Sepsis and septic shock in the general intensive care unit of University hospital of Split : a retrospective study of incidence, mortality and length of stay

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Diploma thesis

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To my thesis supervisor and mentor Assoc. Prof. Nenad Karanovic for his consistent help and guidance.

To my family, for all their love and support.

To my parents, for giving everything they can, always, in order for me to follow my dreams.

To my friends, for always being there and making my life so much more joyous.

1. INTRODUCTION

1.1 Etiology

Sepsis is a severe clinical condition of the body in response to an infection (1). Before the year of 2016, the diagnosis of sepsis was made in a patient with systemic inflammatory response syndrome (SIRS) resulting from an infection.

SIRS is defined by the presence of 2 or more of the following criteria in a patient;

- temperature of above 38°C or below 36°C,
- heart rate of above 90 beats per minute,
- respiratory rate of >20 breaths per minute,
- PaCO2 of below 32 mmHg
- white blood cell count of above 12 x 10^9 or below 4 x 10^9 (2,3)

This definition has since been revised in the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (4). Before this revision the definition of sepsis was concentrated on SIRS reaction to an infection (5-8), these criteria can still aid in identifying patients with sepsis. The revised definition of sepsis states that sepsis is "a life-threatening organ dysfunction caused by a dysregulated response to infection."(4,9-11). Instead of the before used SIRS criteria the definition of sepsis now focuses on the sequential organ failure assessment (SOFA), where sepsis is diagnosed in a patient with an increase of the score by 2 or more (4).

Additionally, septic shock has also been defined in the Sepsis-3 campaign stating that shock as a result of sepsis, in which, great circulatory, metabolic and cellular abnormalities are associated with a higher risk of mortality compared with sepsis alone (4,9).

The etiology of sepsis is generally associated with further conditions such as perforation, compromise, or rupture of an intra-abdominal or pelvic structure (12). Sepsis may also be a consequence of direct introduction through an intravenous infusion.

In the US a study from 1979-2000 showed that the most prevalent isolated pathogens were gram-positive bacteria Streptococcus pneumoniae and Staphylococcus aureus and the gram-negative bacteria Escherichia coli, Klebsiella spp., and Pseudomonas aeruginosa (13,14). With the most common sites of infection being lungs or abdomen (15,16).

1.2 Epidemiology

As the definition of sepsis and septic shock was changed recently the epidemiology can be hard to evaluate (17). Shankar et al. showed that with the new sepsis-3 definition "The extrapolated population incidence of Sepsis-3 sepsis and Sepsis-3 septic shock was 101.8 and 19.3 per 100 000 person-years, respectively, in 2015" (17), the study was carried out in England.

In Croatia there are not a lot of studies regarding epidemiology of sepsis and septic shock especially with the new definition in mind. The studies done are with the old definition and results showed an estimated annual incidence of sepsis in Croatia is 0.06% of the population in 2005 (18).

The incidence of sepsis around Europe is approximately 30% with different numbers between countries (19)The incidence seems to be rising which probably can be attributed to an aging population. The mortality of patients with sepsis is very high and is shown to be around 50% (19,20).

1.3 Pathogenesis

The revised sepsis definition states that sepsis is a severe clinical condition of the body in response to an infection (3). The organ dysfunction is characterized by an increase of the SOFA score of 2 or more from 0, or the patients baseline. The SOFA score system considers the function of respiration, coagulation, liver, cardiovascular, central nervous system and renal (4).

Further, septic shock is defined as "a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone." (4) Patients with septic shock are identified as those who require vasopressors to maintain a mean arterial pressure of 65 mmHg or more and with a serum lactate level of more than 2 mmol/L (4).

Sepsis activates both pro- and anti-inflammatory processes (4,21), usually seen as an early hyper-inflammatory phase over a few days and then a more extended immunosuppressive phase (21,22).

Septic patients recurrently manifest disseminated intravascular coagulation (DIC) (2), they show an alteration of all three of Virchow's classic triad, changes in coagulability,

endothelial cell injury, and abnormal blood flow and thus blood flow to vital organs is reduced. (2).

