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Serum Procalcitonin As Biomarker for Early Diagnosis of Sepsis

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Abstract

Aim: study designed to analyse the Procalcitonin for early detection of sepsis. *Method*: procalcitonin, blood, urine culture, and ultrasound were performed and patients were categorized into groups based on PCT levels. *Results*: 40% had respiratory infections, 30% showed urinary tract infections, 6% gastrointestinal tract infections, 4% soft tissue infections and 6% were with other types of infections. 84% cases with sepsis and 16% cases with no sepsis. Sepsis was observed in 40 % and septic shock in 44% cases. 36% cases were died. Acute febrile illness observed in 6 (12%), ARDS and pyelonephritis with sepsis recorded in 4(8%). vasoactive support (VA) was given to 28 patients. 33.3% sepsis cases more than 10ng/ml procalcitonin was observed while none of the cases with no sepsis showed this level. 9.5% and 57.1% patients with sepsis, the procalcitonin level was below 2ng/ml and 2-10ng/ml respectively. The mean procalcitonin in survivors was 5.47±3.02 ng/ml while it is 10.84± 5.66 ng/ml in non survivors. The mean lactate in survivors was 6.68± 2.04 and it is 8.17± 2.02 in non survivors. The mean procalcitonin level was 3.23 ng/ml in APACHE II (Score<10), 7.50 ng/ml in APACHE II (Score10-20) and increased to 10.29 ng/ml in APACHE II (Score>20). The mean procalcitonin level was 4.14 ng/ml in SOFA (Score<10), 9.57 ng/ml in SOFA (Score10-20) and increased to 13.75 ng/ml in SOFA (Score>20). *Conclusion*: present study showed that procalcitonin is a useful marker in early diagnosis of septic shock, help in management.

Keywords: Sepsis, Serum Procalcitonin, APACHE II, Ventillator Support

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Introduction

Fever is one of the most frequent causes for hospitalization in developing countries. While several etiological causes result in a febrile illness, bacterial infections constitute an important "curable" cause of fever. Systemic bacterial infection, bacterial sepsis and related syndromes are life-threatening illnesses that need early initiation of appropriate antimicrobial therapy (Alladi Mohan and Hari Krishna)[1] Sepsis is a systemic immune response to infection by microbial organisms. Sepsis is defined as the presence of infection together with systemic manifestations of infection. The third International Consensus, sepsis 3 update, organized by Society of critical care medicine and European society of Intensive care medicine, on 2016 found limitations of previous definitions that included excessive focus on inflammation, misleading model that sepsis follows a continuum through severe sepsis to shock and inadequate specificity and sensitivity

to SIRS criteria. The task force concluded the term severe sepsis was redundant (Mervyn Singer *et. al.*)[2]. Sepsis was redefined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Sepsis can be difficult to distinguish from non-infectious conditions in critically ill or comatose patients in the early stages, diagnosis, treatment and outcomes greatly differ between patients with and without sepsis (Harbarth *et. a*l. 2001)[3.] Positive bacteriological cultures, including blood cultures, may not be available before 24 to 48 hours, interpretation of local colonization may be ambiguous; and traditional markers of infection, such as body temperature and white blood cell (WBC) count, may not be specific (Castelli *et. al.* 2004)[4]. Furthermore, there are concerns about possible blood culture–negative clinical sepsis, particularly in the setting of increased prophylactic and empirical antibiotic use (Muller *et. al.* 2007)[5]. Conversely, differentiating true infection from contamination after growth of common skin commensals in blood cultures, poses a diagnostic problem (Muller *et. al.* 2000)[6]. Since early identification of infections and sepsis is crucial for patient management, an effective marker specific for bacterial infection is very useful in the critical care settings.

There are several markers of sepsis. An ideal biomarker for bacterial infections should facilitate early rapid diagnosis, predict the course and prognosis of the disease and guide therapeutic decisions. Leucocyte count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), soluble triggering receptor expressed on myeloid cells 1 (sTREM-1), proadrenomedullin (ProADM), serum procalcitonin (PCT), mid-regional pro-atrial natriuretic peptide (ANP), pancreatic stone protein (PSP)/regenerating protein (reg), interleukin-6 (IL-6), IL-8, IL-27, soluble urokinase-type plasminogen activator receptor (suPAR) among others, have been studied as potential biomarkers to facilitate diagnosis and aid prognostication in bacterial sepsis. Mahua Sinha, *et. al.* (2011[7] showed that the PCT assay conducted by them revealed moderate sensitivity (86%) and high specificity (95%) at a cut-off ≥ 2 ng/ml and concluded that the PCT assay was found to be a useful biomarker for diagnosis of sepsis. The overall studies carried out subsequently also showed that PCT is the superior biomarker over the other biomarkers tested.

The present study was an attempt to assess the usefulness of serum Procalcitonin (PCT) as an early diagnostic marker in patients suspected of sepsis using the semi-quantitative, rapid immune chromatographic kit at the Department of Emergency Medicine.

This prospective study was to determine the Procalcitonin as a biomarker for the early detection / diagnosis of sepsis.

Materials and Methods

Study Design

The present study was a prospective study on atraumatic patients admitted in the Emergency Department (ED) for Narayana Medical College and Hospital, Nellore District, Andhra Pradesh. Informed consent was taken from all the patients / guardians of the patients for participation in the study.

Study Population

The study was performed from November, 2014 to October, 2016 in the Emergency Department of Narayana Medical Collage and Hospital, Nellore. All adult atraumatic patients admitted in the ED suspected of sepsis were only included in the study. The patients who were dead on arrival and those referred from other wards were excluded from the study.

Methodology:

All the patients were clinically examined and demographic information such as age, sex, residence and other information on signs and symptoms, case history, past medical history, complaints etc., was collected and recorded in the Proforma prepared for this study purpose. Pulse rate, heart rate, temperature, Blood Pressure and respiratory rate were also recorded. Blood samples were collected to study complete blood picture including WBC, hemoglobin and also to study for biochemical parameters such as creatinine, CBG, lactate levels, LDH, amylase, lipase and PCT. Blood and Urine Culture were also set up for microbial analysis.

