

**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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ABSTRACT

Acute rejection is an important risk factor for allograft failure. Renal biopsy is the best method to predict outcome 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:-**

- . Acute Allograft Rejection.
- . Chronic Allograft Nephropathy.
- . Urinary Interleukin-18.

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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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List of Abbreviations

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 filtration 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:	Tumor 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 (**McInnes 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