Relationship between Reduced Albumin and Inflammatory Response in Critically Ill Patients

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Abstract: Background: The inflammatory response plays an important role in the pathophysiology of sepsis, and the impact of inflammation that can worsen chronic illness, which is a major determinant of adverse, long-term outcomes. Thus, biomarkers that can be used as independent prognostic factors to evaluate the mortality of patients with severe sepsis or septic shock should be measured objectively to reflect the inflammatory processes as well as responses to therapeutic intervention. As the level of C-reactive protein increases markedly in response to infection, and the magnitude of the increase may correlate with the severity of the infection, the prognostic value of CRP levels has been investigated in many diseases. **Aims:** To determine the relationship between reduced albumin and inflammatory response and its effect on morbidity and mortality in critically ill patients. **Patients and Methods:** This is a prospective randomized study that was conducted on patients who were admitted to ICU in Ain Shams University Hospitals. An informed written consent was obtained from patients and/or relatives. All patients subjected to daily hemodynamic monitoring of the mean arterial blood pressure, heart rate and temperature. Serum albumin level, Procalcitonin, CRP, TLC, ESR, blood gases and lactate were collected in first, third, seventh. **Results:** A sample size of 43 achieves 81% power to detect a difference of 0.30 between the correlation of 0.4 as regarding decreased albumin and increased inflammatory response measured by procalcitonin, c-reactive protein, ESR and total leucocytic count and the alternative hypothesis correlation of 0.7 using a two-sided hypothesis test with a significance level of 0.05. It was noticed that serum albumin had negative significant correlation with baseline inflammatory markers; CRP (r= -0.65; P= 0.04), ESR (r= -0.45; P= 0.01), TLC (r= -0.42; P= 0.01) and Procalcitonin (r= -0.34; P= 0.02). **Conclusion:** It was noticed that pro-calcitonin was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease. It was noticed that serum albumin had negative significant correlation with baseline inflammatory markers.

Key Words: Albumin, Sepsis, Inflammatory markers, Procalcitonin.

1. Introduction

Sepsis, including severe sepsis and septic shock, remains a major cause of morbidity and mortality worldwide. The mortality rate of severe sepsis is 20–30%, accounting for about 30-50% of hospital deaths. Even though the mortality rate of severe sepsis has decreased markedly since the introduction of early resuscitative treatments, including early goal-directed therapy (EGDT), survivors are still at increased risk of death [1].

The inflammatory response plays an important role in the pathophysiology of sepsis, and the impact of inflammation that can worsen chronic illness, which is a major determinant of adverse, long-term outcomes. Thus, biomarkers that can be used as independent prognostic factors to evaluate the mortality of patients with severe sepsis or septic shock should be measured objectively to reflect the inflammatory processes as well as responses to therapeutic intervention. As the level of C-reactive protein increases markedly in response to infection, and the magnitude of the increase may correlate with the severity of the infection, the prognostic value of CRP levels has been investigated in many diseases [2].

More than 170 biomarkers have been proposed and assessed clinically, including various cytokines, cell surface markers, receptors, complement factors, coagulation factors, acute phase reactants, and many others, but none has 100% specificity for sepsis. CRP is sensitive but not very specific, being increased in all inflammatory disorders, including after uncomplicated surgery. Procalcitonin is a more specific marker than CRP, although it is also increased in other inflammatory conditions, such as pancreatitis or after polytrauma or major surgery [3].

Albumin is also a potent prognostic marker of outcomes in infection-related disease, as its levels

decrease during the response to acute phase infections [4].

Albumin levels are associated with the chronic nature of disease, and represent the inflammatory status. In patients with community-acquired bloodstream infections, with severe sepsis or septic shock, hypoalbuminemia is the strongest predictor of mortality [5].

Albumin could be an independent reliable prognostic predictor of mortality in a wide range of clinical and research such as community-acquired pneumonia, hemodialysis and coronary heart disease. In hospitalized patients, hypoalbuminaemia is associated with increased length of stay, higher complication rates and higher mortality. Decreased serum albumin concentration correlates with increased length of stay in the intensive care unit (ICU) and with complication rates, such as ventilator dependency and the development of new infection. The daily trend of serum albumin can be a useful tool in predicting the weaning capability of patients needing mechanical ventilation [3].

