



# **Update on Role of Albumin in ICU**

## **Essay**

submitted in Partial Fulfillment of Master Degree in ICU

By

**Ahmed Osman Abd El Kader**

M.B., B.Ch. (2006)

**Supervised by**

**Dr. Ayman Mokhtar Kamaly**

Professor of Anesthesiology, Intensive Care and Algology  
Faculty of Medicine, Ain Shams University

**Dr. Sahar Mohamed Kamal**

Professor of Anesthesiology, Intensive Care and Algology  
Faculty of Medicine, Ain Shams University

**Dr. Dina Salah El Din Mahmoud**

Lecturer of Anesthesiology, Intensive Care and Algology  
Faculty of Medicine, Ain Shams University

Faculty of Medicine  
Ain Shams University

2014



## **Acknowledgments**

My deepest gratitude and thanks to **ALLAH** the most merciful for guiding me through and giving me the strength to complete this work.

It is my pleasure to express my deepest thanks and profound respect to my honored professor **Dr. Ayman Mokhtar Kamaly** Professor of Anesthesiology , Intensive Care and Algology ,Faculty of Medicine , Ain Shams University, for helping me to choose the subject of this work and for this continuous guidance, support and valuable advice.

I would also like to express my outmost thanks to **Dr. Sahar Mohamed Kamal** Professor of Anesthesiology, Intensive Care and Algology, Faculty of Medicine, Ain Shams University, for her endless support and advice. It has been an honor and a privilege to work under his generous supervision.

I would also like to thank **Dr. Dina Salah El Din Mahmoud** Lecturer of Anesthesiology, Intensive Care and Algology, Faculty of Medicine, Ain Shams University, for her valuable advice, enriching observations and close scientific supervision during every step of this work.

Last, I would like to express my love and everlasting gratitude to my family for their love, support, continuous encouragement and patience.

## **LIST OF FIGURES**



Figure no.	Figure title	Page no.
1.1	<b>Amino acid sequence of Human Serum Albumin</b>	<b>2</b>
1.2	<b>Albumin production</b>	<b>5</b>
1.3	<b>Decay pattern of labelled albumin versus time.</b>	<b>9</b>
1.4	<b>Forces governing distribution of water across the capillary membrane</b>	<b>13</b>
1.5	<b>Crystal structure of rHSA</b>	<b>17</b>
1.6	<b>Muehrcke's lines</b>	<b>24</b>
2.1	<b>Recent advances in our understanding of hepatorenal syndrome</b>	<b>32</b>
3.1	<b>Schematic representation of causes of hypoalbuminaemia in critically ill patients</b>	<b>50</b>

## **LIST OF TABLES**



Table no.	Table title	Page no.
1.1	<b>Factors that modify albumin metabolism</b>	<b>7</b>
1.2	<b>Distribution of extra-vascular albumin in the body</b>	<b>10</b>
2.1	<b>Types of refractory ascites</b>	<b>34</b>
2.2	<b>Human serum albumin products for clinical use.</b>	<b>44</b>
2.3	<b>Aluminum content in some albumin (Human) Products</b>	<b>45</b>

## **LIST OF ABBREVIATIONS**



Abbrev.	Full term
AASLD	:American Association for the Study of Liver Diseases
ALI	:Acute Lung Injury
ALIAS	:Albumin in Acute Stroke
ALISAH	:Albumin in Subarachnoid Hemorrhage
ARDS	:Acute Respiratory Distress Syndrome
ATP	:Adenosine Triphosphate
AVG	:Arginine Vasopressin
CO	:Cardiac Output
COP	:Colloid Osmotic Pressure
CVP	:Central Venous Pressure
EABV	:Effective Arterial Blood Volume
FDR	:Fractional Degradation Rate
FSR	:Fractional Synthesis Rate of albumin
GFR	:Glomerular Filtration Rate
GTP	:Guanosine-5'-Triphosphate
HES	:Hydroxyl Ethyl Starch
HOCL	:Hypochlorous acid
HRS	:Hepato Renal Syndrome
HSA	:Human Serum Albumin
ICU	:Intensive Care Unit
LCFAs	:Long Chain Fatty Acids



