Assessment of Thyroid dysfunction in patients with chronic viral hepatitis (B and C) in Egypt

Thesis

Submitted for the partial fulfillment of Master Degree
In Tropical Medicine

BY

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M.B.B.CH

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Introduction:

Thyroid dysfunction (TD) represents an extrahepatic manifestation of chronic hepatitis C (CHC). Moreover, the currently approved treatment of CHC is often associated with TD ***(Vezali et al., 2009).*** However, it remains debatable if TD is mainly virus- or treatment-related.

HCV is a major cause of chronic liver disease. HCV infection frequently leads to chronic hepatitis with increasing risk of developing liver cirrhosis and HCC ***(Wang-Sheng et al., 2005).*** HCV is a global health problem, with an infection rate of 3% of the world population ***(WHO, 2009).***

Egypt has the highest prevalence of hepatitis C in the world reaching 13% of the population ***(Deuffic-Burban et al., 2006; Mohammed, 2004).***

HCV is both a hepatotropic as well as a lymphotropic virus and its chronic infection is known to be responsible for both hepatic and extrahepatic diseases ***(Zignego and Craxì, 2008).***

A high prevalence of thyroid autoimmunity and hypothyroidism ***(Antonelli et al., 2004),*** as well as of papillary

thyroid carcinoma ***(Antonelli et al., 2006),*** has been reported in patients with chronic HCV infection.

HBV infection can be self limited or chronic. Hepatitis B is a serious liver infection that is usually spread through contact with blood and/or body fluids of some one who has the infection, also hepatitis B can be transmitted from unprotected sexual contact with an infected partner. People who use IV drugs can get hepatitis B when they share needles with some one who has the virus ***(American Academy of family physicians 2010).*** However, in most reports, no comparison has been made between TD in chronic HCV infection and hepatitis B. Autoimmune phenomena against the thyroid gland in patients with HBV infection are not well understood.

Antonelli et al. (2004) found that patients with chronic hepatitis C were more likely to have hypothyroidism (13%), anti-thyroglobulin antibodies (TgAb 17%) and antithyroperioxidase antibodies (TpoAb 21%) than individuals in any control group.

Antonelli et al. (2006) found that prevalence of various thyroid disorders and serum antithyroid bodies were generally higher in patients with chronic hepatitis C than in those with hepatitis B.

The relationship between chronic liver diseases and TSH hormone are debated. Particularly, no defined data are available about TSH hormone level in viral liver disease patients.

In the present study, the level of TSH will be assessed in patient with chronic viral hepatitis (B and C).

AIM OF WORK:

This study aims to :

1- Assess the frequency of thyroid dysfunction in Egyptian patients with chronic viral hepatitis (B and C).

2- Evaluate the value of anti thyro globulin and thyroproxidase antibodies in early diagnosis of subclinical hypothyrodism in Egyptian patients with chronic viral hepatitis (B and C).

Patients and methods:

Patient Recruitment:

- **Study Design:** This is a Cross Sectional Study.

- **Study Setting:** Eighty (equally divided) chronic viral hepatitis (B and C) patients will be selected. This work will be carried on patients attending in outpatient clinic of Tropical Medicine Department Ain-Shams university and Professor Doctor Yassin Abdel Gaffer Charity Center for Liver Disease and Research.

- **This study will be carried on** (80) patients with chronic viral hepatitis and will be classified into 2 groups as follow:

Group 1: patients with chronic compensated hepatitis C

Group 2: patients with chronic compensated hepatitis B

As well as a control group; will includes 40 normal healthy volunteers.

Inclusion Criteria:

Clinical, laboratory and ultrasonographic criteria suggestive of chronic liver disease [Child A].

Exclusion Criteria:

1- Previous combined interferon and ribavirin therapy.

2- Decompensated chronic viral hepatitis (Child B and C).

3- Other causes of liver diseases, including: autoimmune hepatitis, alcoholic liver disease, drug-induced hepatitis.

