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Impact of Direct Acting Antivirals Therapy on Novel Fibrosis Index for Assessment of Hepatic Fibrosis in Comparison with AST to Platelet Ratio and Fibrosis-4 (FIB-4) Indexes in Egyptian Patients with Chronic Hepatitis C Infection in Correlation with Fibroscan

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ABSTRACT

Background: Scarring or progressive fibrosis and cirrhosis develop over time as a result of chronic viral infection, which induces inflammation and tissue healing via deposition of extracellular matrix. There has been an increase in the sustained virological response (SVR) and the rate of eradication of HCV because of the effectiveness of direct-acting antiviral drugs (DAAs). Reduced hepatic fibrosis is associated with increased SVR rates. There are a variety of non-invasive fibrosis imaging, scoring, and marker methods: transient elastography, aminotransferase platelet ratio index (APRI), as well as fibrosis-4 (FIB-4) score.

Objective: The purpose of this research was comparing the novel fibrosis index to APRI, (FIB-4) score and fibroscan in predicting the degree of hepatic fibrosis in Egyptian chronic HCV patients who were managed by DAAs.

Patients and methods: 100 Egyptians with chronic HCV infection participated in a our 3-month long prospective Cohort research using the IFN-free DAA combination of Sofosbuvir and Daclatasvir ± Ribavirin.

Results: There was significant regression of fibrosis with DAAs treatment in all patients achieving SVR by fibroscan, APRI and fib4. Novel fibrosis index is reliable and good tool in estimation of liver fibrosis in correlation to fibroscan, with the cutoff value in prediction of hepatic fibrosis stage 4 was >3.1 and has sensitivity of 81.5% while the specificity was 74.1%.

Conclusion Novel fibrosis index has been found to be good reliable marker for assessment of liver fibrosis with high accuracy of predicting f4 fibrosis stage. There was significant marked reduction of fibrosis degree by fibroscan, APRI and FIB4 after DAAs treatment.

Keywords: DAAs, SVR, NFI, liver fibrosis indexes.

INTRODUCTION

Hepatitis C virus (HCV) infection is a prominent cause of chronic liver disease globally, and in certain cases has been linked to liver cancer [(1)]. Management lines for chronic hepatitis C virus (CHC) infection have shifted from the use of peginterferon and ribavirin (PegIFN/RBV, PR) to that of direct antiviral medicines (DAAs) [(2)].

High ratios of sustained virological response (SVR) are accompanied by a minimizing risks of hepatic fibrosis as well as decreasing risky consequences such hepatic failure and portal hypertension [(3)].

Studies have demonstrated that patients with CHC who are managed with IFN and achieve SVR had a lower risk of advancing hepatocellular carcinoma (HCC) and other liver-related problems, and an enhanced health-related quality of life [(4)].

Liver fibrosis stage is a well-established predictor of disease severity and problems in chronic HCV infection; F4 fibrosis is most typically linked to ascites, hepatic encephalopathy, portal hypertension, and other implications. Proper staging of hepatic fibrosis in chronic HCV infection is crucial for achieving timely treatment and optimal therapeutic outcomes. In addition, in low and middle-income countries, where complete eradication of virus in each instance is crucial, a correct diagnosis of fibrosis is especially vital in deciding when to commence antiviral therapy in patients with chronic HCV infection [(5)].

Liver biopsy has mostly been superseded by less invasive methods, such as fibrosis scores, imaging methods, and novel blood fibrosis markers [(3)]. The aminotransferase (AST)/platelet ratio index (APRI) and fibrosis-4 (FIB-4) scores are two of the most common methods used to assess liver damage in individuals with viral hepatitis C, especially those with advanced fibrosis and cirrhosis [(6)]. Rapid and noninvasive, transient elastography (TE) has found widespread application in clinical practice due to its excellent sensitivity and specificity for detecting advanced fibrosis [(7)].

