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Evaluation of Red Cell Distribution Width (RDW) to Platelet Ratio as A Novel Non-Invasive Index for Predicting Hepatic Fibrosis in Patients with Chronic Hepatitis C before and after Antiviral Treatment

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ABSTRACT
Background: For the purpose of making decisions and providing treatment for individuals infected with HCV, liver fibrosis must be accurately staged. Prior to starting medication, the degree of the fibrosis should be evaluated. cirrhosis patients must be identified in order to establish treatment plans and to monitor HCC patients after treatment.
Objective: This study aimed to find a readily accessible haematological CBC markers, a regular, low-cost method of predicting severe fibrosis and cirrhosis.
Patients and methods: The study included 50 patients with chronic hepatitis C virus. They were divided into two groups: Group I included 25 Non-cirrhotic patients having chronic HCV infection and group II that included 25 cirrhotic CHILD A patients having chronic HCV infection.
Results: Before treatment, sensitivity and specificity for RDW/Platelet ratio, APRI and FIB_4 for fibrosis cases (F1, F2 & F3) were evaluated by constructing ROC curve, which showed an excellent (in FIB_4) and good (in RDW/Platelet ratio & APRI) degree of accuracy. The areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were (0.857, 0.821 and 0.911) respectively. For APRI at cut off point 0.35, the sensitivity was 75%. For FIB_4 at cut off point 1.39, the sensitivity was 100%. After treatment, sensitivity and specificity for RDW/Platelet ratio, APRI, FIB_4 for fibrosis cases (F1, F2) and sensitivity & specificity for RDW/Platelet ratio, APRI, FIB_4 for cirrhotic cases (F3, F4) were evaluated. For APRI at cut off point 0.65, the sensitivity was 100% For FIB_4 at cut off point 1.895, the sensitivity was 100%. **Conclusion:** According to our findings, RDW/PLT might accurately determine the degree of liver fibrosis and cirrhosis prior to HCV therapy. While following HCV therapy, we may rely on RDW/PLT to predict the degree of advanced liver fibrosis and cirrhosis (F3 & F4) with great accuracy.
Keywords: Fib-4, APRI, HCV, HCC, CHC, RDW/Platelet ratio.

INTRODUCTION

Worldwide, around 71 million persons have chronic hepatitis C virus (HCV) infection. A high proportion of patients who are persistently infected develop cirrhosis or liver cancer. Each year, around 399, 000 people die from liver cirrhosis and hepatocellular carcinoma [(1)].

Assessment of hepatic fibrosis in chronic HCV infection is regarded as an important aspect of patient treatment and a major decision-making tool. Higher levels of fibrosis have been linked to hepatic decompensation [(2, 3)]. The proper staging of hepatic fibrosis is critical for successful decision-making and management of HCV patients [(2)]. The degree of fibrosis should be determined prior to medication; identifying individuals with cirrhosis is critical in defining treatment regimens and post-treatment monitoring of HCC patients [(4)].

For many years, liver biopsies were considered the gold standard for staging liver fibrosis. Information on necro-inflammatory activity and characteristics like steatosis and iron overload may also be obtained by histological investigation. Nevertheless, taking a liver biopsy is an intrusive procedure that carries some risk. Following a liver biopsy, around 25% of patients have discomfort in the right upper quadrant or right shoulder. Mild sequelae are also very frequent. Severe consequences are rare and include death rates of less than 0.15% and major bleeding rates ranging from 0.05% to 5.3% [(5)]. Furthermore, there is a considerable amount of intra- and inter-observer variability and sampling error associated with liver biopsies [(6)].

For the assessment of liver fibrosis in chronic HCV infection, a number of noninvasive indicators have been proposed. Imaging method and serum biomarkers are the two categories into which these indicators may be separated. Serum biomarkers are often obtained by combining clinical or laboratory parameters in a particular model with normal laboratory testing. For example, the APRI (AST to platelet ratio) score, the modified APRI score (age, AST, PLT, Albumin), and the Fib-4 score (ALT, AST, PLT). Transient hepatic elastography (TE) using fibroscan is an imaging technology that demonstrates a strong relationship between TE and fibrosis stage as determined by the METAVIR grading system [(7)].

RDW to PLT ratio has a comparatively high accuracy in predicting fibrosis in individuals with CHB [(8, 9)].

This study aimed to use readily accessible haematological CBC markers, a regular and low-cost method of predicting severe fibrosis and cirrhosis.

PATIENTS AND METHODS

50 adult patients with chronic hepatitis C virus were split into two groups for this investigation: Group (I) included 25 non-cirrhotic patients having chronic HCV infection and group II that included 25 cirrhotic CHILD A patients having chronic HCV infection. The patients

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were enrolled from Ain Shams University's Gastroenterology Outpatient Clinic at Al Demerdash Hospital.

Inclusion criteria: Adult (18-75) years-old-pts form males and females who were willing to participate and to give an informed consent. Patients who had both positive PCR HCV (RNA) and positive HCV antibody. Patients within the clinical spectrum consistent with chronic HCV. Patients planned to take antiviral treatment. Non cirrhotic & CHILD A cirrhotic patients.

