Study of Neutrophil gelatinase-associated Lipocalin in non septic patients with risk of Acute Kidney Injury in ICU.

Thesis

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بسم الله الرحمن الرحيم

وَلَقَدْ خَلَقْنَا الْإِنسَانَ مِن سُلَالَةٍ مِّن طِينٍ {١٢} ثُمَّ جَعَلْنَاهُ
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خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا
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List Of Abbreviations

ACEI	*Angiotensinogen Converting Enzyme Inhibitor*
ADQY	*Acute dialysis quality initiative*
AKI	*Acute kidney injury*
AKIN	*Acute kidney injury network*
ARB	*Angiotensin II Receptor Blocker*
ARF	*Acute renal failure*
ATN	*Acute tubular necrosis*
ATP	*Adenosine triphosphate*
AUC	*Area under curve*
BNP	*Brain natriuretic peptide*
BUN	*Blood urea nitrogen*
CI	*Confidence interval*
CIN	*Contrast induced nephropathy*
CKD	*Chronic kidney disease*
CNI	*Calcineurin inhibitor*
CO	*Cardiac output*
CRP	*C reactive protein*
DM	*Diabetes mellitus*
DNA	*Deoxyribonucleic acid*
DOP	*dopamine*
dop	*doputamine*
eGFR	*Estimated glomerular filtration rate*
epi	*epinephrine*
ESKD	*End stage kidney disease*
FENa	*Fractional excretion of sodium*
GFR	*glomerular filtration rate*
HELLP	*Haemolysis, elevated liver enzymes and low platelets*

HPF	*High power field*
HTN	*Hypertension*
ICU	*Intensive care unite*
IgA	*Immunoglobulin A*
IL-18	*Interleukin 18*
INOS	*Inducible nitric oxide sensetase*
K	*potassium*
KDIGO	*Kidney disease improving global outcome*
KG	*Kilogram*
KIM	*Kidney injury molecule*
LPF	*Low power field*
LPS	*Lipopolysaccharides*
M MOL/	*Millimole/liter*
MAP	*Mean arterial blood pressure*
ML	*Milliliter*
ML/min	*Milliliter/minute*
MO	*Milliosmol*
mRNA	*Messenengerribonucleic acid*
Na	*Sodium*
NCEPOD	*National confidential enquiry into patient outcome and death*
NGAL	*Neutrophil gelatinae associated lipocalin*
NICE	*National institute for health and critical excellence*
NIISS	*Neonatal therapeutic intervention scoring system*
NO	*Nitric oxide*
NSAID	*Non steroid anti-inflammatory drug*
p-NGAL	*Plasma neutrophil gelatinae associated lipocalin*
RBF	*Renal blood flow*
ROC	*Receiver Operating Characteristic*

ROS	*Reactive oxygen species*
RTE	*Renal Tubular Epithelium*
RVR	*Renal vascular resistance*
SAF	*Saline versus albumin fluid evaluation*
sCr	*Serum creatinine*
SD	*Standard deviation*
SIRS	*Systemic inflammatory response syndrome*
SLE	*Systemic Lupus Erythematosis*
SLED	*Sustained low efficiency dialysis*
SOFA	*Sequential organ failure Assesment*
TLRS	*Tall likereceptors*
TNF	*Tumor necrosis factor*
UF	*Urine flow*
UNa	*Urine sodium*
u-NGAL	*Urinary neutrophil gelatinae associated lipocalin*

Introduction

Acute kidney injury (AKI) represents a major clinical problem, with rising incidence and high mortality rate despite significant advances in medical care. It affects some 3-7% of patients admitted to the hospital and approximately 25-30% of patients in the intensive care unit **(Brenner and Rector., 2007)**.

This apparent lack of improvement may result from the use of more aggressive medical and surgical interventions in an ever-ageing population **(Kolhe et al., 2008)**.

On the other hand, potentially effective therapeutic interventions for AKI may currently fail because they are applied late in the course of injury after an obvious increase of serum creatinine (sCr) is observed **(Johanna et al., 2007).**

Due to the delayed rise in sCr following injury, recent efforts have focused on identification of an early and reliable promising novel biomarker of kidney injury with potentially high sensitivity and specificity **(Bouman et al., 2010)**.

Neutrophil gelatinase-associated lipocalin (NGAL) is a novel renal biomarker showing promising results in prediction of AKI in patients across different clinical settings **(Nagi et al., 2011).**

NGAL measured at ICU admission predicts the development of severe AKI similarly to serum creatinine-derived eGFR. However, NGAL adds significant accuracy to this prediction in combination with eGFR alone or with other clinical parameters and has an interesting predictive value in patients with normal serum creatinine **(De Geus et aL., 2011).**

Aim of the work

To identify the frequency of elevated serum NGAL in non septicpatients with risk of AKI in the ICU setting and its relation to AKI development & patients outcome (mortality and morbidity).

CHAPTER (1)
Acute kidney injury

Introduction

Acute kidney injury (AKI) has now replaced the term acute renal failure and a universal definition and staging system has been proposed to allow earlier detection and management of AKI. The new terminology enables health care professionals to consider the disease as a spectrum of injury. This spectrum extends from less severe forms of injury to more advanced injury when acute kidney failure may require renal replacement therapy (RRT) (**Lewingtonand Kanagasundaram ., 2011**).

Clinically AKI is characterized by a rapid reduction in kidney function resulting in a failure to maintain fluid, electrolyte and acid-base homoeostasis. There have previously been many different definitions of AKI used in the literature which has made it difficult to determine the epidemiology and outcomes of AKI. Over recent years there has been increasing recognition that relatively small rises in serum creatinine in a variety of clinical settings are associated with worse outcomes **(Praught and Shlipack ., 2005).**

To address the lack of a universal definition for AKI a collaborative network of international experts representing nephrology and intensive care societies established the Acute Dialysis Quality Initiative (ADQI) and devised the RIFLE definition and staging system for AKI, Shortly after this many of the original members of the ADQI group collaborated to form the Acute Kidney Injury Network (AKIN) **(Mehta et al., 2007).**

The AKIN group modified the RIFLE staging system to reflect the clinical significance of relatively small rises in serum creatinine. Most recently the international guideline group, Kidney Disease Improving Global Outcomes (KDIGO) has brought together international experts from many different specialties to produce a definition and staging system that harmonises the previous definitions and staging systems proposed by both ADQI and AKIN **(Lewington and Kanagasundaram ., 2011).**

It is anticipated that this definition and staging system will be adopted globally. This will enable future comparisons of the incidence, outcomes and efficacy of therapeutic interventions for AKI.

To date there is a paucity of data on the incidence of AKI whether community or hospital-acquired. The reported prevalence of AKI from US data ranges from 1% (community-acquired) up to 7.1% (hospital-acquired) of all hospital admissions **(Nash et al., 2002).**