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Diagnostic Accuracy of Liver Fibrosis Based on Red Cell Distribution Width to Platelet Ratio Versus Fibroscan in Chronic Hepatitis Patients

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Abstract

Red cell Distribution Width (RDW) and platelet ratio (RPR) are generally accurate predictors of liver fibrosis and cirrhosis in persistent hepatitis B or C. RPR outperformed AST and ALT ratio, AST and RPR index, and FIB-4 as non-invasive techniques to predict liver fibrosis. The aim was to assess the reliability of the diagnosis of liver fibrosis in persistent hepatitis patients with various etiologies using the RDW to RPR with fibroscan. This cross-sectional research enrolled 60 patients with liver cirrhosis brought on by chronic hepatitis C with HCV antibody +ve, chronic hepatitis B with HBs Ag +ve ≥ 6-month bilharzial hepatic cirrhosis and 20 apparently healthy subjects without evidence of any liver disease as controls. Patients and controls were chosen from inpatient and outpatient clinic of Sheben El Kom Fever Hospital and Menoufia Liver Institution. There was a highly statistically substantial positive correlation between FIB 4 and RDW\ Platelet ratio (R = 0.836, P <0.001) and statistically a highly statistically substantial positive correlation between FIB 4 and Liver stiffness (R = 0.337, P 0.009). A reliable test for predicting fibrosis in chronic liver condition was the RDW/ Platelet Ratio. Liver stiffness and RDW/Platelet ratio showed a statistically substantial positive correlation.

Keywords: RPR; hepatic fibrosis; noninvasive; RDW.

1. Introduction

Chronic liver disease causes morbidity and death. Elastography can evaluate hepatic fibrosis. Ultrasound-based elastography is expensive in basic or community hospitals. Serologic tests are cheaper and more available than elastography in these institutes. RDW to platelet ratio (RPR) is a simple serologic test for detecting hepatic fibrosis. [1].

Cirrhosis is the final stage of chronic liver illnesses with significant inflammation, fibrosis, and renewing nodules. These modifications diminish the liver's functional mass and modify its vascular

architecture. [1]. Chronic liver disease causes 2 million deaths annually worldwide. Chronic hepatitis B/C, alcohol-related liver disorders, and NAFLD are common causes [2]. A liver biopsy can detect persistent hepatitis. Intrusive diagnostic procedure with high risk, high cost, potential effects (such as bleeding, pneumothorax, hemothorax, and mortality), and poor acceptance [3]. Non-invasive evaluation of liver fibrosis is important. Serological assays may be non-invasive ways to determine liver fibrosis since needle liver biopsy has risks/limitations [4]. Noninvasive liver tests performed in general care may enhance early identification of advanced liver fibrosis, reduce the need to send patients with moderate sickness, and be cost-effective and efficient [5]. Ultrasound-based elastography is used instead of liver biopsy to evaluate hepatic fibrosis. It can also predict cirrhotic problems [6]. Fibroscan is the best noninvasive tool for predicting liver fibrosis, according to Ramzy, Fouad et al. Other non-invasive technologies may improve Fibroscan's accuracy. RPR showed promising results, especially for identifying advanced fibrosis, and deserves additional evaluation [7]. Calculation includes RDW to platelet ratio. RDW is correlated with chronic liver disease severity [8].

A greater RDW signifies abnormal red blood cell survival and faulty erythropoiesis. RDW may be caused by oxidative stress, inflammation, hypertension, malnutrition, dyslipidemia, and erythrocyte disorders [9]. Platelet transfusion improved cirrhotic patients' liver function and reduced fibrosis [10].

Thrombocytopenia indicates chronic liver disease progression. Liver cirrhosis lowers platelet count. [11].