Exclusion criteria: Pregnancy and lactation. HIV coinfected patients. HBV coinfected patients. Younger than 18 and older than 75 years old.

Every patient in the study underwent the following:

1. Detailed history and clinical examination:

- Age, sex, and residence. Symptoms related to chronic liver disease as jaundice, bleeding tendency, history of encephalopathy.

2. Examination: Full Clinical examination will be performed for all patients including manifestations of chronic liver disease.

3. Biochemical laboratory investigations:

A) Complete blood picture (TLC, RBCs, hemoglobin, RDW, platelets).
B) Biochemical liver profile: (s. bilirubin, s. aminotransaminases (ALT, AST), alkaline phosphatase, s. albumin, and prothrombin time.
C) Anti HCV Ab, HbsAg.
D) PCR HCV (RNA) before and after treatment.
E) RPR=RDW% / platelet (10^9/L) before and after treatment.
F) The FIB-4 score was calculated using Sterling's formula as: Age (y) × AST (IU/l) /platelet count (×109/liter) ×√ALT (IU/l)) before and after treatment.
G) The APRI score was calculated using Wai's formula: (AST/upper limit of normal)/platelet count (expressed as platelets × 109/L) × 100 before and after treatment.

4. Pelvi abdominal ultrasound.

5. Fibroscan before and after treatment.

Ethical approval: The Ethics Committee of Ain Shams University's Faculty of Medicine granted the study approval. Following a detailed description of the study's aims, all participants gave informed consents. The Helsinki Declaration was followed throughout the study's conduct.

Statistical methods:

Data management and analysis were performed using SPSS V. 22.0. We used the Shapiro Walk test to see if the data were normally distributed. The frequencies and relative percentages were used to depict the qualitative data. Apply the χ^2-test to determine the difference in qualitative characteristics between two or more groups. The formula for quantitative data were represented as mean ± SD. The normally distributed variables (parametric data) in two independent groups were compared using the independent samples t-test. When it was equal to or less than 0.05, the p-value was deemed significant. Every p-value is bidirectional. A significance level of $P < 0.05$ was applied. Agreement (sensitivity, specificity) for RDW/Platelet ratio, APRI, FIB_4 for cirrhotic and non-cirrhotic cases before and after treatment was done using ROC curves.

RESULTS

Non-Cirrhotic Group: Table (1) showed that the mean age was 41.6 ± 11.69 ranged between 25 and 71 years. Positive PCR before treatment was 14897483.4 ± 28839543.79.

Table (1): Age distribution and HCV PCR in the studied non-cirrhotic group before treatment

	Age	PCR before treatment
Min.- Max.	25 - 71	11000 - 94702300
Mean ± SD	41.6 ± 11.69	14897483.4 ± 28839543.79
Median	40	4000000.00

The correlation between RDW/Platelet and APRI & FIB 4 in non-cirrhotic group before treatment revealed statistically significant difference (P = 0.008 and <0.001 respectively). With moderate positive Pearson correlation between RDW/Platelet and APRI (r 0.520) and Strong positive Pearson correlation between RDW/Platelet and FIB 4 (r 0.762). The Correlation between RDW/Platelet and APRI, FIB 4 in non-cirrhotic group after treatment revealed statistically significant difference (P <0.001) with moderate positive Pearson correlation between RDW/Platelet and APRI (r 0.697) and strong positive Pearson correlation between RDW/Platelet and FIB 4 (r 0.804) (Table 2).

Table (2): Correlation between RDW/Platelet and APRI, FIB_4 before and after treatment

Variables	RDW/Platelet before		RDW/Platelet after	
	r*	P	r*	P
APRI	0.520	0.008**	0.697	<0.001**
FIB_4	0.762	<0.001**	0.804	<0.001**

* r (Pearson correlation) **significant

The correlation between RDW/Platelet and fibroscan in non-cirrhotic group before treatment revealed statistically insignificant difference (P = 0.06). There was a weak positive Spearman correlation (rs 0.381) between RDW/Platelet and fibroscan. The correlation between RDW/Platelet and fibroscan in non-cirrhotic group after treatment revealed statistically insignificant difference (P = 0.426). There was a weak positive Spearman correlation (rs 0.166) between RDW/Platelet and fibroscan (Table 3).

Table (3): Correlation between RDW/Platelet and fibroscan before and after treatment

	RDW/Platelet before		RDW/Platelet after	
	rs*	P	rs*	P
Fibroscan	0.381	0.06	0.166	0.426

* rs (Spearman correlation)

The relation between fibroscan before and after treatment in non-cirrhotic group revealed statistically significant difference (P < 0.001) (Table 4).

