



STUDY OF ACUTE RENAL FAILURE IN SEPSIS SYNDROME

Medicine

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ABSTRACT

Sepsis syndrome is very often associated with a downward spiral through a spectrum of systemic inflammatory response syndrome (SIRS) culminating in organ failure and death¹. **Aims and Objectives:** To study the clinical manifestations, epidemiological and lab profile of acute renal failure in different stages of sepsis syndrome. **Methods:** We conducted a prospective 6-month study in 20 multidisciplinary intensive care units to assess the prognosis of patients hospitalized with acute renal failure due to sepsis. Sepsis syndrome and septic shock were defined according to the criteria of the Society of Critical Care Medicine Consensus Conference. Severity scoring indexes (SAPS, APACHE II, and organ system failure (OSF)) were measured on ICU admission and on inclusion. The end-point was hospital mortality **Conclusion:** Diabetes mellitus, hypertension, older age (>60 years), pre-existing CKD, nephritic syndrome, HIV infection, malignancy and nephrotoxic drug intake were important risk for the development of sepsis, AKI or both.

KEYWORDS

Acute Renal Failure, Sepsis Syndrome

Introduction

Sepsis syndrome is very often associated with a downward spiral through a spectrum of systemic inflammatory response syndrome (SIRS) culminating in organ failure and death¹. They are frequently encountered disorders in critical care environment and are associated with increased morbidity and mortality^{2,3,4}. The mortality in sepsis syndrome increases as SIRS progress to an established state of shock associated with failure of an increasing numbers of organ systems¹.

Sepsis and particularly septic shock are important risk factors for the development of acute kidney injury (AKI). AKI in sepsis is generally not an isolated event but often a component of the multiple organ dysfunction syndrome (MODS) that may complicate sepsis⁵.

Complicating AKI in sepsis adversely affects the outcome^{1,5,6}. Preexisting renal insufficiency also serves as a common risk factor in the development of AKI in sepsis syndrome⁶. It is of interest to note that while survival from isolated AKI has improved, mortality rates over the last 30 years, despite significant improvements in resuscitation and renal support⁵.

Aims and Objectives

1. To study the clinical manifestations, epidemiological and lab profile of acute renal failure in different stages of sepsis syndrome.
2. To study the common focus of infection in sepsis syndrome.
3. To study the risk factors contributing AKI in sepsis syndrome.
4. To study the treatment modality and outcome in patient with AKI in sepsis syndrome.

Methods: We conducted a prospective 6-month study in 20 multidisciplinary intensive care units to assess the prognosis of patients hospitalized with acute renal failure due to sepsis. Sepsis syndrome and septic shock were defined according to the criteria of the Society of Critical Care Medicine Consensus Conference. Severity scoring indexes (SAPS, APACHE II, and organ system failure (OSF)) were measured on ICU admission and on inclusion. The end-point was hospital mortality

Results: 50 patients of septicaemia with renal involvement were studied. 3% of patients belonged to the age group of 31-45 yrs. While 26% of patients were in the age group of 40-60 yrs.; and 26% were above the age of 60 yrs. 18% of patients belonged to the age group of 15-30 yrs. Sex distribution of 50 septicaemic patients with renal involvement is There was a male preponderance found with the M : F ratio being 2.3:1

The commonest source of infection was respiratory tract (26%) followed by kidney and Urinary tract (22%) and skin and soft tissue (22%). This was followed by intra-abdominal causes (20%), OBGY causes (10%), post operative (8%), orodental (2%) were the less common source of infection. The focus of infections was not known in 4% of patients and 14% of patients had more than one site as a source.

Table 1. Blood culture findings in sepsis syndrome in the patients are as follows :

Blood culture	N=50 [%]
Positive	30 [60]
Negative	20 [40]

Table 2 : Renal Manifestation in Different Subgroups of Sepsis Syndrome

Renal Manifestation	Sepsis/SI RS (n=19) [%]	Severe Sepsis/ Severe SIRS (n=2) [%]	Septic Shock/ SIRS shock (n=15) [%]	MOD S (n= 2) [%]	Refractory septic shock (n=12) [%]	Total (n=50) (%)
Pyuria	8[42]		2[13]			10[20]
Oliguria	17[89]	2[100]	14[93]	2[100]	12[100]	47[94]
Hematuria	4[21]			1[50]		5[10]
Proteinuria	8[42]	2[100]	5[33]			15[30]
Azotemia	19[100]	2[100]	15[100]	2[100]		50[100]
Uraemia	4[12]		3[20]	1[50]	12[100]	12[24]
Fluid overload	3[15]	1[50]			4[33]	4[8]
Metabolic acidosis	17[89]	1[50]	15[100]	1[50]		44[88]
Hyponatremia	3[15]	1[50]	2[13]		10[83]	10[20]
Hypernatremia					4[33]	2[4]
Hypokalemia	1[5]	1[50]	1[6.6]		2[16]	4[8]
Hyperkalemia	10[52]	1[50]	5[33]		1[18]	21[42]
Hypocalcemia	12[63]		5[33]		5[41]	18[36]
Hyperphosphatemia	8[42]	1[50]	2[13]		1[8]	12[24]
Hyperuricemia	9[47]		1[6.6]		1[8]	11[22]
Anaemia	16[84]	2[100]	9[60]	2[100]	6[50]	35[70]

