**Ain Shams University**
**Faculty of Medicine**
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# PERIPHERAL BLOOD T-CELL CD4 AND CD8 LEVELS IN SEROPOSITIVE HCV RENAL TRANSPLANTED PATIENTS

*Thesis*

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بسم الله الرحمن الرحيم

# قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢


*First of all I have to express my all thanks to* ***Allah*** *the most merciful the most helpful allowing me perform this work.*

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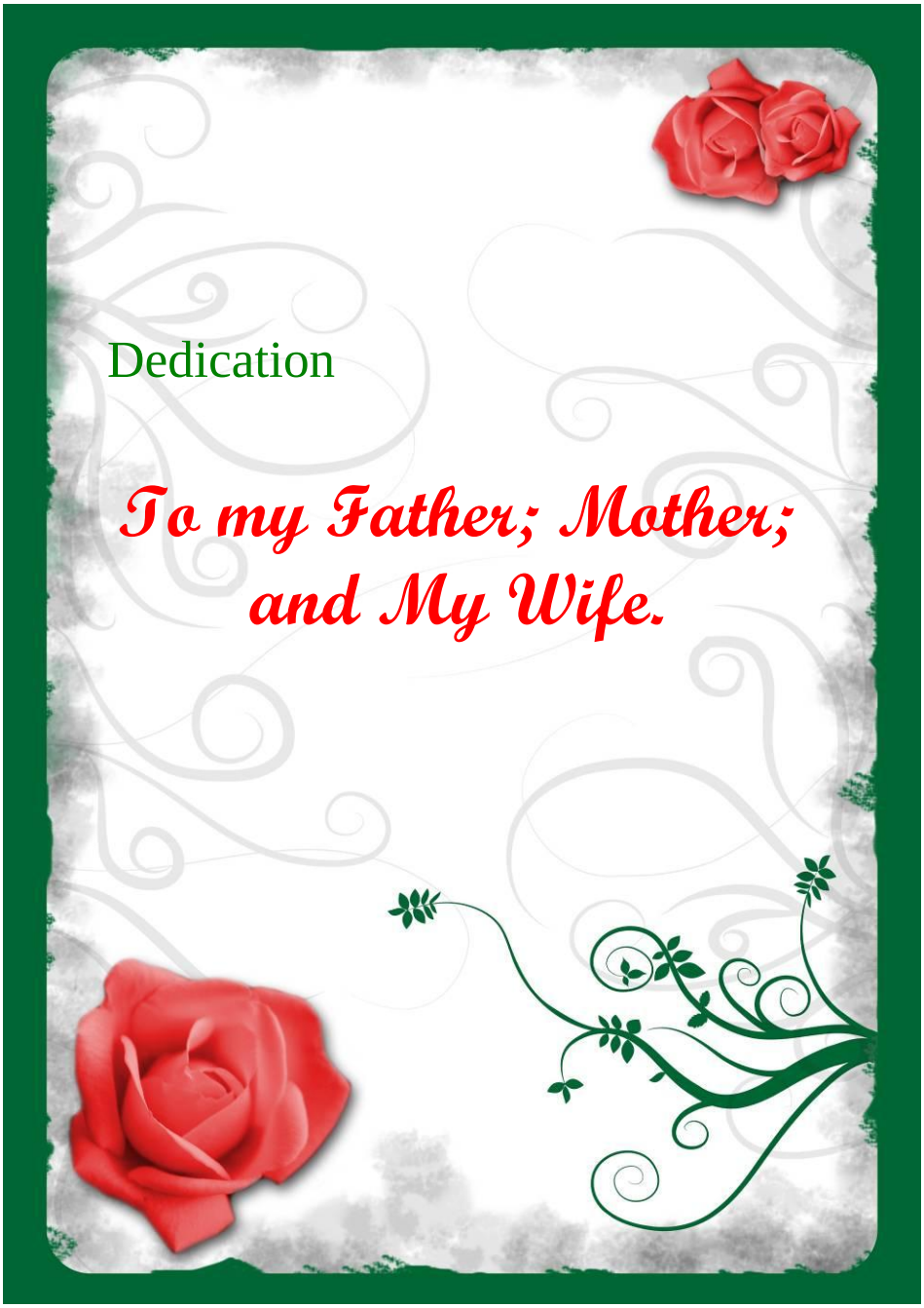
Dedication

*To my Father; Mother; and My Wife.*



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# List of Abbreviations

| | |
|---|---|
| **ACE** | Angiotensin converting enzyme |
| **ACR** | Acute cellular rejection |
| **ALG** | Antilymphoblast globulin |
| **ALT** | Alanine amino transferase |
| **APC** | Antigen-presenting cell |
| **ARB** | Angiotensin receptor (AT2) blockers |
| **AT2** | Angiotensin receptor |
| **ATG** | Antithymocyte globulins |
| **AZA** | Azathioprine |
| **CCL3** | Chemokine (C-C motif) ligand 3 |
| **CHC** | Chronic hepatitis C |
| **CNIs** | Calcineurin inhibitors |
| **CI** | Confidence interval |
| **CsA** | Cyclosporine |
| **CTL** | Cytotoxic T Lymphocytes |
| **CXCL8** | Chemokine (C-X-C motif) ligand 8 |
| **CyA** | Cyclosporin A |
| **DC** | Dendritic cells |
| **DGF** | Delayed graft function |
| **DM** | Diabetes mellitus |
| **E** | Envelope |
| **ESRD** | End stage renal disease |
| **EIA** | Enzyme immunoassay |
| **ELISA** | Enzyme-linked immunosorbent assay |
| **FAE** | Follicle-associated epithelium |
| **FoxP3** | Forkhead box p3 |
| **GM-CSF** | Granulocyte/macrophage colony-stimulating faactor |