Table (4): Relation between fibroscan before and after treatment

			Fibroscan2		Monte Carlo test	P value
			F1 (n=17)	F2 (n=8)		
Fibroscan1	F1 (n=14)	Count	14	0	MC 14.988	<0.001*
		% within Fibroscan1	100.0%	0.0%		
	F2 (n=7)	Count	2	5		
		% within Fibroscan1	28.6%	71.4%		
	F3 (n=4)	Count	1	3		
		% within Fibroscan1	25.0%	75.0%		

ROC curve (figure 1) represented the trade-off between sensitivity and specificity for RDW/Platelet ratio, APRI, and FIB_4. The test would be more accurate the closer the ROC plot is to the upper left corner. The scores represented in this figure had curves that were reasonably near to one another, with just minor variations across the various cutoff points. Assuming an outstanding (in FIB_4) and good (in RDW/Platelet ratio, APRI) degree of precision, they were around the upper left corner. Table (5) revealed that the areas under the ROC curve for RDW/Platelet ratio, APRI, FIB_4 were (0.857, 0.821 and 0.911) respectively with standard errors of (0.080, 0.142 and 0.060) respectively. The best cut off points for RDW/Platelet ratio, APRI, FIB_4 were 0.000689, 0.35 and 1.39 respectively. These cut off points were detected by the ROC curve descriptions in the SPSS program version 21. In RDW/Platelet ratio at cut off point 0.000689, the sensitivity was 100% and specificity was 78.6%. For APRI at cut off point 0.35, the sensitivity was 75% and specificity was 42.9%. For FIB_4 at cut off point 1.39, the sensitivity was 100% and specificity was 0.143.

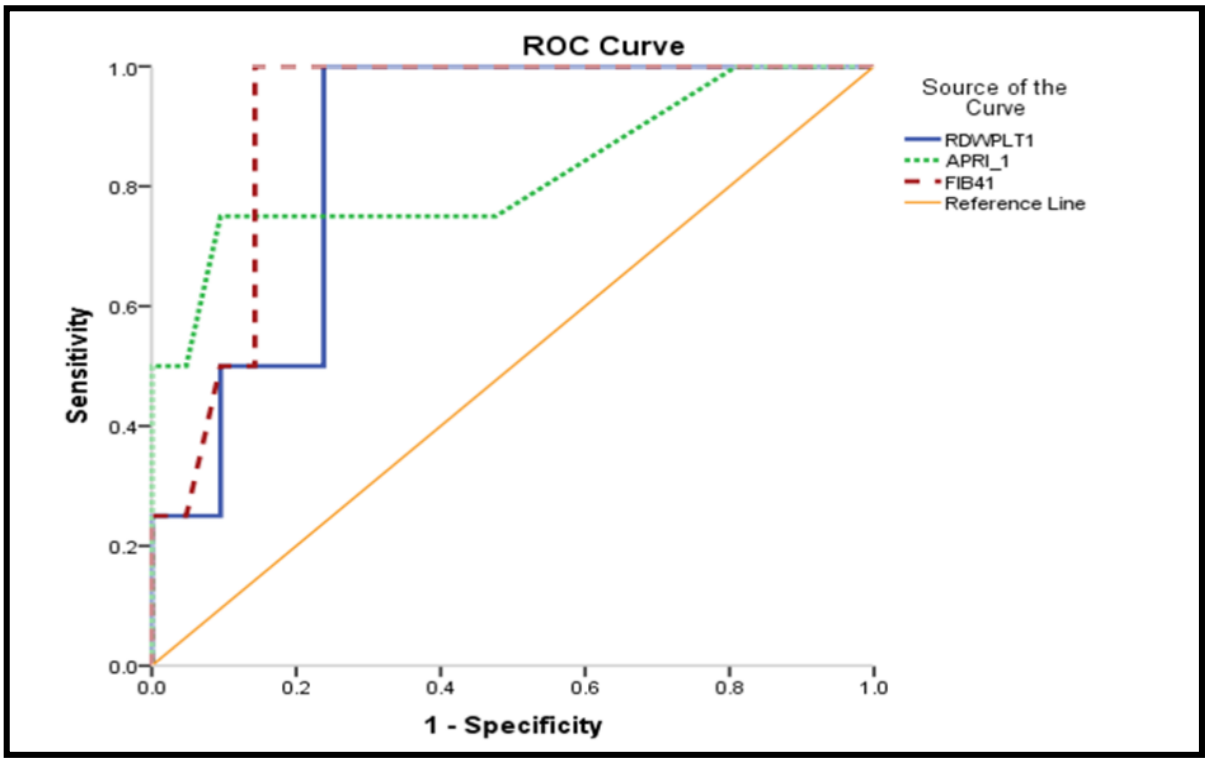

Figure (1): Area under ROC curve denoting sensitivity and specificity for RDW/PLT ratio, APRI, FIB_4 as predictors of fibrosis (before ttt) (F1, F2, F3).

Table (5): Agreement (sensitivity, specificity) for RDW/ PLT ratio, APRI, FIB_4 for fibrosis cases before treatment (F1, F2, F3).