Apart from the pro- inflammatory and anti-inflammatory processes seen in sepsis, major changes in nonimmunologic pathways such as cardiovascular, neuronal, autonomic, hormonal, bioenergetic, metabolic and coagulation (4,23), Singer et al. further claims that the organ dysfunction seen in the patients is not associated with substantial cell death (4).

1.4 Clinical manifestations

The clinical manifestations of sepsis and septic shock can be plenty and unspecific. Any of the SIRS criteria can be seen in the patient as well as the SOFA score system. These include changes in respiration with a decrease of PaO2 pressure, dysfunction of coagulation with a decrease in platelet count, liver dysfunction, shown as an increase in bilirubin, as well as in AST and ALT levels, cardiovascular dysfunction and hypotension, mental alteration, renal dysfunction shown as decrease in urine output and an increase in serum creatinine levels (4,24).

Depending on the origin of infection manifestation of the local infection may also be seen, i.e. peritonitis in abdominal origin.

Septic shock manifests in the patient with sepsis by persistent hypotension even with the use of vasopressors (4,25-27).

1.5 Risk factors

The most obvious risk factor for sepsis and septic shock are infection of any origin. The risk of developing sepsis and septic shock is also increased in patients with renal disease, indwelling urinary catheter, hematologic malignancy, neutropenia, solid tumors, liver disease, pulmonary disease and pneumonia. (28-30).

1.6 Diagnostic methods

1.6.1 Definition

As sepsis has been hard to define (4,6,7), no clear diagnostic methods or tests exists (4,10) and diagnosis is still mostly made up of clinical signs and symptoms.

The SIRS criteria can still help in aiding with diagnosis of sepsis even though they are considered to be nonspecific (4).

The 2001 task force noted that various examination findings and laboratory test results are indicative of organ dysfunction (7) which then can be used in the diagnosis of sepsis. These are included in the SOFA scores and so the diagnosis of sepsis is thus made in a patient with assumed infection, and an increase in SOFA scores of 2 or more (4,24).

1.6.2 SOFA score

The diagnostic methods for sepsis and septic shock are thus based on the clinical criteria from the task force in 2016 (10,11). With the help of the SOFA score and assumption or proof of an infection in a patient, the diagnosis is made (Table 1.). There is no redefinition of infection and the suspicion or confirmed case of an infection is enough when there is organ dysfunction to diagnose sepsis, as well as the prediction of mortality. Routine microbiologic cultures should however be done when there is a suspicion, preferably before the onset of antibiotic therapy or within 24 hours (9).

Table 1. The SOFA scoring system (4)

Score	0	1	2	3	4
PaO2/FIO2, mmHg (kPa)	400 (53.3)	400 (53.33)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Platelets, x10^3/µL	150	150	<100	<50	<20
Bilirubin µmol/L	20	0-32	33-101	102-204	>204
Cardiovascular	MAP >70 mmHg	MAP <70 mmHg	Dopamine <5 or dobutamine (any dose)	Dopamine 5.1-15 or epinephrine/norepinephrine <0.1	Dopamine >15 or epinephrine/norepinephrine >0.1
Glasgow coma scale score	5	3-14	10-12	6-9	<6
Creatine µmol/L Urine output, mL/day	110	10-170	171-299	300-440 <500	>440 <200

MAP= mean arterial pressure. Vasoactive drugs (dopamine or norepinephrine) are given as µg/kg/min and given for at least 1 hour.

The quick SOFA score (qSOFA) was developed for screening of patients with a suspicion of sepsis outside of an ICU setting (Table 2.). Any 2 of the 3 variables is considered to be positive and should warrant for further investigation in the patient. The criteria being; altered mentation by a Glasgow coma scale (GCS) of less than 13, respiratory rate above 22 breaths per minute and a systolic blood pressure of 100mmHg or less (4, 31).

Table 2. The qSOFA scoring (4)

qSOFA score	
Respiratory rate	>22 per minute
Altered mental state	GCS <13
Systolic blood pressure	<100 mmHg

1.6.3 Definition of septic shock

Septic shock is a subset of sepsis with profound consequences and increased mortality in patients suffering from it (4, 10). When sepsis leads to hypoperfusion and the patient needs to be treated by vasopressors, septic shock is diagnosed (32).

