Hospitalization Type and Subsequent Severe Sepsis. *Am J Respir Crit Care Med*. 2015; 192: 581-588.
 23. Janz DR, Bastarache JA, Sills G, Wickersham N, May AK, Bernard GR, et al. Association between haptoglobin, hemopexin and mortality in adults with sepsis. *Crit Care*. 2013; 17: R272.