Evaluation of Natural Killer Cells in HCV Patients undergoing Hemodialysis

Thesis

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Evaluation of Natural Killer Cells in HCV Patients undergoing Hemodialysis

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Abstract:

Background: Hepatitis C virus (HCV) is a hepatotropic virus and one of the major causes of liver disease and a potential cause of substantial morbidity and mortality worldwide. Patients on hemodialysis are at high risk for HCV, with frequency of infection several times higher than that in non-uremic patients. Natural killer (NK) cells are best appreciated for innate defense against viral infections and in tumor cell surveillance. **Objective:** To study the percentage of peripheral blood natural killer cells among chronic hepatitis C patients undergoing hemodialysis compared to chronic HCV patients with normal kidney functionsby flowcytometry immunophenotyping. **Methodology:** Frequency of CD3- CD56+ cells was assessed in two distinct groups. Group I: 35 chronic HCV patients with end stage renal disease and undergoing hemodialysis, group II: 35 age and sex matched chronic HCV patients with no kidney disease. **Results:** No significant difference was observed between HCV hemodialysis patients with ESRD and HCV patients with normal kidney function regarding the frequency of both NK cells (CD3-CD56+) and NKT cells (CD3+CD56+). However, group I had significantly higher percentage of CD3+ cells than group II. **Conclusion:** no difference was found in this study between HCV patients on hemodialysis and HCV with normal kidney function regarding NK cell frequency. However, assessment of NK cell function in future studies might reveal differences.

Key words: HCV, NK

LIST OF ABBREVIATIONS

Abb.	Full Term
ADCC	antibody-dependent cellular cytotoxicity
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BAT3	B associated transcript 3
BID	BH3-interacting domain
BUN	blood urea nitrogen
CD	cluster of differentiation
cDNA	complementary DNA copy
CHILPs	common helper innate lymphoid progenitors
CILPs	common innate lymphoid progenitors
CLDN	claudin
CLPs	common lymphoid progenitors
DC	dendritic cells
EDTA	ethylenediamine tetra-acetic acid
EIA	enzyme immunoassay
ESRD	end-stage renal disease
FasL	Fas ligand
Fs	forward scatter
GAGs	glycos-aminoglycans
GM-CSF	granulocyte/monocyte colony-stimulating factor
GzmA	granzyme A
GzmB	granzyme B
HCV	Hepatitis C virus
HD	hemodialysis
HLA	human leukocyte antigen

ICAM-1 - : inter-cellular adhesion molecule- 1

IFN ------- : interferon

IL --------- : interleukin

ILC ------- : innate lymphoid cell

ILCP ----- : innate lymphoid cell precursors

ITAM ---- : immunoreceptor tyrosine-based activating motifs

ITIM ----- : immunoreceptor tyrosine-based inhibitory motifs

KIRs ----- : killer cell immunoglobulin-like receptors

LDL-R -- : LDL-receptor

LFA ------ : Lymphocyte function associated antigen

LIRs------ : leukocyte Ig like receptors

LTi ------- : lymphoid tissue-inducer

LTiPs ---- : lymphoid tissue inducer progenitors

mDCs ---- : myeloid DCs

MHC ----- : major histocompatibility complex

MICA/B - : major histocompatibility complex class I-related chain A/B

NADPH - : Nicotinamide Adenine Dinucleotide Phosphate

NCR------ : natural cytotoxicity receptor

NK ------- : natural killer

NKP------ : NK cell precursors

NS proteins: non-structural proteins

NS -------- : non-significant

PBMCs -- : peripheral blood mononuclear cells

PCR ------ : polymerase chain reaction

pDCs ----- : plasmacytoid DCs

PFN ------ : perforin

RIBA----- : recombinant immunoblot assay

RNA ----- : ribonucleic acid

S ---------- : Significant

SD -------- : standard deviation

SPSS ----- : statistical package for social science

SR-B I --- : scavenger receptor class B type I

Ss --------- : side scatter

TAP ------ : transporter associated with antigen

TGF-B 1- : transforming growth factor- B 1

TNF ------ : tumor necrosis factor

TRAIL--- : tumor necrosis factor-related apoptosis-inducing ligand

TRAIL-R : TNF-related apoptosis-inducing ligand-receptor

UTR ----- : untranslated regions

VCAM--- : vascular adhesion molecules

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INTRODUCTION

Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV) that primarily affects the liver ***(Lavanchy, 2011).*** HCV spreads primarily by blood-to-blood contact associated with intravenous drug use, poorly sterilized medical equipment, needle stick injuries in healthcare and transfusions. ***(Maheshwari and Thuluvath, 2009).***

Chronic kidney disease is a progressive loss in renal function over a period of months or years. All individuals with a glomerular filtration rate of less than 15/ml/min/1.73 m2 for 3 months are classified as having end-stage renal disease (ESRD) ***(Levin et al., 2008).***

In Egypt, the prevalence of dialysis patients is presumed to be increasing and the main causes of ESRD in Egypt, other than diabetic nephropathy, include hypertensive kidney disease, chronic glomerulonephritis, unknown etiology, chronicpyelonephritis, schistosomal obstructive uropathy, and schistosomal nephropathy ***(Afifi et al., 2004).***

