Abdelhaleem *et al. Egyptian Liver Journal* (2023) 13:21
https://doi.org/10.1186/s43066-023-00255-x

Egyptian Liver Journal

ORIGINAL RESEARCH ARTICLE

Open Access

Effect of HCV treatment with DAAs on serum intestinal fatty acid binding protein (I-FABP) as a marker of intestinal permeability in HCV/HIV co-infected patients

Hanan Abdelhaleem[1], Marwa Khairy[1], Mahmoud Abdo[1], Ahmed Cordie[1], Marwa Elsharkawy[2], Shereen Abdel Alem[1], Aisha Elsharkawy[1], Lamiaa Al sehemy[1*] and Gamal Esmat[1]

Abstract

Background HCV and HIV co-infected patients develop cirrhosis more rapidly than HCV mono-infection. Intestinal injury and microbial translocation are postulated mechanisms for the rapid progression of cirrhosis.

Aim Study the effect of HCV treatment with DAAs on serum intestinal fatty acid binding protein (I-FABP) as a marker of intestinal injury in HCV/HIV co-infected patients and its relation to hepatic fibrosis. Comparing the level of I-FABP in HCV mono-infection and HCV/HIV co-infection was a secondary aim.

Methods I-FABP levels were measured in 50 non-cirrhotic HCV/HIV co-infected patients pre- and post-HCV treatment (*SVR* 12) (25 patients were HIV treatment naive, and 25 patients were on HAART) and in 25 chronic HCV patients as a control group. Hepatic fibrosis was assessed by FIB4 score, APRI score, and transient elastography.

Results HCV/HIV co-infected patients had significantly higher levels of I-FABP compared to the HCV-mono-infected patients ($P=0.001$). After HCV treatment in HCV/HIV co-infected patients, I-FABP level was significantly elevated ($P<0.001$) and was positively correlated with baseline FIB4 values and serum ALT levels ($r=0.283$, P-value $=0.047$) and ($r=0.340$, P-value $=0.016$), respectively.

Conclusion HCV/HIV co-infection is associated with significantly higher intestinal injury and subsequent hepatic fibrosis than HCV mono-infection. HIV infection is associated with intestinal epithelial injury and microbial translocation and may play a role in the persistence of systemic inflammation after HCV eradication.

Keywords I-FABP, HCV/HV co-infection, Hepatic fibrosis, ALT, FIB4

Introduction

Elevated levels of many blood markers indicative of pathological bacterial translocation or systemic inflammation have been detected in HIV-infected patients such as lipopolysaccharide and intestinal fatty acid binding protein [1]. Cross-sectional transient elastography data in HIV-infected patients have yielded a high percentage of advanced fibrosis in HIV-infected patients that may be explained by the direct hepatotoxic effect, dyslipidemia, or insulin resistance associated with HIV infection, even without alcohol abuse or underlying viral hepatitis [2].

*Correspondence:
Lamiaa Al sehemy
Lamiaaalsehemy@kasralainy.edu.eg
[1] Endemic Medicine Department and Hepatology Unit, Faculty of Medicine, Cairo University, Cairo, Egypt
[2] Clinical and Chemical Pathology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Data about the prevalence of HCV in persons living with HIV in Egypt is scarce. However, the prevalence of HIV among HCV-infected Egyptian patients was 0.66% in one study [3].

HCV/HIV co-infected patients are more prone to accelerated progression of their hepatic fibrosis to cirrhosis [4]. One proposed mechanism is that co-infected persons have impaired intestinal barriers, allowing the translocation of bacteria into the portal circulation with consequent hepatic and systemic inflammation [5].

Previous studies have measured markers of microbial translocation, including I-FABP (a marker of intestinal epithelial damage and is associated with microbial translocation), and found that these markers were significantly elevated in HCV/HIV co-infected patients than in patients with HCV mono-infection [6, 7].

Understanding the association between HCV, HIV, microbial translocation, and liver fibrosis may be beneficial in identifying interventions to reduce the harmful consequences of microbial translocation [7].

Studies assessed the effect of HCV treatment with DAAs in HCV/HIV co-infected patients on microbial translocation and found improvement in the severity of liver stiffness measurement and plasma inflammatory markers such as IL-18 and IL-8 [8, 9].

Objectives

We studied the effect of HCV treatment with DAAs on serum intestinal fatty acid binding protein (I-FABP) as a marker of intestinal injury in HCV/HIV co-infected patients and its relation to hepatic fibrosis. Comparing the level of I-FABP in HCV mono-infection and HCV/HIV co-infection was a secondary aim.

