HEPATITIS C VIRUS IN HAEMODIALYSIS PATIENTS

THESIS

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BY

SAHAR MOHAMED FIKRY LOTFY
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SUPERVISED BY

PROF. DR. OSAIMA EL-SAYED SELIEM
PROFESSOR OF CLINICAL PATHOLOGY

PROF. DR. ABDEL RAHMAN EL-ZAYADI
PROFESSOR OF TROPICAL MEDICINE

DR. MONA MOHAMED RAFIK
ASSISTANT PROFESSOR OF CLINICAL PATHOLOGY

AIN SHAMS UNIVERSITY
FACULTY OF MEDICINE
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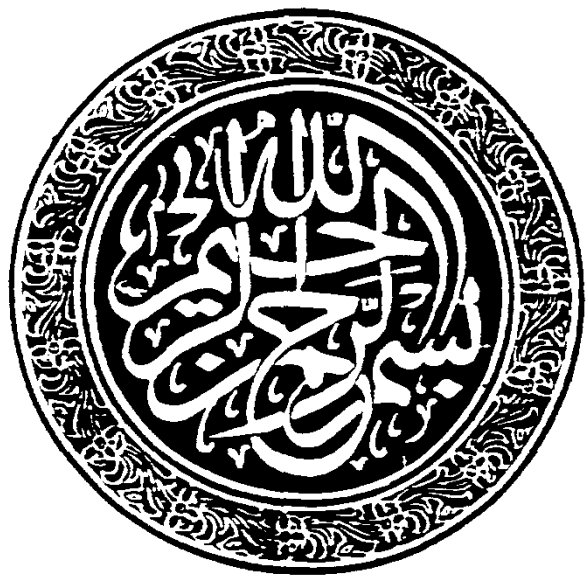