Radiological examinations including ultrasound were also performed when ever needed. The PCT was estimated and the patients were catergorized based on PCT levels. The details of the cases who recovered (Survivors) and died (Non- Survivors) were also recorded.

*Subjects***:** The patients who fulfilled the following conditions were only included for the study

*Inclusion Criteria***:**

The Inclusion Criteria of the patients were as

follows:

1. Patients aged >18 years with suspected sepsis.
2. Clinical or Laboratory features suggestive of sepsis based on American college of chest physician guidelines & new classification according to society of critical care medicine and European Society of Intensive care Medicine in recent Sepsis 3 Update.
3. Clinical Presentation of sepsis and patients with Positive Blood or urine culture.

*Exclusion Criteria***:**

Patients with history of malignancy,Trauma, Recent Surgery, Burns, Cardiogenic shock, Acute pancreatitis.

Statistical analysis

Statistical analysis has been done by using IBM SPSS Version 22.0. For categorical variables, the data values are represented as number and percentages. To test the association between the groups, chi-square test was used. For continuous variables, the data values are shown as mean and standard deviation. To test the mean difference between two groups, Student's t-test was used. To test the correlation between the groups, Pearson's correlation test was used. To test the mean difference between three or more groups, ANOVA test was used. All the p values having less than 0.05 are considered as statistical significant.

Results

Out of 50 critically ill patients admitted in the Emergency Department, 31 (62 %) are males as against 19 (38%) females. The cases are subjected to Arterial Blood Gas Analysis and out of 50, 48% (24) are with metabolic acidosis and 26%are with respiratory acidosis.

In 82% of cases cultures were set up for diagnosis and in 18% of cases (n=9) no cultures were carried out. Out of 50 cases, 40% (20) showed respiratory infections, 30% showed urinary tract infections, 6% gastrointestinal tract infections, 4% soft tissue infections and 6% are with other types of infections. In 14% of cases (7) no source was detected. The results showed 84 % (n=42) of cases with sepsis and 16% of cases with no sepsis.

The outcome of the patients admitted in the E.D was studied and recorded that 64% (32) only survived and the remaining 36% (18) did not survive.

Diagnosis of study group

Pneumonia was found in 14 patients , acute febrile illness was observed in 6 out of 50(12%) cases while ARDS was found in 1 patient, cellulitis was recorded in 2 patients, gastroenteritis with AKI was recorded in 1 patient, Pyelonephritis with sepsis was recorded in 4/50 (8%) in each case.

Out of 50 patients vasoactive support was given to 28 patients. 13 patients survived and 15 patients died in spite of VA support. Out of 50 patients ventilator support was given to 30 (60%) patients.15 Patients survived and 15 patients died in spite of ventilator support.

In 11/50 (22%) Hypertension (HTN) was recorded followed by Diabetes Mellitus (DM) in 9/50 (18%), CAD in 5/50 (10%), CKD in 4/50(8%), Hypothyroidism in 2/50(4%), Hyperthyroidismin (2%) cases. More than one sign/symptom was observed in some cases. In 4/50 (8%) DM and HTN were noted followed by CKD and HTN and HTN and Hypothyroidism in one case each (1/50, 2%).

The mean age was 48.02 years in patients with sepsis and 44.25 years in patients with no sepsis. The difference in the age between the two groups was insignificant. The mean HR(per minute) was 127.02 in patients with sepsis and 110.75 in patients with no sepsis. The difference in the HR between the two groups was significant. The mean RR(per minute) was 34.48 in patients with sepsis and 28.50 in patients with no sepsis. The difference in the RR between the two groups was significant. The mean MAP (mm of Hg) was 67.88 in patients with sepsis and 73.25 in patients with no sepsis. The difference in the MAP between the two groups was insignificant. The mean urea (mg/dl) was 67.62 in patients with sepsis and 49.13 years in patients with no sepsis. The difference in the urea between the two groups was insignificant. The mean serum creatinine(mg/dl) was 3.60 in patients with sepsis and 2.13 in patients with no sepsis. The difference in the creatinine between the two groups was significant. The mean bilirubin (mg/dl) was 3.13 in patients with no sepsis and 6.26 in patients with sepsis. The difference between the two groups was statistically significant. The mean GCS in patients with sepsis is 10.62 and in patients with no sepsis was 13.25. The difference was statistically significant between the two groups. The mean PaO2/FiO2 ratio in patients with sepsis was 261.31 and in patients with no sepsis it was 335. The difference between the two groups was significant. The mean lactate value (mmol/l)) for patients with no sepsis