Patients and methods

Patient's selection

This cross-sectional prospective study was conducted on patients with chronic HCV candidates for HCV treatment with DAAs directed to the Kasr Al-Aini Viral Hepatitis Center (KAVHC) — Faculty of Medicine — Cairo University as one of the approved centers for HCV treatment during the period from March 2019 to April 2021.

The included patients were adults above the age of 18 years of both sexes and able to give informed consent and compliant to study procedures. Patients included in the study were non-cirrhotic by FIB4 score to eliminate the effect of liver cirrhosis on the I-FABP level. HCV infection was diagnosed by the presence of positive HCV antibody for more than 6 months and detectable HCV viremia. The recommended protocol for HCV treatment was sofosbuvir and daclatasvir for 12 weeks. HIV infection was diagnosed by third-generation HIV antibody ELISA testing and confirmed by HIV PCR.

Exclusion criteria were patients refusing or unable to write the informed consent, pregnancy, breast-feeding, history of chronic intestinal diseases such as celiac disease or inflammatory bowel diseases and other inflammatory conditions, patients having an active intestinal infection or on antibiotic treatment for the past 4 weeks, chronic liver diseases due to causes other than HCV infection, history of using NSAIDS for 2 weeks before visit, and alcohol drinking (more than 4 drinks per week by a man or > 3 drinks per week by a woman).

Patients grouping

The enrolled patients were divided into two groups based on HIV infection, as follows:

- Group 1 (25 patients): Non-cirrhotic chronic HCV mono-infected patients
- Group 2 (50 patients): Non-cirrhotic chronic HCV/HIV co-infected patients. This group was further divided into 25 patients on HAART and 25 patients who were HAART naive. We divided this group to determine whether there was a difference between both groups.
- Twenty-five healthy participants were recruited as a control group for the measurement of baseline I-FABP level.

Consent

Written informed consent was obtained from all patients. The study was performed in compliance with the ethical principles of the 1975 Declaration of Helsinki and its later amendments with good clinical practice (GCP) guidelines.

The approval of the Institutional Review Board (IRB) of Kasr Alainy School of Medicine, Cairo University, was obtained for our study (D-43–2019) and for the umbrella project entitled "HCV prevalence among patients infected with HIV registered for HAART in Imbaba fever hospital in Cairo" (N-149–2018).

Methodology

Patients were subjected to thorough history-taking with special emphasis on the presence of comorbidities, special habits of medical importance, and drug abuse. Blood samples were obtained for complete biochemical, serological, and virological testing.

FIB4 and APRI scores were calculated. FIB-4 score was calculated using the following formula: FIB-4 = age [years] × AST [U/l]/platelet count [Plt × 10

⟧ ^9/l] × (ALT1/2 [U/l]) [9]. The APRI score was calculated using the following formula: APRI = (AST/upper limit of normal × 100)/platelet count [10].

I-FABP testing was done by ELISA kit that uses the sandwich-ELISA method. The micro-ELISA strip plate provided in this kit has been pre-coated with an antibody specific to I-FABP. Standards or samples were added to the appropriate micro-ELISA strip plate wells and combined with the specific antibody. Then, a horseradish peroxidase (HRP)-conjugated antibody specific for I-FABP was added to each micro-ELISA strip plate well and incubated. Free components are washed away. The TMB (tetramethylbenzidine) substrate solution was added to each well. Only those wells that contain I-FABP and HRP-conjugated I-FABP antibodies will appear blue in color and then turn yellow after the addition of the stop solution.

The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value was proportional to the concentration of I-FABP. Calculations of the concentration of I-FABP in the samples were performed by comparing the OD of the samples to the standard curve.

The reference range of the used kits was < 2 ng/ml. Calibration of the I-FABP testing level was performed based on the I-FABP results of 25 healthy subjects as a control group; the calibration range of the control group was 6.09 ± 1.90 ng/ml.

Liver fibrosis and steatosis were assessed by *FibroScan*® (EchoSens, Paris, France) with the standard M probe and XL probe for obese patients. Measurements were performed through the intercostal spaces, where patients lye in the dorsal decubitus position with the right arm in maximal abduction. Measurements were performed after overnight fasting. Patients were further categorized into the following:

1. Nonsignificant fibrosis (< *F2*)
2. Significant fibrosis (≥ *F2*) [11]

Assessment of steatosis by CAP (controlled attenuation parameter) and results were categorized into the following:

- S0: No steatosis (0–237 dB/m)
- S1: Mild steatosis (238–259 dB/m)
- S2: Moderate steatosis (260–292 dB/m)
- S3: Severe steatosis (≥ 293 dB/m) [12]

Laboratory workup, transient elastography, and I-FABP testing were performed at baseline for the two patient groups and post-HVC treatment (SVR 12) for group 2.

