

**To study the role of Absolute Lymphocyte Count as a prognostic marker in comparison with APACHE II and SAPS 3 scores in severe sepsis**

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**Abstract**

**Background:** Severe sepsis is the most common cause of hospitalization in the ICU around the world, patients are often hospitalized for extended period of upto 2-3 weeks.

**Methods:** This study was planned to establish Absolute Lymphocyte Count as a prognostic marker in comparison with APACHE II and SAPS 3 score in severe sepsis patients admitted in Medical Intensive Care Unit under Department of Medicine, Jawahar Lal Nehru Medical College & Hospital, Ajmer.

**Results:** On day 0, Absolute Lymphocyte Count  $< 1300 \text{ cells}/\mu\text{L} \times 10^6$  were independent and reliable markers of mortality in patients with severe sepsis

**Conclusion:** Absolute lymphocyte count can be used as a prognostic marker at admission and subsequently on day 4 and day 7 in severe sepsis, which are cheap, easily available and routinely done as a part of management of sepsis patients.

**Keywords:** ALC, Sepsis, APACHE II, SAPS 3

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**Introduction**

Severe sepsis is the most common cause of hospitalization in the ICU around the world, patients are often hospitalized for extended period of upto 2-3 weeks.<sup>(1)</sup> In spite of use of rational antimicrobial therapy and advance life support, mortality in patient with sepsis has remained high.<sup>(2)</sup> Sepsis is characterised by SIRS(Systemic Inflammatory Response Syndrome) and the presence of known or suspected infection. Severe sepsis and septic shock reflect the end result of complex interactions between infecting microorganism and host response and signify a primarily inappropriate response by the host to a microbial insult. The mismatch of the host response to the intensity of pathogenic stimuli is the key component that describes the pathophysiological events in septic shock that results in organ injury or dysfunction with or without hypotension.<sup>(3)</sup> Biomarkers for sepsis and by extension bloodstream infections hold much promise for

increasing the rapidity with which sepsis is diagnosed and for risk stratification and prognostication.

Multiple scoring system are available for assessment and prognosticate the severity of illness, can help to determine the chances of survival. Worsening sepsis is associated with increased mortality as multiple organ system fail. The degree of severity is often quantified by the APACHE II and SAPS 3 score which can predict the severity and outcome of multiple organ failure.<sup>(4)</sup>

Neutrophilia is well recognised as an infection marker whereas clinicians are less familiar with absolute lymphocyte count as a possible marker in sepsis. Absolute lymphocyte count may predict early and late mortality and may serve as a biomarker for sepsis induced immunosuppression.

#### Material and methods

This study was planned to establish Absolute Lymphocyte Count as a prognostic marker in comparison with APACHE II and SAPS 3 score in severe sepsis patients admitted in Medical Intensive Care Unit under Department of Medicine, Jawahar Lal Nehru Medical College & Hospital, Ajmer.

**Study Design:** Observational prospective cohort study.

**Duration of the study:** 1 year

**Study Size:** 100 patients with severe sepsis were included. Among 100 subjects, survivors and non-survivors were included and Absolute Lymphocyte Count, Platelet Indices and other parameters were compared among the 2 groups.

#### Inclusion Criteria

- Critically ill medical patient who meets criteria of severe sepsis (according to surviving sepsis campaign).
- Age more than 18yrs.

#### Exclusion Criteria

- Patient with concomitant immunological and hematological diseases (hematological
- Malignancies, ITP, reactive thrombocytosis and hypersplenism).
- Patient receiving platelets and FFP.
- Patients taking drugs (thrombocytopenia-amiodarone, carbamazepine, diclofenac, digoxin, ethambutol, rifampin, fluconazole, furosemide, hydrochlorothiazide, linezolid, sulfa drugs; neutropenia-alkylating agents, antimetabolites, anticonvulsants, antibiotics) affecting platelets and lymphocyte count.
- Pregnant and breast-feeding women.
- Treatment with chemotherapy agents or corticosteroids within 6 months prior to hospitalization.
- Patients those not given consent.

All relevant data were entered in a predesigned proforma which was subsequently analyzed & discussed to arrive at conclusions.

#### Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The independent t test (for quantitative data within two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Multiple regression analysis was used for prediction. Level of significance was set at  $P \leq 0.05$ .

**Results**

Table 1: Association of ALC with final outcome (n=100) on day 0

	0 DAYS	Final Outcome		Total n (%)	p value
		Survived n (%)	Died n (%)		
ALC	<1300	33 (49.3)	34 (50.7)	67 (100)	<0.001(S)
	1300-3500	32 (97)	1 (3)	33 (100)	

Absolute lymphocyte count among non-survivors was significantly lower than that of survivors. Total 34 of 67 patients died who had absolute lymphocyte count less than 1300 cells/ $\mu\text{L} \times 10^6$ , while only one patient out of 33 patients died who had lymphocyte count  $>1300$  cells/ $\mu\text{L} \times 10^6$ .

Table 2: Association of ALC with final outcome (n=100) on day 4

	4 DAYS	Final Outcome		Total n (%)	p value
		Survived n (%)	Died n (%)		
ALC	<1300	31 (50)	31 (50)	62 (100)	<0.001(S)
	1300-3500	34 (100)	0	34 (100)	

- Absolute lymphocyte count on day 4 among non-survivors was significantly lower than that of survivors. Total 31 of 62 patients died who had absolute lymphocyte count less than 1300 cells/ $\mu\text{L} \times 10^6$ , while no patient out of 33 patients died who had lymphocyte count  $>1300$  cells/ $\mu\text{L} \times 10^6$ .