2. Subjects and Methods

After taking a written consent from patient of studied groups to share in the study, our study was cross-sectional study caried out on 60 chronic hepatitis C patients with liver cirrhosis with HCV antibody +ve, chronic hepatitis B with HBs Ag +ve ≥6 months and 20 apparently healthy subjects without evidence of any hepatic disease as controls. The patients and controls were consecutively included from inpatient and outpatient clinic of Sheben El Kom fever hospital and Menoufia liver institution. Exclusion criteria were BMI > 30 kg / m2 as the abdominal wall fat represents a physical limitation to the liver stiffness measurements by the fibroscan, presence of ascites, cancer, Hepatoma, Coinfection with HIV, Cardiovascular diseases, heart failure, Hemorrhagic fever, Blood transfusion 3 months prior to admission and Liver transplantation. All patients and controls were subjected to complete detailed history in the form of the name, age, sex, residence, history of the present illness and past history. Full clinical and local examination of chest, abdomen, heart, and nervous system. Laboratory investigations included complete blood count (CBC) with the values of RDW (%) hemoglobin level (gm/dl), white blood cell count (WBC), and platelet count /mm3, Liver functioning tests(Aspartate amino transferase (AST), Alanine amino transferase (ALT), Renal functioning tests (urea, creatinine) , Lipid profile (serum cholesterol, serum triglycerides and serum low density lipo protein) ,serum bilirubin, serum albumin, total proteins**.**Radiological investigations included pelvi abdominal ultra sound and fibroscan. Fibroscan examination: The right lobe of the liver was tested via the intercostal plane on patients sleeping in the dorsal decubitus posture with the right arm in maximum abduction to determine the stiffness of the liver using an Echosens. With coupling gel applied, the probe transducer's tip was positioned on the skin between the ribs at the position of the right lobe of the liver. The operator found a section of the liver that was at least 6 cm thick and devoid of significant vascular structures with the use of ultrasound time-motion and A-mode pictures generated by the device. The

measuring region was situated at a depth of 25-65 mm, and the operator clicked the probe button to start an acquisition. Only when 10 successful tests and a measure rate of success of greater than 65% are attained can this result be believed. The ratio of the number of successful acquisitions to the total number of acquisitions was used to compute the success rate. The average value was retained as the liver elastic modulus standard. Less than five minutes were allotted for the test. F0 (No fibrosis), F1 (mild fibrosis): 0-7.1 kPa, F2 (Fibrosis medium): > 7.1-9.3 kPa, F3 (severe fibrosis): > 9.3-14.5 kPa, and F4 (Cirrhosis): > 14.5 kPa are the different categories for liver fibrosis. The liver fibrosis in this research was split into two groups (F ≤2 is referred to as a mild-moderate group and F> 2 is referred to as a severe group). Statistical method: Data which were collected was analyzed utilizing SPSS (Statistical Package for Social Science). Data was entered as numerical or categorical, as appropriate. Quantitative data were represented in Mean, Standard Deviation of the mean (x ± SD). Qualitative data were represented in number and percent (%). Chi-square analysis and the student t-test were employed in analytical statistics to compare two groups that included quantitative variables. Statistics were deemed substantial at a P value of <0.05. The Spearman correlation coefficient (rs) was employed to show the relationship between two continuous variables.

3. Results

In all, 80 adults participated in the research. They were classified into two groups; patient group including 74 patient (78.33%) suffered from HCV, while thirteen patients (21.67%) suffered from HBV) and a control group including 20 apparently healthy. Age of patients ranged from 25 to 66 that include 66 males and 14 females. There was substantial elevation in the Mean ± SD of RDW (14.217±2.401) when compared to that of the control group (13.105±0.923) (P < 0.05). Also, there was a highly substantial elevation in the Mean ± SD of RDW\Platelet ratio of patients (0.092±0.045) when compared to that of the control group (0.066±0.011) (P < 0.01). [*table1*]. There was a highly substantial elevation in the mean ± SD of AST of the patient (45.383 ± 28.987) when compared to that of the control group (22.350 ± 6.319) (P < 0.01). There was substantial elevation in the mean ± SD of ALT of the patient (45.683 ± 35.062) when compared to that of the control group (27.400±6.573) (P < 0.05). There was a highly substantial reduction in the mean ± SD of Albumin of the patient (4.087 ± 0.501) when compared to that of the control group (4.430±0.447) (P < 0.01). There was a highly substantial elevation in the mean ± SD of INR of the patient (1.100 ± 0.139) when compared to that of the control group (1.025±0.055) (P < 0.01). There was a substantial elevation in the mean ± SD of creatinine of the patient (0.886 ± 0.226) when compared to that of the control group (0.765±0.142) (P < 0.05). There was a substantial elevation in the mean ± SD of creatinine of the patient (0.886±0.226) when compared to that of the control group (0.765±0.142) p-value 0.028 (P < 0.05). There was a substantial reduction in the mean ± SD of cholesterol of patient (193.383±24.803) when compared to that of the control group (205.450±0.142) (P < 0.05). There was a substantial reduction in the mean ± SD of triglyceride of patient (99.100±27.649) when compared to that of the control group (120.450±28.951) (P < 0.05). There was a highly substantial reduction in the mean ± SD of LDL of patient (120.800±17.698) when compared to that of the control group (133.850±13.220) (P < 0.01) [*table2*]. Among the studied group with chronic liver disease 5.00% of patient were F0 when compared to that 45.00% of control, 3.33% of patient were F0-F1 when compared to that 5.00% of control, 11.67% of patient were F1 when compared to that 30.00% of

