

HEPATITIS C VIRUS (HCV)
AMONG EGYPTIAN BLOOD DONORS

THESIS

SUBMITTED FOR PARTIAL FULLFILMENT OF MASTER DEGREE
IN CLINICAL AND CHEMICAL PATHOLOGY

By

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M.B., B.CH. [1986]

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List of Abbreviations.

ALT	Alanine Aminotransferase.
AVH	Acute Viral Hepatitis.
CAH	Chronic Aactive Hepatitis.
CMV	Cytomegalovirus.
CPH	Chronic Persistant Hepatitis.
DNA	Deoxyribonucleic Acid.
EBV	Epstein-Barr Virus.
ELISA	Enzyme Linked Immunosorbant Assay.
HAV	Hepatitis A Virus.
HBC	Hepatitis B core.
HBV	Hepatitis B Virus.
HCV	Hepatitis C Virus.
HIV	Human Immundeficiency Virus.
NANBH	Non-A, non-B Hepatitis.
PCR	Polymerase Chain Reaction.
PTH	Post-Transfusion Hepatitis.
RIBA	Recombinant Immunoblot Assay.
RNA	Ribonucleic Acid.
YFV	Yellow Fever Virus.

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INTRODUCTION AND AIM OF WORK

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Introduction

Infection with hepatitis C virus presents a special challenge to physicians, because it is frequently asymptomatic in both acute and chronic infection. This hampers any policy of medical intervention to deal with the disease (Hoofnagle, 1990).

Hepatitis C virus (HCV) is one of Non-A, non-B hepatitis viruses. It is a lipid enveloped small single stranded RNA virus of approximately 30-60 nm in diameter. It belongs to togavirus or flavivirus category (Hollinger, 1990).

There are 2 distinct types of HCV, one is transmitted parenterally, while the other is sporadic or community acquired. Sexual, vertical (mother to child transmission) has also been reported (Zuckerman, 1989). Non-A, non-B accounts for a substantial proportion of hepatitis cases among patients with frequent parenteral exposure to blood ^{et al.} (Esteban, 1989).

Around 80% of patients with chronic HCV do not have any serious problems, although they may have abnormal liver tests. Difficulty arises with the other 20% of patients who end up with severe problems as cirrhosis, and hepatocellular carcinoma (Hoofnagle, 1990).

In the past, a variety of imperfect surrogate tests have been tried in order to identify the units of blood capable of NANB hepatitis transmission. Recently, a recombinant hepatitis C ELISA test has been approved which detects antibodies to HCV in blood. This test is being used by blood banks and labs to identify post-transfusion and spontaneous NANB cases (Lee, 1991).

Aim of our work

To assess the prevalence of HCV among Egyptian blood donors.

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REVIEW OF LITERATURE

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1- Hepatitis C Virus

Historical Aspects:

For many years, it was presumed that at least two unknown viruses cause post-transfusion hepatitis (PTH), which can eventuate in cirrhosis (Lee, 1991). Since the development of diagnostic tests for hepatitis A (HAV) and B (HBV) viruses in 1975, it was apparent that most cases of PTH are not caused by these agents or any other known hepatotropic virus such as Cytomegalovirus (CMV) or Epstein-Barr virus (EBV). Hence, it was ^{termed} non-A, non-B hepatitis (NANBH) (Knodell et al, 1975)

Additional studies indicated that the agent(s) of NANBH caused 90% of PTH and were transmitted primarily by the percutaneous route. Other studies indicated that 1-7% of healthy blood donors might be infective and that there was a correlation between the presence of elevated serum alanine aminotransaminase (ALT) level and antibodies to HB core antigen (Anti-HBc) in the donor and the risk of NANBH developing in the recipient (Wick et al, 1985).

Recently, however, epidemiologic studies established the occurrence of NANBH more frequently outside the transfusion settings. Intravenous drug users have displayed particular risk and comprised 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). Moreover, approximately 40% of cases have no identifiable origin (Maddrey et al, 1990).

The cloning of an agent designated hepatitis C virus (HCV), from the plasma of a chronic NANBH chimpanzee led to the development of a recombinant antigen (C 100-3), which was used in an assay to identify antibodies to HCV (anti-HCV) (Bradley et al, 1985). Initial studies detected anti-HCV in 0.2-1.2 % of random blood donors (in USA, Europe and Japan), 15-25 % of acute NANBH patients and 67-85 % of chronic NANBH patients (Choo et al, 1989). Individual blood or plasma donors or patients (based on clinical evaluation) may be tested for anti-HCV. The ABBOTT HCV Enzyme Immuno Assay (EIA) detects antibodies to protein expressed by the C100-3 clone region of HCV genome. The presence of these antibodies indicates that the individual (donor or patients) has been infected with HCV, may harbor infectious HCV, and may be capable of transmitting NANBH. Finally, in 1989, with the isolation and cloning of the actual agent, the specific diagnosis of viral C hepatitis was established (Alter, 1989).

Physico-chemical characterization of Non-A, Non-B hepatitis Viruses:

It has been well documented that chloroform 10 % inactivate NANB viruses (Feinstone et al., 1983; Bradley et al., 1985).

In addition, heating serum at 100°C for 5 min (Yoshizawa et al., 1982) and at 60°C for 10 hours (Tabor and Gerety 1982) apparently are sufficient to inactivate small quantities of NANBH agents. However, Purcell and Coworkers (1985) showed that heating to 60°C for 30 up to 72 hours in the lyophilized state did completely prevent NANBH transmission. However, when a dry- heated factor VIII was administered to humans, Colombo and Coworkers, (1985) demonstrated that 11 of 13 developed NANBH.

Schimpf et al., (1987) demonstrated that material heated in solution in the presence of glycine and sucrose caused neither Hepatitis B nor NANBH.

More complete inactivation occurs following the use of :

- a) A combination of β -propiolactone and ultraviolet irradiation, with or without lipid solvents or detergents (Prince et al., 1986).
- b) More recently, attention has been focused on the use of an organic solvent such as tri-(n-butyl)-

phosphate (TNBP), in combination with the detergent sodium cholate (Prince et al., 1986).

- c) Steam-heat or pasteurization (Schimpf et al., 1987).
- d) Prolonged storage at room temperature resulted in a reduction in detectable HCV-RNA concentrations of more than 3 log, whereas freezing and thawing caused a half-log reduction (Farci et al., 1991).

HCV:-

Hepatitis C virus has been identified by recombinant gene technology as one of the causative agents of NANBH (Kuo et al., 1989). HCV is 30-60 nm in diameter. It has a lipid containing envelope that is essential to its replication (chloroform-sensitive), and has a RNA genome. Evidence that it is a RNA virus, was based on hybridization of the cloned cDNA with total RNA, but not DNA, extracted from infectious liver. The signal was lost following treatment with ribonuclease but not with deoxyribonuclease. Hybridization also occurred with the nucleic acid extracted from the pelleted starting material. The RNA is a single-stranded genome of at least 10,000 nucleotides (Hollinger, 1990).

The nucleotide sequence of the genomic RNA was determined by isolating overlapping cDNA clones using hybridization probes based on the sequence of previous