Acta Tropica 176 (2017) 283–287

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Impact of old Schistosomiasis infection on the use of transient elastography (Fibroscan) for staging of fibrosis in chronic HCV patients

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ARTICLE INFO

Keywords:
HCV
Schistosomiasis
Fibroscan
Fibrosis
Periportal tract thickening
Liver biopsy

ABSTRACT

Background and aim: In tropical regions, Hepatitis C virus (HCV) − Schistosomiasis coinfection remains one of the health problems. With the new era of HCV treatment and the variety of methods of assessment of liver fibrosis so we aimed to evaluate the effectiveness of FibroScan for staging hepatic fibrosis in HCV-Schistosomiasis coinfected patients.

Methodology: Three groups of patients were enrolled. Group 1: chronic HCV with out antischistosomal antibody (122 patients), Group 2: chronic HCV with positive antischistosomal antibodies and without periportal tract thickening (122 patients), Group 3: chronic HCV with positive antischistosomal antibodies and ultrasonographic picture of periportal tract thickening (108 patients). Routine laboratory workup, serum Antischistosomal antibody, and Schistosomal antigen in serum were performed. Ultrasound guided liver biopsy with histopathological examination; abdominal ultrasound and fibroscan examination were done for all patients.

Results: The agreement between results of liver biopsy and results of fibroscan in the staging of fibrosis was the best in group 1 (55.7%), Although the agreement was higher among those with no periportal tract thickening (70.7%) and the disagreement was higher among those with positive schistosomal serology (66.5%), yet this relation was not statistically significant. Multivariate logistic regression analysis showed that disagreement is significantly associated with older age, higher BMI (≥30), and increase in anti Schistosomal antibody titer.

Conclusion: Fibroscan is a reliable, non-invasive tool for staging hepatic fibrosis among HCV-schistosomiasis co-infected patients with no effect of the induced periportal tract thickening on the readings. Only higher anti-schistosomal antibody titres may cause disagreement between liver biopsy and fibroscan.

1. Introduction

The hepatitis C virus (HCV) is a major public health problem and a leading cause of chronic liver disease. (Ghany et al., 2009).

In Egypt about 13.3% of population are chronically infected with HCV and are at risk of liver complications. Individuals living in rural areas had significantly more anti-HCV seropositivity (36.1%) than those living in urban areas (24.7%) (Guerra et al., 2012; Mohamed, 2004). Egypt has the highest reported prevalence of hepatitis C virus (HCV) globally (Esmat et al., 2013a; Obach et al., 2015).

Liver fibrosis represents a major health problem worldwide (Friedman 2000).Assessment of liver fibrosis by Liver biopsy and histological analysis, was considered the gold standard technique. However, it is a painful and invasive procedure, prone to sampling errors and may have some life-threatening complications, (Strader et al., 2004).

A variety of methods including the measurement of liver stiffness, using transient elastography (TE), and serum markers especially FibroTest, and aspartate-to platelet ratio (APRI) are the most widely used and validated non-invasive methods for assessment of liver fibrosis (Castera 2012; Castera 2009)

Patients with hepatosplenic Schistosomiasis were found to be 7–10 times more susceptible to co-infection with hepatitis (Agha et al., 2006).The reasons for this interaction between Schistosomiasis and hepatitis viruses include the direct stimulation of viral replication by soluble egg antigen, defects in cell mediated immunity and the high

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http://dx.doi.org/10.1016/j.actatropica.2017.08.019
Received 9 November 2016; Received in revised form 8 August 2017; Accepted 21 August 2017
Available online 26 August 2017
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exposure of Schistosomal patients to repeated specific parenteral therapy, blood transfusion and non specific therapy (El-Awady et al., 2006).

The impact of this schistosomiasis coinfection in our Egyptian population on the performance of fibroscan is not well studied so our aim was to evaluate the effectiveness of FibroScan for staging hepatic fibrosis in chronic HCV infected patients with or without schistosomiasis.

2. Subjects and methods

This study was conducted on 352 Egyptian patients with chronic hepatitis Patients were subjected to history taking, clinical examination and routine laboratory work up including Complete blood count (CBC), blood glucose, kidney functions tests and liver functions tests. Antischistosomal antibodies by the indirect haemagglutination test (IHAT) was done and considered positive if titre ≥1/160 with a sensitivity up to 95% and specificity up to 99%. (Sorgho et al., 2005; Kinkel et al., 2012), Schistosomal antigen in serum was done using the fast (ELISA) with a sensitivity 93%, specificity 89%, and efficiency 91%. (Attallah et al., 1999).

The diagnosis of chronic hepatitis C (CHC) was established by the presence of HCV RNA using polymerase chain reaction assays. All patients underwent a pretreatment liver biopsy within 6 months prior to the initiation of therapy. All patients underwent a pretreatment abdominal ultrasound and fibroscan examination. Patients with HCV genotype other than genotype 4, chronic liver disease other than HCV, decompensated liver cirrhosis and hepatocellular carcinoma, were excluded from the study.

