ANTINUCLEAR ANTIBODY POSITIVITY IN PATIENTS WITH CHRONIC HEPATITIS C: CLINICALLY RELEVANT OR AN EPIPHENOMENON ?

Thesis

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بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

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LIST OF ABBREVIATIONS

AASLD	:	American Association for the Study of Liver Diseases
ACAs	:	Anti centromere antibodies
AIH	:	Autoimmune hepatitis
AIHA	:	Autoimmune haemolytic anaemia
AITP	:	Autoimmune thrombocytopenia
ALT	:	Alanine transaminase
ANA	:	Antinuclear antibody
Anti-HBc	:	Antihepatitis B core
Anti-HBs	:	Antihepatitis B surface
Anti-HCV	:	Anti hepatitis C virus
AST	:	Aspartate transaminase
BOC	:	Boceprevir
cANCA	:	Antineutrophil cytoplasmic antibodies
CBC	:	Complete blood picture
CLD	:	Chronic liver disease
CTD	:	Connective tissue disease
DAA	:	Direct acting antiviral
ds DNA	:	Double-stranded Deoxyribonucleic acid.
EASL	:	European Association for the Study of the Liver

LIST OF ABBREVIATIONS (CONT.)

EHM	:	Extrahepatic manifestation
ELISA	:	Enzyme-linked immunosorbent assay
ENA	:	Extractable nuclear antigens
ESR	:	Erythrocyte sedimentation rate
HCC	:	Hepatocellular carcinoma
IASL	:	International Association for the Study of the Liver
IIF	:	Indirect immunofluorescence
INF	:	Interferon
INR	:	International Normalized. Ratio
LKMA	:	Liver kidney microsomal antibody
MC	:	Mixed cryoglobulinemia
NHL	:	Non-Hodgkin lymphoma
NOSAs	:	Non organ specific auto- antibodies.
pANCA	:	Perinuclear Anti-Neutrophil Cytoplasmic Antibodies
PBC	:	Primary biliary cirrhosis
PCR	:	Polymerase chain reaction.
RF	:	Rheumatoid factor
SLE	:	Systemic lupus erythematosus

LIST OF ABBREVIATIONS (CONT.)

SMA	:	Smooth muscle antibody
SS	:	Sjögren's syndrome
SS CL	:	Systemic sclerosis
SVR	:	Sustained virological response
WHO	:	World health organization

INTRODUCTION

The hepatitis C virus (HCV) is a major public health problem and a leading cause of chronic liver disease. An estimated 180 million people are infected worldwide **(Williams, 2006)**. Hepatitis C is an infectious disease primarily affecting the liver, chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years. In some cases, those with cirrhosis will go on to develop liver failure or other complications, including liver cancer or life-threatening esophageal varices and gastric varices **(Ryan and Ray, 2004)**.

Chronic hepatitis C is defined as infection with the hepatitis C virus persisting for more than six months based on the presence of its RNA. Chronic infections are typically without symptoms during the first few decades, and thus it is most commonly discovered following the investigation of elevated liver enzyme levels or during a routine screening of high risk individuals**(Kanwal and Bruce, 2011)**.

Several immunologic abnormalities, such as production of autoantibodies, like cryglobulins, are associated with HCV infection. Hepatitis C virus infection plays an

important role in the pathogenesis of the immunologic derangement **(Boyer and Marcellin, 2000)**.

Hepatitis C Virus infection frequently causes Organ-specific and non-specific autoantibodies (NOSA) were first described in autoimmune disorders, but many of them may also be found during other viral infections, Hepatitis C Virus (HCV) seems to be highly auto immunogenic because numerous autoantibodies have been detected in HCV-infected patients **(Chretien et al.,2009)** .

Antinuclear antibodies (ANA) and smooth muscle antibodies (SMA) are the most common non-organ-specific autoantibodies (NOSA) in patients with HCV related chronic liver disease (CLD) **(Peng et al .,2001)** .

Antinuclear antibody is one of the most frequently detected autoantibodies. The prevalence of ANA in HCV infected individuals ranges from 21% to 34%. Although ANA is the diagnostic hallmark of systemic lupus erythrematosus (SLE) and type 1 autoimmune hepatitis, its role in chronic HCV infection is unclear **(Peng et al., 2001)** .

The presence of serum ANA is associated with various factors including advancing age, genetic predisposition

environmental agents, oestrogen-androgen balance, chronic infection and neoplasm **(Hsieh et al., 2008)** .

In some studies ANA positivity had no observed effect on HCV clinical outcome. ANA positivity was associated with being in the group of patient exhibiting quicker progression of HCV fibrosis although this did not reach statistical significance . Associations of ANA positivity with non-response to therapy were not observed **(Yee et al., 2004)** .

AIM OF THE WORK

This work aims to study the frequency of occurrence of ANA in an Egyptian sample of patients with chronic hepatitis C virus infection as well its correlation with biochemical, histological and clinical features of the disease and their relation to antiviral therapy.