Study Of Anticardiolipin Antibodies In Chronic Active Hepatitis

Thesis
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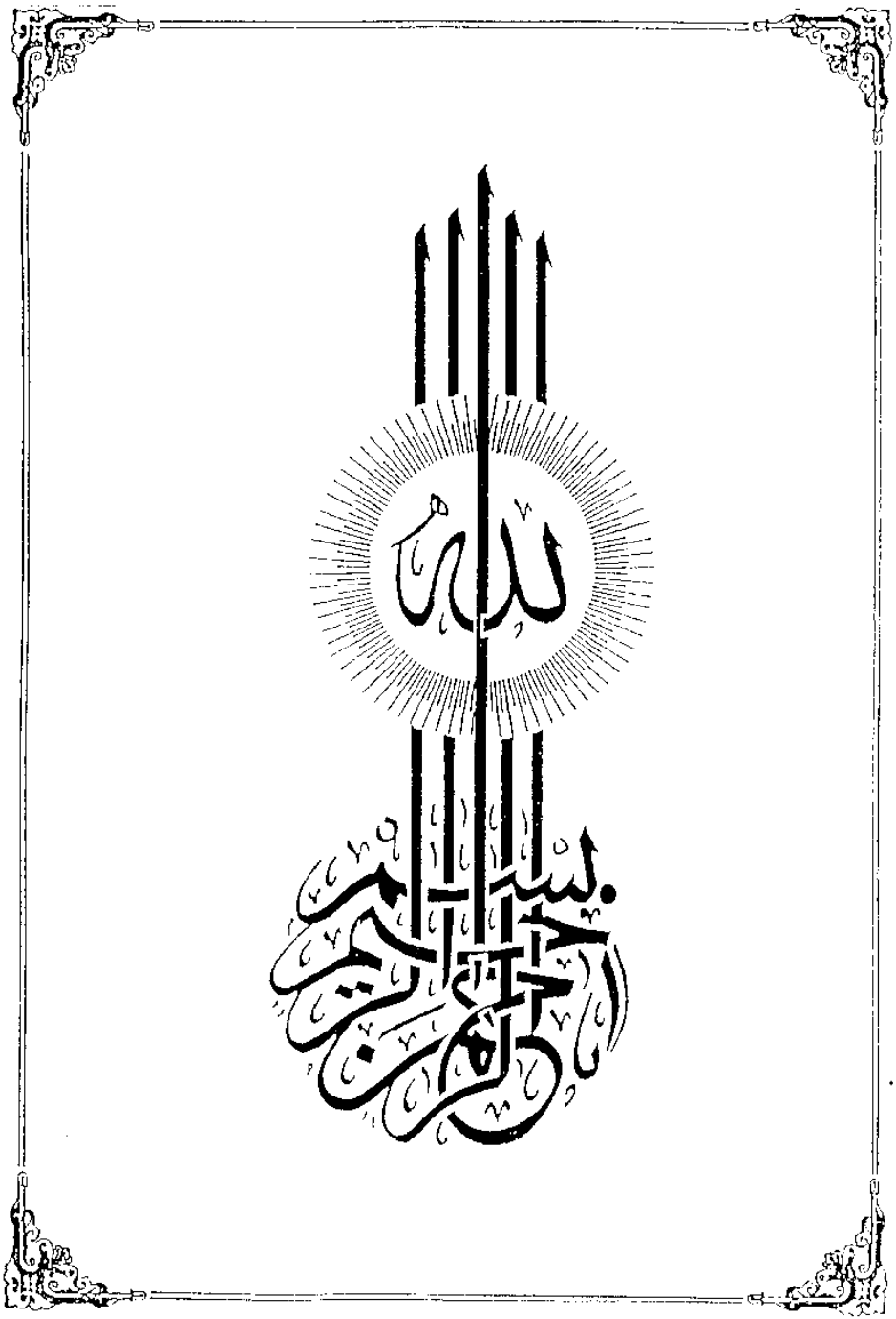
List of abbreviations