Since the results of the novel fibrosis index correspond with the expected fibrosis stages, F3 and F4, go with the FibroScan® test and are highly confirmed by clinical data in patients with chronic HCV infection, it is a valuable and reliable tool for predicting fibrosis progression [(8)].

AIM OF OUR STUDY

The purpose of this research was to compare the novel fibrosis index to APRI, (FIB-4) score and fibroscan in predicting the degree of hepatic fibrosis in Egyptian chronic HCV patients who were managed by DAAs.

PATIENTS AND METHODS

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This prospective study included 100 Egyptians with chronic hepatitis C infection who were recruited from the Hepatology and virology outpatient clinic at Ain Shams University Hospital. None of the volunteers were younger than 18 years old.

Inclusion criteria: DAA (Sofosbuvir & Daclatasvir ± Ribavirin) treatment for 3 months in 100 patients who are 18 years old or older with chronic hepatitis C virus infection.

Exclusion criteria: Decompensated liver cirrhosis in pregnant women (child-pugh score C). Hepatocellular Carcinoma Patients, Patients with a history of heavy alcohol use, patients taking agents that decrease lipids (such as fibrates or statins), patients taking long-term steatosis-inducing drugs (such as corticosteroids, tamoxifen, and amiodarone), patients abusing intravenous drugs, patients with diabetes, patients with chronic kidney disease whose estimated GFR is less than 30 ml/min/1.73 m, and patients who refused to participate.

Methods:

All patients was subjected to the following:

Full history taking included history of lower limb edema, abdominal enlargement, encephalopathy, bleeding etc..).

Full clinical examination: any palapable mass, ascites, jaundice, edema, etc…).

Laboratory investigations including Complete blood count, Liver function tests including: serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), alkaline phosphatase, total and direct bilirubin, INR as well as serum albumin. Before and after treatment completion, serum HCV RNA concentrations were measured using PCR technique. Alpha fetoprotein, creatinine, and prothrombin time in the serum.

- Calculation of novel fibrosis index:

$$NFI = \left[\frac{Bilirubin \times (ALP)^2}{Platelet\ Count (Albumin)^2}\right]$$

- **APRI**= [{AST (IU/L)/AST_ULN (IU/L)}×100]/platelet count (10^9/L).

The APRI score less than 0.5 rule out cirrhosis and greater than 1.5 rule in cirrhosis.) In between values are less helpful.

- FIB-4=[age(years)×AST (IU/L)]/[platelet count(×10^9/L)×ALT (IU/L)1/2].

(The negative predictive value of the FIB-4 score was 90% for advanced fibrosis when it was less than 1.45. Instead, a FIB-4 >3.25 would be 97% specific and 66% predictive of advanced fibrosis).

Radiological investigation:

Abdominal ultrasonography and Fibroscan before and after the end of treatment.

Fibroscan: To perform ultrasound elastography, a standard ultrasound probe is adapted to monitor the speed of a shear wave generated by a vibratory source. Liver fibrosis stages can be estimated by the liver's stiffness using ultrasonography. Kilopascals (kPa) are used to measure the results, and the range is from 2 to 75. FibroScan® readings typically fall within a range of 2 to 7 kPa. There are 4 distinct phases of scarring. The absence of scarring is denoted by the letter F, while mild fibrosis (F1), moderate fibrosis (F2), severe fibrosis (F3), and cirrhosis (F4) are all more severe forms of scarring.

Patients were prescribed Direct Acting Antiviral therapy courses that met the standards set by the National Committee for the Control of Viral Hepatitis C. Care following treatment: Sustained Virologic Response was determined by testing all patients 12 weeks after therapy ended for HCV RNA (SVR).

Statistical methods:

Descriptive statistics

Quantitative information was presented as a description of qualitative data in terms of numbers (frequency and percentage). Range, median, and standard deviation were used to characterize the quantitative data.