control, 1.67% of patient were F1-F2 when compared to that 0% of control, 6.67% of patient were F2 when compared to that 15.00% of control, 18.33% of patient were F3 when compared to that 50.00% of control, 3.33% of patient were F4 when compared to that 0.0% of control (P < 0.01). Liver stiffness split into two groups regarding to degree of liver fibrosis (group 1) (F0- F2) 28.33% of patient when compared to that 95.00% of control with non-advanced fibrosis and (group 2) (F3-F4) 71.67% of patient when compared to that 5.00% of control with advanced fibrosis and there was highly substantial elevation between these groups (P <0.01). There was highly substantial elevation in the mean ± SD of liver stiffness (19.665 ±14.838) when compared to that of the control group (1.915 ± 1.942) (P < 0.01). There was highly substantial elevation in the mean ± SD of IQR % (6.871 ± 6.868) when compared to that of the control group (1.915 ± 1.587) (P < 0.01). There was highly substantial elevation in the mean ± SD of FIB 4 (2.432 ± 2.293) when compared to that of the control group (0.879 ± 0.292) (P < 0.01). There was statistical substantial variation regarding mean liver stiffness values between patients and control (P > 0.05) [*table2*] There was a statistically substantial positive correlation between Liver stiffness and RDW\Platelet ratio (R = 0.273, P< 0.05). There was highly statistical substantial positive correlation between Spleen examination by abdominal ultrasound and RDW\Platelet ratio (R = 0.570, P <0.001) and highly statistical substantial positive correlation between Spleen and Liver stiffness) (R = 0.525, P 0.003). There was highly statistical substantial positive correlation between abdominal ultrasound of portal vein and RDW\Platelet ratio (R = 0.525, P <0.001). There was highly statistically substantial negative correlation between Platelet count in CBC and RDW\Platelet ratio (R = 0.525, P <0.001). There was statistical substantial variation between AST and Liver stiffness (R = 0.321, P 0.013). There was highly statistically substantial negative correlation between Albumin and RDW\Platelet ratio (R = -0.523, P <0.00 1). There was highly statistically substantial positive correlation between Bilirubin and RDW\Platelet ratio (R = 0.536, P <0.001).There was highly statistically substantial positive correlation between INR and RDW\Platelet ratio(R= 0.711, P <0.001) and highly statistically substantial positive correlation between INR and Liver stiffness (R = 0.363, P-0.004).There was highly statistically substantial positive correlation between random blood sugar and RDW\Platelet ratio (R = 0.397, P 0.002) and highly statistically substantial positive correlation between random blood sugar and Liver stiffness (R = 0.379, P0.003). There was statistically substantial negative correlation between Cholesterol and RDW\Platelet ratio (R = -0.332, P 0.009) and there was statistically substantial negative correlation between Cholesterol and Liver stiffness (R = -0.252, P 0.052). There was statistically substantial negative correlation between Triglyceride and RDW\Platelet ratio(R = -0.326, P 0.011) and highly statistically substantial negative correlation between Triglyceride and Liver stiffness (R = -0.490, P <0.001).There was highly statistically substantial negative correlation between Low-density lipoprotein and RDW\Platelet ratio (R = -0.465, P <0.001) and highly statistically substantial negative correlation between Low-density lipoprotein and Liver stiffness (R = -0.510, P <0.001).There was highly statistically substantial positive correlation between FIB 4 and RDW\Platelet ratio (R = 0.836, P <0.001) and statistically substantial positive correlation between FIB 4 and Liver stiffness(R = 0.337, P 0.009) [*table3*] Table 4 shows that RPR test can detect liver fibrosis with Cutoff >0.1, high specificity (94%) and high PPV (94%). Table 5 shows that RPR accuracy between patient and control was 70% with high Specificity 95 and PPV 96 with cutoff >0.08. Liver stiffness accuracy between patient and

control was 91.8% with a high Specificity of 100, sensitivity of 73 and PPV of 100 with cutoff > 9.

