

Renal Failure and Renal Replacement therapy in Intensive Care Unit

Essay

*Submitted for Partial Fulfilment of Master Degree
In General Intensive Care*

By

Eslam Metwally Elsayed Elhendawy
M.B.B.CH. (Cairo University)

Supervised by

Dr. Gamal Eldin Mohammad Ahmad Elewa

*Professor of Anesthesia,
Intensive Care and Pain Management
Faculty of Medicine, Ain Shams University*

Dr. Mostafa Mansour Hussein

*Lecture of Anesthesia,
Intensive Care and Pain Management
Faculty of Medicine, Ain Shams University*

**Faculty of Medicine
Ain Shams University**

2017

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببناك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**,
the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and
profound gratitude to **Dr. Gamal Eldin
Mohammad Ahmad Elewa**, Professor of
Anesthesia, Intensive Care and Pain Management,
Faculty of Medicine, Ain Shams University for his
keen guidance, kind supervision, valuable advice
and continuous encouragement, which made
possible the completion of this work.*

*I am deeply thankful to **Dr. Mostafa
Mansour Hussein**, Lecturer of Anesthesia,
Intensive Care and Pain Management, Faculty of
Medicine, Ain Shams University, for his great help,
active participation and guidance.*

*Last but not least, I would like to express my
hearty thanks to all my family for their support till
this work was completed.*

Eslam Metwally

Contents

Title	Page No.
List of Abbreviations	5
List of Tables	10
List of Figures	11
Introduction	1
Aim of the Essay	3
Chapter (I): Acute Kidney Injury In Intensive Care: Causes and Diagnosis	4
Chapter (II): Prophylactic Measures to avoid Renal Failure In Intensive Care	66
Chapter (III): Management of Renal Failure in Intensive Care and Renal Replacement Therapy Modalities	79
Summary	150
References	157
Arabic summary	

