DIAGNOSTIC AND PROGNOSTIC VALUE OF PRESEPSIN IN THE EMERGENCY DEPARTMENT

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DIAGNOSTIC AND PROGNOSTIC VALUE OF PRESEPSIN IN THE EMERGENCY DEPARTMENT (Abstract): Sepsis syndrome is a common situation and has devastating implications on health care systems worldwide. Biomarkers may have an important role to highlight the presence, absence or severity of sepsis. **Material and methods**: Retrospective study is conducted on a group of 95 suspected sepsis patient (0.16%) out of a total of 56,996 patients that were presented in the Emergency Department / Emergency County Hospital "St. Spiridon" from Iaşi during 01.01.2012-01.12.2012. The study aims to establish the following: the incidence of sepsis diagnosis, analysis of prognostic factors, relationship between the presepsin value and clinical outcome. **Results**: In men, there was a distribution of cases between the age of 22 years up to 89 years with an average confidence interval between 59.32 and 67.23 years, and the distribution of cases varies among women from age of 40 years up to 93 years, with an average confidence interval between 65.53 and 75.47 years The most frequent primary source of infection is localized at the pulmonary level, in a total of 21.1%, followed by abdominal location occurring in a total 14.7%. Area under the curve in ROC curve analysis regarding mortality showed significant values of area for presepsin (0.859), leukocytes (0.790), traumatic injuries association (0.761) and the presence of gastrointestinal history. **Conclusions**: Presepsin has diagnostic value, early prognostic value and is an early marker of mortality in septic patients. Trauma associated with severe systemic infection leads to an increase in mortality. **Keywords**: SEPSIS, BIOMARKER, PRESEPSIN, MORTALITY.

The progress made over the last two centuries in fighting against infectious pathology may suggest at first glance an optimistic vision of this type of pathology compared to the early era of antibiotics. Sepsis is defined as an infectious disease, caused by bacterial microorganism, evolving as a serious systemic infection and will progress to severe sepsis (acute organ dysfunction caused by an infection or suspected to be caused by an infection) and to septic shock (severe sepsis associated with hypotension that does not respond to fluid resuscitation therapy), installed as a result of discharging in the blood flow of pathogens, toxins and cellular disintegration products. Sepsis and its clinical forms must be regarded as stages of the same disease (1).

Sepsis syndrome is a common in Intensive Care Units and has devastating implications on health care systems worldwide.

Estimated average annual cost for care of patients with sepsis was calculated to be worth $ 16.7 billion in 2008 (2).

Severe systemic infection and sepsis are challenging overcrowded emergency services, and in literature is described various causes of severe *sepsis*, even after intrauterine devices insertion (3). Other issue is the fact that septic infections were characterized by etiologic polymorphism and resistance to antibiotics (4). Failure to recognize these entities at the appropriate time, followed by early initiation of therapy and supportive etiological treatment can lead to degradation of vital parameters or even death in these patients. Hence the need for the use of laboratory diagnostic methods easy to use with high sensitivity and specificity to allow an early diagnosis prior installation of septic shock phase.

Biomarkers may have an important role to highlight the presence, absence or severity of sepsis, and can differentiate a bacterial infection of viral or fungal, in addition helps the differential diagnosis of sepsis (systemic infection) with a local infection.

Presepsin (sCD14-ST) - CD 14, is a glycoprotein expressed on the cell membrane surface of monocytes and macrophages present in macrophages, monocytes and granulocytes, is responsible for intracellular signal transmission triggered by the presence of endotoxins. Soluble fraction was called soluble CD14 subtype or presepsin has increased plasma levels in infections.

Cut-off value of presepsin allowing systemic inflammatory response syndrome differentiation within bacterial infectious diseases and nonbacterial was determined to be 600 pg/ml, the clinical sensitivity and specificity were 87.8% and 81.4% (5).

MATERIAL AND METHODS

This study is a retrospective study conducted on a group of 95 (0.16%) patients with suspected sepsis out of a total of 56,996 patients that were presented in the Emergency Unit - Emergency County Hospital “St. Spiridon” from Iaşi during 01.01.2012 -01.12.2012.

The study aims to establish the following:

- Incidence of sepsis diagnosis presented in the Emergency Unit - Emergency County Hospital "St. Spiridon "- Iasi;
- Clinical-tracking according to the precocity of when the patients are diagnosed and how long the therapy is initiated;
- Analysis of prognostic factors;
- Analyzing the relationship between trauma and sepsis on survival;
- The relationship between the obtained presepsin value and clinical outcome (on early diagnosed and properly treated patients).