Septic shock is diagnosed in a patient with sepsis where hypotension is persistent (mean arterial pressure of below 65mmHg) even with the use of vasopressors and where fluid resuscitation has been adequate, as well as an increase in serum lactate. Hyperlactemia is defined as a value of more than 2 mmol/L (18 mg/dL) (4, 11).

The mortality is significantly higher in patients with septic shock, due to the unresponsiveness to therapy as well as the multiple organ dysfunction of the patient (1).

1.7 Treatment

1.7.1 Resuscitation

Early resuscitation of a septic patient, within 6 hours of recognizing sepsis should be initiated (9). The initial amount of crystalloids should be aimed at a quantity of 30 ml/Kg, given rapidly, within the first 3 hours (higher amounts and quantity may be necessary in some patients). Albumin can further be added in those patients who require a continuous and substantial amount of crystalloids to maintain adequate mean arterial pressure, even though this is a recommendation with weak evidence of effectiveness (9). The fluid challenge should be continued as long as an improvement is seen in the patient. After the initial resuscitation,

continuous fluid therapy should be given after frequent reassessment of hemodynamic status (9).

1.7.2 Antibiotics

Blood cultures should preferably be taken before initiation of antimicrobial therapy. If possible, imaging studies should be performed to confirm site of infection. The initiation of antimicrobial therapy should be started within an hour of diagnosis for both sepsis and septic-shock. The recommendation is to use broad-spectrum therapy with the use of more than one antimicrobial therapy to cover as many pathogens as possible until blood cultures are back, and a specific antibiotic therapy can be introduced (9). Treatment duration of 7-10 days is adequate for both sepsis and septic shock (9). Procalcitonin levels can be used to shorten the duration of antibiotics therapy (9).

1.7.3 Vasopressors

Norepinephrine is recommended as the first vasopressor of choice (9). Vasopressin or epinephrine can be added to raise the mean arterial pressure (MAP) to the target value of 65 mmHg in patients with shock (9).

The targeted mean arterial pressure in patients with septic shock is, as stated before, 65 mmHg and should be achieved with a combination of different vasopressors along with aggressive fluid therapy. Lactate could be used in guiding of resuscitation and used as a marker for hypoperfusion of tissues (9).

The guidelines states that norepinephrine should be initiated and titrated up to 35-90µg/min until target MAP is achieved (9). If the target MAP is not achieved by the use of norepinephrine, vasopressin should be added. The dose of vasopressin should be up to 0.03 units/min. In a patient whom the MAP is not satisfactory the third step is to add epinephrine at a dose of 20-50 µg/min (9). Phenylephrine should be considered as further therapy if epinephrine does not help to reach the target MAP, a dose of up to 200.300 µg/min can be given in this case (9).

1.7.4 Acute respiratory distress syndrome (ARDS)

Acute respiratory distress syndrome can be a grave consequence of sepsis and septic shock in patients with organ dysfunction of the lungs. The recommended therapy is mechanical ventilation. It is then recommended to use a higher PEEP flow rather than a low flow but, with a low tidal volume. The recommendation states that a target tidal volume of 6ml/kg body weight should be achieved (32). It is also recommended to put the patient in a prone position rather than supine, when compared to intubated patients in a supine position it was noticed that mortality was improved in patients put in a prone position (9), this can, however, be hard to achieve in patients who are critically ill. Contrary to the recommendation of strong fluid resuscitation, in patients with established ARDS, the guidelines rather recommend a conservative fluid therapy as it was shown that in these patients the restricted fluid therapy lead to shorter need for mechanical ventilation (9). This can of course only be performed in patients with established ARDS and who are not suffering further from septic shock.

1.7.5 Other therapies

Symptomatic therapy should be initiated depending on which organs are affected. In patients with renal failure and increased creatine values it is not recommended to start renal replacement therapy if the only symptoms are oliguria and increased creatine levels unless other definitive indicators of dialysis therapy are present (9).