Overall oliguria, azotemia, metabolic acidosis, hyperkalemia, hypocalcemia, anaemia are the most common manifestations and pyuria, hematuria, proteinuria, fluid overload, hyperuricemia,

hyperphosphatemia are less common and hypokalemia, hypernatremia are least common manifestations.

In septic shock/SIRS shock, (60%) patients had intrinsic renal failure, (33.5%) patients had prerenal and (6.5%) patients had AKI on CKD.

In MODS (50%) patients had prerenal and intrinsic renal failure each. In refractory septic shock (66.5%) patients had intrinsic renal failure, (25%) had prerenal failure and (8.5%) had AKI on CKD.

Outcome of different subgroups of sepsis syndrome were studied and the results obtained. (100%) mortality was observed in patients with severe sepsis/severe SIRS and refractory septic shock while mortality was (50%) in MODS, (40%) in septic shock/SIRS shock and (31.5%) in sepsis/SIRS. (50%) patients with MODS AND (46.5%) with septic shock/SIRS shock and (21%) patients with sepsis/SIRS had complete recovery.

(42%) of patients with sepsis/SIRS and (6.75%) patients with septic shock/SIRS shock were left with CRF. (5.5%) patients with sepsis/SIRS and (6.75%) patients with septic shock/SIRS shock were lost to follow up.

Severity of AKI according to serum creatinine levels with the outcome is determined in the patients are as follows. Mortality in patients with mean serum creatinine of $> 3 \text{ mg\%}$ was found to be higher (59.2%) than patients with serum creatinine value of $1.2-3 \text{ mg\%}$ that is (40.7%). Mortality in patients with sepsis induced AKI was higher (61.5%) in patients above 60 years of age compared to those younger than 60 years (51.4%). Mortality in patients with known risk factor with sepsis syndrome was 55.4% as compared to 52.4% of those patients without any risk factor.

DISCUSSION

Renal involvement in sepsis syndrome especially in critically ill patients is common and sepsis still remains a major problem both as a precipitating and complicating factors in acute kidney injury.

In the present study, 50 patients of sepsis syndrome with renal involvement were studied. The mean age (in years) was 44.4 with an age range of 15 to 80 years, with male; female ratio being 2.3:1. A study by Karnik A.M et al¹ has also reported a male predominance in their study of 35 patients with systemic inflammatory response syndrome (SIRS), especially below the age of 40 years. They have concluded that premenopausal women seem to be protected.

As per the 1992 & 2001, ACCP/SCCM consensus conference definition criteria⁷ of sepsis 38% of patients had sepsis/SIRS, 30% HAD SEPTIC SHOCK SIRS shock, 24% were in refractory septic shock and 4% had severe sepsis and MODS respectively in our study. The commonest focus of infection in the present study was respiratory tract (26%) followed by kidney and urinary tract (22%) and skin and soft tissue (22%). This was followed by intra-abdominal causes (20%), OBGY infection (10%) and postoperative causes (8%), Oro-dental (2%) was the least common source of infection. This report is in accordance with the National Nosocomial Infection Surveillance (NNIS) system report (1992 to 1997) where nosocomial pneumonia was ranked second most common hospital acquired infection just behind the urinary tract infection and both types of infection are frequent causes of sepsis due to gram negative bacteria². Patients having refractory septic shock had higher prevalence of intra-abdominal (50%) and multiple sources (25%) of infection as compared to those with sepsis/SIRS (4.2% each) while the prevalence of kidney and urinary tract as a source of infection was lower (0%) in refractory septic shock as compared to those with sepsis SIRS (42.1%). This is in accordance with a higher prevalence of intra-abdominal (28%) and multiple sites of infection (7%) in severe sepsis compared to those with sepsis (15% and 1% respectively) and a lower prevalence of urinary tract source (12%) in severe sepsis as compared to (25%) in sepsis reported by B. Buisson et al⁸ in their study. Skin and peritoneal infections were also reported as more common source of infection for patients with SIRS and AKI by Karnik A.M et al¹.