4- Hepatocellular carcinoma

5- Any other depilating disease (cardiac or renal).

Methods :

All patients will be subjected to the following:

I- Careful Full medical history taking including risk factors of occurrence HCV (right hypochondrial pain, parentral antibilharzial therapy, blood transfusion and previous operation).

II- Thorough Clinical examination with special stress on signs of liver cell failure, hepatomegaly, splenomegaly and/or ascites.

III- Laboratory investigations:

1- Routine liver function tests (ALT, AST, Alkaline Phosphatase, Total and direct bilirubin, albumin and prothrombin time).

2- Complete blood picture and erythrocyte sedimentation rate.

IV- Viral markers:

1- Anti-HCVAb & HBsAg.

2- Quantitative PCR for HCV-RNA if available.

3- Quantitative PCR for HBV-DNA if available.

V- Thyroid profile:

1- TSH.

2- Anti thyro globulin Ab

3- Thyroperoxidase Ab

VI- Tumour marker: Alfa fetoprotein (If needed).

VII-Imaging: Abdominal ultrasound.

<u>Sample Size and randomization</u>:

It will include (80) patients (equally divided) with chronic viral hepatitis (B or C) according to the pre-designed inclusion criteria.

Ethical Considerations:

An informed consent will be obtained from each of the participants or one of the responsible relatives before recruitment in the study.

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بسم اللّه الرحمن الرحيم

[قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ

(صدق اللّه العظيم)

سورة البقرة الآية (٣٢)

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Shaimaa Salah
November, 2014

بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لاَ
عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ
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(صدق الله العظيم)

سورة البقرة الآية (٣٢)

List of Abbreviations

AA protein : Amyloid A protein

AFP : Alpha fetoprotein

AH : Autoimmune hepatitis

AITD : Autoimmune thyroid disease

ALT : Alanine transaminase

Anti-HBc : Hepatitis B core antibody

AST : Aspartate transminase

AUC : Area under curve

BP : Bullous pemphigoid

CAH : Chronic active hepatitis

CCCDNA : Covalently closed circular DNA

CHB : Chronic hepatitis B

CHC : Chronic hepatitis C

CI : Confidence interval

CMV : Cyto megalo virus

CTL : Cytotoxic T lymphocytes

DNA : Deoxyribonucleic acid

EBV : Epestein barr virus

ECM : Essential cryoglobulinemia

EHMS : Extra hepatic manifestations

FT3 : Free T3

FT4 : Free T4

GBS : Guillain-Barre Syndrome

G-CSF : Granulocyte colon-stimulating factor

GN : Glomerulonephritis

HBcAg : Hepatitis B core antigen

HBsAg : Hepatitis B surface antigen

HBV : Hepatitis B virus

HCC : Hepato cellular carcinoma

HCV : Hepatitis C virus

HIV : Human immunodeficiency virus

HSV : Herpes simplex virus

INF-β : Interferon beta

INF-δ : Interferon gamma

IVIG : Intra venous immunoglobulin

LDL : Low density lipoprotein

LP : Lichen planus

MALT : Mucosal associated lymphoid tumors

MC : Mixed cryoglobulinemia

MGN : Membranous glomerulonephritis

MPGN : Membrano proliferative glomerulonephritis

OLP : Oral lichen planus

PAN : Polyarteritis nodosa

PE : Plasma exchange

PEG-INF : Pegylated interferon

RIBA : Ribavirin

RNA : Ribo nucleic acid

ROC : Receiver operator characteristics

SD : Standard deviation

SE : Standard error

SVR : Sustained virology response

T_2DM : Type 2 diabetes mellitus

TAs : Thyroid antibodies

TD : Thyroid dysfunction

TgAb : Thyroglobulin antibody

TpoAb : Thyroperoxidase antibody

TSH : Thyroid stimulating hormone

WHO : World health organization

αINF : Alpha interferons