Detection of Cytomegalovirus infection among renal dialysis patients

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LIST OF ABREVIATION

A	Adenine
AIDS	Acquired immunodeficiency syndrome
APC	Antigen presenting cells
BP	Base pair
C	Complement
CF	Complement fixation test
CPE	Cytopathogenic effect
CNS	central nervous system
DB	Dense bodies
DNA	Deoxyribonucleic acid
EHV	Equine herpes virus
EIA	Enzyme Immunoassay
ELISA	Enzyme linked immunosorbent assay
ESRD	End stage renal disease
FC	Fraction complement binding site
FITC	Fluorescein isothiocyanate
G + C	Guanine + Cytosine
GI	Gastrointestinal
HBV	Hepatitis B virus
HBSAg	Hepatitis B surface antigen
HCMV	Human Cytomegalovirus
HCV	Hepatitis C virus
HHV	Human herpes virus
HIV	Human immunodeficiency virus
HLA	Human leucocyte antigen
HRP	Horseradish Peroxidase
HSV	Herpes simplex virus
IEA	Immediate early antigen
IFA	Indirect fluorescent antibody
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IHA	Indirect hem agglutination
IL	Interleukin
IR	Internal repeat

LA	Late antigen
MAB	Monoclonal antibody
MHC	Major histocompatibility complex
NK	Natural killer
PBS	Phosphate buffer saline
PCR	Polymerase chain reaction
PML	Polymorphonuclear leucocytes
TCR	T cell receptor
TMP	Titramethyle benzedian
TR	Terminal repeat
UL	Unit long
US	Unit short

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INTRODUCTION

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Human cytomegalovirus (HCMV) is one of the remarkable group of viruses, which infects human beings universally and stay for life. Although most CMV infections are asymptomatic, certain patient groups such as fetus, new born infant or immunocompromised patients are at high risk for serious even life-threatening illness **(Stagno et al ., 1999) .**

Hallmarks of the biology of HCMV are silent primary infection, persistence, latency and reactivation of the virus. HCMV seems to require considerable disturbance of immunoregulation for symptomatic reactivation **(Jawetz et al., 2001).**

Cytomegalovirus (CMV) infections have been noted in many types of immunocompromised patients but are most notable in organ transplant recipients, CMV is still the most important infectious agent following renal transplantation**(Cerná et al., 2002).**

It is obvious that HCMV infection may be mild or it may be fatal specially for allograft recipients. The wide spectrum of clinical manifestations of HCMV disease and the potential adverse consequences to a successful graft and to a patient survival requires sensitive and specific diagnostic procedures that allow early diagnosis of viral infection. In addition the availability of specific antiviral drugs whose effectiveness is highly increased by early administration, stress the need for procedures and rapid methods to identify patients early so that therapy can be instituted and monitored **(Cerna et al., 2002).**

HCMV may be found in both cervical secretions and in breast milk. Most infants become infected in utero appear healthy but may manifest late sequelae. Ten

percent of infant who infected in utero and born with symptomatic cytomegalic inclusion disease have a very poor prognosis **(Stagno et al., 2003).**

Patients undergoing dialysis (hemo or peritoneal) due to renal failure are immunocompromised and are subjected to blood transfusion. They may suffer from symptomless CMV infection. This may be either due to self reactivation of latent infection or infection with exogenous virus from the blood or renal donor. Therefore pretransplantation evaluation can minimize risks and help to anticipate special problems **(Mayoral et al.,2006).**

Because of its direct effect, morbidity and mortality are caused by CMV syndrome and disease. Its indirect effect contribute to the net states of immunosuppression which independently increases the risk of opportunistic superinfection.**(Drew and Robacck, 2007).**

Cytomegalovirus is presumed to be transmitted latently in donor leucocytes. Immunological data suggested that packed RBCs transfusion may itself be immunosuppressive and lead to reactivation of endogenous CMV. The importance of HCMV as a pathogen has increased over the past two decades as immunosuppressive post-transplant therapies, as well as acquired immunodeficiency syndrome (AIDS) and other immunodeficiency states have become prominent medical concerns. These conditions predispose individuals to primary CMV infection or to reactivation of latent infections resulting in fulminant, life threatening acute disease.**(Drew and Robacck, 2007).**

There are several diagnostic laboratory tests available to support a diagnosis of CMV infection. Conventional tissue culture is considered the gold standard but is time consuming. The rapid shell vial technique provides a more timely result but is less sensitive than culture for some specimens as blood. Serology is most useful in

active infections and CMV antigenemia testing is very labor intensive, subjective and is performed on blood specimens. Qualitative CMV/DNA by polymerase chain reaction (PCR) is a direct method for virus detection. **(Drew et al, 2009).**

Aim of the work

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The aim of this study was :

1- to detect the incidence of HCMV infection among first time renal dialysis patients, and follow up HCMV IgM negative patients by HCMV IgM and HCMV DNA assays after 4-6 weeks of hemodialysis.

2- to compare diagnostic value of serological test IgM& IgG and HCMV DNA detection by PCR


REVIEW OF LITERATUR

HUMAN CYTOMEGALOVIRUS

History

In 1904, Jesionek reported the finding of characteristic enlarged cells in a variety of tissues from neonates and infants. These cells were called protozoan like cells and were thought to be protozoa. **In 1921, Good pasture and Talbot** suggested that these cells were of viral etiology because of the similarities of these cells to those infected by varicella zoster virus and herpes simplex virus. They suggested the name "cytomegalia" to describe the condition. **(Weller et al ., 1957).**

Farber and Wolbock, (1932) proposed the name " salivary gland virus" because the typical inclusion-bearing cells were frequent incidental finding in the salivary gland of children dying from a variety of causes. Finally Cytomegalovirus (CMV) was isolated by tissue culture techniques and was given the name cytomegalovirus by **(Weller et al ., 1957).**

Human cytomegalovirus (HCMV) is a member of the Betaherpesvirinae, subfamily of the herpesvirinae **(Mocarski,2001)**.

Classification:

According to the criteria or host range, duration or reproductive cycle, cytopathology and characteristics of latent infection, herpesviruses have been divided into 3 subfamilies: Alpha, Beta and Gamma herpesvirinae **(Davision and Clements,1998)**.

(I) Alpha - herpesvirinae :

They have a variable host range, short growth cycle, spread rapidly with destruction of infected cells and are neurotropic in that they have capacity to