Analytical statistics

SPSS V17 was used to display and analyze statistical data from this study, including means, standard deviations, t-tests, ANOVAs, and linear correlation coefficients. If the P-value is larger than 0.05, the result is not statistically significant; if it is between 0.05 and 0.01, the result is significant; and if it is less than 0.01, the result is very significant.

Ethical approval:

Using the FWA assurance number FWA 000017585, the FMASU Research Ethics Committee (REC) is a nationally recognized organization. The REC was founded and works in compliance with guidelines from the International Council for Harmonization (ICH), the Islamic Organization for Medical Sciences (IOMS), the U.S. Office for Human Research Protections, and the U.S. Code of Federal Regulations.

RESULTS

Table 1 highlights the baseline data of chronic HCV patients involved in the study with mean age was 47.720±10.604 years and majority of them were males 79%, mean value of PCR was 1261843.290±304531.124IU\ml.

Table (1): Baseline data of enrolled patients in our study

All patients (n= 100)	
Age (year)	47.720±10.604
Sex Male Female	 79 (79%) 21(21%)
PCR (IU/ml) Baseline	1261843.290±3531.124

Data expressed as frequency (percentage), mean ± SD

The following table 2 show laboratory data of our patients before and after DAAs treatments with significant improvement of the value of platelet, AST, ALT and ALP after treatment. Also these were changes in value of hemoglobin with P-value 0.01 and albumin with P-value 0.15.

Table (2): Baseline and follow up laboratory data of enrolled patients

	Baseline (n= 100)	**Follow up (n= 100)**	***P* value**
Leukocytes (10^3/ul)	3.7 ±0.9	3.8±0.82	0.063
Hemoglobin (mg/dl)	14.330± 1.319	14.649±0.903	0.010
Platelets (10^3/ul)	159.490±37.213	206.180±43.714	<0.001
INR	1.068± 0.166	1.041± 0.239	0.283
Bilirubin (mg/dl)	0.930± 0.211	0.936± 0.201	0.873
ALT (u/l)	38.540 ± 8.701	28.100±6.143	<0.001
AST (u/l)	46.330±11.432	22.290±5.263	<0.001
Albumin (g/dl)	3.972±0.224	4.046±0.240	0.015
ALP	97.279±22.353	66.572± 15.32	<0.001

Prior to treatment with DAAs, there was a positive and statistically significant association between fibroscan fibrosis scores and APRI, FIB4, and NFI. Also, the fibrosis stages related significantly to platelets count and INR. These results showed in table 3.

Table (3): Correlation between different laboratory, Age and HCV PCR, BMI, HBA1c before DAAs treatment and baseline fibroscan stages.

Fibroscan	
Age (years)	**1.271(0.298)**
HCV PCR level (u/l)	1.418 (0.242)
BMI (kg/m2)	0.874 (0.457)
Hemoglobin (mg/dl)	-0.051 (0.617)
Leukocyte (103/ul)	1.595 (0.196)
Platelets (103/ul)	5.268 (0.002*)
INR	6.073 (0.001*)
Bilirubin (mg/dl)	1.856 (0.142)
ALT (u/l)	0.603 (0.614)
AST (u/l)	0.658(0.580)
Albumin (g/dl)	3.662 (0.015)
ALP	**2.502 (0.064)**
FIB-4 index baseline	**7.361 (< 0.001*)**
APRI score baseline	**3.295(0.024)**
NFI	14.306(0.001*)
HBA1C	2.619(0.055)

With follow up after treatment with DAAs, the indices of fibrosis were significantly decreased as FIB-4 index and APRI score with p value less than 0.001, and also the degree of fibrosis estimated by fibroscan showed marked improvement with P value was 0.001. These results were shown in the following table 4.