2.1. Patients were classified into three groups

Group 1: chronic HCV with negative antischistosomal antibody (122 patients).

Group 2: chronic HCV with positive antischistosomal antibodies and without periportal tract thickening (122 patients).

Group 3: chronic HCV with positive antischistosomal antibodies and ultrasonographic picture of periportal tract thickening fibrosis (108 patients).

Abdominal ultrasound was done to all patients to assess the degree of periportal tract thickening: grade I if thickness = 3–5 mm, grade II = greater than 5–7 mm, and grade III = greater than 7 mm. (Abdel-Wahab et al.1992; Frank et al., 2000)

Institutional Review Board (IRB) study approval was obtained prior to commencement of the study and signed informed consent was obtained from all study patients.

3. Histological classification

Histopathological examination of ultrasound-guided percutaneous liver biopsy using 16-G semi-automated biopsy needles. Liver specimens of a minimum of 15 mm in length with at least four portal tracts were fixed in 10% neutral formalin, processed then embedded in paraffin. Sections were stained with hematoxylin–eosin and Masson-trichrome for detection of fibrosis. Histopathological examination according to the METAVIR scoring system demonstrated different stages of fibrosis (F0–F4) and grades of necroinflammatory changes activity (A0–A3) (Bedossa and Poynard, 1996)The histopathological examination of all the liver biopsies was performed by a single expert pathologist.

4. Fibroscan (ultrasound transient elastography)

Liver stiffness measurements were done for all patients with FibroScan® (ECHOSENSE, FIBROSCAN 502, Paris, France) located in Kasr Alainy Viral Hepatitis Center, Cairo university. Ten valid measurements were performed, and median of liver stiffness expressed in kilopascals (kPa) was reported (Sandrin et al., 2003). Only examinations with success rate > 60% and interquartile range (IQR) < 30% were included in this study and were considered reliable. Cut offs used are those used by (De ledinghen and vergniol, 2008) as follows:

F0 < 5.5 kpa
F0-F1 = 5.5 till 5.9 kpa
F1 = 6 till 6.9 kpa
F1-F2 = 7 till 8.7 kpa
F2 = 8.8 till 9.4 kpa
F3 = 9.5 till 12.4 kpa
F3-F4 = 12.5 till 14.4 kpa
F4 ≥ 14.5 kpa

5. Statistical analysis

The quantitative data were described with mean and standard deviation (SD) and compared by the Student's *t*-test. Qualitative variables were described by number and percent. They were compared by the chi-squared or Fischer's exact test, when appropriate. Multivariate logistic regression was used in which the disagreement between fibroscan and liver biopsy was the dependent variable. In all tests, p value < 0.05 was considered significant.

6. Results

Our study included 352 Egyptian patients with chronic hepatitis C infection categorized in three groups. The demographic features of the studied patients are shown in Table 1.

Regarding the laboratory parameters Hb, WBCs, Bil T, and albumin, all showed statistically significant difference between groups as shown in Table 2. Serum schistosomal antigen (AG) was negative in (around 90%) of HCV-schistosomiasis, coinfected patients (group 2 + 3)

Portal tract thickening by abdominal ultrasound was found in 108 patients (group 3) (47% of HCV-schistosomiasis coinfected patients) mainly grade 1 in 101 patient of them.

No statistically significant difference was observed in the mean liver stiffness among the three groups.

The agreement between results of liver biopsy and results of fibroscan in the staging of fibrosis was the best in group 1 (55.7%), however this relation was not statistically significant among groups.

Among those with positive antischistosomal antibody, titres were reported to be ≥1/160 in 58 patients (25% of group 2 + group3), ≥1/320 in 80 patients (35% of group 2 + group3), ≥1/640 in 51 patients (22% of group 2 + group3) and ≥1/1280 in 41 patient (18% of group 2 + group3)

Agreement between the reading of liver biopsy (METAVIR) and the results of fibroscan through the different stages of fibrosis are shown in Table 3.

The relations between agreement and different parameters of schistosomal infection are shown in Table 4.

Table 1
Demographic features of the studied groups.

	HCV	HCV + SCHISTO	HCV + SCHISTO + PPT	P value
	(group 1)(122)	(group 2) (122)	(group 3)(108)	
Age(Mean ± SD)	39.9 ± 10	43.9 ± 10	41.9 ± 11	0.015
SEX				
Female	53 (43.4%)	36 (29.5%)	18 (16.7%)	0.001
Male	69 (56.6%)	86 (70.5%)	90 (83.3%)	
BMI(Mean ± SD)	28.5 ± 3	26.8 ± 3	27 ± 3	0.376

BMI: body mass index.

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