Aim of the Work

To determine the relationship between reduced albumin and inflammatory response and its effect on morbidity and mortality in critically ill patients.

Patients And Methods

This is a prospective randomized study that was conducted on patients who were admitted to ICU in Ain Shams University Hospitals.

An informed written consent was obtained from patients and/or relatives.

O **Inclusion Criteria:**

• All patients were adult, more than 18 years old, admitted to ICU, with critical illness that have clinical picture of inflammation.

O **Exclusion Criteria:**

• Patients less than18 years old.
• Patients or relatives refused, to be included in this study.
  • Nephrotic syndrome patients
  • Hepatic cirrhosis patients
  • Heart failure patients
  • Malnutrition patients

The diagnosis of sepsis was established according to the definitions of the American College of Chest Physicians Consensus Conference. All patients received standard supportive treatment following recommendations of the Surviving Sepsis Campaign released in 2016.

Sepsis diagnosis requires the presence of infection (which can be proven or suspected) and 2 or more of SOFA points.

Study design:

All patients were subjected to the followings:

1. Full history, including personal data, special habits as smoking, and co-morbidities as diabetes, hypertension, renal impairment or cardiac disease.

2. Hemodynamic monitoring, daily hemodynamic monitoring of the patients:
  ➢ Mean arterial blood pressure.
  ➢ Heart rate.
  ➢ Temperature.

3. Daily clinical examination: daily full clinical examination.

4. Lab profile: Routine laboratory investigations on the day of admission and during stay in ICU:
  • CBC, serum electrolytes.
  • Liver function tests.
  • Coagulation profile.
  • Kidney function tests.
  • Blood gases.
  • Cultures and sensitivity according to source of sepsis.

5. Radiological.
  • CXR, some patients underwent CT chest, abdominal U/S & echo.

6. Early Goal directed therapy will be initiated for all patients:
  • Early empirical broad spectrum antibiotics.
  • Aiming mean blood pressure > 65 mmHG.
  • Aiming CVP 8-12 cm H_2O.
  • Aiming UOP 0.5-1 ml/kg/hour.

7. Patient data were collected as regard.
  ☒ Causes of admission.
  ☒ Infection data.
  ☒ Infection site (pulmonary, genitourinary, abdomen and surgical wound).
  ☒ Pathogenic bacteria (Gram +ve, -ve Bacteria and fungi) detected by cultures from (blood, urine, sputum and wound swap).
  ☒ Morbidity and mortality.
  ☒ Length of ICU stay.

8. Scoring System: At ICU admission, severity of the illness was evaluated by the Acute Physiology and Chronic Health Evaluation (APACHE) II score, considering the worst data point for the first 24 hours in the ICU. Failure of organs and severity of multiple organ dysfunction syndromes was assessed by the Sequential Organ Failure Assessment (SOFA) scale.

9. All patients were managed with fluid therapy, antibiotics, and other supportive treatment according to:

• Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2016.

Data collection:

• Serum albumin level, Procalcitonin, CRP, TLC, ESR, blood gases and lactate were collected in first, third, seventh.

The statistical analysis

• A sample size of 43 achieves 81% power to detect a difference of 0.30 between the correlation of 0.4 as regarding decreased albumin and increased inflammatory response measured by procalcitonin, c-reactive protein, ESR and total leucocytic count and the alternative hypothesis correlation of 0.7 using a two-sided hypothesis test with a significance level of 0.05.

• Quantitative data were expressed using mean and standard deviation, while qualitative data were expressed in frequency and percent.

• The statistical analysis was performed using a standard SPSS software package version 17 (Chicago, IL). Normally distributed numerical data are presented as mean ± SD and differences between groups were compared using the independent Student's *t*-test, data not normally distributed were compared using Mann-Whitney test and are presented as median (IQR) and categorical variables were analyzed using the χ^2 test or fisher exact test and are presented as number (%).

• Comparison of variables between the study groups and its significance was done using P value. All *P* values are two-sided. *P*<0.05 is considered statistically significant.