It is strongly recommended to have a strict glucose control of patients with sepsis in the intensive care unit with continuous controls of plasma glucose level every 1-2 hours until blood glucose is stable and every 4 hours after that. If there are 2 continuous measurements of plasma glucose levels above 10mmol/L, insulin therapy should be initiated, with the aim of a level below 10mmol/L rather than a target blood glucose below 6.1mmol/L (9).

When it comes to nutrition in a septic patient, early use of parenteral nutrition is not recommended, alone, or in combination with enteral feedings (9). It is rather recommended to initiate early enteral feedings when possible. In patients where enteral feeding is not feasible the guidelines recommend starting intravenous glucose first and try enteral feedings as soon possible over the first 7 days in the critically ill patient. In patients with feeding intolerance, vomiting or aspiration of gastric content, the use of prokinetic agents are recommended. If

after the initial 7 days enteral feedings cannot be initiated satisfactorily parenteral feedings should be considered (9).

Sepsis is a condition with strong reactions, both with proinflammatory and anti-inflammatory processes, therapy with agents that decrease cytokines, by the use of a hemadsorption device, for blood purification, e.g. cytosorb, can be given as adjunctive therapy (33). In patients with septic shock, it was seen that purification with cytosorb reduced blood lactate levels as well as stabilized the patients faster (33).

Corticosteroid therapy in hemodynamically unstable patients are also recommended (9,34,35). The dosage recommended is 200mg per day, it was shown that patients treated with corticosteroids had a decreased 28-day mortality and that they faster reached hemodynamic stability (9,34,35). However, it was shown that administration of corticosteroids in boluses lead to hyperglycemia, so strict blood glycemic control needs to be applied, this increase was not seen when corticosteroids were given as an infusion (9).

2. OBJECTIVES

The objective of this study is to determine the incidence of sepsis and septic shock at the general Intensive Care Unit of the University Hospital of Split (UHS), Croatia. The study will be retrospective and focus on cases between 2015 to the first quarter of 2018.

Furthermore, we want to know about the most prevalent pathogens causing sepsis, age, gender, mortality rate and length of stay of the patients with sepsis and septic shock. Additionally, a comparison between the non-septic patients and septic patients will be done, in order to compare mortality rates, age, gender and length of stay in the department to distinguish differences between these two groups.

3. METHODS

3.1 Study type

The study is a retrospective study that looks at the cases of sepsis and septic shock at the Department of Anesthesiology, Resuscitation and Intensive Care of UHS general Intensive Care Unit during the period of 2015 up to the first quarter of 2018. The study material is gathered by going through patient files during this period and gather information about the patients with sepsis and septic shock and further gather information about patient age, gender, origin of pathogens if microbiology was managed, mortality and length of stay. As well as age, gender, mortality and length of stay of all patients, during the same timeframe, who did not have sepsis.

3.2 Ethical issues

No personal information about patients was gathered, as the information is for statistical purposes and no personal information is necessary, thus there is no ethical issues with this study.

3.3 Statistical analyses

The statistical analyses were performed using the statistical software Medcalc for Windows [MedCalc Statistical Software version 18.5 (MedCalc Software bvba, Ostend, Belgium).

3.4 Data presentation

The data will be presented in forms of tables, figures as well as in text. The statistical tests that will be performed are Chi-square test, Mann-Whitney U-test with a statistical significance level of $P<0.05$.

4. RESULTS

In total, the general intensive care unit had 1038 patients during the year 2015 to the first quarter of 2018, out of which 200 (19.0%) had sepsis. In 2015, 57 patients out of 315 (18%), 2016, 61 patients out of 330 (18.5%), 2017, 64 patients out of 316 (20%) and during the first quarter of 2018, 18 patients out of 77 (23%), patients had sepsis (Figure 1.).

Median age of patients with sepsis was 66 years (95% CI 63.0 to 67.8). The median duration of stay at the intensive care unit for patients with sepsis was 11 days (95% CI 9-13). Most patients with sepsis were males, the majority of patients with sepsis developed septic shock. Just over half of the patients with sepsis did not survive. Most diagnosis of sepsis was confirmed with an hemoculture. Almost half of the patients with confirmed microbiology where found to have multiple microorganismal infection (Table 3.).