Abbreviation	Full name
Ab	Antibody
ACLA	Anticardiolipin antibody
ADCC	Antibody dependent cellular cytotoxicity
ADP	Adenosine diphosphate
αFP	Alpha feto-protein
Ag	Antigen
AI-CAH	Autoimmune chronic active hepatitis
ALP	Alkaline phosphatase
AMA	Anti-mitochondial antibody
ANA	Anti-nuclear antibody
APLA	Antiphospholipid antibody
APS	Antiphospholipid syndrome
APTT	Activated partial thromboplastin time
ASMA	Anti-smooth muscle antibody
CAH	Chronic active hepatitis
CAS	Catastrophic antiphospholipid syndrome
CPH	Chronic persistent hepatitis
DIC	Dissiminated intravascular coagulopathy
DM	Diabetes mellitus
DNA	Deoxyribonucleic acid
DVT	Deep venous thrombosis
ELISA	Enzyme-linked immunosorbant assay
G-PL	G-phospholipid
H & E	Haematoxline and eosin
HBcAb	Hepatitis B core antibody
HBcAg	Hepatitis B core antigen
HBeAb	Hepatitis B e antibody
HBeAg	Hepatitis B e antigen
HBsAb	Hepatitis B surface antibody
HBsAg	Hepatitis B surface antigen
HBV-DNA	Hepatitis B virus deoxyribonucleic acid
HCV	Hepatitis C virus



HCV RNA	Hepatitis C virus ribonucleic acid
HIV	Human immundeficiency virus
HLA	Human leukocyte antigen
IDDM	Insulin dependent diabetes mellitus
IgG-ACLA	Immunoglobulin G anticardiolipin antibody
IgM-ACLA	Immunoglobulin M anticardiolipin antibody
IL_2	Interleukin-$_2$
ITP	Immune thrombocytopenic purpura
LA	Lupus anticoagulant
LMP	Liver membrane protein
LSP	Liver soluble protein
M-PL	M-phospholipid
PAPS	Primary antiphospholipid syndrome
PCR	Polymerase chain reaction
PGI_2	Prostaglandin I_2
PT	Prothrombin time
SGPT	serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic-puruvate transaminase
TIAs	Triansient ischemic attacks
TTP	Thrombotic thrombocytopenic purpura
TXA_2	Thromboxane A_2
VDRL	Venereal disease research laboratory

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Introduction :-

The disturbed blood coagulation in patients with chronic liver disease is particularly complex and multifactorial and depends on the balance between hepatic synthesis and clearance of activated coagulation proteins and their inhibitors, the presence or absence of dysfibrinogenaemia, thrombocytopenia, abnormal platelet function and DIC ***(Kelly et al., 1986).***

Abnormalities in platelet number, structure and function are common with all forms of liver disease. They are mainly related to increased splenic pool ***(Sherlock and Dooley, 1993).*** Furthermore, there are few reports of the presence of platelet antibodies (IgG) in patients with chronic active hepatitis ***(Pfueller et al., 1983).***

The presence of antiphospholipid antibodies in various liver disease has been reported by many authors. Vascular hepatic lesions, liver cirrhosis, hepatomas and chronic active hepatitis have been reported to be associated with antiphospholipid antibodies ***(Mackworth-Young et al., 1986).***

Aim of the Work :-

The aim of this study is the determination of anticardiolipin antibodies, and platelet aggregation with ADP in patients with chronic active hepatitis in an attempt to study the relation between them and their impact on the disease status.

Review of Literature

THE BLOOD PLATELETS

Blood platelets are small discoid non-nucleated cytoplasmic fragments of megakaryocytes. That are derived from pleuripotential stem cells in the bone marrow ***(Wright, 1966).***

Functional anatomy of blood platelets :