Table 1. Showing independent Variables in patients with sepsis and no sepsis

Clinical Diagnosis		N	Mean	Std. Deviation	t-value	P value
AGE(yrs)	No Sepsis	8	44.25	18.030	-0.620	0.538 (Not Sig.)
	Sepsis	42	48.02	15.369		
	Total	50	47.42	15.686		
HR(per min)	No Sepsis	8	110.75	17.661	-2.514	0.036 (Sig.)
	Sepsis	42	127.02	11.077		
	Total	50	124.42	13.548		
RR(per min)	No Sepsis	8	28.50	7.329	-2.504	0.045 (Sig.)
	Sepsis	42	34.48	7.578		
	Total	50	33.52	7.786		
MAP(mm of Hg)	No Sepsis	8	73.25	21.049	0.924	0.360 (Sig.)
	Sepsis	42	67.88	13.777		
	Total	50	68.74	15.036		
UREA(mg/dl)	No Sepsis	8	49.13	28.256	-1.928	0.06 (Not Sig.)
	Sepsis	42	67.62	24.238		
	Total	50	64.66	25.544		
Sr. Creatinine (mg/dl)	No Sepsis	8	2.13	1.727	-2.768	0.008 (Sig.)
	Sepsis	42	3.60	1.308		
	Total	50	3.36	1.467		
Bilirubin (mg/dl)	No Sepsis	8	3.13	3.834	-2.246	0.029 (Sig.)
	Sepsis	42	6.26	3.582		
	Total	50	5.76	3.766		
GCS	No Sepsis	8	13.25	3.151	2.521	0.015 (Sig.)
	Sepsis	42	10.62	2.622		
	Total	50	11.04	2.850		
PAO2 / FIO2	No Sepsis	8	335.00	100.854	2.518	0.036 (Sig.)
	Sepsis	42	261.31	86.239		
	Total	50	273.10	91.764		
Lactate (mmol/l)	No Sepsis	8	5.3438	1.85230	-2.903	0.006 (Sig.)
	Sepsis	42	7.5743	2.01481		
	Total	50	7.2174	2.13756		
Platelet Count (per cumm)	No Sepsis	8	131250.00	67170.891	2.465	0.017 (.Sig)
	Sepsis	42	77245.24	54831.864		
	Total	50	85886.00	59667.504		
WBC (cells/cumm)	No Sepsis	8	8855.00	1770.448	-1.780	0.081 (.Sig)
	Sepsis	42	11587.10	4242.312		
	Total	50	11149.96	4065.754		
Procalcitonin (ng/ml)	No Sepsis	8	2.98	2.294	-4.806	0.0001 > (VHS)
	Sepsis	42	8.25	4.782		
	Total	50	7.40	4.868		
qSOFA	No Sepsis	8	2.25	707.	-1.477	0.146 (.Sig)
	Sepsis	42	2.60	587.		
	Total	50	2.54	613.		

Cont.../-

SOFA	No Sepsis	8	5.50	1.852	-7.052	0.0001 > (VHS)
	Sepsis	42	13.07	5.514		
	Total	50	11.86	5.813		
APACHE II	No Sepsis	8	8.63	916.	-8.707	0.0001 > (VHS)
	Sepsis	42	18.95	7.395		
	Total	50	17.30	7.778		
(LOS (in Days	No Sepsis	8	1.00	000.	-4.946	0.0001 > (VHS)
	Sepsis	42	3.64	3.463		
	Total	50	3.22	3.315		

Table 2. Summary of different parameters in patients with sepsis and no sepsis

Parameters	**No sepsis N (%)**	**Sepsis N (%)**	**Total N (%)**	**Chi-square**	**P value**
Sex					
Males	4 (50.0)	27 (64.3)	31 (62.0)	0.582	0.445
Females	4 (50.0)	15 (35.7)	19 (38.0)		(Not Sig.)
CULTURE					
Bal	0 (0.0)	1 (2.4)	1 (2.0)		
Blood	0 (0.0)	9 (21.4)	9 (18.0)		
CSF	1 (12.5)	1 (2.4)	2 (4.0)		< 0.0001
ET	0 (0.0)	3 (7.1)	3 (6.0)	34.706	VHS
None	7 (87.5)	2 (4.8)	9 (18.0)		
Pus	0 (0.0)	2 (4.8)	2 (4.0)		
Pus/Drain	0 (0.0)	2 (4.8)	2 (4.0)		
Sputum	0 (0.0)	13 (31.0)	13 (26.0)		
Urine	0 (0.0)	9 (21.4)	9 (18.0)		
CLINICAL DIAGNOSIS					
Respiratory Tract Infection	0 (0.0)	20 (47.6)	20 (40.0)		
Urinary Tract Infection	0 (0.0)	15 (35.7)	15 (30.0)		< 0.0001
Gastrointestinal Tract Infection	0 (0.0)	3 (7.1)	3 (6.0)	45.04	VHS
No Source Found	7 (87.5)	0 (0.0)	7 (14.0)		
Soft Tissue Infection	0 (0.0)	2 (4.8)	2 (4.0)		
Miscellaneous	1 (12.5)	2 (4.8)	3 (6.0)		
Vasoactive Support					
No	7 (87.5)	15 (37.5)	22 (44.0)	7.314	0.007
Yes	1 (12.5)	27 (64.3)	28 (56.0)		(Sig.)
Ventillatory Support					
No	6 (75.0)	14 (33.3)	20 (40.0)	4.861	0.027 (Sig.)
Yes	2 (25.0)	28 (66.7)	30 (60.0)		
qSOFA					
Score - 1	1 (12.5)	2 (4.8)	3 (6.0)	2.191	0.334
Score - 2	4 (50.0)	13 (31.0)	17 (34.0)		(Not Sig.)
Score - 3	3 (37.5)	27 (64.3)	30 (60.0)		
Procalcitonin Scoring					
< 2 (ng/ml)	3 (37.5)	4 (9.5)	7 (14.0)	6.457	0.040
2 - 10 (ng/ml)	5 (62.5)	24 (57.1)	29 (58.0)		(Sig.)
> 10 (ng/ml)	0 (0.0)	14 (33.3)	14 (28.0)		

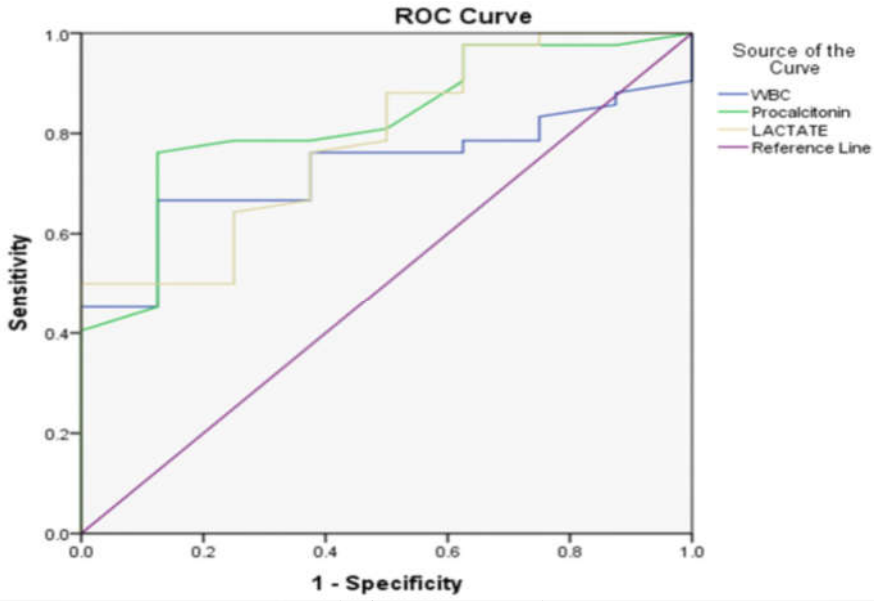

Fig. 1. Roc Curve For Sepsis (Wbc, Pct, Lactate)