The bacteria most commonly seen in hemocultures are coagulase negative Staphylococcus species, *Acinetobacter baumanii* and methicillin resistant Staphylococcus epidermidis (MRSE) (Table 5.).

Median age for patient group without sepsis was 63 years (95% CI 62 to 64). The median duration of stay at the intensive care unit for the patient group without sepsis was 4 days (95% CI 4 to 5). Most patients without sepsis survives their stay at the intensive care unit and are transferred to other departments (Table 4.) Most patients in the ICU are males (Table 4.)

There is a significant difference between mortality of the patient group with sepsis and the patient group without sepsis, $P < 0{,}001$. The duration of stay is significantly longer in the patient group with sepsis $P < 0{,}001$. There is no significant difference between median age of the patient group with sepsis compared to the patient group without sepsis, $P = 0{,}286$.

There is no significant difference between genders in the patient group with sepsis compared to the patient group without $P = 0{,}346$.

Table 3. Patients with sepsis

Variable		n	%
Gender	Male	148	74
	Female	52	26
Septic shock	Yes	126	63
	No	74	37
Mortality	Deceased	104	52
	Survived	96	48
Diagnosis based on hemoculture	Confirmed	152	76
	Clinical diagnosis	48	24
Patients with multiple microorganisms confirmed		66	43

Values represent number and percentage of septic patients for each variable.

Table 4. Patients without sepsis

Variable		n	%
Gender	Male	592	70.6
	Female	246	29,4
Mortality	Deceased	150	17,9
	Survived	686	82,1

Values represent the number and percentage of patients for each variable.

Table 5. Microbiological origin from hemoculture of patients with sepsis.

Microbiology	n	%
Coagulase negative Staphylococcus species	55	28%
Methicillin resistant Staphylococcus epidermidis	48	24%
Acinetobacter baumanii	39	20%
Pseudomonas aeruginosa	24	12%
Klebsiella pneumoniae ESBL+	19	10%
Proteus mirabilis	8	4%
Enterococcus faecalis	8	4%
Methicillin resistant Staphylococcus aureus	7	4%
Enterococcus species	5	3%
Methicillin sensitive Staphylococcus aureus	4	2%
Klebsiella pneumoniae	4	2%
Clostridium species	3	2%
Methicillin sensitive Staphylococcus epidermidis	3	2%
Propionibacterium species	3	2%
Corynebacterium species	3	2%
Streptococcus viridans	2	1%
Acinetobacter species	2	1%
Morganella morgagni	2	1%
Escheria coli	2	1%
Escheria coli ESBL+	2	1%
Propionibacterium acnes	2	1%
Methicillin resistant coagulase - staphylococcus Species	1	1%
Enterobacter cloacae	1	1%
Streptococcus pyogenes	1	1%
Serratia marcescens ESBL+	1	1%
Clostridium innocum	1	1%
Serratia marcensens	1	1%
Providentia sturartii ESBL+	1	1%
Sphingomonas paucimobilis	1	1%
Candida species	1	1%
Candida glabrata	1	1%
Staphylococcus lugdudensis	1	1%
Gram negative bacilli	1	1%
Candida parapsilosis	6	3%
Candida albicans	6	3%
Toxoplasmosis IgG+	1	1%
CMV IgG +	1	1%

Values represent number and percentage of patients with each specific microorganism found on hemoculture.

