Research Paper

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Study of Clinical Course and Prognostic Factors Affecting Course of Septicemia

Medical Science

KEYWORDS : Septicemia, Sepsis, Organ failure, Procalcitonin

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ABSTRACT

The prognosis of the patient with sepsis is related to the number of dysfunctional organs and only during those critical "golden hours" definitive recognition and treatment will provide maximal benefit in terms of outcome. Therefore study enrolled 60 patients with routine biochemical and microbiological investigations and were treated. Patients were monitored with APACHE II and MODS and followed up. In results there were total (n=60) 45 males and 15 females from age groups of 15 to 90 yrs. Total mortality was 56.66% and Pneumonia being most common etiology . There was significant correlation of clinical parameters with severity scores (p=<0.05). APACHE II and MODS were shown to have significant association (r=0.65). To conclude, early recognition of clinical parameters like hypotension, oliguria, prerenal azotemia, metabolic acidosis, ALI and / or ARDS are of much importance; Levels of Procalcitonin , Lactate with standard severity scores will help to prognosticate the disease process and will guide in management strategies.

INTRODUCTION

Sepsis is the combination of a known or suspected infection and an accompanying systemic inflammatory response. Sepsis, severe sepsis, and septic shock are terms used to describe the body's systemic responses to infection. Severe sepsis is sepsis with acute dysfunction of one or more organ systems and septic shock is a subset of severe sepsis. It is common and frequently fatal. Underlying illness, increased age, and multisystem organ failure are major risk factors for mortality from sepsis.[1,2]

The prognosis of the patient with severe sepsis is related to the number of dysfunctional organs. Progression from signs of the inflammatory response to sepsis / severe sepsis and septic shock is associated with an incrementally higher mortality risk. Therefore, early recognition of sepsis is of paramount importance in reducing mortality.[3] Sepsis with acute organ dysfunction is common and frequently fatal and represents a significant health care burden in our country. The incidence and associated mortality and morbidity rates of severe sepsis are commonly underestimated . This is a function of number of factors .

Important methods for reducing mortality identified by recent studies include aggressive fluid resuscitation, early goal-directed therapy (EGDT), early administration of antibiotics, and the administration of activated protein C to eligible patients with recently introduced PIRO grading system for assessment of *P*redisposition, severity of *I*nfection, physiologic *R*esponse, and *O*rgan failure (PIRO).[4] Despite of appropriate antibiotics, source control and organ support , the mortality rate in patients with severe sepsis remains at 18 % to 50 % and that of septic shock ranges from 30% to 87%.[5]

Thus this study was done by evaluating clinical features and prognostic factors affecting course of septicaemia. Which would be useful in predicting the prognosis and deciding the management policies.

MATERIAL & METHODS

This study was a single centre prospective study on septicemia conducted at Govt. Medical College and Hospital, Pune, Maharashtra. Total 60 Cases were selected from Govt. Hospital Intensive Care Unit / M.I.C.U. and wards. After selection of cases detailed history, clinical examination and then investigations were carried out.

INCLUSION CRITERIA :

Criteria For Selection Of Casess

1. Presence or suspicion of infection , coupled with evidence of systemic response to the infection manifested by a systemic inflammatory response of the following :

- Alteration of body temperature : either < 36 ^{0} c or > 38 ^{0} c
- Increased heart rate - > 90/min
- Increased respiratory rate (> 24 /min) or Evidence of hypoventilation (PaCO2 > 32 mmHg).
- Changes in WBC count < 4000 /cmm or > 12000 /cmm or increased no. of immature polymorphonuclear leucocytes

Note : These criteria are incorporated in definition of sepsis by Sepsis Consensus Conference 2001

2. Along with above mentioned criteria presence of one or more of the following :

I. Arterial hypotension that responds to intravenous fluid administration.
II. Systolic blood pressure < 90 mmHg or mean blood pressure < 70 mmHg
III. Acute oliguria – Urine output < 0.5 ml/kg/hr for at least 1 hr despite adequate fluid resuscitation
IV. PaO2 / fiO2 = < 250 or ,if the lung is only dysfunctional organ then < 200
V. Platelet count < 80000 / cmm or < 50 % of highest value recorded over previous 3 days
VI. Unexplained metabolic acidosis – pH < 7.30 or Base deficit > 5 meq /L and plasma lactate levels > 1 mmol/L

All the patients were treated with appropriate antibiotics either according to suspicion of infection site or documented culture sensitivity.