Statistical methods

Data were coded and entered using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data were summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were performed using an unpaired *t*-test when comparing 2 groups and an analysis of variance (ANOVA) with multiple comparisons post hoc test when comparing more than 2 groups [13].

To compare categorical data, the chi-square (χ^2) test was performed. An exact test was used instead when the expected frequency was less than 5. For comparing categorical data measured before and after treatment, McNemar test was used [14]. Correlations between the quantitative variables were peformed using the Pearson correlation coefficient [15]. *P*-values less than 0.05 were considered statistically significant.

Results

Demographic characteristics of the two groups of patients being studied (Table 1)

The highest median age was in the HCV mono-infected group (53 years), while the median age of the HCV/HIV co-infected groups was 32 and 29 years respectively for

Table 1 Demographic characteristics of the studied population

	Group 1 HCV only (*n* = 25)		Group 2a HCV/HIV on HAART (*n* = 25)		Group 2bHCV/HIV HAART naive (*n* = 25)		*P*-value for groups 1 & 2
Median age (IQR)	53.0 (35.0–56.0)		32.0 (29.0–44.0)		29.0 (26.0–37.0)		**< 0.001**
	Count	**%**	**Count**	**%**	**Count**	**%**	***P*-value**
Gender							
Male	11	44.0%	20	80.0%	23	92.0%	**< 0.001**
Female	14	56.0%	5	20.0%	2	8.0%	
Smoking	7	28.0%	18	72.0%	23	92.0%	**< 0.001**
IV drug abuse	0	0.0%	18	72.0%	20	8.0%	**< 0.001**

group 2 a and b. Regarding gender distribution, male participants were more in HCV/HIV co-infected groups (80 & 92%) respectively, while in the HCV mono-infection group, female participants were more than male participants (56 versus 44%).

Regarding the risk factors for HCV and HIV infection acquisition, 72 & 80% of patients in HCV/HIV co-infected groups were IV drug abusers, 40% had a history of surgical intervention, 38% performed dental procedures, and 10% of the patients received a blood transfusion. Risky sexual behavior was denied by the studied patients in the HIV-infected groups.

Comparison between groups 2 a and b regarding I-FABP levels (Table 2)

We first compared both HCV/HIV co-infected groups (2 a & b); there was no significant difference between both groups in I-FABP levels (*P*-value for comparison before HCV treatment was 1.000 and after HCV treatment was 0.776) so both groups were combined into one group and compared with the HCV mono-infected group.

Baseline characteristics of the two studied groups of patients (Table 3)

Analyzing laboratory parameters of the two groups, no statistically significant difference was noticed between the serum transaminase level and bilirubin levels in both groups, while the mean HCV RNA PCR was *statistically significantly* higher in group 2 than in group 1 with a *P*-value of 0.016.

Regarding the assessment of hepatic fibrosis, the mean stiffness value and significant fibrosis (≥ F2) were significantly higher in group 2 compared to group 1 with a *P-value < 0.001*. However, no statistically significant difference was detected between the two groups using the

Table 2 Comparison between group 2 a and b regarding I-FABP results

	Group 2a HCV/HIV on HAART (*n* = 25)			Group 2b HCV/HIV HAART naive (*n* = 25)			*P*-value
	Median	1st quartile	3rd quartile	Median	1st quartile	3rd quartile	
I-FABP (before HCV treatment)	11.00	7.12	11.90	8.60	7.50	14.00	1.000
I-FABP (after HCV treatment)	17.86	15.00	31.00	18.20	15.10	21.40	0.776

Table 3 Baseline characteristics of the studied two groups of patients and posttreatment follow-up

	Group I HCV (*n* = 25)	Group 2 HIV/HCV (*n* = 50)		P1 value	P2 value
		Pre-HCV treatment	Post-HCV treatment		
AST (< 35 IU/ml)	39.04 ± 25.04	39.46 ± 22.72	27.30 ± 8.99	0.942	**< 0.001**
ALT (< 35 IU/ml)	57.92 ± 71.10	62.14 ± 50.96	27.76 ± 10.99	0.769	**< 0.001**
HCV RNA PCR	0.772 ± 0.1004	1.595 ± 1.89	Undetectable	**0.016**	-
I-FABP reference range (< 2 ng/ml)	6.91 ± 1.25	11.76 ± 7.26	20.11 ± 7.30	**0.001**	**< 0.001**
I-FABP control range (6.09 ± 1.90 ng/ml)	6.91 ± 1.25 (*p* = 1.00)	11.76 ± 7.26 **(*p* < 0.001)**	20.11 ± 7.30	**	**< 0.001**
Transient elastography (kPa)	4.42 ± 0.44	5.51 ± 1.26	5.48 ± 2.04	**< 0.001**	0.928
Fibrosis stages					
< F2 *n*(%)	25 (100.0%)	41 (82.0%)	43 (86.0%)	**0.025**	0.727
≥ F2 *n*(%)	0	9 (18.0%)	7 (14.0%)		
CAP (dB/m)	196.84 ± 39.06	212.92 ± 48.75	210.10 ± 48.44	0.156	0.634
Steatosis grades					
< S2 *n*(%)	23 (92.0%)	44 (88.0%)	44 (88.0%)	0.711	1
≥ S2 *n*(%)	2 (8.0%)	6 (12.0%)	6 (12.0%)		
FIB4	1.21 ± 0.57	0.96 ± 0.62	0.82 ± 0.45	0.107	**0.019**
APRI score	0.50 ± 0.45	0.40 ± 0.30	0.25 ± 0.11	0.252	**< 0.001**