Table 3: Statistical analysis of WBC Count, Procalcitonin and Lactate levels in patients with Sepsis

Test Result Variable(s)	Area	Std. Error	P VALUE	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
WBC	.729	.073	.042 (sig)	.587	.871
Procalcitonin	.823	.072	.004 (sig)	.681	.965
Lactate	.786	.081	.011 (sig)	.627	.944

Sig: Significant

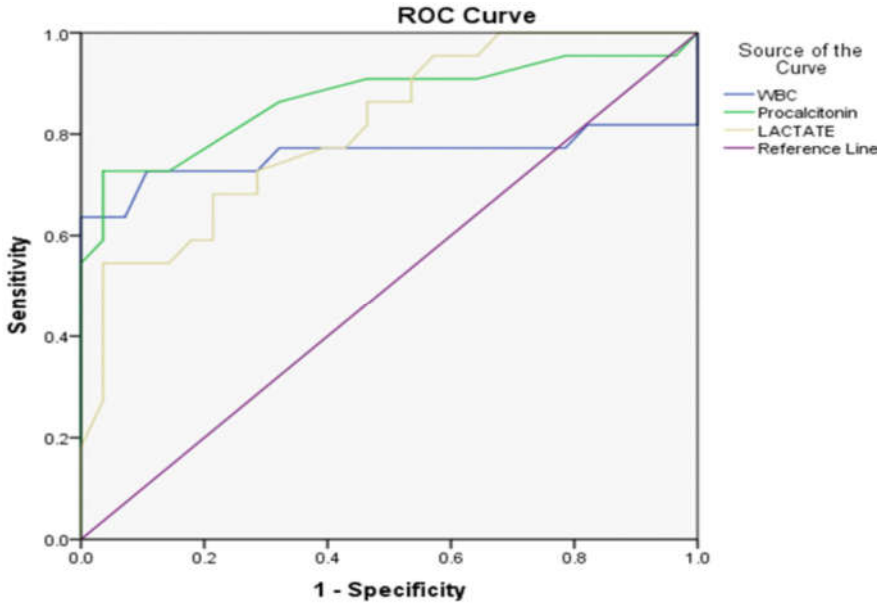

Fig. 2. Roc Curve For Septic Shock (Wbc, Pct, Lactate)

Table 4. Statistical analysis of WBC count, Procalcitonin and Lactate levels in patients with Septic shock

Test Result Variable(s)	Area	Std. Error	P Value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
WBC	.760	.086	0.002 Sig	.592	.927
Procalcitonin	.868	.058	0.000 VHS	.754	.981
Lactate	.812	.060	0.000 VHS	.695	.930

Sig: Significant, VHS: Very High Significant

Table 5. Showing values for independent variables in survivors non survivors of critically ill patients:

Outcome		N	Mean	Std. Deviation	t-value	P value
Age (in yrs)	Survivors	32	45.53	16.262	-1.139	0.26 (Not Sig.)
	Non-Survivors	18	50.78	14.433		
	Total	50	47.42	15.686		
HR (per min)	Survivors	32	120.44	13.735	-2.987	0.004 (Sig.)
	Non-Survivors	18	131.50	10.107		
	Total	50	124.42	13.548		
RR (per min)	Survivors	32	30.44	5.880	-4.367	< 0.0001 (VHS)
	Non-Survivors	18	39.00	7.874		
	Total	50	33.52	7.786		
MAP (mm of Hg)	Survivors	32	71.28	14.195	1.620	0.112 (Not Sig.)
	Non-Survivors	18	64.22	15.825		
	Total	50	68.74	15.036		
UREA (mg/dl)	Survivors	32	61.28	25.431	-1.254	0.216 (Not Sig.)
	Non-Survivors	18	70.67	25.333		
	Total	50	64.66	25.544		
Sr. Creatinine (mg/dl)	Survivors	32	2.91	1.422	-3.174	0.003 (Sig.)
	Non-Survivors	18	4.17	1.200		
	Total	50	3.36	1.467		
Bilirubin (mg/dl)	Survivors	32	4.50	3.213	-3.497	0.001 (Sig.)
	Non-Survivors	18	8.00	3.710		
	Total	50	5.76	3.766		
GCS	Survivors	32	12.00	2.578	3.528	0.001 (Sig.)
	Non-Survivors	18	9.33	2.544		
	Total	50	11.04	2.850		
PAO2 / FIO2 ratio	Survivors	32	303.66	79.442	3.476	0.001 (Sig.)
	Non-Survivors	18	218.78	88.775		
	Total	50	273.10	91.764		
LACTATE (mg/dl)	Survivors	32	6.6825	2.04112	-2.480	0.017 (Sig.)
	Non-Survivors	18	8.1683	2.01908		
	Total	50	7.2174	2.13756		

