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Review Article

Urosepsis During Covid-19 Pandemic

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Abstract

The COVID-19 pandemic is a unique situation in the recent history of mankind, which has put unprecedented pressure on the health system. Urosepsis itself represents a challenge for the health system requiring a multidisciplinary approach and important logistical resources. The present study aims to compare the evolution of patients diagnosed with urosepsis in the pre-pandemic period and during the covid-19 pandemic. Given the low accessibility, low addressability , the relocation of human and logistical resources towards the treatment of patients with SARS CoV-2 and the increased waiting time at the emergency room, the specific surgical or medical act was delayed during the pandemic period. This led to more expensive periods of hospitalization,longer intensive care admission, and a higher mortality rate for pacientes treated for urosepsis during covid-19 pandemic. Although the negative impact of the COVID-19 pandemic is demonstrated, we can learn during this period and make more efficient use of human and material resources when treating patients with urosepsis, so that some of them, whose clinical status allows it, can be treated in an outpatient setting.

Keywords: COVID-19 pandemic; Charlson Comorbidity Index; Hospitalization cost; Mortality; SOFA score; Urosepsis

Introduction

The COVID-19 pandemic is a unique situation in the recent history of mankind, which has put unprecedented pressure on the health system. During this period,not only the lifestyle, but also the accessibility and addressability of patients for specialized treatment have changed. In this study we try to understand the impact of changes in the health system due to the COVID-19 pandemic on the patient with urosepsis. Urosepsis is defined as life-threatening organ dysfunction due to the host abnormal response to infections originating in the urinary tract or male genitals [1]. Of the total cases of sepsis, urosepsis represents 9%-31% [2]. Sepsis has an increased mortality rate and is the second leading cause of death in patients treated in intensive care units [3,4]. Urosepsis has an overall mortality that can range from 7,5% to 30% [5]. In addition, morbidity, as well as the increased costs of managing this disease, make it important to assess it promptly and rigorously and, of course, to provide rapid access to treatment [6]. The management of this pathology is multidisciplinary and requires good collaboration between the departments of urology, intensive care, imaging and laboratory medicine [7]. Thus this pathology in itself represents a challenge for the health system.

Urology practice was affected by the COVID-19 pandemic. In one of the busiest departments of urology in Bergamo, Italy, there was a major change in surgical scheduling. This was related to many factors. First, the anesthesiologists need to work with patients with acute COVID-19 disease. Second, the number of beds used for urological patients was reduced. Third, there was intent not to expose urology patients to hospital contamination and fourth, the number of urology ward staff was reduced [8]. The false-negative rates of the early COVID-19 tests and the presence of asymptomatic carriers did not allow to create a "COVID-free" space [9]. Changes have occurred in clinical and academic settings across the major urological centers in Europe. It was recommended to cancel most of the elective urological surgeries [10]. There is a negative impact of the pandemic on scientific, academic, and educational activities, as well as on the personal and social life of urologists and other health care providers [11]. That being stated, the present study aims to compare the evolution of patients diagnosed with urosepsis in the pre-pandemic period and during the COVID-19 pandemic.

Materials and Methods

We conducted a retrospective study for patients diagnosed with urosepsis, hospitalized in the Urology Department of the County Emergency Clinical Hospital "Saint Andrew the Apostle" in Galati, Romania, from May 2018 to October 2021. We set the date of February 26, 2020, when the first cases of COVID-19 were diagnosed in Romania, as the reference point that will separate the two periods. Thus we had two periods of time from May 2018 until February 2020, considered to be pre-pandemic and another, of equal length, from March 2020 until October 2021 considered pandemic, and this differentiated our two groups. The inclusion criteria were: diagnosis of urosepsis, age ≥18 years. According to our definition, the patients with urinary tract infection were considered to have urosepsis if they had a bacterial infection proven by blood cultures or diagnosed clinically, and exhibited at least 2 of the following 4 criteria: fever (>38°C) or hypothermia (<36°C); tachycardia (>90 bpm); tachypnea (>20 respirations/minute); or leukopenia (leukocyte count $<4.0\times10^9$/L), leukocytosis (leukocyte count $>12.0\times10^9$/L) or a leftward shift (>10% immature granulocytes) [12,13]. The exclusion criteria were: patients aged<18 years, pregnancy, patients with missing data. Demographics, comorbidities, and clinical and laboratory findings were recorded. All patients' medical records were reviewed, and the relevant clinical and biological data were collected. To describe in a systematic and objective way the clinical condition of the patients at the time of admission we used the Sequential (Sepsis-Related) Organ Failure Assessment (SOFA) score, which evaluates the respiratory, nervous and circulatory systems, the hepatic and renal functions, and coagulation [14]. The utility of the score has previously been validated on large cohorts of critically ill patients. To describe the health status of patients before this acute event we used the Charlson Comorbidity Index (CCI) [15].