| | |
|---|---|
| **GN** | Glomerulonephritis |
| **HCV** | Hepatitis C virus |
| **IFN** | Intreferron |
| **IFN-γ** | Interferon-gamma |
| **IRF3** | Interferon regulatory transcription factor |
| **IL-2** | Interleukin-2 |
| **IL2RA** | Interleukin 2 (IL2) receptor alpha |
| **KDIGO** | Kidney Disease Improving Global Outcomes |
| **MMF** | Mycophenolate mofetil |
| **MN** | Membranous nephropathy |
| **MIP1α** | Macrophage Inflammatory Protein- 1 alpha |
| **MyD88** | Myeloid differentiation primary response gene (88) |
| **NS** | Non structural proteins |
| **MGN** | Membranous GN |
| **MHC** | Major histocompatibility complex |
| **MPGN** | Membranoproliferative glomerulonephritis |
| **mIg** | Membrane immunoglobulin |
| **NGF** | Nerve growth factor |
| **NKreg** | Natural killer regulatory cells |
| **NKT** | Natural killer T |
| **NODAT** | New onset diabetes after transplantation |
| **PDCs** | plasmacytoid dendritic cells |
| **PCR** | Polymerase chain reaction |
| **PEG-IFN** | Pegylated interferon |
| **PNALT** | persistently normal alanine aminotransferase levels |
| **PTDM** | Post transplant diabetes mellitus |
| **PTLD** | Post-transplant lymphoproliferative disorder |
| **RA** | Rheumatoid arthritis |
| **RER** | Rough endoplasmic reticulum |
| **RBV** | Ribavirin |

| | |
|---|---|
| **RNA** | Ribonucleic acid |
| **RR** | Relative risk |
| **RTRs** | Renal transplant recipients |
| **SDF-1** | Stromal cell-derived factor |
| **SRR** | Steroid-resistant rejection |
| **SVR** | Sustained viral response |
| **TAC** | Tacrolimus |
| **TAP1** | Transporter associated with antigen processing 1 |
| **TCR** | T cell receptor |
| **Tc** | T cytotoxic cells |
| **TGFβ** | Transforming growth factor β |
| **Th** | T helper cells |
| **TBK1** | TANK-binding kinase 1 |
| **TG** | Transgenic |
| **TNF-α** | Tumer necrosis factor –alpha |
| **Tr1** | Type 1 regulatory T cells |
| **Treg** | T regulatory cells |
| **USRDS** | United States Renal Data System |

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# Introduction

Renal transplantation offers the potential for improved quality and length of life to patients with end-stage renal disease ***(Shapiro R, 2011).***

Renal transplant recipients represent an important group with high prevalence of HCV infection rates ranging from 10% to 50% ***(Justa S et al., 2010).***

Infectious complications significantly increase morbidity and mortality after renal transplantation ***(Sousa S et al., 2010).***

Approximately 80% of all renal transplant recipients have an infectious complication in the first year following transplantation ***(Sousa S et al., 2010).***

In fact, in the past it was reported that patients with non-A non-B hepatitis had ‘a marked increase of life threatening extrahepatic complications’. This finding has been demonstrated in HCV-positive patients who had more frequent postoperative infections and potentially fatal infections of the central nervous system, lungs and blood stream (such as cytomegalovirus infection, tuberculosis, sepsis) ***(Domı´nguez B and Morales JM, 2009).***

Although prior studies have shown an overall increased risk of death from infection in HCV-infected kidney transplant recipients. This study showed that the increased death rate from infection occurs in the early (6 months) post-transplant period. This raises as yet unanswered questions about the contribution of HCV infection to this increased mortality and suggests that one approach may be to modify the immunosuppression administered during this period ***(Roth D et al., 2011).***

The presence of HCV infection in liver transplant recipients resulted in a significant increase in Regulatory T cells and a decrease in activated T cells in comparison with HCV-negative liver transplant recipients. These 2 findings indicate a potentially important effect of HCV on the immune system after transplantation through an increase in the suppressive role of Regulatory T cells and/or a decrease in activated T cells ***(Ciuffreda D et al., 2010).***

CD4 T cell population was significantly increased in both HCV-negative and HCV-infected transplant recipients (17.6±1.4% and 0.5±0.9%, respectively) in comparison with healthy subjects and non transplanted HCV-infected patients. Interestingly, this activated CD4 T cell population was significantly lower in HCV-infected recipients versus HCV-negative recipients **(*Ciuffreda D et al., 2010).***