Cont.../-

Platelet Count (per cumm)	Survivors	32	107262.50	61972.120	4.577	< 0.0001 (VHS)
	Non-Survivors	18	47883.33	29481.086		
	Total	50	85886.00	59667.504		
WBC (cells/cumm)	Survivors	32	10713.88	2735.928	-0.842	0.409 (Not Sig.)
	Non-Survivors	18	11925.22	5744.763		
	Total	50	11149.96	4065.754		
Procalcitonin (ng/ml)	Survivors	32	5.47	3.020	-3.742	0.001 (.Sig)
	Non-Survivors	18	10.84	5.662		
	Total	50	7.40	4.868		
qSOFA	Survivors	32	2.41	665.	-2.398	0.02 (.Sig)
	Non-Survivors	18	2.78	428.		
	Total	50	2.54	613.		
SOFA	Survivors	32	8.34	3.721	-10.593	0.0001 > (VHS)
	Non-Survivors	18	18.11	2.742		
	Total	50	11.86	5.813		
APACHE II	Survivors	32	12.91	5.170	-8.112	0.0001 > (VHS)
	Non-Survivors	18	25.11	4.969		
	Total	50	17.30	7.778		
LOS (in Days)	Survivors	32	3.78	3.841	1.937	(Sig) 0.056
	Non-Survivors	18	2.22	1.768		
	Total	50	3.22	3.315		

Table 6. Summary of different parameters in survivors and non survivors

Parameters	Survivors N (%)	Non-Survivors N (%)	Total N (%)	Chi-square	P value
Grading					
No Sepsis	7 (21.9)	1 (5.6)	8 (16.0)	17.675	< 0.0001 (VHS)
Sepsis	18 (56.2)	2 (11.1)	20 (40.0)		
Septic Shock	7 (21.9)	15 (83.3)	22 (44.0)		
Vas. Support					
No	19 (59.4)	3 (16.7)	22 (44.0)	8.528	0.003 (Sig.)
Yes	13 (40.6)	15 (83.3)	28 (56.0)		
Vent. Support					
No	17 (53.1)	3 (16.7)	20 (40.0)	6.38	0.012 (Sig.)
Yes	15 (46.9)	15 (83.3)	30 (60.0)		
SOFA					
< 10	22 (68.8)	1 (5.6)	23 (46.0)	21.316	< 0.0001 (VHS)
10 – 20	10 (31.2)	13 (72.2)	23 (46.0)		
>= 20	0 (0.0)	4 (22.2)	4 (8.0)		
APACHE II					
< 10	14 (43.8)	1 (5.6)	15 (30.0)	31.895	< 0.0001 (VHS)
10 – 20	14 (43.8)	0 (0.0)	14 (28.0)		
>= 20	4 (12.5)	17 (94.4)	21 (42.0)		

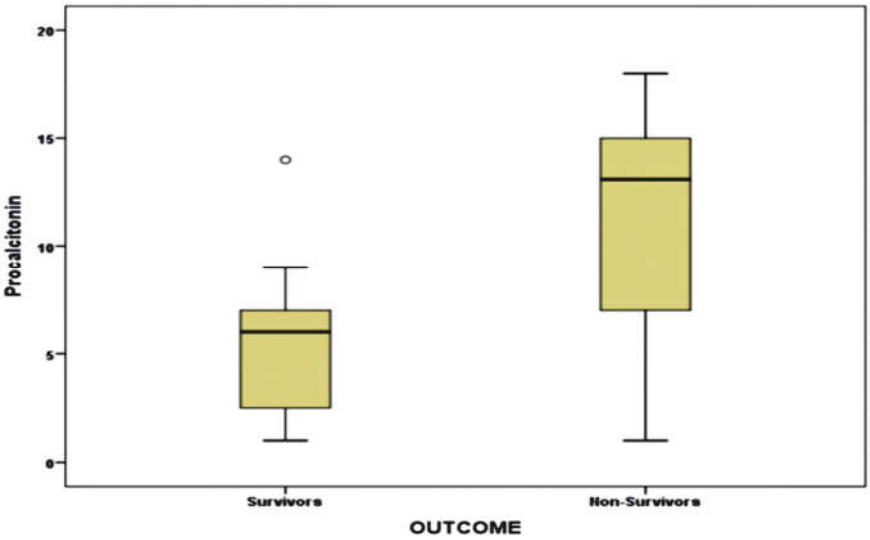

Fig. 3. Shows Mean Procalcitonin levels in Survivors and Non Survivors in the total number of patients in the study

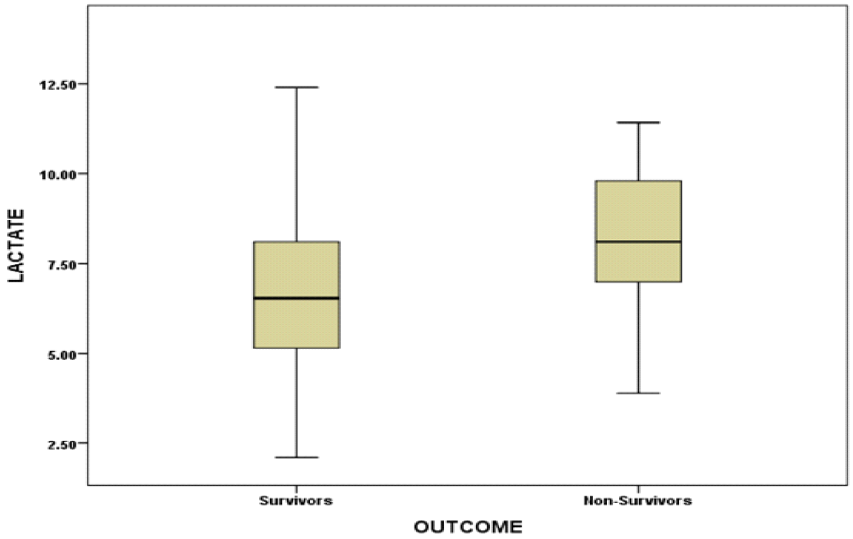

Fig. 4. Shows Mean lactate levels in survivors and non survivors in the total number of patients in the study

was 5.34 and in sepsis it was 7.57. The difference between the two groups was significant. The mean platelet count (per cumm) in patients with sepsis was 77245.24 and in patients with no sepsis it was 131250. The difference between the two groups was statistically significant. The Mean WBC counts (cells/cumm) in patients with sepsis was 11587.10 and in patients with no sepsis 8855. The difference between the two groups was statistically significant. The mean procalcitonin (ng/ml) was 8.25in patients with sepsis and 2.98in patients with no sepsis. The difference in the procalcitonin between the two groups was significant. The mean qSOFA score was 2.60 in patients with sepsis and 2.25 in patients with no sepsis. The difference in the qSOFA score between the two groups was significant. The mean SOFA score was 13.07 in patients with sepsis and 5.50 in patients with no sepsis. The difference in the SOFA score between the two groups was insignificant. The mean APACHE II was 18.95 in patients with sepsis and 8.63 in patients with no sepsis. The difference in the APACHE II between the two groups was significant. The mean LOS was 3.64 days in patients with sepsis and 1.00 day in patients with no sepsis. The difference in LOS between the two groups was significant.