In order to better understand the evolution of the patients, we also analyzed them in terms of therapeutic management. Thus we divided the patients into 3 groups: those who needed major surgery, those who needed minor surgery and those who did not need surgical treatment. We considered minor surgeries the interventions that did not require general or spinal anesthesia and could be performed with local anesthesia, in an outpatient setting, such as: suprapubic cystostomy, clogged nephrostomy or ureteral stent replacement, dorsal incision, etc. Conservative treatment has been prescribed to patients diagnosed with urological infectious pathology for which surgery is not usually recommended, e.g. uncomplicated acute pyelonephritis, non-abscessed orchiepididymitis, acute prostatitis without associated urinary retention, etc. We conducted a statistical analysis that compared the general information of each group using Kolmogorov-Smirnov Test of Normality, independent samples t-test and Mann-Whitney U test for continuous variables, Chi square test for association between two categorical variables, point-biserial Correlation Calculator to measure the correlation between two variables in the special circumstance that one of your variables is dichotomous, and the Pearson correlation coefficient to measure the strength of a linear association between two variables. The statistical analyses were performed using GraphPad.

Results

A total of 223 patients with urosepsis were enrolled in this study. 146 patients with urosepsis were identified as the pre-pandemic group, and 77 patients as the pandemic group. The mean of patients hospitalized per month was 5.26, Standard Deviation (SD) 2.77, in the pre-pandemic period it was 6.33, SD 3.07 compared to 4.19, SD 1.99 for those treated in the pandemic period. We used independent samples t-test that returned $p<0.01$, thus we proved that there were more patients treated in the pre-pandemic period. This is shown graphically in the Figure below, representing monthly admissions (Figure 1). In the pandemic group 2, patients were diagnosed during hospitalization with SARS CoV2 infection, they developed asymptomatic forms and their evolution was not influenced.

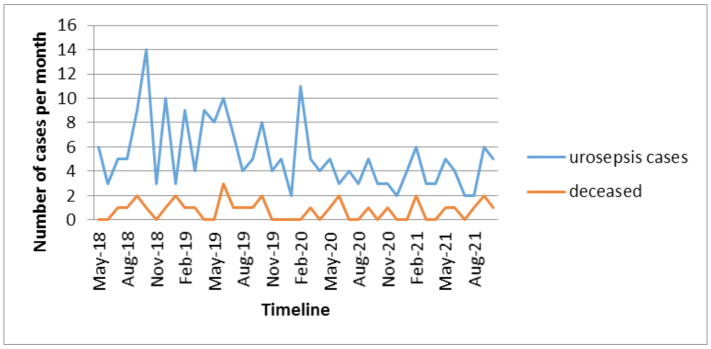

Figure 1: Admissions and deceased monthly.

Leukocyte counts were significantly higher in patients treated during the COVID-19 pandemic (19.06 $x10^9$/L, SD 9.45 $x10^9$/L versus 17.27 $x10^9$/L , SD 7.49 $x10^9$/L, p=0.01).

Organ dysfunction is associated with high rates of morbidity and mortality [16] and, as such, accounts for a high proportion of the ward budget [17]. Organ failure scores, such as the SOFA score can help assess organ dysfunction or failure over time and are useful to evaluate morbidity [18]. Although this scoring system was developed to describe and quantify organ function and not to predict outcome, the obvious relationship between organ dysfunction and mortality has been demonstrated in several studies[19-22]. The SOFA score is an increasingly important tool in defining both the clinical condition of the individual patient and the response to therapies in the context of clinical trials [23]. Sequential assessment of organ dysfunction during the first few days of ICU admission is a good indicator of prognosis. Both the mean and highest SOFA scores are particularly useful predictors of outcome [24]. SOFA score was validated on large cohorts to be an independent mortality predictor [25]. This was also statistically significant in our study; we proved this by using point-biserial correlation that returned p <0.01. Comparing the SOFA score in our two groups we found that the pandemic group had a higher value, which was statistically significant (7.3, SD 3.29 versus 4.58, SD 3.34, p<0.01).