Table (1): Comparison between studied groups and control as regards laboratory findings.

		Group						T-Test	
		Patient			Control			t	P-value
AST, U/L	Range	12	-	153	14	-	38	3.512	0.001*
	Mean ± SD	45.383	±	28.987	22.350	±	6.319		
ALT, U/L	Range	10	-	162	17	-	40	2.309	0.024*
	Mean ± SD	45.683	±	35.062	27.400	±	6.573		
Albumin, g/dL	Range	2.9	-	5.1	3.7	-	5.3	-2.724	0.008*
	Mean ± SD	4.087	±	0.501	4.430	±	0.447		
Bilirubin, mg/dL	Range	0.4	-	2.9	0.5	-	1	1.580	0.118
	Mean ± SD	0.878	±	0.453	0.715	±	0.150		
INR	Range	0.9	-	1.6	1	-	1.2	2.352	0.021*
	Mean ± SD	1.100	±	0.139	1.025	±	0.055		
HbA1C	Range	4.5	-	5.8	4.2	-	5.3	1.042	0.301
	Mean ± SD	5.73	±	0.54	5.40	±	0.48		
Creatinine	Range	0.5	-	1.5	0.6	-	1.1	2.235	0.028*
	Mean ± SD	0.886	±	0.226	0.765	±	0.142		
Cholesterol	Range	111	-	250	180	-	240	-2.032	0.046*
	Mean ± SD	193.383	±	24.803	205.450	±	16.152		
Triglyceride	Range	63	-	160	76	-	170	-2.956	0.004*
	Mean ± SD	99.100	±	27.649	120.450	±	28.951		
LDL	Range	90	-	160	110	-	160	-3.023	0.003*
	Mean ± SD	120.800	±	17.698	133.850	±	13.220		

AST: aspartate aminotransferase, ALT: Alanine aminotransferase, INR: international normalized ratio. LDL: low-density lipoprotein.

Table (2**):** Comparison between studied groups and control as regards fibroscan and FIB 4.

		Group				Chi-Square	
		Patient		Control			
		N	%	N	%	X2	P-value
Fibroscan	F0	3	5.00	9	45.00	33.182	<0.001*
	F0-F1	2	3.33	1	5.00		
	F1	7	11.67	6	30.00		
	F1-F2	1	1.67	0	0.00		
	F2	4	6.67	3	15.00		
	F3	11	18.33	1	5.00		
	F3-F4	2	3.33	0	0.00		
	F4	30	50.00	0	0.00		
Fibroscan	F0-F2	17	28.33	19	95.00	26.936	<0.001*
	F3-F4	43	71.67	1	5.00		
T-Test						T	P-value
Liver stiffness	Range	4.4	- 72	1.6	- 9	4.329	<0.001*
	Mean ±SD	19.665	± 14.838	5.200	± 1.942		
IQR %	Range	0	- 39	0	- 6	3.186	0.002*
	Mean ±SD	6.871	± 6.868	1.915	± 1.587		
Success rate %	Range	71	- 100	95	- 100	-1.219	0.227
	Mean ±SD	98.317	± 5.199	99.750	± 1.118		
FIB 4	Range	0.4	- 11.8	0.4	- 1.7	3.010	0.004*
	Mean ±SD	2.432	± 2.293	0.879	± 0.292		

IQR %: interquartile range FIB 4: Fibrosis-4 score.

Table (3): Correlation between RDW\Platelet ratio and Liver stiffness and some studied variables.

Correlations				
	RDW\Platelet ratio		Liver stiffness	
	R	P-value	r	P-value
Liver stiffness	0.273	0.035*		
Age	0.186	0.155	0.067	0.611
BMI	-0.212	0.104	0.038	0.774
Abd. U/S Spleen	0.570	<0.001*	0.382	0.003*
Abd. U/S PV	0.525	<0.001*	0.205	0.116
RDW	0.178	0.173	-0.092	0.485
Platelet	-0.796	<0.001*	-0.193	0.139
AST	0.205	0.116	0.321	0.013*
ALT	0.021	0.876	0.243	0.062
Albumin	-0.523	<0.001*	-0.239	0.066
Bilirubin	0.536	<0.001*	0.237	0.068
INR	0.711	<0.001*	0.363	0.004*
HbA1C	0.397	0.002*	0.379	0.003*
Creatinine	-0.198	0.129	-0.113	0.388
Cholesterol	-0.332	0.009*	-0.252	0.052*
Triglyceride	-0.326	0.011*	-0.490	<0.001*
LDL	-0.465	<0.001*	-0.510	<0.001*
IQR %	-0.067	0.610	-0.180	0.168
Success rate %	0.131	0.319	-0.043	0.742
FIB 4	0.836	<0.001*	0.337	0.009*

