Study of the Prevalence of Antiphospholipid Autoantibodies in Chronic Hepatitis C Virus Infection and Its Relation to Portal Vein Thrombosis

> Thesis Submitted for partial fulfillment of Master degree of Internal Medicine

> > Bv

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Supervisors

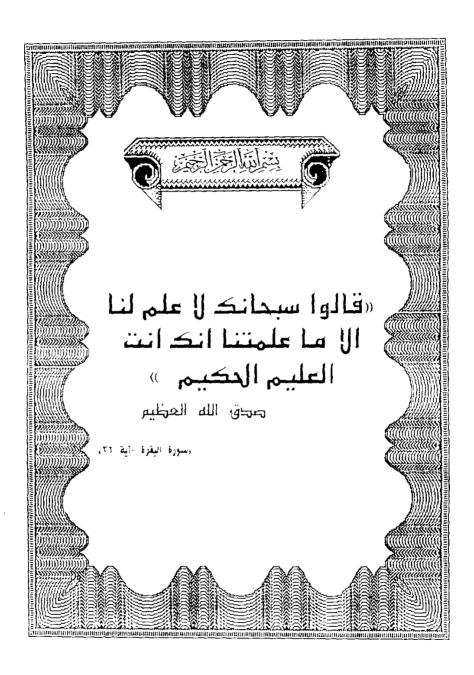
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### List of Abbreviation

A of a 1 of Not 1 to 1	
- Activated partial thromboplastin time	(APTT)
- Alanine aminotransferase	(ALT)
- American rheumatism association	(ARA)
- Anticardiolipin antibodies	(ACLA)
- Antiliver - kidney microsomol antibody	(Anti-LKM)
- Antinuclear antibody	(ANA)
- Antiphospholipid antibodies	(APLA)
- Antiphospholipid syndrome	(APS)
- Antismooth muscle antibody	(Anti-SMA)
- Antithrombin III	(AT-III)
- Autoimmune hepatitis	(AH)
- B2 glycoprotein -1	(B2-GP-1)
- Blood-pool spect imaging	(SPECT)
- Catastrophic antiphospholipid syndrome	(CAS)
- C-Reactive protein	(CRP)
- Cyclic DNA	(cDNA)
- Deep venous thrombosis	(DVT)
- Dermatomyositis	(DM)
- Dissiminated intravascular coagulopathy	(DIC)
- Enzyme immuno assay	(EIA)
- Enzyme linked immunosorbent assay	(ELISA)
- Euglobulin clot lysis time	(ECLT)
- Fulminant hepatic failure	(FHF)
- Gamma phospholipid unit	(GPL)
- Glomerulonephritis	(GMN)
- Glomerular basement membrane	(GBM)
- Guillian- Barre` syndrome	(GPS)
- Hepatitis virus (A,B,C,D,E,G)	(HV)
- Hepatocellular carcinoma	(HCC)
- Human leucocytic antigen	(HLA)
- Idiopathic portal hypertension	(IPH)
- Idiopathic thrombocytopenic purpura	(ITP)
- * * * *	*

- Immunoglobulin (lg)- Interferon alpha (IFN∞) - Interferon gamma (IFNy) - Interleukin (IL) - Interferon (IFN) - Lupus anticoagulant (LAC) - Non-A, non-B hepatitis (NANBH) - Platelet activating inhibitoy factor (PAI1) - Polymerase chain reaction (PCR) - Polymyositis (PM) - Porphyria cutenia tanda (PCT) - Portal vein thrombosis (PVT) - Primary antiphospholipid syndrome (PAPS) - Prostacycline (PGI2) (RIA) - Radioimmuno assay (RIBA) - Recombinant immunoblot assay - Rheumatoid artheritis (RA) - Systemic lupus erythematosus (SLE) - Thromboxan (TXA2) - Tissue factor (TF) (VDRL) - Venereal disease research labratory

#### ACKNOWLEDGMENT

I would like to express my sincere thanks, deepest gratitude and appreciation to prof. Dr. Mohamed Kamel Sabri, professor of internal medicine and immunology, Ain Shams University, who offered me the generous support and many useful criticisms and suggestions throughout this work. His precious guidance and continued supervision which were kindly given are far beyond acknowledgment.

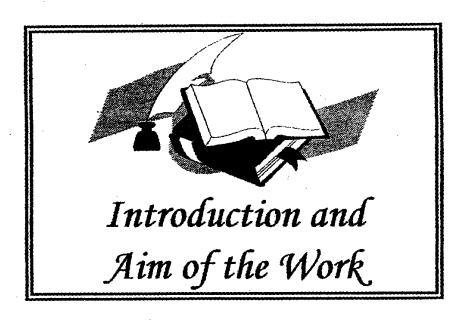
I am honored to express my sincere thanks and deepest gratitude to **Dr. Abd El- Rahman Abd- El- Hamid Soliman**, Assis. Prof. Of internal medicine and immunology, Ain Shams University, for his kind continued supervision, cordial support. most appreciable advice and great help that have contributed a lot to conduct this work to that term. His close continued supervision is beyond acknowledgment.