Table (1): Acute Physiology and Chronic Health Evaluation II score

A Glasgow Coma Scale	B Age Points	C- Chronic Health Points	
Eyes open 4- Spontaneously 3- To verbal 2- To painful stimul 1- No responseverbal 5- Oriented and controversed 4- Disoriented and talks 3- Inappropriate words 2- Incomprehensible Sounds 1- No response Motor 6- Response to verbal command 5- Localizes to pain 4- Withdraws to pain 3- Decorticate 2- Decerebrate 1- No response	Age points <44 0 45-54 2 55-64 3 65-74 5 >75 6	Liver Cardiovascular Pulmonary Kidney Immune If any of the 5 CHE categories is answered with yes give +5 points • Cirrhosis with PHT or encephalopathy • Class IV angina or at rest or with minimal self-care activities • Chronic hypoxemia or hypercapnia or • Chronic peritoneal or hemodialysis • Immunecompromised host	Apache-II Score (sum of A+B+C) A GCS points + B Age points + C Chronic Health Points

Table (2): SOFA score**.**

Variables	0	1	2	3	4
PaO_2/FiO_2 mm Hg	>400	<400	<300	<200with respiratory support	<100 with respiratory support
Platelets x 10^3cells/uL	>150	<150	<100	<50	<20
Billirubin mg/dl	<1.2	1.2-1.9	2-5.9	6-11.9	>12.0
Hypotension	No	MAP <70mmHg	Dopamine<5 or dobutamine any dose	Dopamine>5 Or Epinephrine <0. 1 Or Norepiniphrine <0.1	Dopamine >15 Or Epinephrine >0.1Or Norepinephrine >0. 1
GCS	15	13-14	10-12	6-9	<6
Creat. or UOP (ml)	<1.2	1.2-1.9	2-3.4	3.5-4.9 or <500ml	>5.0 or <200ml

3. Results
Demographic Data of Studied Groups:
   Table 3 shows the demographic data of studied patients. Mean age of survivors was 53.47 ± 14.26 years and 10 (53%) of them were males where mean age of non-survivors was 56.79 ± 11.766 years and 13 (68%) of them were males. Both groups had no significant differences regarding age and sex ($P > 0.05$).

Table (3): Demographic data of studied patients

	Survival group (n= 19)	Non survival group (n= 24)	p-value
Age (years)	53.47 ± 14.26	56.79 ± 11.766	**0.45**
Sex (M/F)	10/ 9	13/11	**1**

Data was expressed in form mean (SD), frequency (percentage). *P* value was significant if < 0.05. **n,** number

Heart Rate in Studied Groups:
   Table 4 shows changes in heart rate in both groups over seven days where it was recorded every eight hours. It was noticed that non- survivors had significantly higher heart rate in comparison to survivors at 3rd, 4th, 5th and 6th days ($P < 0.05$) but at other days both groups had no significant differences ($P > 0.05$).

Table (4): Heart Rate in Studied Groups

Heart rate	Survival group (n= 19)	Non survival group (n= 24)	p-value
1^{st}day			
1	120.79 ± 10.96	115.63 ± 20.39	0.33
2	113.5 ± 26.39	114 ± 19.01	0.97
3	116.68 ± 9.036	11.96 ± 19.3	0.33
2nd day			
1	112.11 ± 10.18	113.13 ± 16.02	0.81
2	111.53 ± 10.2	112.2 ± 15.29	0.94
3	109.25 ± 10.23	113.3 ± 15.24	0.57
3rd day			
1	102.11 ± 8.38	112.04 ± 14.3	**0.01**
2	101.79 ± 8.61	110.75 ± 14.1	**0.02**
3	101.2 ± 8.39	113.13 ± 16.12	**<0.001***
4th day			
1	94.47 ± 7.43	111.25 ± 13.04	**<0.001***
2	94.21 ± 7.2	111.58 ± 11.57	**<0.001***
3	93.79 ± 6.11	110.67 ± 12.37	**<0.001***
5th day			
1	91.21 ± 5.27	110.83 ± 12.04	**<0.001***
2	89.95 ± 2.66	111.4 ± 11.39	**<0.001***
3	88.05 ± 3.63	111.75 ± 11.27	**<0.001***
6th day			
1	84.05 ± 4.64	102.2 ± 20.01	**<0.001***
2	83.84 ± 4.5	98.96 ± 22.34	**<0.001***
3	83.68 ± 4.66	99 ± 23.68	**<0.001***
7th day			
1	82.63 ± 3.86	87.38 ± 28.77	0.48
2	81.68 ± 3.34	89.21 ± 31.66	0.31
3	81.58 ± 3.35	88.2 ± 32.67	0.38