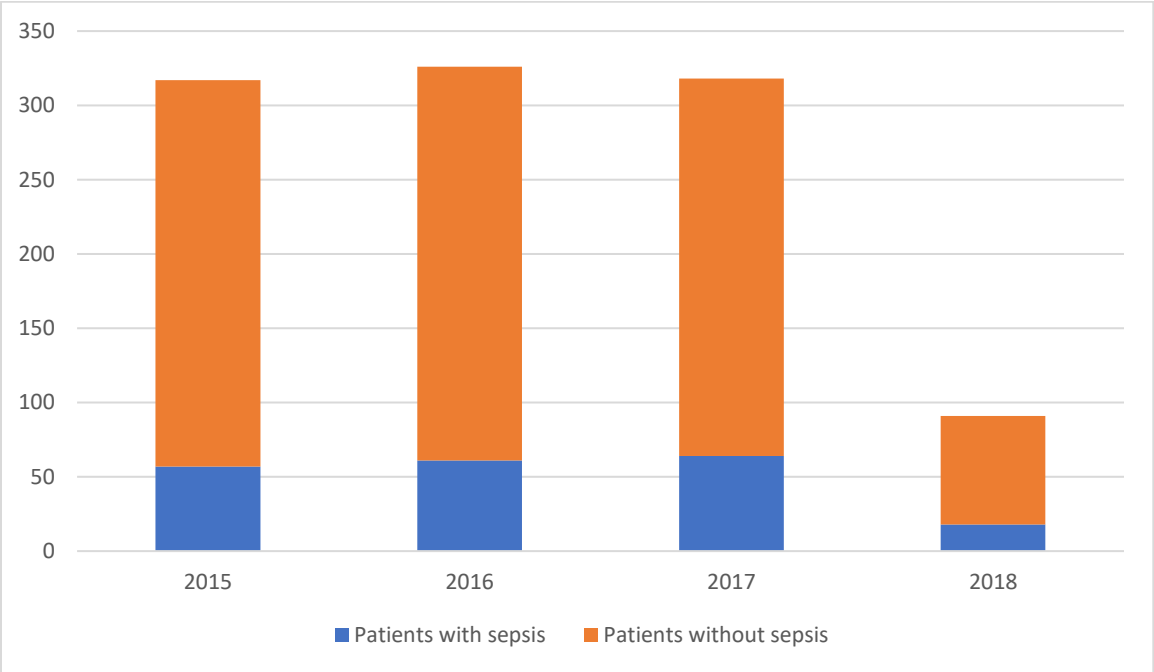

Figure 1. Number of patients with sepsis during years evaluated

5. DISCUSSION

Sepsis continuous to be a debilitating disease with high mortality (19,20,36). The incidence of sepsis appears to be increasing throughout the western world (19). The progressive ageing of the population is seen as one of the causes (19).

In the general Intensive Care Unit at University Hospital of Split, the percentage of patients with sepsis were around 20% per year during the period of 2015 to the first quarter of 2018. There is not a big difference seen between these years, and no big increase or decrease is seen from 2015 up to the first quarter of 2018. According to the SOAP study of sepsis in European intensive care units (20), the amount lies at 37.4%.

The increase in mortality of patients with sepsis compared to those without sepsis is significantly higher, $P < 0,001$. This is consistent with what is seen in Intensive Care Units in the western world (19) and underlines the importance of early recognition and treatment of sepsis in patients before multiple organ dysfunction and resistance to therapy occurs.

As the mortality of sepsis is so high in critically ill patients, it is important to further investigate what can be done to detect sepsis earlier to start antibacterial therapy as early as possible together with early resuscitation.

There were no data taken on whether the patient had sepsis upon admission or later on. This could be a topic for further investigation to distinguish those patients who are admitted with sepsis and those that get sepsis at the department. There was also no checkup on patient mortality in those patients transferred to other departments or discharged, too see if there is also an increased rate of late mortality in patients with sepsis, who are later transferred to other departments.

It is noticed that a high percentage of the septic patients went into septic shock and this could explain the high mortality rate as patients with septic shock show persistent hypotension resistant to vasopressor making resuscitation at this stage very hard and resulting with multiple organ dysfunctions (4,25-27). These patients are much harder to treat and so the importance of early treatment of sepsis is further emphasized by these results.

Most patients diagnosed with sepsis had a confirmed infection on the hemoculture, according to the SOAP study of sepsis in European intensive care units, there were 60% confirmed hemoculture (20). This result is consistent with what was found at the UHS where the percentage of confirmed hemocultures were 76%. The negative cultures could be explained by the fact that hemoculture sampling not always is performed before introduction

of antimicrobial therapy, or those patients in whom a hemoculture was not performed, for example, in the patients who were deceased before hemoculture or any further treatment was started.

