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Relationship between Reduced Albumin and Inflammatory Response in Critically Ill Patients

Thesis

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Mostafa Mohamed Fouad

Contents

List of Abbreviations

Abb.		Full term
KD	:	Dissociation konstant
ICU	:	Intensive care unit
PN	:	Parenteral nutrition
SOFA	:	Sepsis-related Organ Failure assessment
CIC	:	Circulating immune complexes
FcRn	:	Fc receptor
MELD	:	Model for end stage liver disease
IgG		Immunoglobulin G
TNF	:	Tumor necrosis factor
IL-6	:	Interleukin-6
PAMPs	:	Pathogen-associated molecular patterns
DAMPs	:	Danger-associated molecular patterns
MAC	:	Membrane attack complex
C 3	:	Comlement 3
C 4	:	Complement 4
PCT	:	Procalcitonin
CT	:	Calcitonin
MW	:	Molecular weight
CCP	:	Calcitonin carboxyl
CGRP	:	Calcitonin gene related peptide
PAM	:	Peptidylglycine alpha-amidating monooxygenase
SIRS	:	Systemic inflammatory response syndrome
MOF	:	Multi organ failure

Abb.		Full term
LPS	:	Lipopolysaccarides
CD 14	:	Cluster of differentiation 14
AMP	:	Adenosine monophosphate
NO	:	Nitric oxide
iNOS	:	Inducible nitric oxide synthase
CRP	:	C reactive protein
EGDT	:	Early goal directed therapy
COX	:	Cyclooxygenase
TLR	:	Toll like receptor
ESRD	:	End stage renal disease
ESR	:	Erythrocyte sedimentation rate
CAP	:	Community acquired pneumonia
ROS	:	Reactive oxygen species
RNS	:	Reactive nitrogen species
MAP	:	Mean arterial pressure
APACHE	:	Acute Physiology and Chronic Health Evaluation
SPSS	:	Statistical Package for the Social Science
TLC	:	Total leucocytic count

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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 7^{th} days in comparison to 1^{st} 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.

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 **(Kaukonen et al., 2014).**

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 **(Stearns-Kurosawa et al., 2011).**

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 **(Vincent, 2016).**

Albumin is also a potent prognostic marker of outcomes in infection-related disease, as its levels decrease during the response to acute phase infections **(Mayr et al., 2014).**

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 **(Kim et al., 2015).**

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 **(Vincent et al., 2016).**

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.

Chapter (1):

Serum Albumin

Albumin is the most abundant protein in human plasma with diverse functions including antioxidant activity, buffering properties, binding and transport capacities for numerous substances (free fatty acids, various ions, NO, bilirubin, peptides, uremic toxins and drugs **(Fanali et al., 2012).**

Albumin is synthesized in the liver as preproalbumin, which has an N-terminal peptide that is removed before the nascent protein is released from the rough endoplasmic reticulum. The product, proalbumin, is in turn cleaved in the Golgi vesicles to produce the secreted albumin **(Mendez et al., 2005).**

The reference range for albumin concentrations in serum is approximately 3.5-5 g/dL (35-50 g/L). It has a serum half-life of approximately 20 days (**Banks et al., 2010).**

Physiological functions of albumin

1- Colloid osmotic pressure

The molecular weight of albumin (66.5 kD) is less than half that of gamma globulin (160 kD); hence, the