List of Abbreviations

Abb.	Full term
AA	<i>Amino Acids</i>
ACD-A.....	<i>Acid citrate dextrose-A</i>
ACE.....	<i>Angiotensin converting enzyme</i>
ACT.....	<i>Activated clotting time</i>
ADH	<i>Antidiuretic hormone</i>
ADQI.....	<i>Acute dialysis quality initiative</i>
AIN	<i>Acute interstitial nephritis</i>
AKIN.....	<i>Acute kidney injury network</i>
ANA	<i>Antinuclear antibody</i>
ANCA.....	<i>Anti neutrophil cytoplasmic antibodies</i>
ANP.....	<i>Atrial natriuretic peptide</i>
Anti-HIV Ab.....	<i>Anti-human immunodeficiency virus antibody</i>
APTT.....	<i>Activated partial thromboplastin time</i>
ARB.....	<i>Angiotensin II receptor blocker</i>
ARF.....	<i>Acute renal failure</i>
ATN	<i>Acute tubular necrosis</i>
BNPs.....	<i>β-type natriuretic peptide</i>
BOLD.....	<i>Blood oxygen level dependent</i>
CAVHD.....	<i>Continuous arteriovenous hemodialysis</i>
CAVHDF.....	<i>Continuous arteriovenous hemodiafiltration</i>
CAVHF	<i>Continuous arteriovenous hemofiltration</i>
CEUS.....	<i>Contrast enhanced ultrasound</i>
CKD	<i>Chronic kidney disease</i>
CPB.....	<i>Cardiopulmonary bypass</i>
CPG.....	<i>Clinical practice guidelines</i>
CRIAKI	<i>Creatin increase AKI</i>
CRP.....	<i>C reactive protein</i>
CRRT.....	<i>Continuous renal replacement therapy</i>
CTD.....	<i>Connective tissue disease</i>
CVP.....	<i>Central venous pressure</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>CVVH</i>	<i>Continuous venovenous hemofiltration</i>
<i>CVVHD</i>	<i>Continuous veno-venous hemodialysis</i>
<i>CVVHDF</i>	<i>Continuous venovenous hemodiafiltration</i>
<i>C3/C4</i>	<i>Complement C3 and C4</i>
<i>DGF</i>	<i>Delayed graft function</i>
<i>dsDNA</i>	<i>Double stranded DNA</i>
<i>ECG</i>	<i>Electrocardiography</i>
<i>EDD</i>	<i>Extended daily dialysis</i>
<i>EDDf</i>	<i>Extended daily dialysis with filtration</i>
<i>EDTA</i>	<i>Ethylene diamine tetracetic acid</i>
<i>eGFR</i>	<i>Estimated glomerular filtration rate</i>
<i>EGPA</i>	<i>Eosinophilic granulomatosis with polyangiitis</i>
<i>ELISA</i>	<i>Enzyme linked immunosorbent assay</i>
<i>EMA</i>	<i>European Medicines Agency</i>
<i>EN</i>	<i>Enteral nutrition</i>
<i>ERBP</i>	<i>European renal best practice</i>
<i>ESRD</i>	<i>Endstage renal disease</i>
<i>FDA</i>	<i>Food and Drug Administration</i>
<i>GBM</i>	<i>Glomerular basement membrane</i>
<i>GFR</i>	<i>Glomerular filtration rate</i>
<i>GN</i>	<i>Glomerulonephritis</i>
<i>GPA</i>	<i>Granulomatosis with polyangiitis</i>
<i>GST</i>	<i>Glutathione-S-transferase</i>
<i>HA</i>	<i>Human albumin</i>
<i>HCT</i>	<i>Hematocrit</i>
<i>HD</i>	<i>Hemodialysis</i>
<i>HDF</i>	<i>Hemodiafiltration</i>
<i>HES</i>	<i>Hydroxy ethyl starch</i>
<i>HIT</i>	<i>Heparin induced thrombocytopenia</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>HIV</i>	<i>Human immunodeficiency virus</i>
<i>HUS</i>	<i>Hemolytic uremic syndrome</i>
<i>HV-HF</i>	<i>High volume hemofiltration</i>
<i>ICU</i>	<i>Intensive care unit</i>
<i>IDMS</i>	<i>Isotope dilution mass spectroscopy</i>
<i>IgA</i>	<i>Immunoglobulin A antibodies</i>
<i>IGFBP7</i>	<i>Insulin like growth factor binding protein 7</i>
<i>IgG</i>	<i>Immunoglobulin G antibodies</i>
<i>IgM</i>	<i>Immunoglobulin M antibodies</i>
<i>IHD</i>	<i>Intermittent hemodialysis</i>
<i>IL</i>	<i>Interleukin</i>
<i>IRRT</i>	<i>Intermittent renal replacement therapy</i>
<i>I.V</i>	<i>Intravenous</i>
<i>KD</i>	<i>KILODALTON</i>
<i>KDIGO</i>	<i>Kidney disease improving global outcome</i>
<i>KIM-1</i>	<i>Kidney injury molecule-1</i>
<i>Kt/V</i>	<i>K: Dialyzer clearance of urea, t: Dialysis time and V: Volume of distribution of urea</i>
<i>L-FABP</i>	<i>Liver type fatty acid binding protein</i>
<i>LMWHs</i>	<i>Low molecular weight heparins</i>
<i>MDRD</i>	<i>Modified diet in renal disease</i>
<i>MI</i>	<i>Myocardial infarction</i>
<i>MPO</i>	<i>Myeloperoxidase</i>
<i>MRA</i>	<i>Magnetic resonance angiography</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>MW</i>	<i>Molecular weight</i>
<i>NAC</i>	<i>N-acetyl cysteine</i>
<i>NCRIAKI</i>	<i>Non-creatin increase AKI</i>
<i>NGAL</i>	<i>Neutrophil gelatinase-associated lipocalin</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>nGST</i>	<i>n glutathione S-transferase</i>
<i>NICE</i>	<i>National Institute of Health and Care Excellence</i>
<i>NSF</i>	<i>Nephrotoxic systemic fibrosis</i>
<i>NSTEMI</i>	<i>Non-ST elevation myocardial infarction</i>
<i>OD</i>	<i>Optical density</i>
<i>PCA-MRI</i>	<i>Phase contrast angiography-MRI</i>
<i>PEEP</i>	<i>Positive end expiratory pressure</i>
<i>PF4</i>	<i>Platelet factor 4</i>
<i>PIRRT</i>	<i>Prolonged (daily) intermittent renal replacement therapy</i>
<i>PN</i>	<i>Parenteral nutrition</i>
<i>PO</i>	<i>Per oral</i>
<i>PR3</i>	<i>Proteinase 3</i>
<i>P-5'-P</i>	<i>Pyridoxine-5'phosphate</i>
<i>RA</i>	<i>Renal angina</i>
<i>RAAS</i>	<i>Renin angiotensin aldosterone system</i>
<i>RAI</i>	<i>Renal angina index</i>
<i>RCT</i>	<i>Randomized controlled trial</i>
<i>RI</i>	<i>Resistive index</i>
<i>RIFLE</i>	<i>Risk, injury, failure, loss, endstage kidney disease</i>
<i>ROS</i>	<i>Reactive oxygen species</i>
<i>RPGN</i>	<i>Rapidly progressive glomerulonephritis</i>
<i>RRT</i>	<i>Renal replacement therapy</i>
<i>SCUF</i>	<i>Slow continuous ultrafiltration</i>
<i>SD</i>	<i>Standard deviation</i>
<i>SID</i>	<i>Strong ion difference</i>
<i>SIG</i>	<i>Strong ion gap</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>SLE</i>	<i>Systemic lupus erythematosus</i>
<i>SLED</i>	<i>Sustained low efficiency dialysis</i>
<i>SLEDD</i>	<i>Slow extended daily dialysis</i>
<i>STEMI</i>	<i>ST elevation myocardial infarction</i>
<i>TIMP-2</i>	<i>Tissue inhibitor of metalloproteinases</i>
<i>TJRB</i>	<i>Transjugular renal biopsy</i>
<i>UF</i>	<i>Ultrafiltration</i>
<i>UFH</i>	<i>Unfractionated heparin</i>
<i>UKM</i>	<i>Urea kinetic modeling</i>
<i>URR</i>	<i>Urea reduction ratio</i>
<i>5HT</i>	<i>5-hydroxytryptamine</i>