The procalcitonin levels observed in patients with sepsis and no sepsis admitted in Emergency Department. In 14/42(33.3%) sepsis cases more than 10ng/ml procalcitonin was observed while none of the cases with no sepsis showed this level. In 4/14(9.5%) and 24/50 (57.1%) patients with

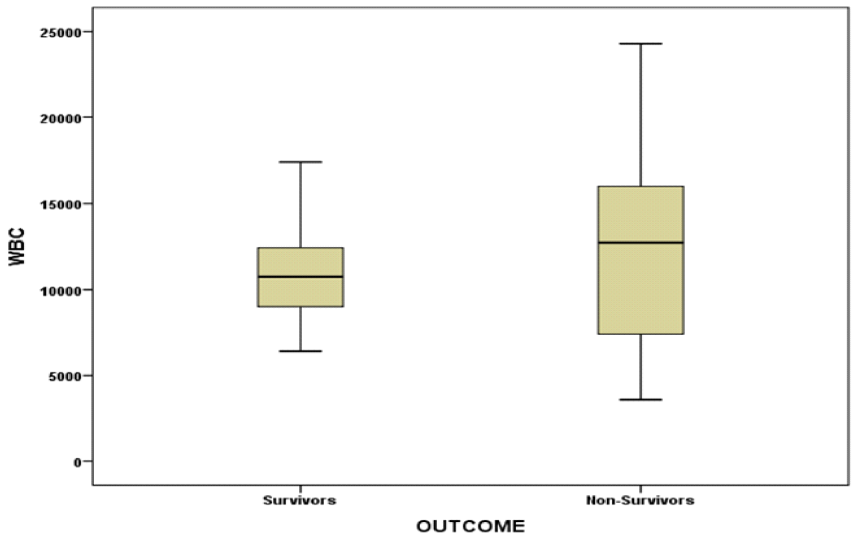

Fig. 5. Shows the mean WBC count in survivors and non survivors in the total number of patients in the study.

Table 7. Statistical analysis of the results on Procalcitonin levels, SOFA and APACHE II when plotted against length of hospital stay days).

Variable	Test	Procalcitonin	Sofa	Apache Ii	Length of Stay (Days)
Procalcitonin	Pearson Correlation	1	.724**	.650**	-.101
	P value		.000	.000	.484
	N	50	50	50	50
SOFA	Pearson Correlation	.724**	1	.918**	-.110
	P value	.000		.000	.449
	N	50	50	50	50
APACHE II	Pearson Correlation	.650**	.918**	1	-.011
	P value	.000	.000		.942
	N	50	50	50	50
Length of Stay (Days)	Pearson Correlation	-.101	-.110	-.011	1
	P value	.484	.449	.942	
	N	50	50	50	50

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

Table 8: Mean procalcitonin values in different groups of APACHE II

Procalcitonin (ng/ml)	N	Mean	Std. Deviation	F value	P value
< 10	15	3.2733	2.30542	13.844	< 0.0001 VHS
10 - 20	14	7.5000	2.47293		
>= 20	21	10.2857	5.37013		
Total	50	7.4020	4.86791		

Table 9: Receiver Operating Curve for HR, RR and MAP in Patients with Sepsis

Test Result Variable(s)	Area	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
HR	.795	.113	.009 SIG	.573	1.000
RR	.747	.112	.028 SIG	.528	.966
MAP	.432	.134	.543 NOT SIG	.169	.694

Table 10:. ROC Curve for Lactate Platelet count and WBC count in patients with Sepsis

Test Result Variable(s)	Area	Std.Error	P VALUE	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
LACTATE	.786	.081	.011 SIG	.627	.944
Platelet Count	.254	.105	.029 SIG	.050	.459
WBC	.729	.073	.042 SIG	.587	.871

sepsis, the procalcitonin level is below 2ng/ml and 2-10ng/ml respectively.

In 3/8(37.5%) and 5/8(62.5%) patients with no sepsis showed below 2ng/dl and 2-10ng/ml procalcitonin level respectively. The statistical analysis of the results using chi-square showed that the increase in procalcitonin level in patients with sepsis is statistically significant when compared to the level observed in non sepsis cases.

Receiver Operator Curve: Analysis of Procalcitonin, WBC and Lactate levels in patients with sepsis with Sensitivity on Y axis and Specificity on X axis.

Sig: Significant

The statistical analysis of the data presented shows that procalcitonin is highly sensitive compared to WBC or Lactate.

Receiver Operator Curve: Analysis of Procalcitonin, WBC and Lactate levels in patients with septic Shock with Sensitivity on Y axis and Specificity on X axis. The Statistical analysis of the data presented showed that Procalcitonin and lactate were highly significant when compared with WBC but maximum sensitivity was for Procalcitonin in patients with Septic Shock.