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
RDW/Platelet	0.857	0.026*	0.701 – 1.00	> 0.000689	100%	78.6%	57.1	100
APRI	0.821	0.045*	0.543 – 1.00	> 0.35	75%	42.9%	27.3	85.7
FIB_4	0.911	0.011*	0.793 – 1.00	> 1.39	100%	85.7%	66.7	100.0

AUC: Area Under a Curve P-value: Probability value CI: Confidence Intervals NPV: Negative predictive value PPV: Positive predictive value *: Statistically significant at $p \leq 0.05$

Table (6) revealed that the areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were 0.603 ± 0.123, 0.685 ± 0.123 and 0.603 ± 0.135 respectively. The best cut off points for RDW/Platelet ratio, APRI and FIB_4 were 0.000408, 0.25 and 0.42 respectively. These cut off points were detected by the ROC curve descriptions in the SPSS program version 21. In RDW/Platelet ratio at cut off point 0.000408, the sensitivity was 100 and specificity was 23.5%. For APRI at cut off point 0.25, the sensitivity was 100% and specificity was 0.824. For FIB_4 at cut off point 0.42, the sensitivity was 100% and specificity was 5.9%.

Table (6): sensitivity, specificity for RDW/PLT ratio, APRI and FIB_4 for fibrosis cases after treatment (F1, F2)

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
RDW/ Platelet	0.603	0.415	0.362 – 0.844	> 0.000408	100%	23.5 %	38.1	100
APRI	0.685	0.210	0.417 – 0.899	> 0.25	100%	17.6%	36.4	100
FIB_4	0.603	0.415	0.338 – 0.867	> 0.42	100%	5.9%	33.3	100

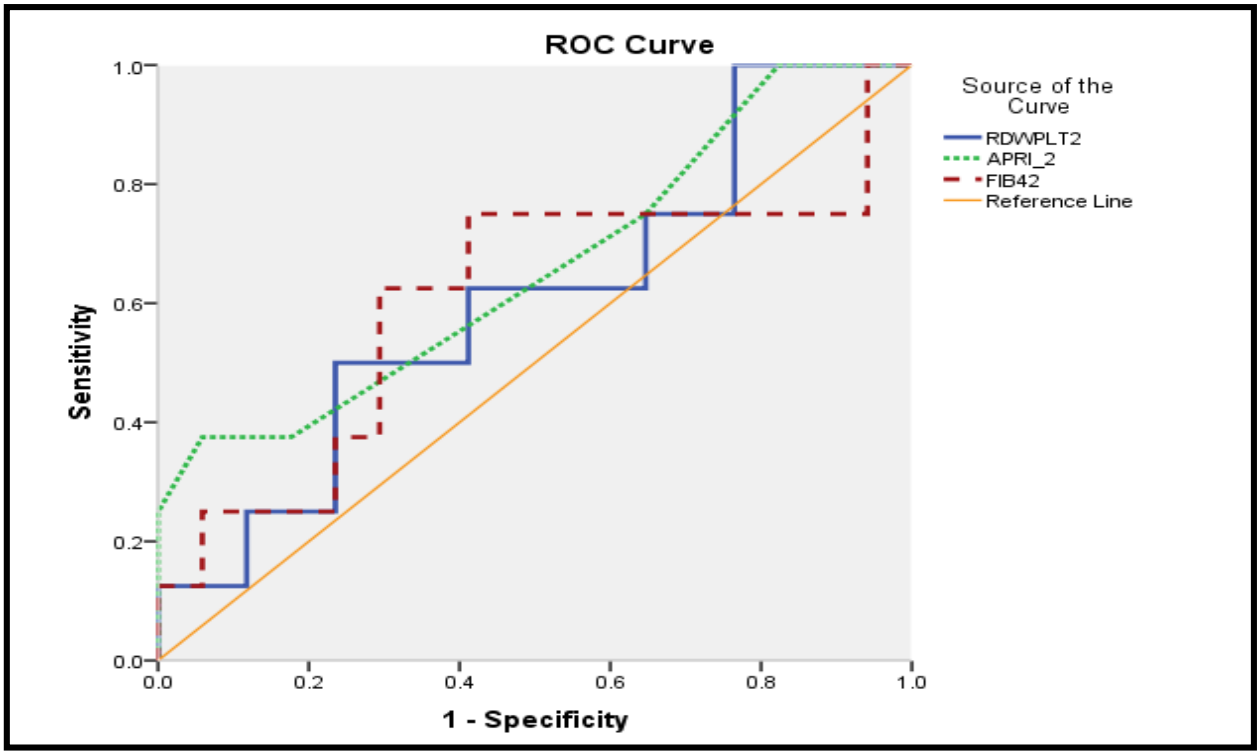

Figure (2): Area under ROC curve denoting sensitivity and specificity for RDW/PLT ratio, APRI, FIB_4 as predictors of fibrosis (after ttt) (F1, F2).

Cirrhotic Group:
Table (7) showed that mean age was 53.7 ± 13.07 ranged between 21 and 76 years and positive PCR before treatment, mean was 3750102.5 ± 5394385.832.