BMI: body mass index, Abd. U/S PV: abdominal ultrasound of portal vein, AST: aspartate aminotransferase, LDL: Low-density lipoprotein, IQR %: interquartile range, FIB 4: Fibrosis-4 score.

Table (4): Diagnostic performance of RPR in the diagnosis of liver fibrosis (F0-F2 and F3-F4) in hepatic Patients.

ROC curve between F3-F4 and F0-F2 in Patient						
	Cutoff	Sens.	Spec.	PPV	NPV	Accuracy
RDW\Platelet ratio	>0.1	37.21	94.12	94.1	37.2	64.9%

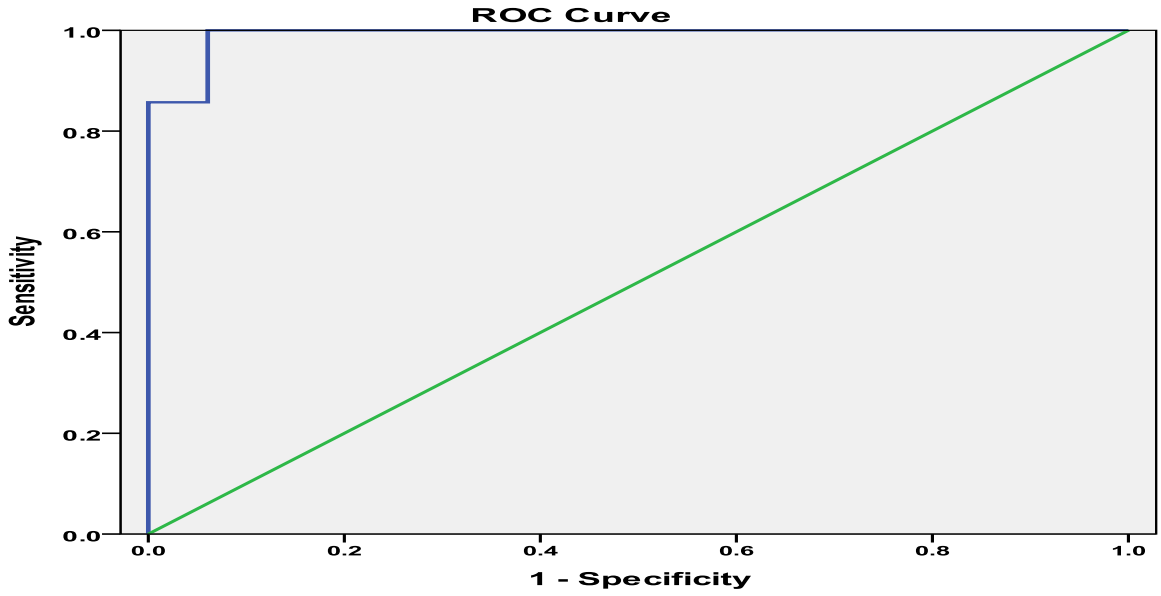

Figure (1): Diagnostic performance of RPR in diagnosis of liver fibrosis (F0-F2 and F3-F4) in hepatic Patient.

Table (5): Diagnostic performance of RPR and Liver stiffness in diagnosis of liver fibrosis between patient and control.

ROC curve between Patient and Control						
	Cutoff	Sens.	Spec.	PPV	NPV	Accuracy
RDW\Platelet ratio	>0.08	43.33	95.00	96.3	35.8	70.6%
Liver stiffness	>9	73.33	100.0	100.0	55.6	91.8%