I am deeply grateful to **Dr. Shahira Mohamed Fathy El-Fedawey**. Lecturer of clinical Pathology & immunology, Ain Shams university for her kind great help, cooperation and close guidance in the practical part of this work.

I wish to express my sincere thanks to **Dr. Maged Abd-El Kariem**. lecturer of community and statistical medicine, Ain Shams University for his valuable kind help in the statistical part of this work.

To all my respectable colleagues and members of internal medicine department in **Dar El- Shifa Hospital**, (ministry of health), to whom I belong, I am deeply grateful.

To all the nursing staff in Dar El-Shifa Hospital, who did help in collecting samples for performance of this work, as well as my patients, I am quiet grateful.



### Introduction

Anticardiolipin autoantibodies are strongly associated with recurrent spontaneous abortions, thrombocytopenia, and thrombotic events including deep venous thrombosis with or without pulmonary embolism, portal or hepatic vein thrombosis, and large vessel arterial occlusions (Mackworth - Young et al; 1989).

The combination of persistantly positive antiphospholipid test results with any of these clinical manifestations is known as the antiphospholipid antibody syndrome. This syndrome which can be part of the clinical spectrum of systemic lupus erythematosus, can also occur in patients with connective tissue diseases. and for these cases the term primary antiphospholipid syndrome has been suggested (Harris et al; 1987).

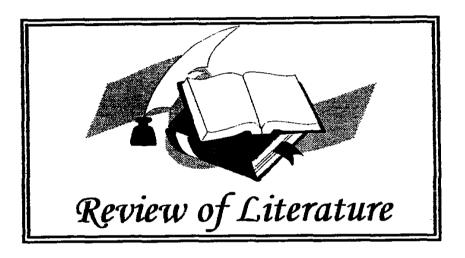
Anticardiolipin autoantibodies have been detected in a variety of infectious diseases, particularly of viral origin, such as human immuno-deficiency virus infection, mumps and hepatitis A. However there is only few data concerning the prevalence, of anticardiolipin autoantibodies in hepatitis C virus infection, which is a process associated with the presence of serum autoantibodies, such as, antinuclear, antimitochondrial, anti-smooth muscle, and liver- kidney microsomal antibodies (McNeil et al; 1991and Prieto et al; 1996).

Although thrombosis is rare in liver cirrhosis, portal vein thrombosis may occur in up to fifth of patients with liver

cirrhosis and the pathogenesis of it is not known (Viola et al; 1994).

#### Aim Of The Work

Evaluation of the prevalence of anticardiolipin autoantibodies in chronic HCV infection and its relation to portal vein thrombosis.



### Hepatitis Viruses

So far, the hepatitis A,B,C,D and E viruses and, most recently, the hepatitis GB viruses A,B, and C. The latter also termed hepatitis G (HGV), have been identified, and there will be others. Hepatitis F has been tentatively reserved for a non-A to E virus associated with fulminant hepatitis (*Dusheiko*; 1996).

one way to group the hepatitis viruses is by their route of transmission. An enteral, i.e. foeco-oral route of transmission is characteristic for the non-enveloped, hepatitis A and E viruses. The hepatitis A virus (HAV) is a picorna virus of 27 nm and hepatitis E virus (HEV), an RNA virus of similar size (27-30 nm), which is closely related to the calcivirus family. Both of these viruses can cause acute hepatitis, in the case of HEV infection of pregnant women even fatal hepatitis, but are never associated—with chronic hepatitis and liver cirrhosis (Krawczynske: 1993).

Parenteral transmitted viruses are the hepatitis B,C and D viruses and the group of recently identified GB viruses. They are enveloped viruses and their lipid envelop, preclude the passage of viable virus from the liver through the biliary system to the intestinal tract which prevent foeco-oral transmission (*Lemon and Thomas*, 1997). With the exception of hepatitis D virus (HDV), which depends on the envelop proteins of the hepatitis B virus (HBV), to maintain its life cycle, this group consists of the main agents responsible for blood transfusion-associated hepatitis. Although they are all capable of inducing acute as well as chronic hepatitis, and hepatocellular

carcinoma, their molecular and biological characterisites differ considerably.

HBV is classified as a hepadnavirus, it is 42 nm double shelled DNA virus

HDV is a very small 36 nm RNA particles, it is not able to replicate on its own, but is capable of infection when activated by the presence of HBV.

HCV is a single stranded RNA virus, 50-60 nm size and is related to the group of together and flaviviridae (*Choo, et al;* 1989).

The newly identified hepatitis GB viruses A,B, and C (HGBV-A, HGBV-B, and HGBV-C) are RNA viruses, placed in the flaviviridae family, as they show less than 25% sequence homology with HCV and other members of this family. HGBV-A and HGBV-B are probably tamarin viruses and HGBV-A and HGBV-B are probably tamarin viruses and HGBV-C is a human one (Leary et al; 1996). Another recently identified agent, hepatitis G virus (HGV), was cloned from a patient with community acquired chronic hepatitis whose plasma had transmitted hepatitis to tamarin monkeys. Sequence of HGBV-C and HGV are more than 95% homologus, that is why they are considered to be closely related isolates of the same virus (*Linnen et al; 1996*)