* P1 value difference between group 1 and group 2 pre-HCV treatment

P2 value difference between pre- and post-HCV treatment in group 2

** *P*-value for group 1 with (calibration) control is 1.000 and for group 2 with calibration (control) < 0.001

FIB4 and the APRI scores in the assessment of hepatic fibrosis (*P*-value 0.107 and 0.252, respectively). Regarding the steatosis assessment by CAP, no statistically significant difference was detected between the two groups with a *P*-value of 0.711.

Comparing the I-FABP level, the mean value was *significantly* higher in group 2 (11.76 ± 7.26) than in group 1 (6.91 ± 1.25) with *P-value = 0.001*. Regarding the I-FABP level in the control group, the I-FABP level in the HCV group was comparable to that in the control group while significantly higher in group 2 than in the control group.

Group 2 characteristics pre- and post-HCV treatment (Table 3)

The mean I-FABP level was *significantly* higher after HCV treatment (20.11 ± 7.30) than before treatment (11.76 ± 7.26) with a *P*-value < *0.001*.

Comparison of laboratory parameters before and after treatment revealed that the mean platelets count after HCV treatment (225.28 ± 60.96) was significantly higher than the mean count before treatment (219.53 ± 58.09) with a *P*-value of 0.016. Mean AST and ALT levels after treatment were (27.30 ± 8.99) and (27.76 ± 10.99), respectively, and both values were significantly lower than the mean values before treatment that were (39.46 ± 22.72) and (62.14 ± 15.96), respectively, with *P*-values of < 0.001 for both.

Assessment of liver fibrosis revealed that mean FIB4 and APRI scores after HCV treatment were 0.82 ± 0.45 and 0.25 ± 0.11, respectively, which were *significantly* lower than the mean values before treatment 0.96 ± 0.62 and 0.40 ± 0.30, respectively, with *P*-value = 0.019 for FIB4 and < 0.001 for APRI score, respectively.

Correlation between serum I-FABP and the parameters under study in group 2 pre- and post-HCV treatment (Tables 4 and 5)

Only significant correlations were found between the baseline FIB4 and ALT level and the posttreatment I-FABP level ($r = 0.283$, *P*-value = 0.047) and ($r = 0.340$, *P*-value = 0.016), respectively, as shown in Figs. 1 and 2.

Concerning the correlation between posttreatment parameters in the HCV/HIV co-infection group and the I-FABP values before and after treatment revealed only *a significant* positive correlation between posttreatment bilirubin level and the pre-treatment I-FABP level ($r = 0.286$, *P*-value = 0.044).

Table 4 Correlation between serum I-FABP and the studied parameters in group 2 pre- and post-HCV treatment

Baseline parameters	Pre-treatment I-FABP level		Post-treatment I-FABP level	
	Pearson correlation (*r*)	*P*-value	Pearson correlation (*r*)	*P*-value
AST (< 35 IU/ml)	0.072	0.618	0.216	0.132
ALT (< 35 IU/ml)	0.064	0.660	0.340	**0.016**
FIB4	0.113	0.436	0.283	**0.047**
APRI score	0.063	0.662	0.245	0.087
FibroScan (kpa)	− 0.090-	0.535	0.035	0.808
CAP (dB/m)	− 0.067-	0.646	− 0.063	0.666
HCV RNA PCR	− 0.040-	0.784	0.085	0.556
CD4 count	− 0.096-	0.508	0.175	0.223
HIV RNA PCR	− 0.170-	0.243	− 0.254	0.078

Abbreviations: *APRI* AST to platelet ratio index, *CAP* Controlled attenuation parameter, *dB/m* decibel per minute, *FIB4* Fibrosis-4, *kPa* kilopascal, *n* number, *ng* nanogram

Discussion

The current study revealed higher serum I-FABP levels detected in the HCV/HIV co-infected patients than in HCV mono-infected patients. Previous studies noticed the same results [6, 16]. This could be explained by the additive effect of both viruses on intestinal mucosal damage. This can also be explained by mucosal CD + 4 T-cell depletion due to HIV infection or may be due to more liver disease progression in co-infected patients [6, 16, 17].

