Serum Ficolin- 2 Concentration and its Relation to Severity of Liver Inflammation and Response to Antiviral Therapy in Egyptian Chronic Hepatitis C Patients

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Abd Elbadea Mohamed Allakany

Contents

List of Abbreviations

AASLD/IDSA/IAS-USA: American Association for the Study of Liver Diseases/ Infectious Diseases Society of America / International Antiviral Society – USA

ac-LDL	:	Acetylated low-density lipoprotein
ARF	:	Alternate reading frame
BOC	:	Boceprevir
CDC	:	Centers for Disease Control and Prevention
CLDN1	:	Claudin-1
CRHD	:	Rheumatic heart disease
CRP	:	C-reactive protein
DAA	:	Directly acting antivirals
DCV	:	Daclatasvir
EASL	:	European Association for the Study of the Liver
EIAs	:	Enzyme-linked immunoassays
FCN2	:	Ficolin 2
GAG	:	Glycosaminoglycans
GlcNAc	:	N-acetyl glucosamine
GT	:	Genotype
HAE-C1-INH	:	Hereditary angioedema due to C1-inhibitor deficiency
HCC	:	Hepatocellular carcinoma
HCV	:	Hepatitis C virus
H-ficolin	:	Hakata antigen or ficolin-3
HIV	:	Human immunodeficiency virus
HLA	:	Human leukocyte antigen
IL28B	:	Interleukin 28B
IRES	:	An internal ribosome entry site
IRRDR	:	Interferon RBV resistance- determining region

List of Abbreviations(Cont.)

IVDU	:	Intravenous drug users
LDL	:	Low-density lipoproteins
LDV	:	Ledipasvir
L-ficolin	:	Liver ficolin or ficolin-2
MASPs	:	Mannan associated serine proteases
MBL	:	Mannose-binding lectin
MELD	:	Model for End-Stage Liver Disease
M-ficolin	:	Monocyte ficolin or ficolin-1
mRNA	:	Messenger RNA
MSM	:	Men who have sex with men
NPC1L1	:	Niemann–Pick C1-like 1
NTR	:	Nontranslated regions
OCLN	:	Occludin
ORF	:	Open reading frame
PCR	:	Polymerase chain reaction
PEG-IFN	:	Pegylated Interferon
PTX3	:	Pentraxin-3
RBV	:	Ribavirin
RTKs	:	Tyrosine kinases
SJS	:	Stevens - Johnson syndrome
SMV	:	Simeprevir
SOC	:	Therapy standard of care therapy
SOF	:	Sofosbuvir
SR-BI	:	Scavenger receptor B type I
SVR	:	Sustained virological response
TE	:	Treatment-experienced
TMA	:	Transcription-mediated amplification
TN	:	Treatment-naïve
TPV	:	Telaprevir
WHO	:	World Health Organization

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Introduction

Chronic hepatitis C (HCV) infection is a major worldwide public health problem. Worldwide, up to 170 million patients are chronically infected and are at risk of developing liver cirrhosis and hepatocellular carcinoma. ***(Shepard et al., 2005).***

Egypt has the highest prevalence of adult HCV infection in the world, averaging 15%-25% in rural communities. ***(Esmat et al., 2012).***

Infection with HCV causes chronic disease in 80% of cases and current treatments are not completely effective. ***(Garcia-Samaniego et al., 2013).***

The innate and adaptive immunity are both involved in defense against HCV infection. The innate immune system provides an immediate line of defense, triggering inflammation and playing a critical role in activating adaptive immunity. ***(Tarr et al., 2012).***

Innate immunity comprises both cellular and humoral components, including complement activation and involving complement C1q, Lectins, Collectins and Ficolins. These molecules activate the complement cascade, neutralize pathogens and recruit antigen presenting cells. Some studies reported that serum mannan-binding lectin (MBL) concentrations are increased in Egyptian chronic hepatitis C patients and related to disease progression and response to interferon-based antiviral therapy. ***(Esmat et al., 2012).***

Ficolin -2 is a kind of human serum complement lectins, which is implicated in innate immunity. Recent studies reported that early increased Ficolin-2

concentrations are associated with severity of liver inflammation and efficacy of antiviral therapy in chronic hepatitis C patients (non Genotype 4). Little is known about the relation of Ficolin-2 to severity of disease and response to interferon-based therapy in Egyptian chronic hepatitis C patients (Genotype 4). ***(Hu et al., 2013).***

Aim of the Work

This work aims to determine the dynamics of Ficolin-2 in Egyptian chronic hepatitis C patients: relation of serum concentration to severity of disease and response to antiviral therapy.

Chapter (1):

Hepatitis C Virus

Epidemiology

Hepatitis C is a disease of significant global impact. According to the World Health Organization there are about 150 million people chronically infected with hepatitis C virus (HCV). There are considerable regional differences: in some countries, e.g., Egypt, the prevalence is >10% ***(WHO, 2013).*** In Africa and the Western Pacific prevalence is significantly higher than in North America and Europe ***(CDC, 2013).*** It is estimated that there are 2-5million HCV-positive persons in Europe. Certain groups are preferentially affected, like injection drug users. In Europe and the United States chronic hepatitis C is the most common chronic liver disease. The majority of liver transplants performed in these regions are for chronic HCV. It is difficult to determine the number of new HCV infections, as most acute cases are not noticed clinically. Recent numbers from Europe still show an ongoing epidemic of acute HCV especially among intravenous drug users (IVDU) and men who have sex with men (MSM) ***(Rockstroh et al., 2012).***

Transmission

Parenteral exposure to hepatitis C is the most efficient means of transmission. The majority of patients infected with HCV in Europe and the United States acquired the disease through intravenous drug use or blood transfusion, which has become rare since routine testing of the blood supply for HCV began. The following possible

routes of infection have been identified in blood donors (in descending order of transmission risk):

1. Injection drug use
2. Blood transfusion
3. Sex with an intravenous drug user
4. Having been in jail more than three days
5. Religious scarification
6. Having been struck or cut with a bloody object
7. Pierced ears or body parts
8. Immunoglobulin injection

Very often in patients with newly diagnosed HCV infection no clear risk factor can be identified. Factors that may increase the risk of HCV infection include greater numbers of sex partners, history of sexually transmitted diseases, and failure to use a condom. Whether underlying HIV infection increases the risk of heterosexual HCV transmission to an uninfected partner is unclear. The seroprevalence of HCV in MSM (men who have sex with men) ranges from about 4 to 8%, which is higher than the HCV prevalence reported for general European populations, increasing globally over the last decade ***(Rockstroh et al., 2012).***

The risk of perinatal transmission of HCV in HCV RNA-positive mothers is estimated to be 5% or less ***(Ohto* et al., *1994).*** Cesarean section has not been shown to reduce transmission. There is no evidence that breast feeding is a risk factor. Hemodialysis risk factors include blood transfusions, the duration of hemodialysis, and the prevalence of HCV infection in the dialysis unit, and the type of dialysis. The risk is higher with in hospital hemodialysis vs. peritoneal dialysis. Contaminated medical equipment, traditional medicine rites, tattooing, and body piercing are considered rare transmission routes. There is