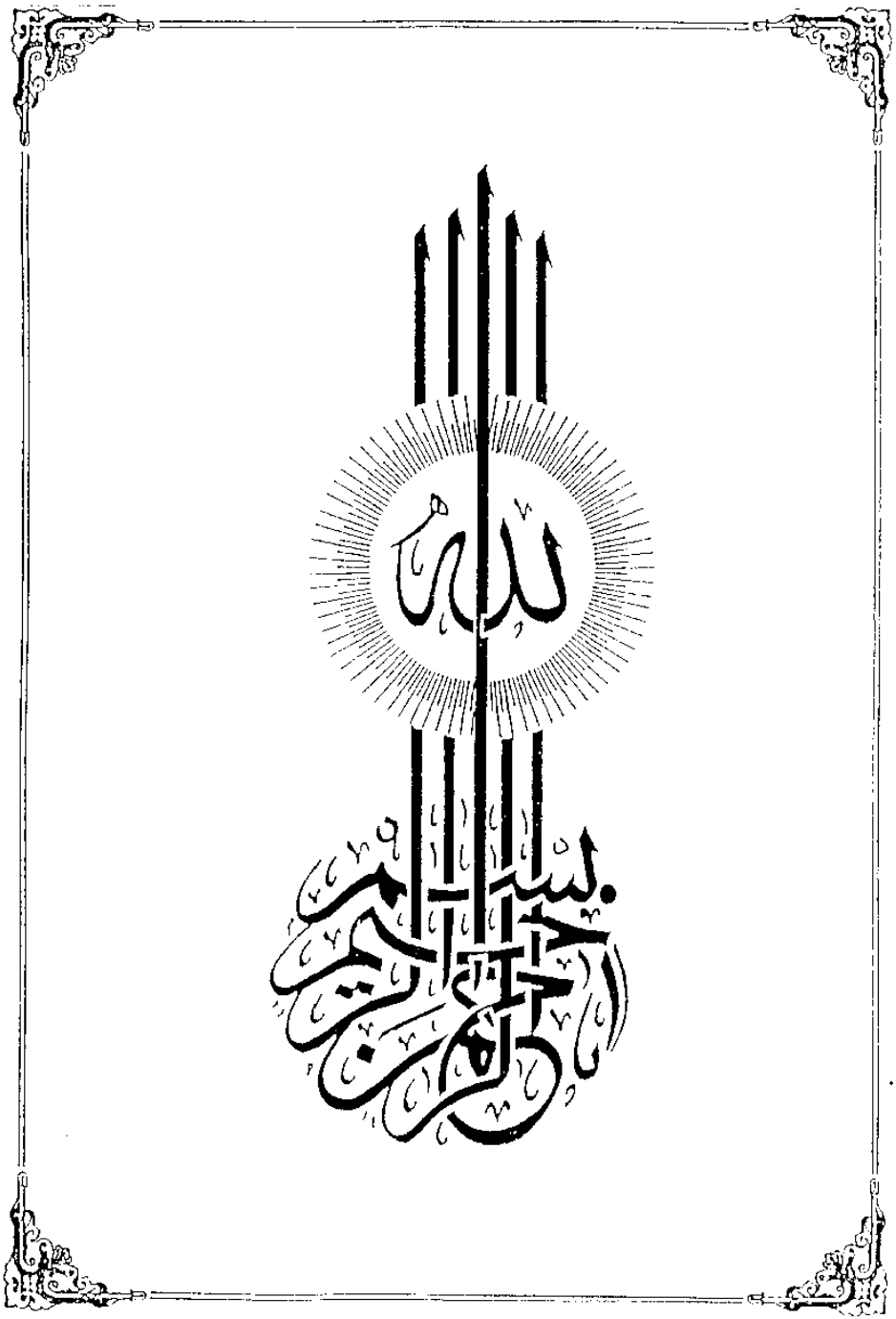

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List Of Abbreviations

ALT	alanine aminotransferase
BUN	blood urea nitrogen
CAH	chronic active hepatitis
CMV	cytomegalo virus
CPH	chronic persistant hepatitis
ANA	deoxyribonucleic acid
EBV	Epstein- Barr virus
ELISA	enzyme linked immunosorbant assay
HAV	hepatitis A vitus
HB_c	hepatitis B core
HB_sAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HDV	hepatitis D virus (the delta virus)
HIV	human immundiffiency virus
IgG	immunoglobulin G
NANB	non-A, non-B
PCR	polymerase chain reaction
RIA	radioimmunassay
RIBA	recombinant immuno blot assay
RNA	ribonucleic acid
TAH	transfusion- associated hepatitis
X^2	chi-square

INTRODUCTION AND AIM OF WORK

INTRODUCTION

Hepatitis C virus (HCV) is a lipid-enveloped small single stranded RNA virus of approximately 30-60 nm. in diameter. It is of the togavirus or flavivirus category (Bradley, 1985).

An antigen has been synthesized which is now being used to screen the HCV antibody by Radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA) in clinical cases. Anti-HCV antibodies seem to be a reliable marker For its diagnosis (Kuhnl et al., 1989).

There are two distinct types of HCV. One is transmitted parenterally, while the other is sporadic or community acquired. Vertical, mother-to-child transmission, has also been reported (Zuckerman, 1988).

Hepatitis C is the most common infectious disease transmitted by blood transfusion. It affects recipients of both red cells and plasma products. HCV accounts for at least 90-95% of transfusion associated hepatitis in USA (Zuckerman, 1989).

Chronic hepatitis C develops in approximately 50% of infected individuals (Alter, 1988), approximately 20% of those with chronic hepatitis have histologic evidence of

cirrhosis (Colombo et al., 1889). It is suspected that HCV may have an important role in the development of some cases of hepatocellular carcinoma (Barrera et al., 1989).

With the recent discovery of the virus, the epidemiology of hepatitis C in Egypt, as in many other countries, is currently being investigated.

Haemodialysis patients belong to the high rist group for acquiring hepatitis C virus infection. The prevalence in different dialysis units in Western countries ranged from 0% to 37% (Schlipkoeter et al., 1990).

AIM OF WORK

The present work aims to study the prevalence of HCV in high risk haemodialysis patients, in Egypt.

REVIEW OF LITERATURE

The term "hepatitis means liver inflammation. In practice it is used for clinical liver diseases in which an essentially reversible inflammatory reaction is localized primarily in or around the portal tract (De Groote, 1979).