Exclusion Criteria:

Patients suffering from Chronic kidney disease and Chronic liver diseases i.e. Cirrhosis etc.

Laboratory investigations :

CBC & Platelets - SYSMEX machine, BSL -Glucose oxidase method, Sr.Electrolytes- Flame photometry method; RFT,LFT-Auto analyser; ABG, Sr.lactate-Randox kit method, Prothrombin Time, Procalcitonin Levels (B·R·A·H·M·S PCT-Q kit). Blood Cultures , Urine Analysis, urine and other cultures, Imaging studies : CXR, USG, CT scan, MRI wherever required.

Monitoring of cases : All patients were monitored on day 1,3,5,10 and 15 . Cases were monitored according to APACHE II and MODS scores .Tables and Charts were formed which included various clinical and biochemical parameters e.g. Heart

rate , fever, temperature, Respiratory rate, Blood pressure, GCS , Lactate , Procalcitonin. Values of various parameters were correlated with each other and there significance with outcome of disease was evaluated statistically.Statistical analysis was done by using Chi-square test for independent attributes , by Spearman's correlation method (Non-parametric technique) and by Co-efficient correlation (r). p value of < 0.05 was considered statistically significant and r = 1 was considered statistically significant.

RESULTS

In this study we have observed the clinical course of sepsis and prognostic factors affecting outcome of disease using APACHE II [6] , Multiple Organ Dysfunction Score (MODS)[7] and Biochemical markers like Scvo2 , Serum Lactate and Serum Procalcitonin levels.

We have included 60 patients randomly irrespective of Age ,Sex and Severity of the disease. The study included criteria for sepsis according to Sepsis CONSENSUS conference 2001. We have excluded the patients of chronic liver and kidney diseases. Appropriate cultures were taken and empirical antibiotics were started, for community acquired pneumonia, third generation cephalosporin in combination with a fluoroquinolone or a macrolide while for some cases Piperacillin and Tazobactum. Gentamicin with Ampicillin or a third generation cephalosporin with gentamicin was used in patients of UTI . Skin infections like wound cellulitis were treated with Vancomycin , Metronidazole , Aminoglycosides and if wound was life threatening a combination of Iminpenem and Cilastatin was used. Ceftriaxone for suspected meningitis, while in few cases combination of Piptaz plus Gentamicin was used. In present study of 60 patients 37 (61.66%) patients (31 males, 6 females) were in age group 30-70 yrs . As the study is too small any correlation of age to sepsis is not possible but it was common in male patients [8]. Most common causes of sepsis are pneumonia in 14 patients (23.33%), urinary tract infections in 12 patients(20%) Skin infections and abscesses (12 patients) rest in list were osteomyelitis , peritonitis, pancreatitis and meningitis etc. Most common organisms found with community acquired pneumonia were K.pneumoniae and P.aeruginosa . out of which some were multidrug resistant pseudomonas. E.coli was the commonest organism found in association with UTI and some cases of pyelonephritis. Staphalococcus aureus was commonly associated with cellulitis and abscesses while in some cultures no organisms were found.

In correlation of temperature with severity of sepsis , 38 (63.33%) patients showed temp. > 101 ^{o}F and APACHE II score > 25. 32 patients (53.33%) with MODS score > 15 and p value=< 0.05 for both scores. Newer advances in therapy has brought down the incidence of both ALI and ARDS and associated mortality rates [9]. We observed incidences of Acute Lung Injury in 32 (53.33 %) patients and ARDS in 11 (18.33 %) patients throughout the course of disease. It showed that the serum procalcitonin levels of patients were significantly high in those who had shown high severity scores (APACHE II and MODS) p =0.013 and <0.001 respectively[10]. Correlation of metabolic acidosis and hypotension throughout course of disease was found to be significant (p = 0.031). Oliguria was observed in 35 patients (58.33%) out of which 10 patients had oliguria for less than 2 days. Most common predisposing factor for oliguria is hypotension , observed in 14 patients (23.33%) other precipitating factors for oliguria are hypovolemia with normal blood pressure , fulminant course of disease, nephrotoxic drugs. Oliguria was significantly correlated with outcome of disease (p= 0.006). 51 Patients (85%) had AKI out of which incidence of prerenal azotemia were found in 45 patients (75%) while in acute tubular necrosis was found in 6 patients (10%) [11]. Correlation of Prerenal azotemia with severity of disease has got strong association (p= <0.001 for MODS score and p= 0.001 for APACHE II score). While correlating AKI (Prerenal azotemia and ATN) with outcome of disease we found that 51 patients (85%) had AKI during course of disease of which 32(53.33%) expired and 19(31.66%) survived , so present study showes mortality rate of 61.66 % is significant with presence of AKI in sepsis with p value = 0.032. APACHE II and MODS scores both have strong significance with the mortality rates in sepsis, higher the scores higher the mortality rates [12,13,14]. (p= <0.05 for both APACHE II and MODS scores). There was no significant correlation of serum procalcitonin levels with central venous oxygen saturation with (p= 0.773). Scvo2 levels were not significantly associated with mortality with 19 (31.66%) out of 34 patients who expired showed levels < 70 % [15]. As our study dealt with central venous oxygen saturation and it has got less predictive value for determination of Svo2 (mixed venous oxygen saturation) and there was no correlation with mortality.