The median age of patients with sepsis was 66 years (95% CI 63.0 to 67.8), while the median age of patients at the intensive care unit in the patients without sepsis was 63 years (95% CI 62 to 64). There is no significant difference between median age of the patient group with sepsis compared to the patient group without sepsis, P = 0,286 showing that in this case, age is not a risk factor for sepsis. This is within the same range as what is seen in intensive care units around Europe and the Western world (19).

In this study it is also shown that the length of stay of patients with sepsis is significantly increased P < 0,001, from a median of 4 days to 11 days in the septic patients. This is an expected result, as patients with sepsis will have a worse general condition and are in need of more specialized care for a longer period of time. This is also seen in studies done in different countries throughout Europe where the length of stay in significantly increased (20,36-39). This is important to recognize as patients staying in the intensive care for a median of a week longer than the general patients is an important cost factor to recognize, as well as to recognize that these patients are severely ill for a longer time, which could also be discussed to contribute to the higher mortality rate as the state of these patients is worse for a longer period with a weaker chance of survival.

The distribution in terms of gender shows that most patients in the intensive care unit are male, and so, also the distribution in terms of gender in the patient group with sepsis were mostly men, there was no significant difference in gender distribution between the groups of patients with sepsis and without sepsis, P = 0,346. This shows that gender is not a risk factor for sepsis at the University hospital of Split. The gender distribution at intensive care units are seen to be majorly male around Europe as well (1,15,19,36,40).

In the hemocultures, 43% of the patients were found to have multiple microorganisms in the blood cultures. We did not study weather this affected the mortality, length of stay or any other factors. As no further data was gathered on the reason for admission of patients, whether they had sepsis upon admission or the origin of infection in patients with sepsis the question of why this could be cannot be answered within the scope of this paper.

The most prevalent microorganisms seen on the blood cultures were coagulase negative Staphylococcal species, seen in 28% of blood cultures, methicillin resistant Staphylococcus epidermidis is seen in 24% of hemocultures, *Acinetobacter baumanii,* seen in 20% of blood cultures and *Pseudomonas aeruginosa* seen in 12% of blood cultures. Most of the other microorganisms are only seen a couple times. According to the SOAP study the most common microorganisms found in Europe were *Staphylococcus aureus*, including MRSA, *Pseudomonas aeruginosa* and *Escheria coli* (20). At the intensive care unit of University Hospital in Split, where the most common being Staphylococcus species but not specifically *Staphylococcus aureus* the prevalence of microorganisms are not too similar even though the most common microorganisms are seen here as well. *Pseudomonas aeruginosa* was seen in 12% of the blood cultures and thus is not one of the most common microorganisms and *Escheria Coli* was only seen in 2% of the blood cultures (Escheria Coli ESBL+ included), even though these seem to be more common around other hospitals in Europe (20). The difference in most prevalent microorganisms could be explained by the geographic differences.

The second most common microorganism seen in the intensive care unit was methicillin resistant Staphylococcus epidermidis, 24%, which is commonly seen in Intensive Care Units. It can be discussed that the reason for this could be either human error when collecting the samples for blood culture, and thus having contaminated samples sent to the lab or that the sterility during different invasive procedures, such as insertion of venous catheter is not done properly. As there was no data gathered on which patients who were infected by which microorganisms and whether they are seen in the patients with sepsis upon admission or those who acquire sepsis at the department, no conclusion can be made on the reason for the high number of methicillin resistant Staphylococcus epidermidis.

The third most prevalent bacteria is *Acinetobacter baumanii*, this is also consistent with nosocomial infections seen around the world, where *Acinetobacter baumanii* is seen to be increasing in the hospital milieu (41,42).

A limitation of this study is that only one person was going through all paper files of patients, rendering this study quite susceptible to human error as over 1000 patient files was looked through. Furthermore, as this was a retrospective study, there was no way to gather information on any information that was missing from the files.