List of Tables

Table No.	Title	Page No.
Table (1):	Kidney disease improving global outcome (KDIGO) classification.....	6
Table (2):	The renal angina index (RAI) score.....	10
Table (3):	The most common causes of acute kidney injury	12
Table (4):	Diagnostic tests to distinguish between prerenal and renal acute kidney injury.....	13
Table (5):	Incidence of causes of hospital-acquired AKI.....	14
Table (6):	Predisposing factors and chronic diseases associated with AKI	17
Table (7):	Classical urinary indices in AKI due to pre-renal causes and intrinsic disease	34
Table (8):	Specific AKI investigations for detection of possible systemic diseases	36
Table (9):	Expectations of novel AKI biomarkers	40
Table (10):	AKI biomarkers in human studies	42
Table (11):	Ultrasound characteristics of specific kidney diseases in B-mode	56
Table (12):	Color Doppler for a semi-quantitative evaluation of intra-renal vascularisation.....	58
Table (13):	Major risk factors for AKI.....	66
Table (14):	Benefits and drawbacks of earlier RRT in critically ill patients with AKI.....	82
Table (15):	Absolute and relative indications for starting RRT in critically ill patients with AKI	84
Table (16):	Techniques suitable for renal replacement therapy in acute kidney injury	108
Table (17):	The “4 Ts” scoring system to estimate probability for heparin induced thrombocytopenia, prior to laboratory testing for HIT antibodies	122
Table (18):	Recommended doses of anticoagulants for CRRT	135

List of Figures

Fig. No.	Title	Page No.
Fig. (1):	Proposed algorithm to aid in clinical decision making on when to initiate RRT in critically ill patients with AKI.	87

INTRODUCTION

Acute kidney injury (AKI) is the abrupt loss of kidney function, resulting in the retention of urea and other nitrogenous waste products and the dysregulation of extracellular volume and electrolytes. The term AKI has largely replaced acute renal failure (ARF), reflecting the recognition that smaller decrements in kidney function that do not result in overt organ failure are of substantial clinical relevance and are associated with increased morbidity and mortality. The term ARF is now reserved for severe AKI, usually implying the need for renal replacement therapy (*Palevsky et al., 2013*).