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance

Mean Arterial Blood Pressure in Studied Groups:

    Table 5 shows changes in mean arterial blood pressure in both groups over seven days where it was recorded every eight hours. It was noticed that non-survivors had significantly lower mean arterial blood pressure in comparison to survivors in all 7 days ($P < 0.05$).

Body Temperature in Studied Groups:

    Table 6 shows changes in body temperature in both groups over seven days where it was recorded every eight hours. It was noticed that non- survivors had significantly higher body temperature in comparison to survivors starting from the 2nd day till the 7th day ($P < 0.05$).

Albumin Level in Both Groups:

    Table 7 shows changes in albumin level in both groups where it was recorded at 1st, 3rd and 7th day. It was noticed that non- survivors had significantly lower albumin level in comparison to survivors ($P < 0.05$). It was noticed that albumin level was significantly increased at 7th days in comparison to 1st day in case of survivors but in case of non- survivor it showed significant decrease.

Table (5): Mean arterial blood pressure in Studied Groups

MABP	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day			
1	74.3±17.63	64.29±14.39	**0.04**
2	74.16±16.99	63.88±14.09	**0.03**
3	74.47± 15.84	64.75±15.31	**0.04**
2nd day			
1	77.21±11.37	66.88± 12.21	**<0.001***
2	77.4±11.1	66.96±12.42	**<0.001***
3	77.2±10.81	66.7± 12.27	**<0.001***
3rd day			
1	77.74±10.14	65.6±11.16	**<0.001***
2	78.42±9.37	65.8±11.43	**<0.001***
3	79.37± 9.59	66.04±11.31	**<0.001***
4th day			
1	80.58±7.58	65.96±10.99	**<0.001***
2	81.26±7.9	65.5±11.3	**<0.001***
3	81.74± 7.84	64.54± 10.37	**<0.001***
5th day			
1	82.53±9.19	62.21±10.66	**<0.001***
2	82.32±8.53	61.04±11.07	**<0.001***
3	82.37± 8.6	60± 11.35	**<0.001***
6th day			
1	83.42± 8.002	58.17±10.55	**<0.001***
2	84.2±8.28	57.46±10.8	**<0.001***
3	84± 8.41	56.17± 10.97	**<0.001***
7th day			
1	85.21±9.61	43.75±23.95	**<0.001***
2	85.86±10.122	38.3±26.07	**<0.001***
3	85.74± 9.86	37.7± 25.75	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance. **MABP**, mean arterial blood pressure

Table (6): Body temperature in Studied Groups

Temperature	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day			
1	38.35±0.58	38.3±0.57	0.76
2	38.02±0.55	38.07±0.54	0.77
3	37.85± 0.49	37.99± 0.53	0.49
2nd day			
1	37.45±0.44	37.76±0.45	**0.02**
2	37.33±0.452	37.88±0.39	**<0.001***
3	37.18 ± 0.34	37.71±0.38	**<0.001***
3rd day			
1	37.03±0.12	37.58± 0.51	**<0.001***
2	37.04±0.23	37.67±0.51	**<0.001***
3	37.05± 0.29	37.65± 0.6	**<0.001***
4th day			
1	37.13±0.57	37.29±0.35	**<0.001***
2	37.2±0.57	37.27±0.29	**<0.001***
3	37.06± 0.23	37.4± 0.45	**<0.001***
5th day			
1	37.29±0.31	37.34± 0.46	**<0.001***
2	37.27±0.11	37.5± 0.48	**<0.001***
3	37.1± 0.45	37.4± 0.57	**<0.001***
6th day			
1	37.03±0.11	37.51± 0.62	**<0.001***
2	37.04±0.27	37.5± 0.59	**<0.001***
3	37.04± 0.21	37.53± 0.54	**<0.001***
7th day			
1	37.13±0.55	37.65± 0.57	**0.01**
2	37.24±0.54	37.63± 0.49	**0.02**
3	37.16± 0.23	37.67± 0.51	**0.03**

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance.