Several viral etiologic agents are capable of inducing the disease, the best known of which are hepatitis A virus (HAV), hepatitis-B virus (HBV), hepatitis-D virus (HDV) and non-A,non-B hepatitis viruses (NANB) (recently called hepatitis C (Choo et al., 1989)).

HISTORICAL ASPECTS

Although NANB hepatitis was extremely difficult to diagnose because it lacked easily identified markers, the illness had distinct clinical and epidemiologic characteristics (Zuckerman, 1989).

NANB hepatitis was originally considered a transfusion-related disease, perhaps as another variant of hepatitis B. Recently, however, epidemiologic studies established its occurrence more frequently outside the transfusion settings. Intravenous drug users have displayed particular risk and comprise the largest known group of infected individuals (42%) (Zuckerman, 1989). Additionally, direct person-to person transmission by intimate or sexual contact has been implicated (Esteban et al., 1989), and HAV- like epidemics

have been reported in Asia, Africa, Mexico, Russia, and the Indian subcontinent. Moreover, approximately 40% of cases have no identifiable origin (Maddrey et al., 1990).

Although the epidemiologic and clinical differences between this and other forms of hepatitis were apparent, the advent of specific serologic tests for HBV and HAV identified the separate and distinct nature of this form of hepatitis.

The early tests for B surface antigen (HBsAg) and the later, more sensitive radioimmunoassays (RIA) which were employed to screen the nation's blood supply failed to produce the expected elimination of transfusion-associated hepatitis.

Furthermore, serologic analysis for anti-HBs in transfusion-associated hepatitis patients demonstrated that many of these individuals had not been exposed to the B virus. These findings led some physicians to believe that HAV was the infective agent in many of these cases, even though the epidemiologic profiles did not match. However, with the HAV antibody testing, this belief was dispelled in 1973.

Of the numerous well-documented cases of non-B, transfusion-associated hepatitis, none could be serologically related to the A virus. Thus, the diagnosis was made by exclusion, establishing non-A,non-B hepatitis as a distinct and

separate entity Stevens et al., 1984

Finally in 1989 with the isolation and cloning of the actual agent, the specific diagnosis of viral C hepatitis was established Alter, 1990

NON-A, NON-B / HCV

Discovery of Virus C:-

The virus(es) causing the parenterally transmitted form of non-A,non-B hepatitis have not been fully characterized, and their mode of replication and antigenic composition were not clear up till now, despite intensive efforts in many laboratories throughout the world. There is no homology between the viruses causing hepatitis A and B, the delta hepatitis virus and the enterically and parenterally transmitted non-A,non-B virus (Zuckerman, 1989).

A claim to have identified the last of these viruses came in the form of a news release by the Chiron Corporation, based in California, followed by a press conference in Washington in May 1988. This described the identification, cloning, and expression of proteins from the virus. However to the intense disappointment of the medical and scientific community, no scientific publication appeared until nearly a year later.

Choo et al., derived a random primed complementary DNA from infectious plasma known to contain the non-A,non-B agent using a construct in the bacteriophage λ gt 11 (Choo et al., 1989). This phage vector permits efficient

expression of polypeptides encoded by complementary DNA and was designed originally by Young and Davis to help isolate complementary DNA clones by well characterized antibodies that bind to clones synthesizing the polypeptides of interest (Young & Davis, 1983). The infectious plasma was ultracentrifuged to make a pellet from which a putative small virus, and nucleic acid was recovered. Since the nature of the genome of the virus was not known, the nucleic acid was denaturated before synthesizing complementary DNA from both RNA and DNA with random primers of reverse transcriptase (Fig. 1).

About a million clones were screened. One was found to produce a protein that reacted with the serum of a patient with chronic non-A,non-B hepatitis, which was presumed to contain antibodies to the virus. The 155 base pair insert in this clone was then cut and used as a hybridisation probe to the original library of complementary DNA, and a larger overlapping clone with 353 base pairs was extracted. This double stranded cloned DNA did not hybridise to host cell DNA or to DNA derived from plasma or liver infected with non-A,non-B hepatitis. One of the strands hybridised specifically to RNA from infected liver, however, and was shown to be homologous to a single stranded RNA in the original pellet obtained by ultracentrifugation of infectious plasma. These and other data indicated that the