Blood culture was positive in 60% and negative in 40% of patients in the present study. This report is supported by the fact that blood stream infection is not a prerequisite for the development of septic shock and only 30-50% of patients with sepsis have positive blood culture result in a study by David Simon et al⁹.

Among the renal manifestations studied Azotemia (100%), oliguria (94%), metabolic acidosis (88%), Anemia (70%), Hyperkalemia (42%), hypocalcemia (36%), proteinuria (30%) were commonly encountered while uraemia (24%), hyponatremia (20%), hematuria (10%), fluid overload (8.1%), hypokalemia (8%), hypernatremia (4%) were less commonly encountered in patients with sepsis syndrome and AKI in present study. Of the various types of renal failure studied in patients with sepsis syndrome, intrinsic renal injury (54%) was commonly encountered followed by pre renal (26%) and AKI on CKD (20%). This can be partly explained by the fact that sepsis affects renal function not only by its systemic hemodynamic effects but also by directly causing an imbalance between the vasodilatory and vasoconstrictory substances locally in the kidney with the aid of myriads of soluble mediators thereby profoundly declining the renal blood flow¹⁰.

A higher mortality of 100% was found in patients with refractory septic shock followed by septic shock group (40%) then with sepsis/SIRS (31.5%). As sepsis syndrome is a continuum of injury response ranging from sepsis to septic shock to refractory septic shock, it is expected that the mortality rate will also increase with progression from sepsis to refractory septic shock as found in present study. Mortality was reported as 17% in patients with sepsis, 20% severe sepsis and 46% in patients with septic in a study on natural history of SIRS by ranger franssio M. Et al.²

A higher mortality in present study can be partly explained by the fact that only patients with sepsis who developed ARF was included in the study and AKI in the setting of sepsis syndrome are proven to be associated with poor outcome.

The present study also showed an increased mortality of 59.2% in patients with serum creatinine value above $3 \text{ mg\%}$ as compared to mortality of 40.7% in those with serum creatinine value less than $3 \text{ mg\%}$. Similar findings of increased mortality of bacteraemic patients with serum creatinine value above $3 \text{ mg\%}$ has been reported by Shmueli et al⁶ in a study on 2722 bacteraemic patients Susan H Hou et al²⁴ has reported a mortality rate of 64% in patients with serum creatinine value above $3 \text{ mg\%}$ compared to 15% in patients with serum creatinine $3 \text{ mg\%}$ in a study of hospital acquired AKI. This finding can be explained by the fact that mortality is higher in patients with severe degree of renal failure. Diabetes mellitus, hypertension, pre-existing CRF, nephritic syndrome, HIV infection, malignancy, nephrotoxic drug use, age 60 years were the various risk factors identified in patients with sepsis induced AKI in the present study. Mortality in patients having any of the above mentioned risk factors was (55.4%) as compared to 52.4% in patients without any risk factor. Elderly age, Diabetes mellitus, malignancy, HIV infection and nephritic syndrome compromise the host defense system and increase the likelihood of infection and potentially the development of sepsis². Old age, hypertension, diabetes mellitus causes afferent arteriolar pathology in the kidney which limits renal autoregulation consequently, glomerular filtration may decrease already at minor reductions of blood pressure. This predisposition causes them to easily develop

Conclusion

Males predominate females by a ratio of 2.3:1 in developing sepsis induced AKI however mortality remains uninfluenced by sex. Age above 60 is associated with increased risk of developing sepsis induced AKI and is also associated with a higher mortality due to same. Respiratory tract, kidney and urinary tract, skin and soft tissue and intraabdominal infection sites are common focus of infection and intraabdominal infection, multiple foci of infection were the more prevalent in patients with refractory septic shock, kidney and urinary tract infection was more prevalent in patients with sepsis. Refractory septic shock had a greater mortality compared to septic shock intum compared to sepsis/SIRS. Azotemia, oliguria, metabolic acidosis, anaemia, hyperkalemia hypocalcemia and proteinuria were the commonly encountered renal manifestations in patients with sepsis syndrome. Intrinsic renal failure is the commonest type of renal failure in sepsis syndrome. Complicating AKI increases the mortality in patients with sepsis syndrome. AKI on CKD group has the lowest mortality. Diabetes mellitus, hypertension, older age (>60 years), pre-existing CKD, nephritic syndrome, HIV infection, malignancy and nephrotoxic drug intake were important risk for the development of sepsis, AKI or both.

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