The study protocol included the following data taken from the group of patients: epidemiological, clinical and laboratory variables, medical treatment administered in the Emergency Department (ED) - Hospital “St. Spiridon” from Iaşi, evolution.

Inclusion criteria: patients over 18 years; patients with clinical signs of infection accompanied by the presence of at least two of the following criteria: temperature > 38°C or < 36°C, heart rate > 90 / min, respiratory rate > 20 /min and leukocytosis (>12,000 mm^3) or leukopenia (<4,000 mm^3).

Exclusion criteria: patients under age of 18 years; patients who are pregnant or lactating.

The diagnosis of sepsis was made based on the clinical signs (specific and usually signs) in conjunction with other investiga-

tions, respecting the diagnostic criteria from Surviving Sepsis Campaign statements (5).

For each patient with suspected sepsis in the ED, approach was standardized based on specific protocols existing on emergency medicine specialties. The patient was clinically evaluated, vital signs was monitored and when clinical suspicion of infection arise the clinicians started to complete a case sheets including clinical and laboratory variables listed according with the definition of sepsis.

For patients who experienced associated traumatic injuries, protocol was applied for diagnosis and treatment of trauma patients according to existing guidelines and protocols.

Data collected from records of patients meeting inclusion criteria were processed statistically using statistical analysis software IBM-*SPSS 22.0.*

RESULTS

Structurally, the study group included 61 men, corresponding to a percentage of 64.21% and 34 women, representing a rate of 35.79%. Statistical analysis highlights an average age of 65.86 years in study participants, the mean age being 63.28 on men and 70.5 years on women (tab. I).

TABLE I

Table comparision mean age male/female

Sex related distribution	Mean	N	Std. Deviation
Male	63.28	61	15.443
Female	70.50	34	14.254
Total	65.86	95	15.351

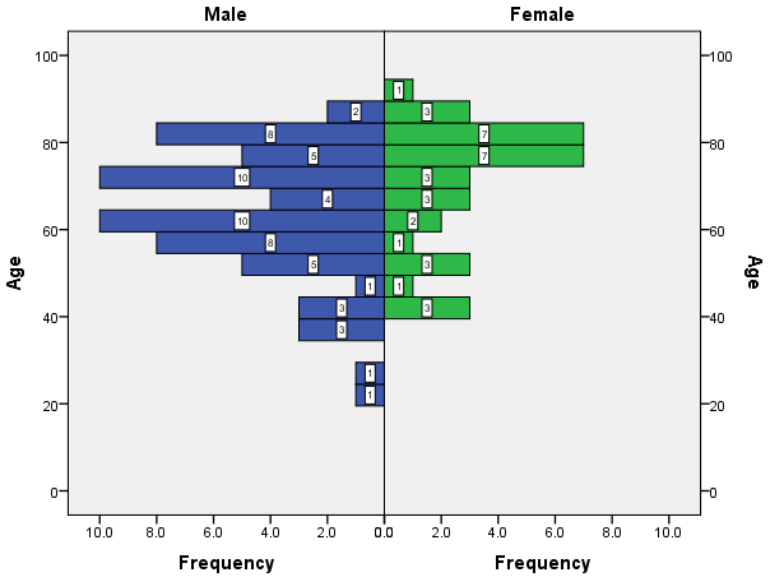

Fig. 1 Distribution of patients according to sex and age group

In men, there was a distribution of cases between the age of 22 years up to 89 years with a average confidence interval between 59.32 and 67.23 years, and for women the distribution of cases varies by age in a range from 40 years up to 93 years, with an average confidence interval between 65.53 and 75.47 years. The highest frequency recorded in men's was in 60-80 years age range and for women the most frequent cases were recorded in the range 70-80 years (fig. 1).

The most frequent primary source of infection is localized in the lung, 21.1%, followed by abdominal location occurring in 14.7%. In a percentage of 45.3% we could not detect during their presence in the E. D."St.Spiridon" the primary source of infection (tab. II).