Table (7): Albumin level in Studied Groups

Albumin (mg/dl)	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day	3.18 ± 0.45	2.83 ± 0.49	**0.01**
3rd day	2.968 ± 0.357	2.42± 0.357	**<0.00***
7th day	3.22± 0.34	2.04 ± 0.26	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance.

C-reactive Protein Level in Both Groups:

Table 8 shows changes in CRP in both groups where it was recorded at 1st, 3rd and 7th day. It was noticed that non- survivors had significantly higher CRP in comparison to survivors ($P< 0.05$). It was noticed that CRP was significantly increased at 3rd and 7th days in comparison to 1st day in case of non-survivors but in case of survivor it showed significant decrease.

Table (8): CRP in Studied Groups

CRP (mg/dl)	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day	139.2 ± 63.39	170.25 ± 78.08	0.16
3rd day	102.2± 47.34	207.29 ± 87.45	**<0.001***
7th day	58.37 ± 23.78	251.8 ± 91.39	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance. **CRP**, C- reactive protein

Total Leucocytic Count Level in Both Groups:

Table 9 shows changes in TLC in both groups where it was recorded at 1st, 3rd and 7th day. It was noticed TLC had no significant between both groups at 1st and 3rd but at the 7th non- survivors had significantly higher TLC in comparison to survivors ($P<0.05$). It was noticed that TLC was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease.

Table (9): TLC in Studied Groups

TLC (X10^9/L)	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day	20 ± 7.57	17.47 ± 5.2	0.2
3rd day	15.34 ± 4.62	18.42± 7.23	0.11
7th day	10.26 ±1.97	22.13± 6.28	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance. **TLC**, total leucocytic count

Erythrocyte Sedimentation Rate Level in Both Groups:

Table 10 shows changes in ESR in both groups where it was recorded at 1st, 3rd and 7th day. It was noticed ESR had no significant between both groups at 1st day but at 3rd and 7th non- survivors had significantly higher ESR in comparison to survivors ($P<0.05$). It was noticed that ESR was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease.

Table (10): ESR in Studied Groups

ESR (ml/hour)	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day	70.26 ± 23.42	57.92 ± 22.89	0.09
3rd day	53.4±14.25	73.5 ± 16.12	**<0.001***
7th day	33.16± 8.85	93.98 ± 13.91	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance. **ESR**, erythrocyte sedimentation rate

Pro- calcitonin Level in Both Groups:

Table 11 shows changes in pro-calcitonin in both groups where it was recorded at 1st, 3rd and 7th day. It was noticed pro-calcitonin had no significant between both groups at 1st day but at 3rd and 7th non- survivors had significantly lower pro-calcitonin in comparison to survivors ($P<0.05$). It was noticed that pro-calcitonin was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease.

Table (11): Pro-calcitonin in Studied Groups

Pro-calcitonin	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day	4.44± 3.07	5.63± 4.76	0.36
3rd day	4.21±3	8.67 ± 5.3	**<0.001***
7th day	2.26± 1.9	9.9 ± 6.8	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance.

Changes in Lactate Level in Both Groups:

Table 12 shows changes in lactate in both groups where it was recorded at 1st, 3rd and 7th day. It was noticed lactate had no significant between both groups at 1st day ($P>0.05$) but it was significantly higher in non- survivors in comparison to survivors at 3rd and 7th days. It showed significant increase at 7th days in comparison to the 1st day in case of non- survivors but showed significant decrease in case of survivors.