Acute kidney injury has emerged as a major public health problem that affects millions of patients worldwide and leads to decrease survival and increase progression of underlying chronic kidney diseases. Patients in particular those in the Intensive Care Unit (ICU) are dying of AKI and not just simply with AKI. Even small changes in serum creatinine concentrations are associated with a substantial increase in the risk of death. Acute Kidney Injury is not a single disease but rather a syndrome comprising multiple clinical conditions. Outcomes from AKI depend on the underlying disease, the severity and duration of renal impairment, and the patient's renal baseline condition (*Singbart and Kellum, 2012*).

Acute tubular necrosis (ATN) is the primary cause of AKI. The rates of AKI have been reported in hospitalized patients to be between 3.2% - 20%, and rises in ICUs up to

22% and even to 67% depending on population studied and the definition used (*Murugan et al., 2011*).

Impairment of kidney function requires special attention in ICUS, because if multi organ failure affects the kidney, it carries a greater risk for worse outcome and furthermore survivors have higher risk than normal population for chronic renal failure. They also have higher mortality and morbidity rates compared to normal population (*Kellum and Ronco, 2011*).

During the acute stage of renal failure, renal replacement therapy (RRT) is the mainstay of therapy. Adequacy of dialysis is likely to be linked to better outcome. Various modalities of RRT are available. Continuous RRT using convective methods are preferred in sepsis-induced ARF, especially in hemodynamically unstable patients. Early initiation of RRT is probably advantageous, although the optimal timing of dialysis is yet unknown. Higher doses of RRT are more likely to be beneficial (*Rajapakse et al., 2010*).

Substantial progress has been made toward understanding the mechanisms whereby sepsis is associated with a high incidence of acute renal failure. Recent investigations in animals and humans suggest that, the effect of CRRT in sepsis may increase survival in patients with sepsis-associated ARF. Moreover, recently identified clinical investigations may decrease the occurrence of ARF and sepsis and the associated high mortality (*Simmi et al., 2011*).

AIM OF THE ESSAY

So, the aim of this essay was to highlight the updates in terminology and classifications of acute kidney injury (AKI), with the possible causes encountered in intensive care and the updates in diagnosis of AKI and the possible modalities of management of such patients in intensive care.

ACUTE KIDNEY INJURY IN INTENSIVE CARE: CAUSES AND DIAGNOSIS

Acute kidney injury (AKI) is a clinical syndrome representing a sudden decline of renal function leading to the decrease of glomerular filtration rate (GFR) (*Bellomo et al., 2012b*). This “conceptual” definition has been utilized for many years in place of a more precise and universally accepted classification: Currently, objective parameters such as urine output and creatinine levels have been included into the so-called KDIGO (Kidney Disease: Improving Global Outcomes) definition (*Kellum and Lameire, 2013*). This recent innovation into clinical practice of AKI is improving uncertainties in epidemiology and clinical management. However, still the literature reports that AKI incidence and mortality varies widely (incidence ranges 1–31 % and mortality ranges 28–82%) (*Lameire and Kellum, 2013*).

This depends on the fact that often patients with different characteristics and severity of renal dysfunction are included in the analyses. Furthermore, AKI etiology and patient clinical condition strongly affect outcome, moving mortality rate from 20 % of the cases with isolated AKI with minimal or absent comorbidities to 80 % in case of AKI associated with severe sepsis or septic shock. Hence, in the description and evaluation of AKI in the clinical context, it becomes very important to diagnose this pathology with a consensus definition, to exactly