TABLE.II

Primary source of infection

Primary source		Frequency	Percent	Valid percent	Total percent
Territory	Unspecified	43	45.3	45.3	45.3
	Pulmonary	20	21.1	21.1	66.3
	Cutanat	7	7.4	7.4	73.7
	Genito-Urinary	7	7.4	7.4	81.1
	Abdominal	14	14.7	14.7	95.8
	Central Nervous System	3	3.2	3.2	98.9
	Cardiac	1	1.1	1.1	100.0

The distribution of the starting point of systemic infection coupled with a mean age of patients shows a high average age for starting point located on pulmonary territory (71.5 years), followed by abdominal starting point (70.64 years), with the lowest average age if systemic infection was with cardiac starting point (22 years) (tab.III).

TABLE III

Epidemiological characteristics by age and primary source of infection

Diagnostic	Mean	N	Std. Deviation	Range	Minimum	Maximum
Unspecified	65.26	43	14.825	68	25	93
Pulmonary	71.50	20	13.690	51	38	89
Cutaneous	59.71	7	14.557	39	40	79
Genito-Urinary	61.86	7	13.434	33	51	84
Abdominal	70.64	14	13.765	45	44	89
Central Nervous System	53.00	3	19.672	39	35	74
Cardiac	22.00	1	.	0	22	22
Total	65.86	95	15.351	71	22	93

In addition to the usual biological constants laboratory determining, presepsin values determination was made in all patients included in the study, we observed an average value of its 2,519.25 pg / ml (tab. IV).

TABLE IV
Biological variables values

	N	Minimum	Maximum	Mean	Std. Deviation
Leucocytes	95	880	66,100	17,778.42	11,012.784
Thrombocytes	95	52,900	60,2000	253,029.47	133,950.395
INR	95	0	2	0.54	0.727
Glycemia	95	46	460	155.55	77.027
pH	95	6.80	7.58	7.3501	0.17002
RA	95	4.9	39.0	21.088	6.9188
Presepsin	95	145	20000	2519.25	3,169.939

We analyzed using Receiver Operating Characteristic curve (ROC) the correlation between the presepsin value and mortality in the group of patients, along with other variables but statistical significance values were obtained only between the value of leukocytes, history of gastrointestinal disease and trauma association in patients with sepsis (tab.V, fig.2). Area under the curve (AUC) showed significant values for presepsin (AUC=0.859), leukocytes (AUC=0,790), traumatic injuries association (AUC=0.761) and the presence of gastrointestinal history.

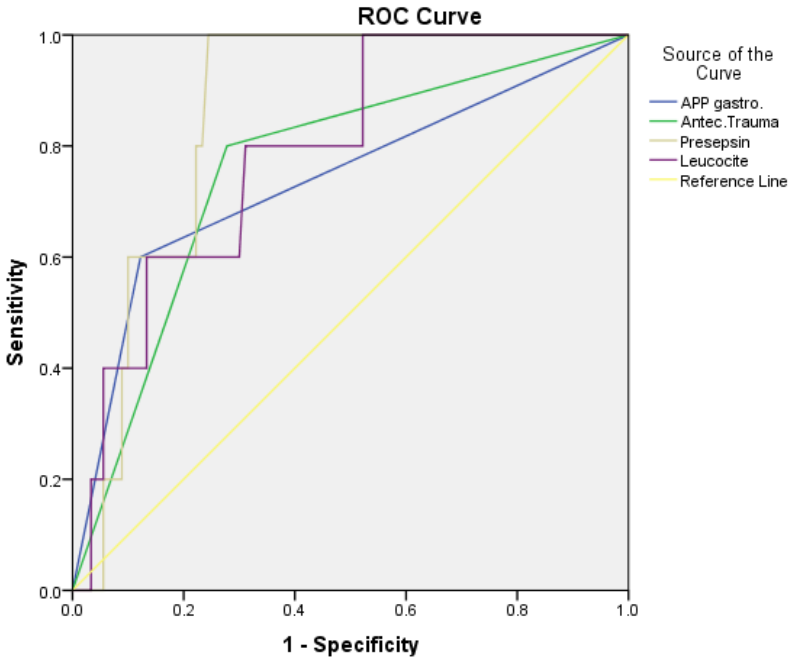

Fig. 2 ROC curve mortality-presepsin, leucocytes, trauma, and history of gastrointestinal disease

TABLE V

ROC Curve Mortality

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Gastro-intestinal history	.739	.134	.073	.477	1.000
Trauma history	.761	.108	.050	.550	.973
Presepsin	.859	.046	.007	.769	.949
Leucocytes	.790	.087	.030	.619	.961

The analysis of correlations between variables was made using Pearson method, significant correlations were detected between traumatic injuries and need for orotracheal intubation maneuver, mortality, low Glasgow coma score (GCS less than 9 points) and admission on intensive care unit. The analysis of presepsin show statistically significant correlations between this values and the presence of septic shock, need for vasopressor medication and need for advanced management on airways orotracheal intubation (OTI) (tab. VI, VII, VIII).