Sig: Significant, VHS: Very High Significant

The mean age was 45.53 years in survivors and 50.78 years in non survivors. The difference in age between the two groups was insignificant. The mean heart rate (HR) was 120.44 per minute in survivors and 131.50 per minute in non survivors. The difference in HR between the two groups was significant. The mean respiratory rate (RR) was 30.44 per minute in survivors and 39.00 per minute in non survivors. The difference in RR between the two groups was highly significant. The mean MAP (mm of Hg) was 71.28 in survivors and 64.22 in non survivors. The difference in MAP between the two groups was insignificant. The mean urea(mg/dl) in survivors was 61.28 and 70.67 in non survivors. The difference in urea between the two groups was insignificant. The mean serum creatinine (mg/dl) for survivors was 2.91 and 4.17 in non survivors. The difference in serum creatinine between the two groups was significant. The mean bilirubin (mg/dl) was 4.50 in survivors and 8.00 in non survivors. The difference in bilirubin between the two groups was significant. The mean GCS was 12.00 in survivors and 9.33 in non survivors. The difference in GCS between the two groups was significant. The mean PAO2/FIO2 ratio was 303.66 in survivors and 218.78 in non survivors. The difference in PAO2/FIO2 between the two groups was significant. The mean lactate (mmol/l) in survivors was 6.68 and 8.17 in non survivors. The difference in lactate between the two groups was significant. The mean platelet count (per cumm) was 107262.50 in survivors and 47883.33 in non survivors. The difference in platelet count between the two groups was highly significant. The mean WBC count (cells/cumm) was 10713.88 in survivors and 11925.22 in non survivors. The difference in WBC count between the two groups is insignificant. The mean procalcitonin (ng/ml) is 5.47 in survivors and 10.84 in non survivors. The difference in procalciton in between the two groups was significant. The mean qSOFA score in survivors was 2.41 and 2.78 in non survivors. The difference in mean qSOFA scores between the two groups was significant. The mean SOFA score in survivors is 8.34 and 18.11 in non survivors. The difference in SOFA score between the two groups was highly insignificant. The mean APACHE II score in survivors was 12.91 and 25.11 in non survivors. The difference in APACHE II score between the two groups is highly significant. The mean LOS was 3.78 days in survivors and 2.22

in non survivors. The difference in LOS between the two groups was insignificant.

The mean Procalcitonin(PCT) values were plotted using a box-chart. The mean values for non survivors was 10.84±5.66ng/ml and in survivors 5.47±3.02ng/ml. The difference between the two groups was statistically significant.

The mean Lactate levels were plotted usig a box-chart. The mean values for non survivors was 8.16 ±2.01mmol/l and in survivors 6.68 ±2.04mmol/l. The difference between the two groups was found to be statistically significant.

The mean WBC counts were plotted using a box-chart. The mean value for non-survivors was 11925.22 ±5744.76 cells/cumm of and in survivors 10713.88 ±2735.92 cells/cumm. The difference between the two groups was statistically significant.

The figure shows number of patients on the Y-axis and the qSOFA in relation to sepsis and no sepsis on the X-axis. Out of the 50 patients, score of 1 who had sepsis were 2 and no sepsis was 1, Patients with a Score of 2 who had sepsis were 13 and no sepsis were 4 and patients with a score of 3 who had sepsis were 27 and with no sepsis were 3. The statistical analysis showed a significant relation between the two variables.

In APACHE II group the survival of patients with sepsis was assessed and the results showed that the patients irrespective of the score died within 2-3 days. Very few patients survived after ten days.

In SOFA group, the survival of patients with sepsis was assessed and the results showed that the patients with more than 3 score died within 2-3 days. Very few patients survived after ten days.

The survival of critically ill patients with sepsis was assessed in relation to PCT and the results showed that the patients with more than 2 ng /dl died within 2-3 days. Very few patients survived after ten days.

7 out of 50 patients showed less than 2ng /ml PCT where as 14 patients showed more than 10ng /ml PCT. 29 patients had PCT levels between 2 and 10ng/ml.

The mean procalcitonin level is 3.23 ng/ml in APACHE II(Group<10), 7.50 ng/ml in APACHE II(Group10-20)and increased to 10.29 ng/ml in APACHE II (group>20).The statistical analysis of the results showed that the procalcitonin level in all the groups is significant and also the differences in procalcitonin levels in between the groups is significant

The mean procalcitonin level is 4.14 ng/ml in SOFA(group<10), 9.57 ng/ml in SOFA(group 10-20) and increased to 13.75 ng/ml in SOFA (group>20). The statistical analysis of the results showed that the procalcitonin level in all the groups is significant and also the differences in procalcitonin levels in between the groups is significant

The HR,RR and MAP are some of the signs used to suspect sepsis. The statistical analysis of the data indicated that HR and MR were found to be statistically significant while MAP was found to be insignificant indicating that HR and RR are better signs to suspect sepsis.

The WBC count, Lactate and platelet count were used to diagnose the sepsis. The statistical analysis of the data indicated that WBC count, lactate and platelet count were found to be statistically significant.

Discussion

TNF-α, CRP and IL-6 have been studied as markers of bacterial infection in critically ill patients admitted in ED. Moscovitz et. al. (1994)[8] studied 100 patients admitted in the Emergency Department (ED) with signs of infection and reported that plasma IL-6 concentrations were able to predict bacteremia and death from infection. A plasma IL-6 concentration ≥ 2.0 ng/ml detected bacteremia with a sensitivity of 42.1%, with a specificity of 96.7%, and with a PPV of 72.7%. Plasma TNF-α concentrations predicted mortality from all causes. The results just reflected the nonspecific nature of TNF-α for identifying infection, and disclosed the potential usefulness of IL-6 as a marker of severe infection.

The details of infections of various systems were studied. Of all the types, acute febrile illness was observed in 6 out of 50(12%) cases while Ards pneumonia and pyelonephritis with sepsis was recorded in 8% in each case. The patients were given vasoactive and ventilator support. Out of 50 patients vasoactive support(VA) was given to 28 patients. 13 patients survived and 15 patients died in spite of VA support. Out of 50 patients ventilator support was given to 30 (60%) patients.15 Patients survived and 15 patients died in spite of ventilator support.