The Charlson Comorbidity Index (CCI) was developed and validated as a measure of 1-year mortality risk and burden of disease [26-28]. The CCI has been extensively used in clinical research to address the confounding influence of comorbidities, predict outcomes, standardise comorbidities abstracted from medical records or administrative databases and for self report of comorbidities [29-33]. In clinical practice, the CCI reduces comorbidities into a single numeric score that may assist health professionals with stratifying patients into subgroups based on disease severity, developing targeted models of care and resource allocation [34]. The CCI has content validity, as the diseases and severity weights were statistically derived from relative risks of a proportional regression model to predict mortality [35]. Although CCI was not used to predict mortality in an acute event, by using point-biserial correlation we wanted to see if this score can predict mortality in patients treated for urosepsis. P value was <0.01, which meant that CCI could be used as an independent mortality predictor for urosepsis. Although there were differences between CCI mean, higher for the pandemic group, thesewere not statistically significant (6.57, SD 3.94 versus 6.06, SD 4.24, p=0.37). Overall mortality in our study was 14.79%, with a higher rate in the pandemic group (19.48% versus 12.32%, p=0.04), which has been proven to be statistically significant. Analyzing the number of patients deceased monthly, we have seen a slight increase during the pre-pandemic period, but this was not statistically significant (0.86, SD 0.85; 0.67, SD 0.73, p=0.44) (Table 1). Although since February 2020 the number of cases hospitalized with urosepsis began to decrease, the number of deceased patients remained relatively the same (18 deaths in the first group versus 15 in the second one), which can also be seen in Figure 1.

		Overall n=223	Pre-pandemic n=146	Pandemic n=77	P value
Demographics	Age (years)	Mean 62.09, SD 15.75	Mean 60.83, SD 16.11	Mean 64.49, SD 14.87	0.09
	Sex	Male 135 (60.53%)	Male 86 (58.9%)	Male 49 (63.63%)	0.49
	Environment	Urban 145 (65%)	Urban 93 (63.69%)	Urban 52 (67.52%)	0.56
	Number of cases treated per month	Mean 5.26, SD 2.77	Mean 6.33, SD 3.07	Mean 4.19, SD 1.99	0.01
Clinical	Leukocyte (10^9/L)	Mean 17.27, SD 7.49	Mean 16.32,SD 6.86	Mean 19.06, SD 9.45	0.01
	SOFA score	Mean 5.52,SD 3.52	Mean 4.58, SD 3.34	Mean 7.3, SD 3.29	<0.01
	CCI	Mean 6.23,SD 4.13	Mean 6.06, SD 4.24	Mean 6.57, SD 3.94	0.37
	Mortality	33 (14.79%)	18 (12.32%)	15 (19.48%)	0.04
	Deceased monthly	Mean 0.76, SD 0.79	Mean 0.86, SD 0.85	Mean 0.67, SD 0.73	0.44

Economical	ICU days	Mean 1.43, SD 3.62	Mean 1.03, SD 3.15	Mean 2.19, SD 4.29	0.02
	Days of hospitalization in the Urology Departmen	Mean 11.51, SD 10.99	Mean 10.6, SD 9.77	Mean 13.25, SD 12.9	0.08
	Cost of hospitalization in the Urology Department (RON)	Mean 10210.31, SD 11038.57	Mean 8370.4, SD 9006.64	Mean 13698.99, SD 13502.9	<0.01

Table 1: Baseline features of the enrolled patients.

Analyzing from the point of view of therapeutic management, we noticed that a total of 137 (61.43%) major surgeries, 22 (9.86%) minor surgeries and 64 (28.69%) conservative treatments were administered. Comparing the two groups, we noticed the tendency to increase the percentage of major surgery during the pandemic period (72.72% versus 55.47%) in detriment of minor surgery (6.49% versus 11.64%) and conservative treatment (20.77% versus 32.86%) (Table 2).

	Overall n=223	Pre-pandemic n=146	Pandemic n=77
Major surgery	137(61.43%)	81 (55.47%)	56 (72.72%)
Minor surgery	22 (9.86%)	17 (11.64%)	5 (6.49%)
Conservative treatment	64 (28.69%)	48 (32.86%)	16 (20.77%)

Table 2: Therapeutic management.

Hospitalization period was higher during the pandemic, but this was not statistically significant (13.25, SD 12.9 versus 10.6, SD 9.77 days; p=0.08). There was a significant incremental cost of hospitalization for patients treated during the pandemic (13698.99, SD 13502.9 versus 8370.4, SD 9006.64 RON; p<0.01). We used the national currency of Romania, RON, 1 RON is approximately 0.2 EURO. We analyzed the Intensive Care Unit (ICU) amount of admission days and concluded that patients with urosepsis during the COVID-19 pandemic needed longer ICU treatment(2.19, SD 4.29 versus 1.03, SD 3.15 days; p=0.02). We also demonstrated that there is a correlation between SOFA score, CCI and ICU hospitalization days (R=0.44, p<0.01, respectively R=0.28,p<0.01) (Table 3). The same output was shown when comparing SOFA score and CCI with days (R=0.41, p<0.01; R=0.24, p<0.01) and cost (R= 0.5, p<0.01; R=0.25, p<0.01) of hospitalization (Table 3).

