Peripheral Blood Natural Killer CD16+ Level In Hepatitis C Virus Seropositive Prevalent Hemodialysis Patients

Thesis

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By

Eman Mohammed Taha
(M.B,B.Ch.)
Faculty of Medicine, Mansoura University

Supervisors

Prof. Mohammed Ali Ibrahim
Professor of Internal Medicine & Nephrology
And Head of Nephrology Department
Faculty of Medicine - Ain Shams University

Prof. Afaf Abd El Alim Mostafa
Professor of Clinical Pathology
Faculty of Medicine - Ain Shams University

Dr. Heba Wahid El Said
Assistant professor of Internal Medicine & Nephrology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
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بسم الله الرحمن الرحيم

﴿ قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴾

[البقرة:٣٢]

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LIST OF ABBREVIATIONS

ALT	Alanine amino transferase
APCs	Antigen-presenting cells
AST	Aspartate amino transferase
BNHL	B-cell non-Hodgkin's lymphoma
Ca	Calcium
CBC	Complete blood count
CHC	Chronic hepatitis C
CRP	C reactive protein
CTLA-4	Cytotoxic T-lymphocyte antigen 4
DBP	Diastolic blood pressure
DL	Deci litre
DM	Diabetes mellitus
ELISA	Enzyme-linked immunosorbent assay
ESRD	End stage renal disease
FITC	Fluorescein isothiocyanate
G	Gram
HB	Hemoglobin
HBV	Hepatitis B Virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HD	Hemodialysis
HIV	Human immunodeficiency virus
I D weight gain	Interdialytic weight gain

IFN	Interferon
K	Potassium
Kg	Kilo gram
L	Litre
LAG-3	Lymphocyte activation gene 3
LCMV	Lymphochoriomeningitis virus
LSM	Liver stiffness measurement
MC	Mixed cryoglobulinemia
mEq	Mili equivalent
MGUS	Monoclonal gammopathy of undetermined significance
MHC	Major histocompatibility complex
Mg	Mili gram
Na	Sodium
NANBH	Non-A, non-B hepatitis
NG	Nano gram
NIH	National Institutes of Health
NK	Natural killer cell
NKRs	Natural killer cell receptors
NS3	Nonstructural protein 3
PCR	Polymerase chain reaction
PD	Peritoneal dialysis
PD-1	Programmed death-1
PE	Phycoerythrin

PEG-IFN	Pegylated-interferon
Pg	Peco gram
PO4	Phosphorus
PTH	Parathyroid hormone
RBV	Ribavirin
RNA	Ribonucleic acid
SBP	Systolic blood pressure
SVR	Sustained virologic response
TCR	T cell Receptor
TMA	Transcription-mediated amplification
U	Unit

INTRODUCTION

Chronic hepatitis C virus (HCV) infection is the major etiology of chronic liver disease, liver cirrhosis, hepatic decompensation, hepatocellular cancer and liver transplantation ***(Hunyady, 2011).***

HCV infection is the most common cause of acute or chronic hepatitis in patients on hemodialysis (HD) ***(Galperim et al., 2010).*** In hemodialysis patients, HCV infection has been associated with increased occurrence of cirrhosis and hepatocellular carcinoma and increased mortality ***(Patel et al., 2010).***

Recent studies have shown that HCV positivity is associated with significantly higher cardiovascular mortality, especially in dialysis patients younger than 65 years ***(Santoro et al., 2009).***

Infections are the major cause of morbidity and the second cause of death following cardiovascular events in HD patients. It seems that the HD procedure

per se as well as disturbances in both innate and adaptive immunity significantly contribute to this susceptibility ***(Eleftheriadis et al., 2011).***

The innate and adaptive immune systems are suppressed by various kinds of mechanisms in HCV patients ***(Kondo et al., 2011).***

T-cell and natural killer (NK)-cell functions are impaired in HD patients **(*Eleftheriadis et al., 2009*).** Chronic uraemia and HD treatment exert a negative effect on natural killer (NK) cells (CD3-, CD16+) count in the peripheral blood. Furthermore, The count of natural killer (NK) cells (CD3-, D16+) in the peripheral blood in patients with chronic renal failure treated with HD could be a prognostic marker of susceptibility to infections and malignancy ***(Liszka et al.,1998).***

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 et al., 2010).***

Approximately 80% of all renal transplant recipients have an infectious complication in the first year following transplantation ***(Sousa et al., 2010).*** HCV-positive patients had more frequent postoperative infections and potentially fatal infections of the central nervous system, lungs and blood stream (such as cytomegalovirus infection, tuberculosis, sepsis) ***(Domınguez and Morales ., 2009).***

However, no previous studies have assessed the effect of HCV seropositivity on intercurrent infection in HD patients.

AIM OF THE WORK

The aim of this study is to assess the possible effect of HCV infection on the level of the peripheral blood NK CD16+ in prevalent HD patients and their association with intercurrent infection**.**

HCV INFECTION

Epidemiology

About 170 million people in the world are infected with hepatitis C virus (HCV). Since the discovery of HCV in 1989 ***(Alter et al, 1999)***, the number of acute HCV cases has fallen by more than 80% ***(Wasley and Alter, 2000).*** However, hepatitis C is still a major health burden because 60–80% of infected people progress to chronic infection ***(Di Bisceglie, 2000).***

Importantly, many individuals are infected with both HIV and hepatitis C virus (HCV) infection. More rapid progression of liver disease is seen, higher levels of HCV RNA encourage transmission and sustained virological responses are lower in coinfected patients. The management of these patients is further complicated by potential interactions between antiretroviral therapy and peginterferon and ribavirin ***(Thomson and Main, 2008).***

HCV is a single-stranded RNA virus belonging to the Flaviviridae family ***(Lindenbach and Rice, 2005).*** The major routes of transmission are injection drug use, blood transfusion, hemodialysis, organ transplantation and less frequently sexual intercourse. Six major genotypes (1–6) of HCV have been identified, and they have varying geographical distribution. Genotypes 1, 2 and 3 are distributed worldwide with genotype 1 accounting for 40–80% of all cases. Genotype 4 is found in the Middle East and Egypt, genotype 5 in South Africa and genotype 6 in South East Asia ***(Wasley and Alter, 2000).***

Geographical trends of HCV genotypes

The geographical trends of HCV genotypes are shown as follow ***(Bostan and Mahmood, 2010).***

Genotype 1: North and South America and in Australia. About 70% of the patients in United States are infected with genotype 1. Genotype 1a is common in United Kingdom. Genotype 1b is mostly found in Europe and Asia and is common in Japan. Studies show that genotype 1 is more resistant to therapy than genotype 2 and 3.