Table (4): Comparison of the degree of fibrosis by fibroscan, APRI and FIB4 before and 12 weeks post DAAs treatment

	Baseline (n= 100)	**Follow up (n= 100)**	***P* value**
Fibroscan			
F1	23.00	48.00	
F2	19.00	2.00	
F3	20.00	22.00	0.001
F4	38.00	28.00	
FIB-4 index	2.480±0.53	1.73 ± 0.36	< 0.001
APRI score	0.764±0.170	1.050±0.211	< 0.001

The next table 5 show the diagnostic performance of each marker in predication of fibrosis stage 4 with cutt of value of noval fibrosis index was more than 3.1, sensitivity was 81.58%, specificity was 74.19%, PPV 66%, NPV 86% which were more than APRI and FIB4. While APRI sensitivity was 63%, specificity was 67%, positive predictive value 54%, negative predictive value 75% and FIB4 sensitivity was 73%, specificity was 64%, PPV 56%, NPV 80%.

Table (5): Diagnostic performance of NFI, APRI and FIB4 in prediction of hepatic fibrosis stage 4 (advanced cirrhosis)

ROC curve between F1&2&3 and F4 Fibro scan Baseline						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
NFI	>3.1	81.58	74.19	66.0	86.8	79.4%
APRI	>0.73	63.16	67.74	54.5	75.0	63.7%
FIB4	>2.21	73.68	64.52	56.0	80.0	73.6%

Data expressed as frequency (percentage).

Table 6 Shows significant correlation between noval fibrosis index baseline and **age** with P-value 0.003, **leukoytes** with P-value 0.048, **Platelets** with P-value <0.001, **INR** with P-value <0.001, **AST** with P-value 0.009, **T.bilirubin** with P-value 0.001, **Albumin** with P-value 0.003, **ALP** with P-value <0.001, **APRI** score with P-value <0.001, **FIB4** with P-value <0.001and **fibroscan** stages with p-valve<0.001.

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Table (6): Correlation between baseline NFI score and Age, Gender, APRI, FIB4,HCV PCR, BMI, Fibroscen, HBA1c and different laboratory parameters

NFI	
Age (years)	**0.299(0.003)**
Gender	-0.277(0.782)
HCV PCR level (u/l)	0.019 (0.849)
BMI (kg/m2)	0.014 (0.889)
Hemoglobin (mg/dl)	-0.054 (0.591)
Leukocyte (103/ul)	**-0.198 (0.048)**
Platelets (103/ul)	**-0.421 (<0.001*)**
INR (baseline)	**0.491 (<0.001*)**
Bilirubin baseline (mg/dl)	**0.318 (0.001)**
ALT baseline (u/l)	0.155 (0.124)
AST baseline (u/l)	**0.258(0.009)**
Albumin baseline(g/dl)	-0.290 (0.003)
ALP baseline	**0.79 (< 0.001)**
FIB-4 index baseline	**0.591 (< 0.001)**
APRI score baseline	**0.497(< 0.001)**
HBA1C	-0.188 (0.61)
Fibroscan	14.306(< 0.001)

Table 7 shows a significant correlation on post treatment noval fibrosis index with age (P=0.003), platelets (P <0.001), international normalized ratio (P <0.001), aspartate aminotransferase (AST) (P <0.001), alanine aminotransferase (ALT) (P <0.001), t-bilirubin (P <0.001), albumin (P <0.001), alkaline phosphatase (ALP) (P <0.001), APRI (P <0.001),fib-4 (P <0.001), fibroscan (P <0.001).

Table (7): Correlation between Post treatment NFI score and Age, Gender, APRI, FIB4, PAUS, Fibroscen HCV PCR baseline, BMI, HBA1c and different laboratory parameters

NFI	
Age (years)	**0.299(0.003)**
Gender	0.558 (0.578)
HCV PCR level (u/l)	0.310 (0.002)
BMI (kg/m2)	0.090 (0.372)
Hemoglobin (mg/dl)	-0.051 (0.617)
Leukocyte (103/ul)	0.095 (0.348)
Platelets (103/ul)	-0.524 (<0.001*)
INR (posttreatment)	0.600 (<0.001*)
Bilirubin posttratment (mg/dl)	0.406 (0.001)
ALT posttreatment (u/l)	0.499 (<0.001*)
AST posttreatment (u/l)	0.556(<0.001*)
Albumin posttreatment(g/dl)	-0.547 (<0.001*)
ALP posttreatment	**0.482 (< 0.001*)**
FIB-4 index posttreatment	**0.718 (< 0.001*)**
APRI score posttreatment	**0.699(< 0.001*)**
Fibroscan posttreatment	5.591(0.001)