There was strong significance of higher serum procalcitonin levels and disease mortality[16]. Those who are having procalcitonin values >10 ng/ml all 20 (33.33%) patients expired because of septicemic shock as complicating event.(p = < 0.001). It showed that the lactate levels of patients who expired are significantly higher than the patients who survived [17,18]. While correlating APACHE II and MODS scores it was found that both severity scores correlates significantly with each other at presentation (Pearson's correlation coefficient (r) is 0.675 i.e < 1 , p-value < 0.001 there is Significant good positive correlation between the APACHE II and MODS).

Table 1 : Correlation of procalcitonin levels with severity of disease (APACHE II & MODS)

Severity scores (n= 60)		Procalcitonin				p-value
		< 0.5 ng/ ml	0.5 - 2 ng/ml	2 - 10 ng /ml	>10 ng/ml	
APACHE II	< 10	0	0	0	0	0.013
	10 – 25	1	12	3	5	
	26 – 40	1	11	9	10	
	> 40	0	2	3	5	
MODS	< 5	0	0	0	0	< 0.001
	5 – 15	2	16	4	2	
	16 – 20	0	3	14	18	
	> 20	0	1	0	0	

Conclusion :-

p-value < 0.05 by using Chi-square test with Yates's correction there is association between the procalcitonin and APACHE II score and p-value < 0.05 there is association between procalcitonin and MODS score.

Correlating complications of sepsis e.g. DVT, PE, G.I.Bleed, Nosocomial infections , critical illness neuropathy with outcome of sepsis , we found that they had no significance with mortality rates. p= > 0.05.

DISCUSSION

The present study deals with a sample of 60 septicemic patients admitted and treated in Govt medical college and Hospital wards and in MICU. Study was designed as to find out the clinical profile of septicemic patients in the hospital and to judge the use of lab parameters to prognosticate the disease process.

After evaluating the biochemical and microbiological profile of these septicemic patients, lab parameters were correlated with the clinical course and outcome of sepsis. In study, patients showed Pneumonia and UTIs are being the commonest sources of sepsis in hospitalised patients. Clinical parameters like Heart rate , respiratory rate , temperature correlated well with severity of disease process and correlated significantly with outcome of the sepsis. 43 out of 60 patients showed increased incidences of sepsis associated ALI and ARDS. In patients who were having oliguria, there is increased incidence of prerenal azotemia and ATN i.e. in 85 % of patients. Both prerenal azotemia and ATN were bad prognostic indicators.

While correlating biochemical markers of sepsis Serum procal-

citonin had significant correlation with both severity scores and also was strong predictor of sepsis and its mortality. Scvo2 i.e. Central venous oxygen saturation was not proved to be a predictor of sepsis outcome in present study probably because of its less predictability of Svo2 (mixed venous o2 saturation) .Thus it showed no significance in our study regarding outcome of sepsis. Mean lactate levels of critically ill patient were significantly higher from onset of sepsis and correlated well with both APACHE II and MODS severity scores and also with serum procalcitonin levels thus can be considered as the reliable indicator of unfavourable prognosis.

CONCLUSION-

Despite of recent advances and higher generation of antibiotics , the clinical course and outcome in septicemic patients is dreadful and thus early recognition of clinical parameters like oliguria, hypotension, metabolic acidosis, ALI and / or ARDS; and sepsis markers (like Sr. Procalcitonin, Sr. Lactate) will help to prognosticate the disease process and will guide in management strategies.

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