In our HCV mono-infected group, the serum I-FABP level was higher than the reference range of the kits but not significantly higher than that of healthy control participants. Our results agree with a previous similar study by Wurcel, where the mean I-FABP levels were 294 pg/ml and 386 pg/ml in HCV patients and the control group, respectively, and the difference was not statistically significant [16]. On the contrary, Reid et al. found a significant elevation of the serum I-FABP level in HCV mono-infected patients compared with the control group. This may be explained by the difference in the study population, as the latter study included cirrhotic patients, and we excluded cirrhotic patients in our study as elevated I-FABP levels may be related to enterocyte damage and microbial translocation that are known to occur in liver cirrhosis [7].

In our exploratory analysis, the baseline FIB4 score was positively correlated with the posttreatment serum I-FABP levels in HCV/HIV co-infected patients. This positive correlation suggests a relationship between increased I-FABP and increased liver disease severity. Similar results were confirmed by previous studies by Wurcel and French et al. [16, 17].

Table 5 Correlation between serum I-FABP and the posttreatment parameters in group 2 pre- and post-HCV treatment

Posttreatment parameters	Pre-treatment I-FABP level		Post-treatment I-FABP level	
	Pearson correlation	*P*-value	Pearson correlation	*P*-value
Bilirubin total (0.3–1.2 mg/dl)	0.286	**0.044**	0.018	0.900
AST (< 35 IU/ml)	0.006	0.967	0.047	0.748
ALT (< 35 IU/ml)	0.100	0.489	0.195	0.176
FIB4	0.068	0.638	0.233	0.104
APRI	0.140	0.331	0.219	0.126
FibroScan (kpa)	− 0.066-	0.649	− 0.070-	0.629
CAP (dB/m)	− 0.030-	0.834	− 0.077-	0.594

Another potential explanation for the observed statistical correlation between I-FABP in HCV/HIV co-infection and FIB4 score is the effect of antiretroviral therapy (ART) on the liver in this group. Recent ART-related clinical syndromes such as NAFLD and non-cirrhotic portal hypertension have increased in patients on ART, and observational studies have proposed long-term ART-related hepatic injury [18].

Significant improvement in the elevation of serum transaminases and improvement of platelet count in HCV/HIV co-infected patients after HCV eradication that was noted in our study is in concordance with the study by Brochado-Kith et al., who concluded that at the end of follow-up after all-oral DAA therapy, HCV/HIV-coinfected patients exhibited a significant decrease (*P*-value < 0.05) in AST and ALT, and substantial increase in platelet count was observed [19].

Regarding the improvement of hepatic fibrosis in HCV/HIV co-infected patients after HCV treatment with DAAs, the significant improvement in the FIB4 and APRI scores could be explained by the amelioration of HCV-induced necro-inflammation and