6. CONCLUSION

1. The incidence of sepsis at the general intensive care unit at the University hospital in Split was around 20% during the years 2015 to the first quarter of 2018. No great increase or decrease is seen during this period.
2. Sepsis lead to a significant increase in mortality as well as length of stay in the patients at the general intensive care unit at the University hospital in Split.
3. The mortality seen in the patient group with sepsis was 52% and the length of stay 11 days (95% CI 9 to 13 days).
4. There was no significant difference in age distribution and gender distribution between the patient group with sepsis and the patient group without sepsis. The median age of the patient group with sepsis was 66 years (95% CI 63 to 67.8) and most patients admitted to the department where male.
5. Of the patients diagnosed with sepsis 76% had a confirmed blood culture and 43% of all septic patients were found to have multiple microorganismal infection.
6. Of all the patients with sepsis 63% also went into septic shock during their stay at the intensive care unit.
7. The most commonly seen bacteria in the hemocultures were coagulase negative Staphylococcal species, methicillin resistant Staphylococcus epidermidis and *Acinetobacter baumanii*.

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8. SUMMARY

Objectives: The aim of this paper is to learn more about the incidence of sepsis and septic shock at the general intensive care unit as well as looking into mortality, pathogen origin, age, gender and length of stay of the patients with sepsis and furthermore compare the results with the patient group who do not have sepsis.

Materials and methods: The study is a retrospective study looking into patient records during the period between 2015 to the first quarter of 2018. Information about age, gender, length of stay and mortality was taken from all patients records during this period as well as blood cultures and whether the patients with sepsis also had septic shock. The statistical analyses were made using Medcalc.

Results: Mortality was 52% in patients with sepsis, 43% of patients with sepsis had multiple microorganismal infection shown on blood culture. There was no significant difference between age and gender distribution in the patient group with sepsis and the patient group without. The most frequent bacteria seen in the blood cultures were coagulase negative staphylococcal species and methicillin resistant Staphylococcus epidermidis, of all the patients with sepsis 63% also had septic shock.

Conclusion: Mortality was significantly increased in patients with sepsis compared to those who did not suffer from sepsis. The length of stay was significantly longer in patients with sepsis and patients stayed approximately a week longer in the intensive care unit when suffering from sepsis. The difference in age distribution and gender distribution was not significantly different in the patient group with sepsis compared to those patients who did not suffer from sepsis.

9. CROATIAN SUMMARY

Naslov: SEPSA I SEPTIČKI ŠOK U JEDINICI INTENZIVNE NJEGE KLINIČKOG BOLNIČKOG CENTRA SPLIT, RETROSPEKTIVNA STUDIJA INCIDENCIJE, MORTALITETA I DUŽNI BORAVKA

Ciljevi: Cilj ovog istraživanja su nova saznanja o incidenciji sepse i septičkog šoka u jedinici intenzivne njege, te usporedba mortaliteta, patologije, dobi, spola i duljine boravka kod pacijenata koji su imali sepsu i onih koji je nisu imali.

Materijali i metode: Obuhvaća retrospektivni studij u kojoj su korišteni podaci pacijenata u periodu između 2015. do prve četvrtine 2018. godine. Korištene su informacije o dobi, spolu, dužini boravka, mortalitetu, nalazi hemokulture, te podatak koliko je pacijenata oboljelih od sepse imalo septički šok. Za statističku analizu korišten je Medcalc.

Rezultati: Mortalitet pacijenata sa sepsom je 52%, kod njih 43% hemokulturom su izolirani multipli patogeni. Dokazano je da ne postoji značajna razlika između dobi i spola pacijenata koji su imali sepsu i oni koji je nisu imali. Najučestalija bakterija izolirana u hemokulturi je koagulaza negativni stafilokok i meticilin rezistentni Staphylococcus epidermidis, 63% pacijenata oboljelo od sepse je imalo septički šok.

Zaključci: Mortalitet je značajno veći kod pacijenata oboljelih od sepse u usporedbi sa onima koji nisu oboljeli od iste. Duljina boravka je značajno duža kod pacijenata koji su imali sepsu, tjedan dana duže su boravili u jedinici intenzivne njege. Razlike u godinama i spolu nisu bile značajne medju pacijentima sa sepsom i onima koji je nisu imali.

10. CURRICULUM VITAE

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Work:

January-February 2018: Nurse assistant in a pediatric emergency ward

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