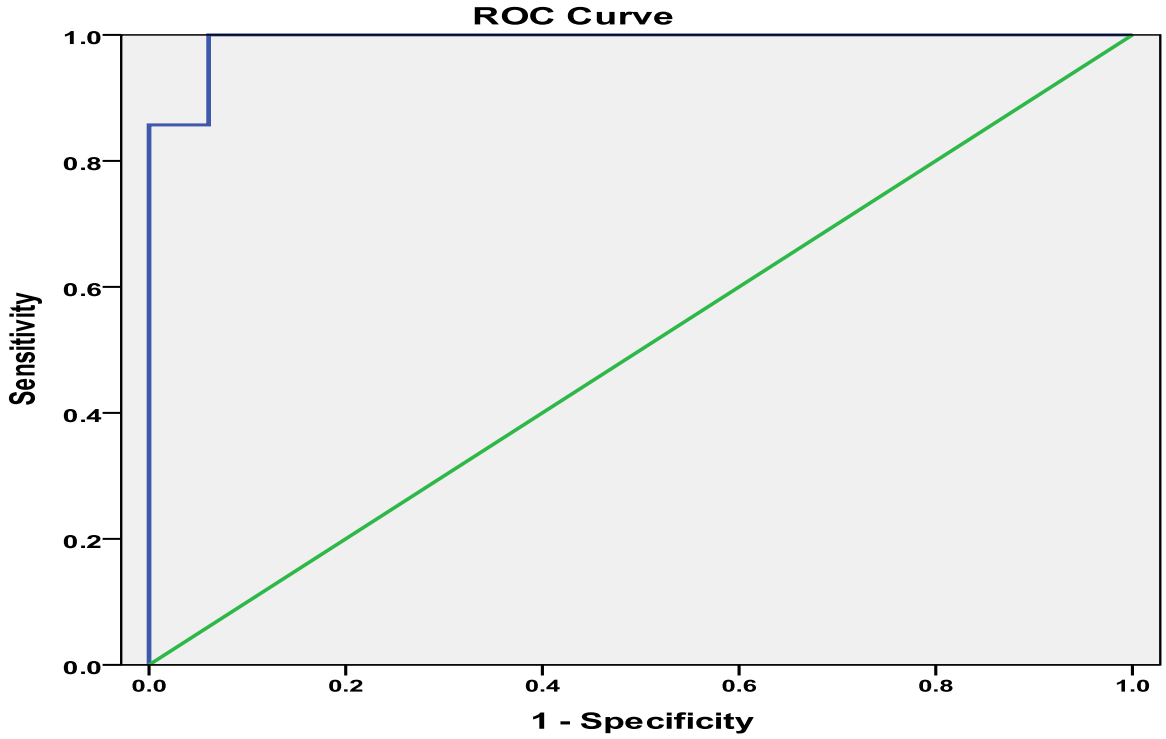

Figure (2): Diagnostic performance of RPR in diagnosis of liver fibrosis between patient and control.

4. Discussion

Fibroscan is the greatest noninvasive liver fibrosis predictor. Non-invasive technology can increase fibroscan's prognostic usefulness. RPR results were encouraging for advanced fibrosis. [7]. This study compared RDW to platelet ratio to fibroscan for predicting liver fibrosis in CHC and CHB patients. This study comprised 60 patients with chronic hepatitis B and C and 20 healthy controls. Ages ranged from 25-66, with 66 males and 14 females. RDWPlatelet ratio differed significantly between patients and controls. As per lab results, ALT, INR, and creatinine increased, whereas cholesterol, triglycerides, LDL, and albumin decreased. Liver stiffness, IQR, and FIB4 showed highly statistical differences. Nallagangula et al. discovered that liver disease is the most common source of elevated transaminase activity in blood [12]. PT and INR reflect coagulopathy due to synthetic dysfunction in end-stage liver disease patients. INR is a reliable indication of liver disease death (as part of MELD) [13]. Cheng et al. discovered that FIB-4 and TE in the same CHC group determined fibrosis stages. TE correlated better with splenomegaly than FIB-4 [14]. In this investigation, RDWPlatelet ratio and liver stiffness were positively connected as regards ultrasonography, local liver

examination, and palmer erythema with substantial mean + SD increases. In this study, RDWPlatelet ratio was connected with local spleen examination, jaundice, spider nevi (mean +SD increased) and child categorization, esophageal varices grading (mean +SD decreased). Zhu et al. disagreed with that conclusion and found RDW was inversely related to albumin and positively related to total bilirubin and Child-Pugh score in hepatocirrhosis participants [15].

RDWPlatelet and Liver stiffness revealed statistically significant positive correlation with (Spleen examination by abdominal ultrasound, INR, RBS) and negative correlation with (cholesterol, triglyceride, LDL).