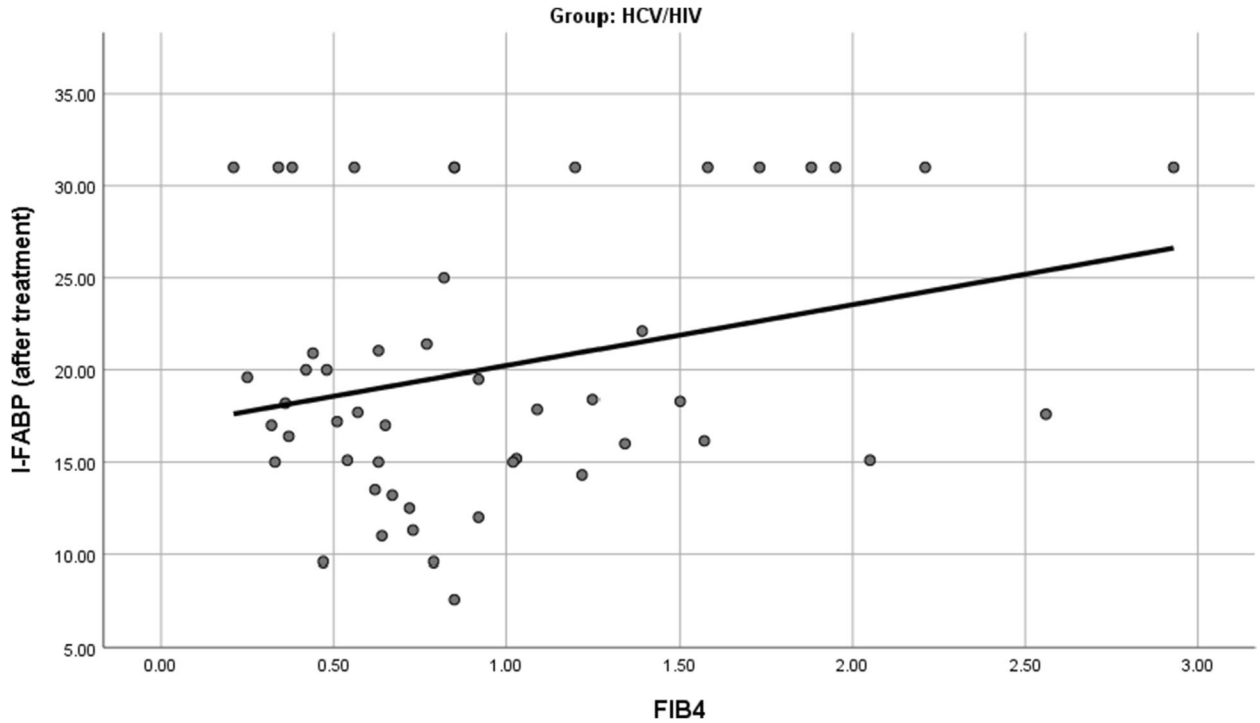

Fig. 1 Significant positive correlation between baseline FIB4 score with posttreatment I-FABP level in HCV/HIV co-infected group ($r = 0.283$, *P*-value = 0.047)

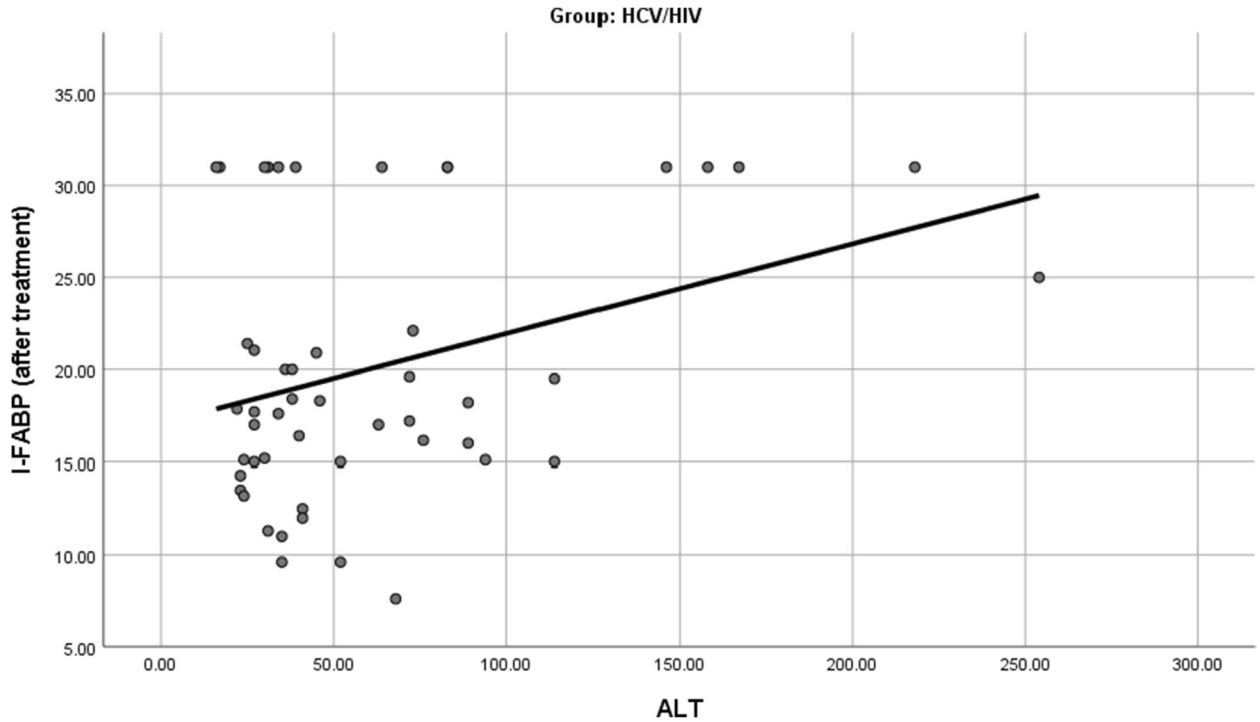

Fig. 2 Significant positive correlation between the baseline ALT and posttreatment I-FABP level in HCV/HIV co-infected group ($r = 0.340$, P-value = 0.016)

fibrosis [20-22]. However, this improvement was not reflected in the results of transient elastography and steatosis measured by CAP. This may be due to confounding effects of ART that may induce hepatic steatosis that consequently affects stiffness and steatosis measurements.