Table 3: Association of ALC with final outcome (n=100) on day 7

	7 DAYS	Final Outcome		Total n (%)	p value
		Survived n (%)	Died n (%)		
ALC	<1300	24 (68.6)	11 (31.4)	35 (100)	<0.001(S)
	1300-3500	40 (100)	0	40 (100)	

- Absolute lymphocyte count on day 7 among non-survivors was significantly lower than that of survivors. Total 11 of 35 patients died who had absolute lymphocyte count less than 1300 cells/ $\mu\text{L} \times 10^6$ , while no patient out of 40 patients died who had lymphocyte count  $>1300$  cells/ $\mu\text{L} \times 10^6$ .

Table 4: Association of ALC with APACHE II on day 0

			ALC		Total
			<1300	1300-3500	
APACHE II	0-15	N	32	21	53
		%	60.4%	39.6%	100.0%
	16-25	N	16	9	25
		%	64.0%	36.0%	100.0%
	26-35	N	11	3	14
		%	78.6%	21.4%	100.0%
	>35	N	8	0	8
		%	100.0%	.0%	100.0%
Total	N	67	33	100	
	%	67.0%	33.0%	100.0%	

P value=0.15

- Absolute lymphocyte count  $<1300 \text{ cells}/\mu\text{L} \times 10^6$  was associated with higher APACHE II score, however this difference was not statistically significant (p value-0.15).

Table 5: Association of ALC with SAPS III on day 0

			ALC		Total
			<1300	1300-3500	
SAPS III	21-40	N	2	0	2
		%	100.0%	.0%	100.0%
	41-60	N	35	29	64
		%	54.7%	45.3%	100.0%
	61-80	N	19	4	23
		%	82.6%	17.4%	100.0%
	81-95	N	9	0	9
		%	100.0%	.0%	100.0%
	>96	N	2	0	2
		%	100.0%	.0%	100.0%
Total	N	67	33	100	
	%	67.0%	33.0%	100.0%	

P value=0.01 (S)

Table 6: Association of ALC with SAPS III on day 4

			AL		Total	
			<1300	1300-3500		
SAPS III	21-40	N	1	1	2	
		%	50.0%	50.0%	100.0%	
	41-60	N	33	30	63	
		%	52.4%	47.6%	100.0%	
	61-80	N	20	3	23	
		%	87.0%	13.0%	100.0%	
	81-95	N	7	0	7	
		%	100.0%	.0%	100.0%	
	>96	N	1	0	1	
		%	100.0%	.0%	100.0%	
	Total		N	62	34	96
			%	64.6%	35.4%	100.0%

P value=0.008 (S)

- Absolute lymphocyte count on day 4 less than  $1300 \text{ cells}/\mu\text{L} \times 10^6$  was associated with higher SAPS III score, and this difference was statistically significant (p value-0.008).
- Absolute lymphocyte count  $<1300 \text{ cells}/\mu\text{L} \times 10^6$  was associated with higher SAPS III score, and this difference was statistically significant (p value-0.01).

Table 7: Association of ALC with APACHE II on day 7

			ALC		Total	
			<1300	1300-3500		
APACHE II	0-15	N	23	27	50	
		%	46.0%	54.0%	100.0%	
	16-25	N	8	10	18	
		%	44.4%	55.6%	100.0%	
	26-35	N	3	3	6	
		%	50.0%	50.0%	100.0%	
	>35	N	1	0	1	
		%	100.0%	.0%	100.0%	
	Total		N	35	40	75
			%	46.7%	53.3%	100.0%

P value=0.75

- Absolute lymphocyte count on day 7, less than  $1300 \text{ cells}/\mu\text{L} \times 10^6$  was associated with higher APACHE II score, however this difference was statistically not significant (p value-0.75).

### Discussion

This study was planned to establish Absolute Lymphocyte Count as a prognostic marker in comparison with APACHE II and SAPS 3 score in severe sepsis patients admitted in Medical Intensive Care Unit under Department of Medicine, Jawahar Lal Nehru Medical College & Hospital, Ajmer.

Severe sepsis is the leading cause of death worldwide. Early detection and prompt administration of antibiotics has been shown to reduce mortality and morbidity in patients with sepsis. Hence, various markers have been evaluated for earlier diagnosis of sepsis.

Serum Procalcitonin and C-Reactive Protein are diagnostic markers of sepsis that has been largely studied in adult population and have been established as a marker of sepsis. But it is expensive. There are many other markers of sepsis which are being evaluated for its diagnosis but are either costly or not easily available.

Lymphocytopenia has been described as a marker of bacteremia and mechanisms responsible for lymphocytopenia in sepsis and septic shock involve margination and redistribution of lymphocytes within the lymphatic system and marked accelerated apoptosis. Apoptosis is a prominent feature of sepsis. This process, in which selected cell populations can be actively deleted from certain tissues, has been shown a mechanism of lymphocyte death in animal sepsis models. In blood of sepsis patients, lymphocyte apoptosis is rapidly increased leading to a profound and

persistent lymphocytopenia associated with poor outcome.

### Conclusion

Absolute lymphocyte count can be used as a prognostic marker at admission and subsequently on day 4 and day 7 in severe sepsis, which are cheap, easily available and routinely done as a part of management of sepsis patients.

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