Table (7): Represent the age distribution and HCV PCR in the studied Cirrhotic group before treatment

	Age	PCR before treatment
Min.- Max.	21 - 76	29061 - 28502020
Mean ± SD	53.7 ± 13.07	3750102.5 ± 5394385.832
Median	55	4000000.00

The correlation between RDW/Platelet and APRI & FIB 4 in cirrhotic group before treatment revealed statistically significant difference (P < 0.001 respectively) with strong positive Pearson correlation between RDW/Platelet and APRI (r0.714) and strong positive Pearson correlation between RDW/Platelet and FIB 4 (r0.708).

Regarding the correlation between RDW/Platelet and APRI & FIB 4 in cirrhotic group after treatment, there was statistically significant difference (P <0.001) with strong positive Pearson correlation between RDW/Platelet and APRI (r 0737) and moderate positive Pearson correlation between RDW/Platelet and FIB 4 (r 0.676) (Table 8).

Table (8): Correlation between RDW/Platelet and APRI, FIB_4 before and after treatment

Variables	RDW/Platelet before		RDW/Platelet after	
	r*	P	r*	P
APRI	0.714	<0.001**	0.737	<0.001**
FIB_4	0.708	<0.001**	0.676	<0.001**

Concerning the correlation between RDW/ Platelet and Fibroscan in cirrhotic group after treatment, there was statistically significant difference (P < 0.001) where there was moderate positive Spearman correlation (rs 0.682) between RDW/ Platelet and Fibroscan (Table 9).

Table (9): Correlation between RDW/Platelet and Fibrocsan after treatment

	RDW/Platelet	
	rs*	p
Fibroscan	0.682	<0.001**

The trade-off between sensitivity and specificity for RDW/platelet ratio, APRI, and FIB_4 was shown by the ROC curve in figure (3). The test would be more accurate the closer the ROC plot is to the upper left corner. The scores represented in this figure had curves that were reasonably near to one another, with just minor variations across the various cutoff points. Assuming a high degree of accuracy, they were around the upper left corner.

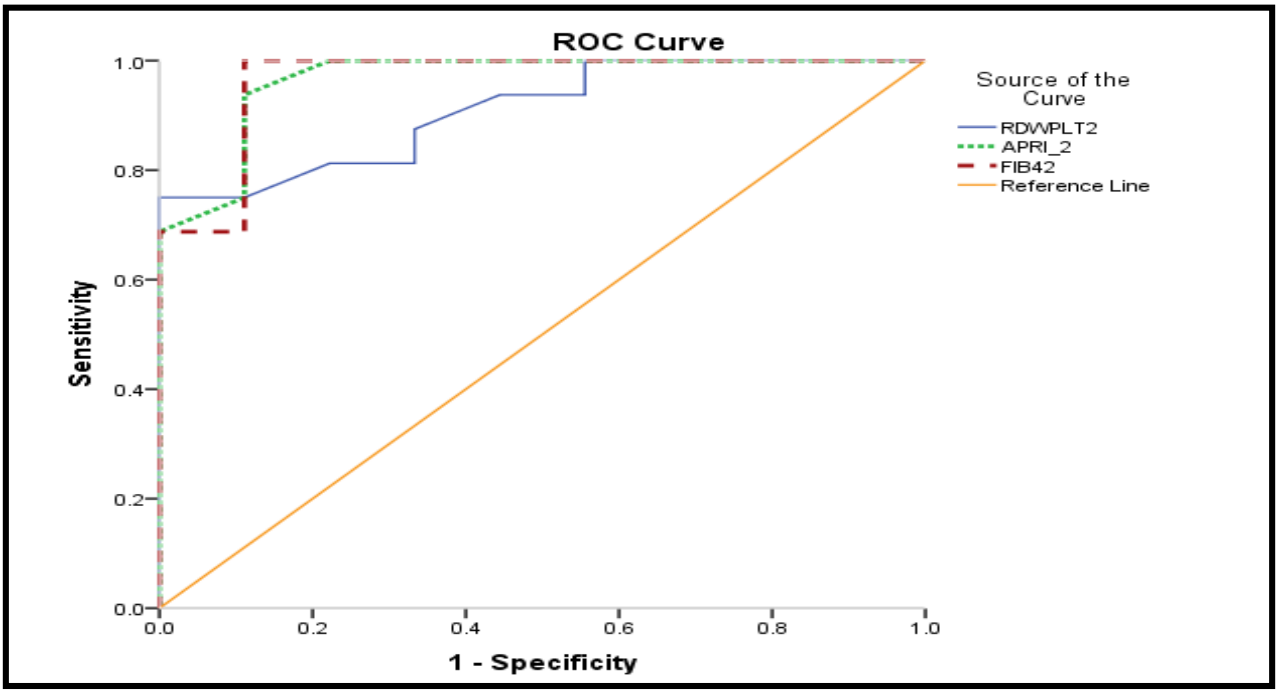

Figure (3): Area under ROC curve denoting sensitivity and specificity for RDW/Platelet ratio, APRI & FIB_4 as predictors of cirrhosis (after ttt) (F3 & F4).