I-FABP level was significantly higher after HCV treatment in HCV/HIV co-infected patients. This may imply that HCV eradication in the liver has potential advantages on the liver (improvement in platelet count, albumin, serum transaminase levels, and hepatic fibrosis), but the enterocyte permeability may persist or even worsen after HCV eradication. Studies have found that despite achieving SVR in HCV-infected patients, monocyte activation (part of systemic inflammation caused by bacterial translocation) may persist [23, 24].

Our results are contrary to Medrano et al., who found no significant change in I-FABP after HCV treatment (P-value = 0.29). This difference may be due to choosing patients with advanced cirrhosis ($LSM \geq 25$ kPa, HVPG ≥ 10 mmHg, or CTP ≥ 7, or prior history of liver decompensation), which may affect baseline I-FABP levels in contrast to our patients who were non-cirrhotic [8].

Limitations to the study

Our study had a financial limitation in measuring I-FABP levels in the HCV-infected group after treatment, which would have been useful in confirming the effect of HCV treatment on I-FABP levels.

Conclusion

In our study of HCV/HIV, co-infected patients had significantly higher I-FABP levels in contrast to HCV mono-infected patients who had I-FABP levels that were comparable to the control group. This may imply that HCV is not the primary driver of impaired permeability in co-infected patients, and this is further confirmed by the lack of improvement of I-FABP after HCV eradication in co-infected patients. Furthermore, advanced baseline liver fibrosis (FIB4 score) was correlated with a higher degree of intestinal injury after HCV treatment with DAAs.

These data provide a starting point for future longitudinal studies looking at how markers of intestinal health and permeability can help monitor the natural history of some diseases and the efficacy of therapy.

Abbreviations

I-FABP	Intestinal fatty acid binding protein
IRB	Institutional research board
KAVHC	Kasr Al-Aini Viral Hepatitis Center
SPSS	The Statistical Package for the Social Sciences

Acknowledgements
Kasr Al-Aini Viral Hepatitis Center (KAVHC) — Faculty of Medicine — Cairo University
project "HCV prevalence among patients infected with HIV registered for HAART in Imbaba fever hospital in Cairo." Institutional review board (IRB) number for the project was (N-149-2018)

Authors' contributions
HAH and GE principal investigators, MK and MA revision of the manuscript, AC data collection, AES data analysis and revision of tables, MES clinical pathological measurement of I-FABP, SAA performed FibroScan, and LAS wrote the manuscript and interviewed the patients. The authors read and approved the final manuscript.

Funding
By Cairo University (N-149–2018).

Availability of data and materials
Are available. Please contact Lamiaaalsehemy@kasralainy.edu.eg.

Declarations

Ethics approval and consent to participate
The approval of the Institutional Review Board (IRB) of Kasr Alainy School of Medicine, Cairo University, was obtained for study conduction and publication (D-43–2019) under the umbrella project entitled "HCV prevalence among patients infected with HIV registered for HAART in Imbaba fever hospital in Cairo" approved by Cairo University (N-149–2018).

Consent for publication
Is not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 27 January 2023 Accepted: 12 April 2023
Published online: 29 April 2023