Table (12): Changes in Lactate in Studied Groups

Lactate	Survival group (n= 19)	Non survival group (n= 24)	p-value
1st day	2.28 ±0.99	3.05 ±1.61	0.07
3rd day	1.94 ±0.68	3.4 ±1.21	**<0.001**
7th day	1.4 ±0.4	5.53 ±2.31	**<0.001***

Data was expressed in form of mean (SD). *P* value was significant if < 0.05. *indicated to high significance.

Correlation between Albumin with Baseline Level of Inflammatory Markers:

It was noticed that serum albumin had negative significant correlation with baseline inflammatory markers; CRP (r= -0.65; P= 0.04), ESR (r= -0.45; P= 0.01), TLC (r= -0.42; P= 0.01) and Procalcitonin (r= - 0.34; P= 0.02).

Table (13): Correlation between serum albumin with inflammatory markers

Inflammatory markers	Reduction in albumin level at 7th day	
	r	P
C-reactive protein	- 0.65	0.04
Erythrocyte sedimentation rate	- 0.45	0.01
Total leucocytic count	- 0.42	0.01
Procalcitonin	- 0.34	0.02

P value indicated to the significance of correlation (if < 0.05, it was significant), r indicated to the strength of correlation

3.　　Discussion

Albumin, the body's predominant serum-binding protein, has several important functions. Albumin comprises 75-80% of normal plasma colloid oncotic pressure and 50% of protein content [6]. Reference serum values range from 3.5-4.5 g/dL. Synthesis occurs only in hepatic cells at a rate of approximately 15 g/d in a healthy person, but the rate can vary significantly with various types of physiologic stress. The half-life of albumin is approximately 21 days. Hypoalbuminemia is an important prognostic indicator among hospitalized patients and correlates with an increased risk of morbidity and mortality [7].

Many studies have shown the predictive power of serum albumin for clinical outcomes especially in the end stage renal disease (ESRD) population. Serum albumin levels below 2.5 g/dL have been associated with a risk of death 20 times greater as compared to the reference level of 4.0-4.5 g/dL in hemodialysis (HD). Serum albumin levels of 3.5-3.9 g/dL were associated with double the risk of death.

Inflammatory response may be defined as a complex biologic response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. Several factors including infection, co-morbidity, genetic factors and diet may contribute to a state of persistent inflammation [8].

Among several markers of inflammation, procalcitonin (PCT) and C-reactive protein (CRP) markers are being studied to investigate their accuracy for the diagnosis of inflammation. PCT is the prehormone of calcitonin, which is normally secreted by the C cells of the thyroid in response to hypercalcemia [9].

While C-reactive protein (CRP) is an acute-phase reactant and CRP level measurements are frequently used to aid in the diagnosis of bacterial infections. CRP is synthesized by the liver, mainly in response to IL-6, which is produced not only during infection but also in many types of inflammation [10].

Our study was a prospective randomized study that was conducted on patients who were admitted to ICU in Ain Shams University Hospitals. Forty-three patients were included in this study and an informed written consent was obtained from patients and /or relatives. All patients were adult, more than 18 years old, admitted to ICU suffering from sepsis or had septic shock.

Our aim was to show the relationship between reduced albumin and inflammatory response and its effect on morbidity and mortality in critically ill patients.

In current study, the mean age of survivors was 53.47 ± 14.26 years and 10 (53%) of them were males where mean age of non-survivors was 56.79± 11.766 years and 13 (68%) of them were males. Both groups had no significant differences regarding age and sex (P> 0.05).

Regarding to demographic data, **Oliveira and his colleagues** [11] reported that in their study, there were 58 (55.8%) men and 46 (44.2%) women and overall mortality was 68.3%, consisting of 35 men (60.3% of the male population) and 36 women (78.3% of the female population) (p=0.082, chi-square test). The age (median; range) was greater for non-survivors (54; 22-91 years) than for survivors (42; 21-81 years) (p<0.01).

In our study, changes in heart rate in both groups over seven days where it was recorded every eight hours. It was noticed that non- survivors had significantly higher heart rate in comparison to survivors at 3rd, 4th, 5th and 6th days (P< 0.05) but at other days both groups had no significant differences (P> 0.05).