Table (10) revealed that the areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were 0.910 ± 0.057, 0.965 ± 0.035 and 0.965 ± 0.037 respectively). Accuracy of scores was considered excellent for prediction of cirrhosis. The best cut off points for RDW/Platelet ratio, APRI and FIB_4 were 0.000741, 0.65 and 1.895 respectively. These cut off points were detected by the ROC curve descriptions in the SPSS program version 21. In RDW/Platelet ratio at cut off point of 0.000741, the sensitivity was 100% and specificity was 44.4%. For APRI at cut off point 0.65, the sensitivity was 100% and specificity was 77.8%. For FIB_4 at cut off point 1.895, the sensitivity was 100% and specificity was 88.9%.

Table (10): Agreement (sensitivity, specificity) for RDW/Platelet ratio, APRI and FIB_4 for cirrhotic cases after treatment (F3 & F4).

	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
RDW/ Platelet	0.910	0.001*	0.779 – 1.00	> 0.000741	100%	44.4%	76.2	100
APRI	0.965	<0.001*	0.897 – 1.00	> 0.65	100%	77.8%	88.9	100.0
FIB_4	0.965	<0.001*	0.892 – 1.00	> 1.895	100%	88.9%	94.1	100.0

As regards sensitivity and specificity for RDW/platelet ratio, APRI, and FIB_4, it was shown by the ROC curve in figure (4). The test would be more accurate the closer the ROC plot is to the upper left corner. The scores represented in this figure had curves that were reasonably near to one another, with just minor variations across the various cutoff points. Assuming a high degree of accuracy, they were around the upper left corner.

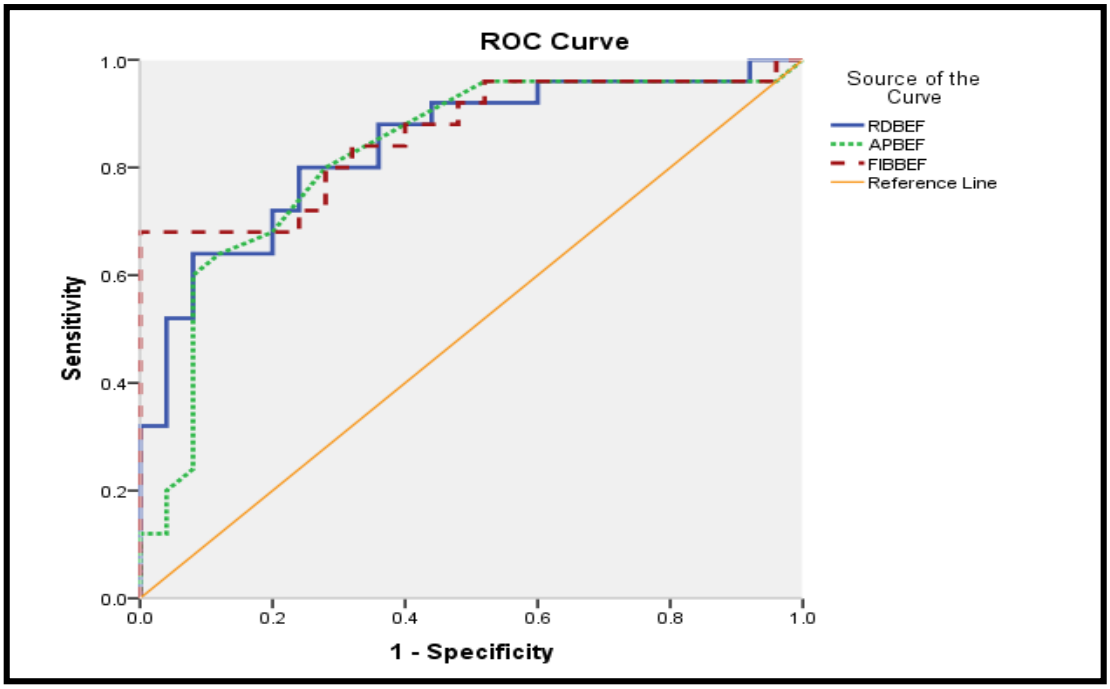

Figure (4): Area under ROC curve denoting sensitivity and specificity for RDW/PLT ratio, APRI, FIB_4 as predictors of cirrhosis (before ttt) (F1, F2, F3, F4).

(Table 11) revealed that the areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were 0.840 ± 0.057, 0.823 ± 0.062 and 0.861 ± 0.054 respectively). Accuracy of scores was considered good for prediction of cirrhosis. The best cut off points for RDW/Platelet ratio, APRI and FIB_4 were 0.000581, 0.45 and 0.8 respectively. These cut off points were detected by the ROC curve descriptions in the SPSS program version 21. In RDW/Platelet ratio at cut off point 0.000581, the sensitivity was 92% and specificity was 56%. For APRI at cut off point 0.45, the sensitivity was 80% and specificity was 72%. For FIB_4 at cut off point 0.8, the sensitivity was 96% and specificity was 48%.