DISCUSSION

Chronic hepatitis C virus (HCV) infection, which may lead to cirrhosis and hepatocellular cancer, is a serious global health concern [(1)]**.** In the treatment of chronic hepatitis C virus (CHC) infection, direct antiviral medications (DAAs) have essentially replaced peginterferon and ribavirin [(2)]**.**

Hepatic fibrosis improves and other problems including hepatic failure and portal hypertension are less likely when the rate of sustained virological response (SVR) is high [(3)]**.**

During the period of October 2020–April 2022, 100 Egyptian individuals with chronic hepatitis C were recruited from the Hepatology and virology outpatient clinic at Ain Shams University Hospital with informed consent from candidates for novel antiviral treatment with DAAs. All study subjects reached sustained virological response with maintaining negative HCV RNA PCR during follow up period.

Similar to the findings of **Dahal *et al.*** [(9)], those of us who looked at the effect of DAA on platelets in individuals with pretreatment thrombocytopenia reported a significant rise in platelet count 12 weeks after therapy with DAA (P< 0.001).

It was also determined by van der **Meer & Berenguer** [(10)] that chronic HCV-infected individuals with advanced liver disease who are properly treated show a steady improvement in histological abnormalities and portal pressure. The fact that individuals who had achieved SVR also had smaller spleens provided additional credence for this theory. After more than 6 months of HCV suppression, SVR may be achieved without worrying about bone marrow suppression brought on by HCV or interferon-based

treatment [11]. Due to an inverse relationship between TPO production and hepatic fibrosis severity, elevated TPO levels may remain important for platelet recovery even after SVR has taken place [12]. While **Menesy *et al.*** [13] found no significant difference between pre- and post-treatment haemoglobin levels (11.4 and 10.84 gm/dl, respectively), in this study there was a significant improvement of haemoglobin level 12 weeks after treatment with DAAs with a P value of 0. 010. On the other hand, **El Sagheer *et al.*** [14] found that the hemoglobin level dropped significantly from 13.6 before treatment to 12.7 after. Another study found that therapy with DAAs resulted in a statistically significant increase in hemoglobin ($p < 0.001$). It had mean values of 13.19 and 12.57 gm/dl before and after treatment respectively done by **Shousha *et al.*** [15]. Additionally, **Alhaddad *et al.*** [16] also reported a significant change in hemoglobin level after DAA therapy. It decreased from 12.28 gm/dl down to 10.09 gm/dl after treatment.

Liver enzymes ALT and AST improved significantly in all SVR patients in the current study with a P value 0.001. These results are consistent with those of **Menesy *et al.*** [13], researchers in Egypt looked at how 100 patients with chronic Hepatitis C responded to DAA treatment, and they discovered a substantial drop in hepatic transaminase levels and an improvement in the patients' BMIs and lipid profiles. With SVR in place, hepatic inflammation should decrease, which could account for this phenomenon. Consistent with our results, several investigations found that hepatic transaminase levels dropped significantly after SVR in response to DAAs [16]. Also **El Kassas *et al.*** [17] who examined the effect of DAA therapy on ALT levels in 1160 patients with chronic hepatitis C Liver enzymes were observed to be significantly reduced in Egyptian individuals treated with interferon-free regimens compared to those treated with interferon-containing regimens. In contrast, **Russo *et al.*** [18] which studied the effect of HCV eradication with DAA on insulin resistance found no difference between pretreatment and post treatment level of AST and ALT.