The procalcitonin levels were estimated in patients with sepsis and no sepsis. In 14/42(33.3%) sepsis cases more than 10ng/dl procalcitonin was observed while none of the cases with no sepsis showed this level. 9.5% and 57.1% patients with sepsis, the procalcitonin level was below 2ng/dl and 2-10ng/dl respectively. In 37.5% and 62.5%

patients with no sepsis showed below 2ng/dl and 2-10ng/dl procalcitonin level respectively. The statistical analysis of the results using chi-square showed that the increase in procalcitonin level in patients with sepsis was statistically significant when compared to the level observed in non sepsis cases.

The WBC count, Lactate and procalcitonin employed to diagnose the sepsis were assessed in the present study and the statistical analysis of the data indicated that WBC count and lactate were found to be statistically significant while procalcitonin was found to be highly significant indicating that procalcitonin is a better biomarker when compared to the other two markers tested. ROC Curve also showed that procalcitonin is highly sensitive compared to other makers i.e., WBC count and Lactate levels. The WBC count, Lactate and procalcitonin levels were also assessed in cases with septic shock. The statistical analysis of the data indicated that WBC count was found to be statistically significant while procalcitonin and lactate levels were found to be highly significant indicating that these are better biomarkers.

The procalcitonin levels in survivors and non survivors of the patients were assessed. The mean procalcitonin in survivors was 5.47± 3.02 ng/dl while it is 10.84± 5.67 ng/dl in non survivors. The difference in procalcitonin levels between survivors and non survivors was analyzed for significance using t-test and the differences were found to be statistically significant. The lactate levels (mg/dl) in survivors and non survivors were assessed. The mean lactate in survivors was 6.68± 2.04 and it is 8.17± 2.02 in non survivors. The difference in lactate levels between survivors and non survivors was analyzed for significance using t-test and the differences were found to be statistically significant. The mean WBC count (cells per mm^3) in survivors and non survivors was also assessed. The mean WBC count in survivors is 10713.88± 2735.93 while it was11149.96± 4065.75 in non survivors. The differences in WBC count between survivors and non survivors was analyzed for significance using t-test and the differences were found to be statistically significant.

The overall results of the present study showed that PCT is auseful biomarkers to diagnose sepsis and septic shock

Extensive studies have shown elevated PCT levels in patients with sepsis, and demonstrated the high levels of PCT correlate with the outcome of the disease. Kibe et. al. (2011)[9] reported that the serum PCT levels have been noted to increase with increasing severity of sepsis. Besides, a rising PCT level might be used as an indicator that an infectious process is not under control.

Some studies have suggested that elevated PCT levels are useful in predicting bacteraemia in febrile patients. Briel et. al. (2008)[10] conducted a multi-center trial in outpatients, including 458 patients for whom the treating physician initially decided to prescribe antibiotics on a routine basis and the control group. In the treatment group, the decision was re-evaluated after presentation of the PCT-guided recommendation (no prescription if PCT <0.1 ng/dl or <0.25 ng/dl). As a result, 72% of patients in the PCT- guided group did not get antibiotics as compared to the control group. They did not have more complications, the number of sick days was the same and fewer side effects, such as diarrhea, were observed (Briel et. al. 2008).

Lu et. al. (2013)[11] showed that PCT can be a useful test in identifying systemic infections among patients with renal dysfunction.

The actual pathophysiologic role of PCT is still under investigation, and it was speculated that PCT might also be an acute phase protein (Nijsten et. al. 2000)[12]. The result of Ling Chang et. al. (2003)[72] showed that PCT might be used as a good marker of infection, but, more importantly, that it is a good marker of the severity of infection. Meisner,(2014)[13] showed that PCT has the highest accuracy for the diagnosis of sepsis in various settings. The lag time for PCT induction is approximately 2 to 4 hr after the onset of sepsis, a time period that has usually passed if patients are presented at the emergency department (ED). Peak levels of PCT occur at 24 to 48 hr after sepsis. Early treatment of sepsis is most effective ("the golden hours of treatment"), and complications like organ dysfunction indicate an already progressed state of the disease. Therefore, early confirmation of systemic inflammation and sepsis, as done by PCT measurement, is most important. Various studies have confirmed that survival rate of patients with sepsis can be significantly improved if antibiotic therapy is initiated immediately using the right antibiotics Kumar et. al. (2006)78. Point-of-care (POC) tests, despite being semi-quantitative, are helpful in situations when quantitative measurements are not going to be available within reasonable time. However, a semi-quantitative POC test should be sensitive enough to indicate or exclude systemic inflammation. This usually requires a lower assay sensitivity of 0.2-0.3 ng/mL. If the clinical impression indicates a possible diagnosis of sepsis, but PCT levels are not elevated, patients should

still be treated for sepsis initially, regardless of the high negative predictive value of normal PCT. Monitoring patients during the next one to two days will indicate whether the initial diagnosis is correct and antibiotics can be discontinued early if sepsis is excluded and PCT remains low. This approach is also supported by the society of critical care medicine (SCCM) sepsis guidelines (Dellinger et. al. 2013)[14]. PCT is also a food and drug administration (FDA)-approved diagnostic marker.

Viallon *et. al.* (2011)[15] observed that for patients presenting to the ED with symptoms of a suspected infection, measuring procalcitonin (PCT) is a useful diagnostic tool to identify bacterial infections, such as sepsis, allowing for early initiation of proper antibiotic treatment. In assessing the severity of sepsis, serum PCT levels are an important diagnostic tool, especially in the early stages. However, if a patient has been pretreated with antibiotics or if a bacterial infection is not accompanied by a systemic inflammatory response, procalcitonin is less useful as a marker. Therefore, a thorough analysis of the patient's clinical characteristics must be carried out, before treatment is initiated.

Conclusion

PCT has shown to be a good biomarker for diagnosing sepsis in febrile subject and also evaluating its severity in an emergency setting while awaiting confirmation from blood culture results. PCT should be interpreted in conjunction with other diagnostic criteria for sepsis.

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