Table (11): Sensitivity and specificity for RDW/ Platelet ratio, APRI and FIB_4 for cirrhotic and non-cirrhotic cases before treatment (F1, F2, F3, F4).

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
RDW/ Platelet	0.840	<0.001*	0.729 – 0.951	> 0.000581	92%	56.0%	67.6	87.5
APRI	0.823	<0.001*	0.702 – 0.945	> 0.45	80%	72.0 %	74.1	78.3
FIB_4	0.861	<0.001*	0.755 – 0.966	> 0.8	96%	48.0%	64.9	92.3

DISCUSSION

Liver fibrosis is a result of persistent liver damage, frequently brought on by several concurrent events. An ideal outcome for assessing the effectiveness of therapy is determining how antiviral medication affects liver fibrosis [10].

A liver biopsy is traditionally the gold standard for determining the degree of fibrosis, despite the fact that it carries a risk of complications and is constrained by sample error and observer variability [11]. Over the last ten years, researchers have worked hard to create a noninvasive diagnostics that can detect liver fibrosis, such as Fibroscan, APRI score, FIB-4 index, and MR elastography. These procedures are limited by these factors, and patients prefer to avoid invasive testing [12].

Non-Cirrhotic group:

In the present study, it was found that mean age was 41.6 ± 11.69 years. This is consistent with **Chen *et al.*** [8] where the mean age was 42.1 ± 11.4 years.

The Correlation between RDW/Platelet and APRI & FIB 4 in non-cirrhotic group before treatment revealed statistically significant difference (0.008 and <0.001 respectively) with moderate positive Pearson correlation between RDW/Platelet and APRI (r 0.520) and strong positive Pearson correlation between RDW/Platelet and FIB 4 (r 0.762). While, after treatment, there was statistically significant difference (P Value <0.001) with moderate positive Pearson correlation between RDW/Platelet and APRI (r 0.697) and strong positive Pearson correlation between RDW/Platelet and FIB 4 (r 0.804).

RDW was linked to an increased risk of death in a number of patient groups. In middle-aged and older persons, the RDW was a good predictor of mortality, according to a prospective research by **Patel *et al.*** [13]. Increased RDW levels were linked to a higher RDW to platelet ratio in individuals with hepatitis B, according to a different research by **Lou *et al.*** [14]. Thus, it can reasonably accurately predict fibrosis in individuals with CHB [8].

Cirrhotic group:

In this study, it was found that mean age was **35.7** ± 13.07 years. While, in **Chen *et al.*** [8], the mean age was 42.1 ± 11.4 years.

The Relation between RDW/Platelet and APRI score in cirrhotic group before and after treatment showed statistically significant difference (P <0.001). The Relation between RDW/Platelet and FIB 4 in cirrhotic group before and after treatment showed statistically significant difference (P <0.001).

The Correlation between RDW/Platelet and APRI & FIB 4 in cirrhotic group before treatment reveal statistically significant difference (P < 0.001) with strong positive Pearson correlation between RDW/Platelet and APRI (r0.714) and strong positive Pearson correlation between RDW/Platelet and FIB4 (r0.708). While after treatment, there was statistically significant difference (P < 0.001) with strong positive Pearson correlation between RDW/Platelet and APRI (r 0737) and moderate positive Pearson correlation between RDW/Platelet and FIB 4 (r 0.676).

Before treatment:

Regarding sensitivity and specificity for RDW/ Platelet ratio, APRI and FIB_4 for fibrosis cases before treatment (F1, F2 & F3), which were evaluated by constructing ROC curve that showed an excellent in FIB_4 and good in RDW/Platelet ratio and APRI degree of accuracy. The areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were 0.857, 0.821 and 0.911 respectively. This is consistent with **Chen *et al.*** [8], who found that in the prediction of substantial fibrosis, the AUCs of the RPR, APRI, and FIB-4 were, respectively, 0.825, 0.740, and 0.826.

The best cut off points for RDW/Platelet ratio, APRI and FIB_4 were 0.000689, 0.35 and 1.39 respectively. In RDW/Platelet ratio at cut off point 0.000689, the sensitivity was 100%. For APRI at cut off point 0.35, the sensitivity was 75%. For FIB_4 at cut off point 1.39, the sensitivity was 100%. While, in **Chen *et al.*** [8] the RDW/PLT ratio sensitivity was 63.1%. APRI sensitivity was 75.4% and FIB4 sensitivity was 67.8%.

Another model of ROC curves was done to detect the sensitivity and specificity for RDW/Platelet ratio, APRI and FIB_4 for cirrhotic and non-cirrhotic cases before treatment (F1, F2, F3 & F4) which showed a good degree of accuracy.

The areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were 0.840, 0.823 and 0.861 respectively. This is consistent with the findings of **Chen *et al.*** [8], who found that the RPR, APRI, and FIB-4 had AUCs of, 0.825, 0.740, and 0.826 respectively in the prediction of severe fibrosis.