	Hospitalization days	ICU days	Cost of hospitalization
SOFA	R=0.41, p<0.01	R=0.44, p<0.01	R= 0.5, p<0.01
CCI	R=0.24,p<0.01	R=0.28,p<0.01	R=0.25, p<0.01

Table 3: Pearson correlation coefficient.

Discussion

The current COVID-19 pandemic underlines the importance of changing some aspects of urology practice, from patient consultation to the triage of urologic surgeries. The pandemic of COVID-19 has serious implications on urology practice and raises particular questions for urologists about the management of different conditions [36].

Severe sepsis and septic shock is a critical situation, with recently reported mortality rates ranging from 28.3% to 41.1%. The infection sites leading to severe sepsis or septic shock are pneumonia in approximately 45% of patients followed by urinary tract infections in 31% of patients [37]. A rapid diagnosis is critical to meet the requirements of the Surviving Sepsis Campaign Guidelines. As the urogenital tract is one of the most frequent sites of infection in sepsis a general assessment of the urinary tract should be regularly carried out in a septic patient [38]. An adequate initial (e.g. in the first hour) antibiotic therapy ensures improved outcome in septic shock [39,40] and is also critical in severe UTI [41] as it has been shown with other infections sites as well [42, 43]. Empirical antibiotic therapy considers the expected bacterial spectrum, the institutional specific resistance rates and the individual patient's requirements [44,45]. If a complicating factor in the urinary tract warranting treatment is identified, control and/or removal of the complicating factor should follow in the first 6 h [46]. In our study we can see a downward trend in patients treated with urosepsis during the pandemic period. Knowing that the incidence of a disease should not change its statistical significance without prophylactic intervention, and that the urgency of treatment is a defining fact, we try to understand this phenomenon. For this purpose we can issue two premises: some of the patients who were to be hospitalized and treated for urosepsis were treated in an outpatient setting and have not been enroled into our database; or some of the patients did not receive specific treatment and the disease progressed to exitus without being diagnosed. For the first hypothesis it could be argued that in the pandemic group a smaller proportion of patients benefited from minor surgery or conservative treatment. We can understand the tendency of the urologist to opt for outpatient treatment, in patients whose clinical condition would have allowed it, in the context of a shortage of resources such as bed occupancy, the unavailability of personal protective equipment and reduced urology ward staff. At the same time, patients would have been tempted to adhere to it because of epidemiological filters that prolong the waiting period for admission, and for fear of contacting COVID-19 during hospitalization.

The increased SOFA score in patients treated during the pandemic argues for the second hypothesis. This certifies that patients treated during the pandemic have arrived at the hospital in a more advanced state of disease. The same is supported by a higher number of days of hospitalization in the ICU during the pandemic. Given the fact that our department is the only emergency Urology Department in the County and knowing that patients diagnosed with urosepsis must receive appropriate treatment as soon as possible [47], a more rigorous triage and outpatient treatment do not explain the difference in number of cases that needed major surgery between the two groups. By extrapolating we can speculate that some of the patients did not survive, so they did not benefit from treatment in our ward. In this context, the mortality rate, which is already higher during the pandemic, could be even higher. In fact, the decrease in the number of patients hospitalized with urosepsis during the pandemic period is probably due to both premises and unfortunately the data we have cannot tell us to what extent.

Leukocytes are generally regarded as useful markers for the diagnosis of sepsis, and are usually used together with blood cultures. However, such methods are sometimes inadequate for early diagnosis, since it takes from 24 to 72 h to obtain the culture results. This delay in diagnosis can be detrimental to the overall health status of the patient. SOFA score and CCI are complex, systematic and describe in an objective way the current clinical status and the comorbidities of the patients, respectively. In our study, increased values of these scores were associated with prolonged ICU hospitalization, increased hospitalization costs, and increased mortality. Patients should be evaluated using these scores in order to act promptly with the therapeutic plan. This study had several limitations: it was a retrospective study and therefore, bias was likely; the data were collected from a single center, as such, it is possible that the results could differ from those of other centers.

Conclusions

The impact of the COVID-19 pandemic over society and the health system should not be assessed solely from the point of view of patients diagnosed with SARS CoV-2. We can see in daily practice changes in approach and difficulties in the management of other pathologies. Being a severe pathology with an uncertain evolution and sometimes leading towards exitus, urosepsis management was indirectly influenced during the pandemic. Patients required a longer period of intensive care hospitalization, there was a higher mortality rateand higher costs for treating these patients. Although the negative impact of the COVID-19 pandemic is demonstrated, we can learn during this period and make more efficient use of human and material resources when treating patients with urosepsis, so that some of them, whose clinical status allows it, can be treated in an outpatient setting. Thus, in the future, this pathology will have a smaller impact on the health system without changing patients' morbidity and mortality.

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