STUDY OF THE ROLE OF URINARY IL-18 AS A MARKER FOR ALLOGRAFT DYSFUNCTION IN THE RENAL-ALLOGRAFT RECIPIENTS

Thesis

Submitted for partial fulfillment of master degree in

Internal medicine

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2012

ABSTRACT

Acute rejection is an important risk factor for allograft failure. Renal biopsy is the best method to predict out come of acute rejection, although; its complications as AVF, even graft loss. Some studies have highlighted the role of urinary IL-18 measurement which elevated in acute kidney rejected allografts as; compared with non-complicated kidney transplanted allografts. Our study value of urinary IL-18 as; a non-invasive tool for early diagnosis of acute rejection or chronic allograft nephropathy.

***Key words:-**

. Acutr Allograft Rejection.

. Chonic Allograft Nephopdthy.

. Urinary Interlukin-18.

Acknowledgement

First of all I thank **Allah**, the most merciful and the most Compassionate for giving me the power to complete this work

I would like to express my deep appreciation and sincere

Gratitude to prof. **Dr. Seham Bakry**, assistant prof. of internal medicine, Faculty of Medicine, Cairo University. She had set the plan, followed the steps of the work, critically discussed the results and taught me the scientific attitude. Her care, perfectionism and invaluable experience were of much guidance to me. I much benefited from her creative thinking, valuable suggestions and constructive criticism.

I would also like to express my gratitude and appreciation toward **Dr. Mohammed Momtaz**, lecturer of internal medicine, Faculty of Medicine, Cairo University for his effective work and sharing in achievement of our thesis .

I would like to thank Prof. **Dr.Laila Rashed**, professor of

Biochemistry, Cairo University for her kindness, sympathy and cooperation to achieve this work.

Lastly,I would like to express my deepest thanks to every-one who helped me to finish this work.

My deepest appreciation and inexpressible gratitude to my family for their never-ending support and care.

This work was done by and for the sake of patients, May Allah alleviate their suffering and accept our honest intention to dedicate this work for the sake of their own benefit. I hope this work offers a chance for a better state of health which they deserve after their long pains and suffering.

Dedication

To

My dear father;the one who really support,help me all my life

May God rest his soul in heaven with Prophets,Ameen.

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ACE:	**Angiotensin converting enzyme**
AGP:	**Allograft glomerulopathy**
AKI:	**Acute kidney injury**
APCs:	**Antigen-presenting cells**
ARB:	**Angiotensin receptor blocker**
ATN:	**Acute tubular necrosis**
CAN)	**Chronic allograft nephropathy**
CkD:	**Chronic kidney disease**
CMV:	**Cytomegalo virus**
CNI:	**Calcineurin inhibitors**
ESRD:	**End stage renal disease**
GFR:	**Glomerular filteration rate**
HLA:	**Human leucocytic antigen**
ICAM-1:	**Intercellular adhesion molecule 1**
IL_18:	**Inter leukin_18**
IRAK:	**IL_1 receptor activating kinase**
IRI:	**Ischemia-reperfusion injury**
MHC:	**Major-histocompatibility-complex**
MMF:	**Mycophenolate mofetil**

m-TOR: Mammalian target of rapamycin

PCR: Polymerase chain reaction

pRIFLE: Paediatric modified risk,injury,failure,loss,end-stage kidney disease

PRISM: Paediatric risk of mortality

PWV: Pulse wave velocity

ROC: Receiver-operating characteristic curves

TNF-α: Tumar necrosis factor-α

USRDS: (United States Renal Data System)

VCAM: vascular-cell adhesion molecules

INTRODUCTION

Kidney transplantation is the treatment of choice for most patients with end-stage renal disease (ESRD), but a shortage of organs limits its availability **(Langone et al, 2003)**

Acute rejection is an important risk factor for allograft failure. The current approach to treatment of acute rejection is uniform, although it is well recognized that some rejection episodes are not fully reversible and lead to long-term graft dysfunction and failure, whereas others are easily treatable and benign **(Opelz, 1997)**

The outcome of acute rejection is difficult to predict, and histologic features that are observed in allograft tissue obtained by core needle biopsy are currently the best predictors **(Hayty, 2000)**

The invasive procedure of allograft biopsy, however, is associated with complications such as bleeding, arteriovenous fistula, and even graft loss **(Beckmgham et al, 1994)**

Macrophage accumulation within acutely rejecting allografts has been reported for many years., and is known to occur through both recruitment from circulation and through proliferation within the rejecting graft.**(Grau et al, 1998)**

IL-18 is a potent pro-inflammatory cytokine, produced by several different cell types, but is primarily a product of macrophages. It is a potent proinflammatory cytokine involved in the host defence by upregulating both innate and acquired immune

responses and may be of particular importance also in mechanisms of kidney allograft rejection **(Mclnnes et al, 2000)**

In a previous study serum levels of IL-18 were significantly elevated in patients with acute rejection of kidney allograft as compared to patients with uncomplicated outcome of kidney transplantation and subjects with acute tubulointerstitial nephropathy **(Ilja et al, 2005)**

Aim of the work

The aim of this work is to study the value of urinary IL_18 as a non-invasive tool for early diagnosis of acute allograft rejection or chronic allograft nephropathy in renal allograft recipients.

ACUTE RENAL ALLOGRAFT DYSFUNCTION

Renal transplantation is the best form of renal replacement therapy for patients with end stage renal disease (ESRD),in comparison to dialysis, as it is associated with higher patient survival, lower hospitalization rate and a superior quality of life ***(Vathsala, 2005)***. The most common complication of renal transplantation is allograft dysfunction, which in some cases leads to graft loss. Although there is a wide intercenter variability, data from the United States indicate that overall one year unadjusted survival of a renal allograft is approximately 90 percent for a deceased donor kidney and approximately 95 percent for a living donor kidney ***(USRDS, 2007)***.

The science of kidney transplantation has progressed considerably in the past half-century largely because of an improved understanding of the role of the immune system in allograft rejection, the disentanglement of the molecular mechanisms underlying graft failure, and better management of immunosuppression. Rejection has always been the major obstacle. Transplantation of tissues or cells from a donor who differs genetically from the graft recipient induces an immune response in the recipient against alloantigens of the donor graft ***(Morris., 2004).***

If not controlled, this response will destroy the graft. Recent discoveries have clarified how T lymphocytes, the principal agents of