Accept the outcome Som et al. [16] reported that alcoholic and non-alcoholic cirrhosis lipid profile parameters were statistically different from the normal group, however only HDL Cholesterol variation was noteworthy. Compared to healthy normals, cirrhotics had lower serum lipid levels. In this study, Liver stiffness and RDWPlatelet ratio P 0.05 and FIB 4 and RDWPlatelet ratio (P-Value 0.001) had a statistically significant positive relationship. RPR was fair in detecting liver fibrosis with Cutoff >0.1, high specificity (94%) and positive prediction value (94%), low sensitivity (37.2) and low negative prediction value (37.2) between F3-F4 and F0-F2 in chronic hepatic patients.

Cai et al. [17] found that RPR accurately predicts liver fibrosis. RPR may accurately identify chronic liver disease patients with cirrhosis, significant fibrosis, and advanced fibrosis (AUC: 0.73, 0.83, and 0.85) [17]. A quantitative meta-analysis included 1282 liver samples from 2010 to 2014. Vascular abnormalities, schistosomiasis, granulomatous liver disease, HBV/HCV, and NAFLD are causes. Five noninvasive patient models were created using laboratory variables. The RPR had the highest accuracy of the five models in predicting hepatic fibrosis (0.75, p.001).

As hepatic fibrosis progressed, RPR climbed. RPR is a useful indicator of hepatic fibrosis severity [18]. Elmdams et al. [19] found RPR has 90% sensitivity for diagnosing cirrhotic liver in CHC patients and 97.4% accuracy for detecting negative cases. [19]. Ramzy, Fouad et al. [7] found that Fib-4, TE, and RPR were reliable diagnostic tools at threshold values of 1.17, 7.75, and 0.07 for predicting significant fibrosis and 1.99, 8, and 0.08 for diagnosing advanced fibrosis. Transient Elastography predicted severe fibrosis.

Fib-4 was only correlated with advanced fibrosis. Using Fib-4, TE, and RPR to predict advanced fibrosis may eliminate liver biopsies. RPR showed adequate sensitivity, specificity, positive and negative predictive values, and overall accuracy [7]. Taefi et al. Most patients had chronic hepatitis C. The research sampled different hepatitis types. RPR can predict fibrosis and cirrhosis in chronic hepatitis. RPR and native liver fibrosis were strongly correlated, according to Taefi et al. This association was the strongest [20]. At ideal cutoffs, the RPR's sensitivity and specificity were high (63.1 percent and 85.5.0 percent, respectively, for severe fibrosis and 73.7 percent and 93.0 percent, respectively, for cirrhosis).

Despite having more variables and computations than the RPR, the two regression models couldn't predict severe fibrosis and cirrhosis. RPR predicts fibrosis better than APRI and FIB-4 [21]. RPR accuracy between patient and control was 70% with Specificity 95 and PPV 96 with cutoff >0.08. Liver stiffness accuracy between patient and control was 91.8% with a cutoff >9. With an AUC of 0.91, liver stiffness best predicted advanced fibrosis (F3-F4), according to Ramzy et al. Fib-4's AUC for advanced fibrosis prediction was 0.82, higher than for substantial fibrosis (F2)20 prediction. FibroScan cutoff values for liver fibrosis were 7 to 8.5 kPa and 11 to 14 kPa for cirrhosis.

This is in accordance with WHO recommendations [22] on the therapy of CHB patients, which found that FibroScan appears reliable for identifying substantial fibrosis or cirrhosis in hepatitis B patients and cutoff values are only marginally different from. FibroScan is a useful diagnostic tool for CHB and liver cirrhosis, according to Li, Q., Huang et al. FibroScan's cutoff values for cirrhosis and severe liver fibrosis had at least 90% sensitivity. FibroScan's cirrhosis and severe liver fibrosis threshold values were 10.8 kPa and 17.8 kPa, respectively [23].
This research has certain limitations since it did not look at the potential factors, including iron or vitamin B12 deficiency, that might have an impact on RDW readings. Additionally, we did not incorporate information on these patients' antiviral treatment, and we did not research any potential effects of antiviral drugs on blood indices. few patients were included.

5. Conclusion

From this study, it was concluded that, RDW\Platelet ratio was a good test for predicting fibrosis in chronic hepatic illness. There was a statistically substantial positive correlation between Liver stiffness and RDW\Platelet ratio.

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