TABLE.VI

Corelation presepsin-TAS

		Presepsin	TAS
Presepsin	**Pearson Correlation**	1	-.308**
	Sig. (2-tailed)		.002
	N	95	95

**. Correlation is significant at the 0.01 level (2-tailed).

TABLE VII

Corelation presepsin-vasopressor

		Presepsin	Vasopressor
Presepsin	**Pearson Correlation**	1	.315**
	Sig. (2-tailed)		.002
	N	95	95

**Correlation is significant at the 0.01 level (2-tailed).

TABLE VIII

Corelation Traum –OTI, GCS, Mortalitate

Trauma asociated		OTI	GCS	Mortality
Trauma	**Pearson Correlation**	.395**	-.251*	.254*
	Sig. (2-tailed)	.000	.014	.013
	N	95	95	95

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

The sepsis average age described in the literature has increased over time, from an average of 68.2 years up to 64.1 years, the average age obtained in the present study were of 65.86 years (7). Men have more susceptibility than women to develop sepsis and severe sepsis, the data of the present study is consistent with international reporting (8).

Most commonly the initial source of infection that developed sepsis is described in the literature to be on pulmonary level, followed by 2nd primary location on gastrointestinal level, the values obtained by us located the same frequency in the top, and also in literature a significant proportion of sepsis cases described the primary infection location as uncertain or not identified (8, 9).

Presepsin is described as the only independent variable that can be associated with survival at 28 days or hospitalization in the intensive care ward and prognostic accuracy is increased compared with procalcitonin and other biomarkers (10, 11, 12). The area under the curve obtained in our study show values comparable to those described in the few studies published up to present date, the value obtained in this study were AUC=0.859, compared with other studies that showed values between AUC=0.640 to AUC= 0.790 (11, 12).

The correlation between the occurrence of septic shock, presepsin value and need for vasopressor therapy was recently described in the literature (13).

The combination of traumatic injuries and further development of sepsis and severe sepsis is described in the literature, with a predominance of this pathology in males, with a mortality still high, ranging from 19.5-23% of cases (14, 15) . Due to the increased severity of this association is explained correlation with the need for advanced airway management and low Glasgow coma score on this category of patients.

CONCLUSIONS

Presepsin early diagnostic value may also have prognostic value over the subsequent evolution of the patient.

Presepsin is an early marker of mortality in septic patients.

Trauma associated with severe systemic infection leads to an increase in mortality compared with patients in the group that did not have a diagnosis of trauma associated (p=0.013).

Endotracheal intubation maneuver needs to be considered in patients with the diagnosis of sepsis associated with trauma (p=0.00076).

Combination of multiple trauma injury and sepsis will lead to a fast deterioration in neurological status of the patient, the Glasgow coma score fell below 9 points in these patients (p = 0.014).

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NEWS

INTERACTION BETWEEN EBOLA VIRUS AND THE EXTRACELLULAR MATRIX

Ebola virus disease (EVD) represents a global public health threat concern. Limited therapeutic and prophylactic options are available for patients suffering from this disease. The EV glycoprotein (GP) is the main determinant causing structural damage of endothelial cells which triggers the hemorrhagic diathesis. However, the molecular mechanisms of this phenomenon remains elusive. In a study by Veljkovic et al. the interaction of GP with endothelial extracellular matrix (ECM) was investigated using the informational spectrum method (ISM), a virtual spectroscopy method for analysis of the protein-protein interactions. The results of the study suggest that Elastin Microfibril Interface Located Proteins (EMILINs) are involved in interaction between GP and ECM. The study concluded that this finding leads to a better understanding of EV/endothelium interaction and its role in pathogenesis, prevention and therapy of EVD (Veljkovic V1, Glisic S1, Muller CP2, Scotch M3, Branch DR4, Perovic VR1, et al. In silico analysis suggests interaction between Ebola virus and the extracellular matrix. Front Microbiol. 2015; 6: 135. doi: 10.3389/fmicb.2015.00135. eCollection 2015).

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