Accuracy of scores was considered good for prediction of cirrhosis. The best cut off points for RDW/Platelet ratio, APRI and FIB_4 were 0.000581, 0.45 and 0.8 respectively. In RDW/Platelet ratio at cut off point 0.000581, the sensitivity was 92%. For APRI at cut off point 0.45, the sensitivity was 80%. For FIB_4 at cut off point 0.8, the sensitivity was 96%. While in **Chen *et al.*** [8], the RDW/PLT ratio sensitivity was 63.1%, APRI sensitivity was 75.4% and FIB4 sensitivity was 67.8%. Our study is in agreement with **Elmdams *et al.*** [15] who found that, the RPR's predictive values were estimated using the ROC curve analysis. Concurrently, the AAR, APRI, and FIB-4—three previously used noninvasive indices—were contrasted with the RPR. Excellent performance was shown in the prediction of substantial fibrosis and cirrhosis by the RPR based on CBC values. In order to forecast the patients under study from having substantial fibrosis and cirrhosis, the area under the ROC curve of each of the four models was examined. The AUCs for the RPR, APRI, FIB-4, and AAR in terms of substantial fibrosis prediction were, in that order, 0.726, 0.704, 0.720, and 0.721. In terms of predicting cirrhosis, the AUCs of the

RPR, APRI, FIB-4, and AAR were 0.989, 0.986, 0.964, and 0.988 respectively. In comparison with the APRI, FIB-4, and AAR, as well as the APRI, FIB-4, and AAR, the RPR showed a greater AUC in both the prediction of cirrhosis and severe fibrosis.

After treatment:

As regards specificity and sensitivity for FIB_4, APRI, and RDW/Platelet ratio in fibrosis patients following therapy (F1, F2), the scores' curves were almost identical, with very minor variations across the various cutoff thresholds. They were, assuming a low level of precision, outside of the upper left corner. For the RDW/Platelet ratio, APRI, and FIB_4, the areas under the ROC curve were 0.603, 0.685, and 0.603 respectively. Therefore, there is contradiction with **Chen *et al.* [8]**, who reported that in the prediction of substantial fibrosis, the AUCs of the RPR, APRI, and FIB-4 were, respectively 0.825, 0.740, and 0.826.

Concerning sensitivity and specificity for RDW/PLT ratio, APRI, FIB_4 for cirrhotic cases after treatment (F3, F4). With very minor variations between the various cutoff criteria, the ROC curves for those scores were relatively similar to one another. They were, supposing exceptional precision, at the upper left corner. The areas under the ROC curve for RDW/Platelet ratio, APRI and FIB_4 were 0.910, 0.965 and 0.965 respectively. Accuracy of scores was considered excellent for prediction of cirrhosis. The best cut off points for RDW/Platelet ratio, APRI and FIB_4 were 0.000741, 0.65 and 1.895 respectively. In RDW/Platelet ratio at cut off point 0.000741, the sensitivity was 100%. For APRI at cut off point 0.65, the sensitivity was 100% and for FIB_4 at cut off point 1.895, the sensitivity was 100%. Our research supports the findings of **Chen and Morgan [16],** who discovered that the AUCs of the FIB-4, APRI, AAR, and RPR were, respectively, 0.825, 0.740, 0.586, and 0.795 in the prediction of severe fibrosis. In the prediction of cirrhosis, the AUCs of the RPR, APRI, AAR, and FIB-4 were 0.884, 0.849, 0.734, and 0.857 respectively. When it came to predicting severe fibrosis in comparison with the APRI and AAR ($p = 0.05$) and cirrhosis in comparison with the AAR ($p = 0.05$), the RPR showed a considerably higher AUC.

In certain research, patients with CHC and CHB might benefit from using other models, such as the FIB-4, FibroTest, ActiTest, and FibroScan, which are all based on chronic hepatitis C patients. However, these models were constrained by the need for intricate calculations or costly equipment [17, 18]. The RDW/PLT is the most straightforward, affordable, and quickly computed noninvasive technique with a reasonably high degree of accuracy; it only needs two common CBC parameters [8, 15].

CONCLUSION

- Before starting HCV therapy, liver cirrhosis and fibrosis may be accurately predicted by RDW/PLT.
- Following HCV therapy, RDW/PLT had a remarkable degree of accuracy in predicting liver cirrhosis (F3 & F4).
- RDW and PLT are not reliable indicators of the onset of early liver fibrosis (F1 and F2) following HCV therapy, even with a poor degree of precision.
- Our findings indicated that RDW/PLT could accurately assess the degree of liver fibrosis and cirrhosis prior to HCV therapy, hence replacing liver biopsy.
- After undergoing HCV therapy, we may rely on RDW/PLT to accurately predict the degree of advanced liver fibrosis and cirrhosis (F3 & F4).
- To determine the accuracy of predicting early liver fibrosis (F1 & F2) following HCV therapy, more research on RDW/PLT is necessary.

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