In our study, changes in mean arterial blood pressure in both groups over seven days was recorded every eight hours. It was noticed that non- survivors had significantly lower mean arterial blood pressure in comparison to survivors in all 7 days ($P< 0.05$). **Houwink et al.** [12] found in their study similar results regarding mean arterial blood pressure.

In our study, changes in body temperature in both groups over seven days was recorded every eight hours. It was noticed that non- survivors had significantly higher body temperature in comparison to survivors starting from the 2nd day till the 7th day ($P< 0.05$). **Schell-Chaple et al.** [13] reported that in early ARDS higher temperature was associated with decreased mortality, **Sanderson et al.** [14] also reported similar result in patients with sepsis.

In our study, changes in albumin level in both groups were recorded at 1st, 3rd and 7th day. It was noticed that non-survivors had significantly lower albumin level in comparison to survivors ($P< 0.05$). Albumin level was significantly increased at 7th days in comparison to 1st day in case of survivors.

Hedlund and Hansson et al. [15] found that serum albumin was decreased until the sixth day of hospitalization, in patients with CAP. **Sullivan et al**. [16] in their prospective study found lower albumin level upon patient discharge from the hospital (mean 29.1 g/L) compared to the admission (mean 36.6 g/L), in hospitalized elderly patients. **Harimurti et al.** [17] found a significant decrease in mean albumin level on the fifth day of hospitalization where is reduction in albumin level during hospitalization in patients hospitalized due to acute conditions seems to be influenced by the severity of underlying infection/ inflammation, although the role of nutrition could not be eliminated.

In our study, changes in CRP in both groups were recorded at 1st, 3rd and 7th day. It was noticed that non- survivors had significantly higher CRP in comparison to survivors ($P< 0.05$). It was noticed that CRP was significantly increased at 3rd and 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease. **Coelho et al.** [18] was reported that non-survivors presented high CRP levels, while patients with a good outcome the CRP concentration fell sharply.

In our study, changes in TLC in both groups where was recorded at 1st, 3rd and 7th day. It was noticed TLC had no significant between both groups at 1st and 3rd but at the 7th non- survivors had significantly higher TLC in comparison to survivors ($P< 0.05$). It was noticed that TLC was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease.

In our study, changes in ESR in both groups were recorded at 1st, 3rd and 7th day. It was noticed ESR had no significant between both groups at 1st day but at 3rd and 7th non- survivors had significantly higher ESR in comparison to survivors ($P< 0.05$). It was noticed that ESR was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease.

Harimurti et al. [17] found TLC and ESR are higher in patients with decreased albumin level; so we can say that patients with more severe infections tend to experience significant decreased in albumin level during acute phase of infection.

Regarding to procalcitonin, **Demirdal et al.** [19] have found that mean PCT levels were significantly higher in non-survivors compared to survivors. Also in the study of **Boussekey** [20] found that the median value of PCT for non-survivors was higher in comparison to survivors.

In our study, changes in procalcitonin in both groups was recorded at 1st, 3rd and 7th day. It was noticed procalcitonin had no significant difference between both groups at 1st day but at 3rd and 7th non-survivors had significantly lower procalcitonin in comparison to survivors ($P< 0.05$). It was noticed that procalcitonin was significantly increased at 7th days in comparison to 1st day in case of non-survivors but in case of survivor it showed significant decrease.

In our study, changes in lactate in both groups were recorded at 1st, 3rd and 7th day. It was noticed lactate had no significant between both groups at 1st day ($P> 0.05$) but it was significantly higher in non-survivors in comparison to survivors at 3rd and 7th days. It showed significant increase at 7th days in comparison to the 1st day in case of non-survivors but showed significant decrease in case of survivors.

In our study, serum albumin had negative significant correlation with baseline inflammatory markers; CRP ($r= -0.65$; $P= 0.04$), ESR ($r= -0.45$; $P= 0.01$), TLC ($r= -0.42$; $P= 0.01$) and Procalcitonin ($r= -0.34$; $P= 0.02$). **Harimurtietal**. [17] found a negative correlation between high CRP levels with percentage of albumin level decrease during 5 days of hospitalization, although the correlation was not too strong.