LR	:Lactated Ringer
LVP	:Large Volume Paracentesis
MARS	:Molecular Adsorbent Resirculating System
mRNA	messenger RiboNucleic acid
NO	:Nitric Oxide
PPF	:Plasma Protein Fraction
RAAS	:Renin Angiotensin Aldosterone System
RBF	:Renal Blood Flow
rHSA	:recombinant Human Serum Albumin
RtPA	:Recombinant tissue Plasminogen Activator
SAH	:Subarachnoid Hemorrhage
SBP	:Spontaneous Bacterial Peritonitis
SNS	:Sympathetic Nervous System
SOFA	:Sequential Organ Failure Assessment
TBSA	:Total Body Surface Area
TNF	:Tumour Necrosis Factor
tRNA.	:transfer RiboNucleic acid



## **Contents**

- Introduction.
- Aim of work
- Chapter 1: Physiology of Albumin.
- Chapter 2: Role of albumin in hepatic and surgical patients.
- Chapter 3: Relevance of albumin in modern medicine.
- English summary.
- References.
- Arabic summary.





# ***Introduction***



## **Introduction**

The last 25 years have seen major advances in our understanding of albumin. We now know the amino acid sequences of bovine and human albumin, the complete gene sequence of human albumin, and the location of mutations in the gene sequence. During the 1990s, the heart-shaped crystalline structure of albumin has been described and a new protein, termed  $\alpha$ -albumin (afamin) has been added to the albumin super family, which otherwise consists of serum albumin, vitamin D-binding protein and  $\alpha$ -fetoprotein (*Peters, 1996*).



Albumin is the main determinant of plasma oncotic pressure. It plays a pivotal role in modulating the distribution of fluid between compartments. Moreover, it has many biological properties that may be important not only for its physiologic actions but also for its therapeutic effects. The non-oncotic properties of albumin include molecular transportation, free radical scavenging, modulation of capillary permeability, Neutrophil adhesion, activation and hemostatic effects (*Evans, 2002*).

The rate of albumin synthesis is affected by both nutrition and inflammation. Patients with severe sepsis and secondary peritonitis usually suffer from severe hypoalbuminemia and inflammatory process. There is controversy regarding albumin administration among meta-analysis (*Don et al; 2004*).

The function of circulating albumin in critical illness is not fully understood. It may differ significantly from that in healthy subjects. A low serum albumin concentration in critical illness is associated with a poor outcome. Despite theoretical advantages for using human albumin solution as a plasma substitute, studies have shown that correcting hypoalbuminemia has no impact on outcome in the critically ill (*Stockwell et al; 1992*).



Data in the literature are split in its support or opposition to the claim that the serum albumin level is associated with clinical outcome and albumin administration may improve the prognosis of hypoalbuminemic patients (*Dubois et al; 2006*).

Until now, few effective clinical studies have verified positive effects of albumin administration on outcomes or incidence of complications in postoperative patients (*Vincent et al; 2003*).



*Aim of work*



## **Aim of work**

This review will examine the role of serum albumin in health and critical illness. It will also review aspects of the physiology of this protein that may be expected to lead to significant dysfunction in critical illness. Finally, the case for and against the use of exogenous albumin in the management of hepatic, surgical and critically ill patients.





Chapter 1

***Physiology of  
Albumin***



## **Structure of albumin**

In humans, albumin is the most abundant plasma protein, accounting for 55–60% of the measured serum protein. It consists of a single polypeptide chain of 585 amino acids with a molecular weight of 66, 500 Da. The chain is characterized by having no carbohydrate moiety, a scarcity of tryptophan and methionine residues, and an abundance of charged residues, such as lysine, arginine, glutamic acid and aspartic acid (*Murray, 2003*).

The mature, circulating molecule is arranged in a series of  $\alpha$ -helices, folded and held by 17 disulphide bridges. The folding creates sub-domains



of three contiguous  $\alpha$ -helices in parallel (Figure1). A pair of sub-domains face each other to form domains. These can be seen as cylindrical structures with polar outer walls and a hydrophobic central Core (*Murray, 2003*).

The tertiary structure of human albumin crystal has been isolated by x-ray crystallography. It is seen as a heart-shaped molecule  $80 \times 30 \text{ \AA}$ . In solution, the shape is quite different (*Murray, 2003*).