Similar to the findings of **Menesy *et al.*** [13], we found that albumin levels rise significantly after DAA therapy of HCV, and this was statistically significant at the P value of 0.015., as it increased from 3.16 g/dl before therapy up to 3.38 gm/dl after therapy. In contrast **Abdulhameed *et al.*** [19] reported a significant decrease in albumin levels after DAA therapy, however, that result was not clinically significant as both of the pre-treatment and post-treatment values were within the normal range. They had mean values of 4.2 and 4.1 gm/l before and after treatment respectively.

The current study showed no significant change between pretreatment and post treatment levels regarding INR level similar to **Shousha *et al.*** [15] who negated any significant change in INR after DAAs therapy. In contrast to **Menesy *et al.*** [20] revealed that INR showed a significant improvement after DAAs treatment as it decreased from 1.29 down to 1.22 ($p = 0.012$). This may be explained because low number of patients in our study and also the majority of the patients have compensated cirrhosis.

The current study showed no significant change between pretreatment and post treatment levels regarding bilirubin level similar to the studies published by **Menesy *et al.*** [13], **Shousha *et al.*** [15] and **Russo *et al.*** [18] which revealed no significant change of bilirubin level after treatment with DAAs. On the other hand, **Alhaddad *et al.*** [16] reported a significant decrease in serum bilirubin levels after DAA combined with ribavirin treatment ($p < 0.001$). It decreased from 1.5 mg/dl before treatment down to 0.9 mg/dl after treatment. This may be explained because low number of patients in our study and also the majority of the patients have compensated cirrhosis.

Our study demonstrated a significant improvement of alkaline phosphatase levels after DAAs treatment.in contrast with the studies published by **Menesy *et al.*** [13] and **Russo *et al.*** [18] which revealed no significant change of alkaline phosphatase after treatment with DAAs.

In the current study we used transient elastography (fibroscan) to assess the degree of fibrosis of all patients before and after treatment. There was significant regression of degree of fibrosis after treatment with DAAs in all patients achieving SVR with P value of <0.001. This is in keeping with the results published by **Bachofner *et al.*** [21] which shown a dramatic improvement in liver fibrosis scores during and after DAA treatment, while in contrast to our study **Knop *et al.*** [22] showed that true regression of liver fibrosis may takes longer, which may be explained because most of patients in our study was in early stages of fibrosis and also may be due to different HCV genotypes. Similar to the findings of **Huang *et al.*** [23] in 2020, our study found a statistically significant reduction in APRI and FIB4 scores 12 weeks after the completion of DAA treatment compared to their baseline on fibro scan, they looked at the prediction of fibrosis even after SVR by DAAs, and found that APRI and FIB4 Scores decreased significantly following HCV treatment, possibly due to the improvement in inflammation. Median LSM dropped from 12.7 to 8.6 kPa after SVR (P0.001), and FIB-4 and APRI readings also dropped significantly**,** in a study by **Bachofner *et al.*** [21].

Our findings on the significant reductions in LSM, APRI, and FIB-4 following SVR are consistent with those of a previous retrospective study on HCV patients treated with DAAs by **Hsu *et al.*** [24]**,** who found that APRI and FIB-4 declined rapidly and persistently from week 2 until SVR12, and that a study by **Facciorusso *et al.*** [25] assessing the magnitude of change in LSM up to 5 years after therapy.

Our results showed that baseline fibrosis stage by fibroscan was significantly correlated with platelet

count, INR level, albumin and there was significant improvement of liver fibrosis by fibroscan after successful treatment of HCV with DAAs which was significantly correlated with TLC, platelet count, albumin, INR. This is consistent with **Hafez *et al.*** [26] Serum albumin and platelet count were shown to have a strong association with the severity of liver fibrosis stage (p-value 0. 01). Unlike **Tag-Adeen *et al.*** [27] Patients who showed improvement on the LSM scale (n=64) following treatment with direct-acting antivirals for hepatitis C virus genotype 4 had higher baseline levels of bilirubin, ALT, and AST than patients who did not (n=16), but there were no differences in age, albumin, INR, or platelets. Furthermore, in those individuals (n=64), an improve in LSM was linked with a improve in AST and APRI in 91% (p=0.01), and an decrease in Fib-4 in 81% (p=0.04); however, an improvement in LSM was not associated with a decrease in ALT (p=0.9) or an increase in platelets (p=0.06). Given these results, it is clear that FIB-4 and APRI levels are significantly greater in the advanced fibrosis group, and this agrees with the results of research by **Karic *et al.*** [28] **and Daniela et al** [29].