Two studies that correlate CRP and albumin level at the same time showed almost similar results. The study by **Hedlund and Hansson et al.** [15] found significant negative correlation ($r = -0.30$. P 0.0003) between CRP and albumin levels in patients with community-acquired pneumonia at admission. A study by **Kaysen et al.** [21] in patients with end-stage renal disease having hemodialysis also found similar results ($r = -0.554$. $P <0.001$).

Conclusion

This is a prospective randomized study that was conducted on patients who were admitted to ICU in Ain Shams University Hospitals. Forty three patients were included in this study and an informed written consent was obtained from patients and/or relatives.

It was noticed that pro-calcitonin was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease. It was noticed that serum albumin had negative significant correlation with baseline inflammatory markers.

Recommendations

‑ Further studies on large number of cases should be considered.

‑ Inflammatory markers should be followed up daily during ICU stay.

Summary

Albumin is the most abundant protein in human plasma with diverse functions including antioxidant activity, buffering properties, binding and transport capacities for numerous substances [22]. Albumin is synthesized in the liver as preproalbumin, then the product, proalbumin, is in turn cleaved in the Golgi vesicles to produce the secreted albumin [23].

The reference range for albumin concentrations in serum is approximately 3.5-5 g/dL (35-50 g/L). Serum albumin (CP) is the serum analyte that best predicts a poor outcome. Serum albumin also predicts mortality in healthy individuals [24].

Inflammation is a part of the complex biological response of body tissues to harmful stimuli. The function of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process and initiate tissue repair [25].

The role of sepsis markers in diagnosing sepsis, the availability of accurate sepsis biomarkers to facilitate diagnosis could be of use to enable timely appropriate treatment to be started, thus optimizing a patient's chances of survival [26].

Procalcitonin is a 116 amino acid peptide that has an approximate MW of 14.5 kDa and belongs to the calcitonin (CT) superfamily of peptides. Procalcitonin is encoded by CALC-1 gene located on chromosome 11. A microbial infection induces a substantial increase of CALC-1 gene expression in all parenchymal tissue and differentiated cell types in the body producing PCT. Its levels increase significantly in sepsis, systemic infection and severe inflammation, the serum levels of ProCT usually increase markedly [27].

The aim of the study is to determine the relationship between reduced albumin and inflammatory response and its effect on morbidity and mortality in critically ill patients.

Patients and methods

This is a prospective randomized study that was conducted on patients who were admitted to ICU in Ain Shams University Hospitals. Forty three patients were included in this study and an informed written consent was obtained from patients and/or relatives.

All patients were adult, more than 18 years old, admitted to ICU, with critical illness that have clinical picture of inflammation.

We excluded Patients less than18 years old, patients or relatives refused, to be included in this study, nephrotic syndrome patients, hepatic cirrhosis patients, heart failure patients and malnutrition patients.

All patients were subjected to assessment of the demographic data of the patient, ICU length of stay (days), hemodynamic data: heart rate, mean blood pressure and temperature were assessed 3 times daily for seven days. Serum albumin level in the first, third and seventh days, CRP level, TLC and ESR in the first, third and seventh days, procalcitonin level in the first and seventh days, blood gases and lactate level in the first, third and seventh days, morbidity and mortality, causes and site of infection.

Forty three patients were included in this study shows the demographic data of studied patients with mean age of survivors was 53.47 ± 14.26 years and 10 (53%) of them were males where mean age of non-survivors was 56.79 ± 11.766 years and 13 (68%) of them were males.

It was noticed that albumin level was significantly increased at 7th days in comparison to 1st day in case of survivors but in case of non- survivor it showed significant decrease.

It was noticed that pro-calcitonin was significantly increased at 7th days in comparison to 1st day in case of non- survivors but in case of survivor it showed significant decrease. It was noticed that serum albumin had negative significant correlation with baseline inflammatory markers; CRP (r= -0.65; *P*= 0.04), ESR (r= -0.45; *P*= 0.01), TLC (r= -0.42; *P*= 0.01) and Procalcitonin (r= -0.34; *P*= 0.02).

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