References

1. Márquez M, Fernández Gutiérrez del Alamo C, Girón González JA (2016) Gut epithelial barrier dysfunction in human immunodeficiency virus-hepatitis C virus coinfected patients: influence on innate and acquired immunity. World J Gastroenterol 22(4):1433–1448. https://doi.org/10.3748/wjg.v22.i4.1433
2. Rockstroh JK, Mohr R, Behrens G et al (2014) Liver fibrosis in HIV. Curr Opin HIV AIDS 9(4):365–70. https://doi.org/10.1097/COH.0000000000000064
3. Fouad R, Shaker O, Hafez H et al (2013) HIV prevalence among HCV Egyptian infected patients and its impact on the result of HCV treatment. Adv Infect Dis 3(2):71–77. https://doi.org/10.4236/aid.2013.32011
4. LópezDiéguez M, Montes ML, PascualPareja JF et al (2011) The natural history of liver cirrhosis in HIV–hepatitis C virus-coinfected patients. AIDS 25(7):899–904. https://doi.org/10.1097/QAD.0b013e3283454174
5. Balagopal A, Philp FH, Astemborski J et al (2008) Human immunodeficiency virus-related microbial translocation and progression of hepatitis C. Gastroenterology 135:226–233. https://doi.org/10.1053/j.gastro.2008.03.022
6. Tudesq JJ, Dunyach-Remy C, Combescure C et al (2017) Microbial translocation is correlated with HIV evolution in HIV-HCV co-infected patients. PLoS One 12(9):e0183372. https://doi.org/10.1371/journal.pone.0183372
7. Reid M, Ma Y, Scherzer R, Price JC et al (2018) Contribution of liver fibrosis and microbial translocation to immune activation in persons infected with HIV and/or hepatitis C virus. J Infect Dis 217(8):1289–1297. https://doi.org/10.1093/infdis/jix688
8. Medrano LM, Berenguer J, Salgüero S et al (2021) Successful HCV therapy reduces liver disease severity and inflammation biomarkers in HIV/HCV-coinfected patients with advanced cirrhosis: a cohort study. Front Med (Lausanne) 8:615342. https://doi.org/10.3389/fmed.2021.615342. Published 2021 Feb 1
9. Jenabian MA, Mehraj V, Costiniuk CT et al (2016) Influence of hepatitis C virus sustained virological response on immunosuppressive tryptophan catabolism in ART-treated HIV/HCV coinfected patients. J Acquir Immune Defic Syndr (1999) 71(3):254–262. https://doi.org/10.1097/qai.0000000000000859
10. Sterling RK, Lissen E, Clumeck N et al (2006) Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology 43:13171325. https://doi.org/10.1053/jhep.2003.50346
11. Wai CT, Greenson JK, Fontana RJ et al (2003) A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology 38(2):518–526. https://doi.org/10.1053/jhep.2003.50346
12. Park HS, Choe WH, Han HS et al (2019) Assessing significant fibrosis using imaging-based elastography in chronic hepatitis B patients: Pilot study. World J Gastroenterol 25(25):3256–3267. https://doi.org/10.3748/wjg.v25.i25.3256
13. Sansom SE, Martin J, Adeyemi O et al (2019) Steatosis rates by liver biopsy and transient elastography with controlled attenuation parameter in clinical experience of hepatitis C virus (HCV) and human immunodeficiency virus/HCV coinfection in a large US hepatitis clinic. Open Forum Infect Dis 6(4):ofz099. https://doi.org/10.1093/ofid/ofz099. eCollection 2019 Apr
14. Chan YH (2003) Biostatistics102: quantitative data – parametric & non-parametric tests. Singapore Med J 44(8):391–396
15. Chan YH (2003) Biostatistics 103: qualitative data –tests of independence. Singapore Med J 44(10):498–503
16. Wurcel A (2014) Evaluation of the intestinal fatty acid binding protein (I-FABP) in people with HIV, HCV and HIV/HCV co-infection. MD thesis, Tufts University, Massachusetts http://hdl.handle.net/10427/011156. Viewed 7 April 2022
17. French AL, Evans CT, Agniel DM et al (2013) Microbial translocation and liver disease progression in women coinfected with HIV and hepatitis C virus. J Infect Dis 208:679–689. https://doi.org/10.1093/infdis/jit225
18. Kovari H, Weber R (2011) Influence of antiretroviral therapy on liver disease. Curr Opin HIV AIDS 6:272–277. https://doi.org/10.1097/COH.0b013e3283473405
19. Brochado Kith Ó, Martínez I, Berenguer J et al (2021) HCV cure with direct-acting antivirals improves liver and immunological markers in HIV/HCV-coinfected patients. Front Immunol 12:723196. https://doi.org/10.3389/fimmu.2021.723196. eCollection 2021
20. Lee YC, Hu TH, Hung CH et al (2019) The change in liver stiffness, controlled attenuation parameter and fibrosis-4 index for chronic hepatitis C patients with direct-acting antivirals. PLoS One 14(4):e0214323. https://doi.org/10.1371/journal.pone.0214323
21. Márquez-Coello M, Arizcorreta A, Rodríguez-Pardo M et al (2021) Modifications of liver stiffness and CXCL4, TGF-β1 and HGF are similar in HCV- and HIV/HCV-infected patients after DAAs. Sci Rep 11:9824. https://doi.org/10.1038/s41598-021-89370-6
22. El-Garem H, AbdAllah M, Omar H et al (2019) DAAs therapy associated with improved hepatic fibrosis in HCV-GT4 patients co-infected with HIV. Expert Rev Gastroenterol Hepatol 13(7):693–698. https://doi.org/10.1080/17474124.2019.1614441

23. Perez-Matute P, Iniguez M, Villanueva-Millan MJ et al (2019) Short-term effects of direct-acting antiviral agents on inflammation and gut microbiota in hepatitis C-infected patients. Eur J Int Med 67:47–58. https://doi.org/10.1016/j.ejim.2019.06.005. Epub 2019 Jun 17
24. Auma AWN, Shive C, Damjanovska S et al (2021) T-cell activation is correlated with monocyte activation in HCV/HIV coinfection and declines during HCV direct-acting antiviral therapy. Open Forum Infect Dis 8(4):079. https://doi.org/10.1093/ofid/ofab079. eCollection 2021 Apr

Publisher's Note