Patients on hemodialysis are at high risk for HCV, with frequency of infection several times higher than that in non-uremic patients. The spread of HCV in hemodialysis units is

declining, but the prevalence of HCV in hemodialysis patients remains high ***(Selcuk et al., 2006).***

The knowledge about the immunological aspects of the chronic hepatitis C especially in ESRD patients on regular hemodialysis needs further study ***(Poordad et al ., 2004).***

The immunophenotyping of peripheral blood has been employed in studies focusing on the pathogenesis of chronic hepatitis C. The study of natural killer (NK) cells, a type of cytotoxic lymphocyte critical to the innate immune system, in hepatitis C pathogenesis has been the focus of several studies ***(Larrubia et al .,2007).***

AIM OF THE WORK

The aim of this work is to study the percentage of peripheral blood natural killer cells among chronic hepatitis C patients undergoing hemodialysis compared to chronic HCV patients with normal kidney functions by flowcytometry immunophenotyping.

HEPATITIS C VIRUS

Hepatitis C virus is a hepatotropic virus and one of the major causes of liver disease and a potential cause of substantial morbidity and mortality worldwide. Moreover, it is estimated that >184 million people have been infected with HCV (on the basis of positive anti-HCV antibody results), representing >2.8% of the world population ***(Thrift et al., 2017).***

Chronic HCV is one of the major causes of advanced liver disease, including cirrhosis, hepatocellular carcinoma, and related complications. In the United States, approximately one-third of cirrhosis cases and one-fourth of hepatocellular carcinoma cases are due to chronic HCV infection ***(Armstrong et al., 2000).***

A. Structure of HCV:

Hepatitis C virus is a member of the Hepacivirus genus (of the family Flaviviridae). Other members of this family include viruses that cause yellow fever, dengue, Japanese encephalitis and tickborne encephalitis ***(Rogo et al., 2011).***

HCV is an enveloped, small (55-65nm in size), positive sense, single stranded ribonucleic acid (RNA) virus. The HCV particle consists of a core of genetic material “RNA”, surrounded by an icosahedral protective shell of protein, and further encapsed in a lipid envelope of cellular origin. Two viral envelope

glycoproteins, E1 and E2, are embedded in the lipid envelope ***(Budkowska, 2017)*** (Fig.1).

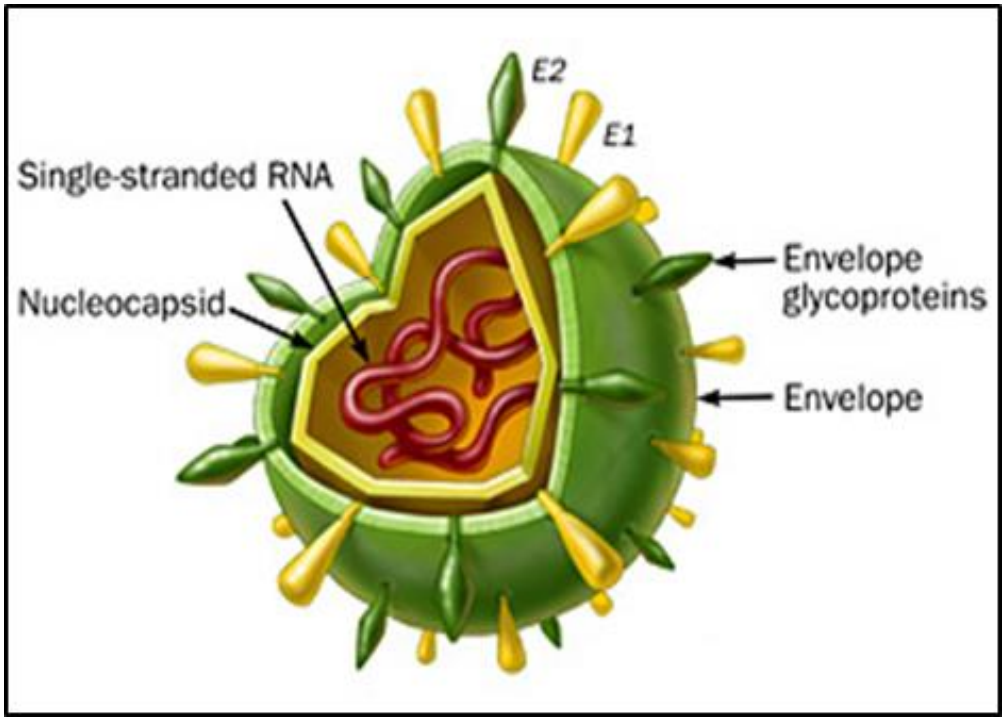

Figure (1): Structure of Hepatitis C virus
(https://microbewiki.Kenyon.edu/index.php/modern_treatments_for_hepatitis_c_virus)

The genome of HCV is an open reading frame of 9600 nucleotide bases that has at its 5' and 3' ends untranslated regions (UTR) that are not translated into proteins but are important to translation and replication of the viral RNA. The 5' UTR has a ribosome binding site that starts the translation of a 3011 amino acid containing protein that is later cut by cellular and viral proteases into 10 active structural and non-structural smaller proteins ***(Rogo et al., 2011)*** (Fig. 2).