In our study we found that novel fibrosis index is significantly correlated to different stages of fibrosis by fibroscan with high sensitivity(81.5%) in detection severe fibrosis F4 by fibroscan similar to the study published by **Azhar *et al.*** [8] which examined the effectiveness of the Novel Fibrosis Index (NFI) in comparison to other fibrosis serum indices and with transient elastography (fibroscan) in assessing liver fibrosis, concluded that the NFI was more effective in staging fibrosis. Our results, like those of the studies, showed a considerable decline in NFI following HCV treatment with DAAs, indicative of a marked reduction in liver fibrosis following DAA treatment.

Our research confirmed the validity of using APRI and FIB 4 to evaluate liver fibrosis. In predicting hepatic fibrosis stage 4, the cutoff values for APRI and FIB4 are respectively >0.73 (sensitivity 63.16 percent, specificity 67.74 percent, PPV 54.5 percent, NPV 75.0 percent, and test accuracy 63.70 percent) and >2.21 (sensitivity 73.68 percent, specificity 64.52 percent, PPV 56 percent, NPV 80 percent, and test accuracy 73.6 percent). These findings are consistent with those of studies reported by **Rungta *et al.*** [30], where they found that APRI and FIB-4 outperformed Fibroscan in identifying patients without liver fibrosis and gave satisfactory results in identifying severe fibrosis. Consistent with the findings of **Papadopoulos *et al.*** [31], who demonstrated that the APRI/FIB-4 combination was useful for predicting substantial fibrosis.

With a threshold value of >3.1 for the prediction of hepatic fibrosis stage 4, our research showed that the noval fibrosis index is a reliable and good instrument in assessing liver fibrosis, in particular substantial fibrosis, with a sensitivity of 81.5% and a specificity of 74.1%. Results showed a 66 percent PPV, an 86 percent NPP and .An accuracy of 79.4% on the test indicates continuity. According to the findings of **Azhar *et al.*** [8], NFI correctly predicted F3, and its prediction of F4 fibrosis stage was more sensitive and specific than those of other FIs.

The research by **Kumar *et al.*** [32] found that both the noval fibrosis index (NFI) and the (APRI) were good predictors for liver fibrosis in patients with NAFLD, with coefficient indices of 0.5174 and 0.5369, respectively**. Singh *et al.*** [33] also found agreement with our result when they compared the effectiveness of the noval fibrosis index and fibroscan in predicting liver fibrosis. This research shows that NFI is the most reliable marker for predicting fibrosis progression in HCV patients.

No enough studies discussed the correlation of NFI and liver fibrosis in chronic HCV patients after direct acting antiviral treatment. So we need more researches on large population sample with different geographic distribution to highlight the importance and the efficiency of noval fibrosis index in follow up liver stiffness after DAAs therapy.

CONCLUSION

There was significant regression of fibrosis with DAAs treatment in all patients achieving SVR by fibroscan, APR and fib4. Novel fibrosis index is reliable and good tool in determining of liver fibrosis in correlation to fibroscan, with the cutoff value in prediction of hepatic fibrosis stage 4 was >3.1 and has sensitivity of 81.5% while the specificity was 74.1%.

Novel fibrosis index has been found to be good reliable marker for assessment of liver fibrosis with high accuracy of predicting f4 fibrosis stage.

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Author contribution: Authors contributed equally in the study.

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