Blood platelets are the smallest formed bodies in the blood and they are non-nucleated fragments of megakaryocytes, the largest of all haemopoietic cells which are derived from pleuripotential stem cells in the bone marrow, that is derived from committed progenitor cells. The latter is directed to a unilinear megakaryocytic stem cell, the megakaryocytic colony forming unit (CFU-M). The CFU-M proliferate into diploid megakaryocyte precursors, the megakaryoblasts, the earliest precursors of megakaryocytes. At some point, the diploid megakaryocyte precursors lose the capacity for cell division and acquire the capacity for endoreduplication of DNA. This phenomenon is unique to megakaryocytic lineage. The cells undergo an unusual form of mitosis in which the DNA, but not the cell itself, divides, and with each nuclear division, there is increased membrane formation and increased maturation of the cytoplasm with the appearance of all the characteristic features of the platelets themselves ***(Hutton et al., 1989).*** The increased membrane is accompanied by progressive invagination of the membrane that forms the demarcation membranes of the individual platelets. The final stage of development is the platelet-releasing mature megakaryocytes. Those extend pseudopodia through the walls of marrow sinusoids and either

individual platelets or larger fragments of the cytoplasm are broken off, the latter being carried in the blood stream to the lungs where the final breakdown to individual platelets is completed mechanically in the pulmonary circulation. The fully mature megakaryocyte may give rise to as many as 3000 platelets ***(Hutton, 1989).***

Platelets circulate in the blood for an average of 8-10 days and during this period they undergo changes in both biochemical composition and function. There is progressive reduction in proteins, phospholipids, cholesterol, ATP, enzymes and membrane-glycoproteins ***(Karpatkin et al., 1972).*** Young platelets generally show greater functional capacity as the ability to aggregate in response to collagen. The biochemical and functional changes that occur in platelets during aging are probably related to their eventual removal by reticuloendothelial system in the liver and the spleen which is, like that of the red cells, age related rather random process ***(Harker, 1978).***

The ultrastructure of the blood platelets :

To relate structure to function, the electron microscopic anatomy of the platelets can be considered under 4 basic divisions :

I- The Peripheral Zone :

It is the physical barrier that protects the platelet interior from the surrounding plasma. It consists of an exterior coat, a trilaminar or unit plasma membrane and a submembrane region containing specialized filamentous elements. The peripheral zone has an important role in platelet function. It maintains platelet integrity; provides receptor sites for

various stimulant and inhibitory agents; it is responsible for platelet immunological specificity; it mediates platelet-platelet and platelet-surface interactions, and finally it provides a phospholipid surface for blood coagulation.

(a) The exterior coat :

It is the outermost layer of the peripheral zone and in direct contact with plasma.

(b) Plasma membrane :

It is a trilaminar membrane about 7-9 nm in thickness. It consists mainly of a phospholipid bilayer with randomly dispersed transmembrane protein components ***(White, 1985).*** In addition to protecting the integrity of the platelets, it also contains enzymes that are involved in membrane transport and c-AMP metabolism. Also, it plays an important role in platelet adhesion ***(Silver, 1965)***; contraction and in supplying a lipid activator for blood coagulation ***(Marcus et al., 1966).***

(c) The submembrane region :-

Chemical and hypotonic stresses revealed submembrane filaments closely associated with the under side of the inner layer of the lipid bilayer ***(White, 1969).*** Also, actin-binding protein and actinin, another platelet contractile protein, have been identified in close association with the undersurface of the plasma membrane ***(Schollmeyerand White, 1971).***

II- The Sol-Gel Zone :-

This zone comprises the viscous matrix inside the platelet. It is composed mainly of proteins assembled into fibrous elements. Three different fiber systems can be identified which differ only in their state of polymerization and site in the cell, the submembrane filament, the microtubules, and the microfilaments ***(Nachmias et al., 1980).***

(a) The submembrane filaments :

They are involved in maintaining the platelet discoid shape, pseudopod formation and clot retraction.

(b) The microtubules :

They form a circumferential band located in the equatorial planes just beneath the cell wall in the resting platelet. They are formed of tubulin, polymerized into a coiled tubules of approximately 250 A in diameter ***(White, 1968).*** They function as both cytoskeleton for the platelet ***(White, 1967)*** and intrinsic contractile apparatus ***(Behnke et al., 1967).***

(c) The microfilaments :

They are present in platelet cytoplasm and formed of contractile protein thrombosthenin (platelet actomycin). They are about 50 A in diameter and are essential element of the platelet contractile mechanism ***(Zucker and Grusky, 1972).***