Predictive Value of Red Cell Distribution Width-to-Lymphocyte Ratio for Diagnosis of Post Hepatic Cirrhosis

Original Article

Sonya Ahmed Ali El-Gaaly, Essam Mohamed Bayoumi Hilal, Shaimaa Shazly Massoud and Mohamed Nabil Badawy Al-Ashram

Department of Gastroenterology and Hepatology, Faculty of Medicine, Ain Shams University

ABSTRACT

Background: As a promising noninvasive biomarker for diagnosing chronic hepatic diseases, including post-hepatatic cirrhosis, the Red Cell Distribution Width-to-Lymphocyte Ratio (RDW-to-LR) has been emerged. Chronic liver diseases, such as post-hepatatic cirrhosis, are associated with impaired liver function and pose significant global health challenges. Traditional liver biopsy is invasive, highlighting the need for safer diagnostic approaches.

Aim: This study goal is to evaluate the RDW-to-LR predictive value in diagnosing post-hepatatic cirrhosis and explore its potential mechanisms in reflecting pathophysiological modifications.

Methods: The study perfomed on 60 hepatitis B patients from Ain Shams University Hospital, divided into three groups: 30 with HBV-related cirrhosis, 30 healthy controls, and 30 with chronic hepatitis B, and. Laboratory evaluations measured total bilirubin, liver enzymes (ALT, AST), GGT.

Results: Regarding liver enzyme levels significant differences were found across the groups, with increased AST, ALT, and GGT in the hepatitis and cirrhosis groups. Correlation analysis showed RDW-to-LR's association with liver function parameters and its inverse relationship with hematological health indicators. Logistic regression identified RDW-to-LR as a significant predictor for cirrhosis. its high specificity and sensitivity in distinguishing cirrhosis from hepatitis and controls was confirmed via ROC analysis.

Conclusion: This study supports for diagnosing HBV-related cirrhosis the RDW-to-LR as a noninvasive, reliable biomarker.

Key Words: Post hepatatic cirrhosis, red cell distribution, width-to-lymphocyte ratio.

Received: 24 January 2025, **Accepted:** 20 March 2025.

Corresponding Author: Sonya Ahmed Ali El-Gaaly, Department of Gastroenterology and Hepatology, Faculty of Medicine, Ain Shams University, Cairo, Egypt. **Tel.:** +2 01095016910, **E-mail**: sonya.elgaaly@yahoo.com

ISSN: 2735-3540, Vol. 76, No. 2, June 2025.

INTRODUCTION

Hepatitis B virus (HBV) continues to be a critical issue that can result in liver cirrhosis (LC), hepatocellular carcinoma (HCC), and chronic active hepatitis. Hepatic fibrosis accurate assessment in chronic hepatitis B (CHB) individuals is essential to ascertain antiviral medication necessity and for establishing a prognosis[1].

At the moment, for cirrhosis diagnosis liver biopsies remain the gold standard. The procedure invasiveness, sampling errors, discrepancies in diagnoses among different pathologists, and complications brought on using a needle for biopsy are just a few of the hectic problems that this method is related to[2].

To hinder consequences as mortality due to CHB, including the HCC development, CHB cases have to check the liver fibrosis grade periodically. As a result, research focuses on noninvasive methods for diagnosing LC. There are various popular noninvasive techniques, each with advantages and disadvantages[3].

Imaging is customarily applied to assess liver fibrosis. Results from imaging broadly exhibit powerful agreement with those from liver histology. However, some imaging techniques claim for specialized equipment and qualified interpreters. The second approach involves laboratory assessment for YKL-40, collagen, hyaluronic acid, and laminin[4].

Conglomerate diagnostic panels can be estimated from regular laboratory information and are further in use. These measurements include the the aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AAR) and AST to platelet (PLT) ratio index (APRI), and[5].

DOI: 10.21608/ASMJ.2025.353749.1371

The fibrosis index based on four components (FIB-4) and APRI are two measurements that are now in use that are particularly beneficial for detecting LC. Furthermore, it provids a comprehensive description of the LC diagnosis utilizing a combination of blood marker tests as well as imaging modalities[6]. Another study also revealed that ideally, a single noninvasive approach to reach diagnosis should be discovered[7].

Few studies have compared the LMR, NLR, RDW, APRI diagnostic benefit, as well as FIB-4 for LC linked to CHB, though. The CHB development and the LC increased risk are generated by HBVineffective immune clearance. HBV infection resulted in immune-mediated liver injury, and earlier research has revealed that throught both cirrhosis and CHB lymphocyte count is lowered. Countless investigations have demonstrated that RDW rises as LC developes[8].

Biochemical characteristics such as red blood cell distribution width (RDW) are commonly ordered. RDW is usually utilized to investigate the causes of anaemia, specifically for the anaemia differential diagnosis caused by iron deficiency. Recent research suggests that RDW may be utilized to anticipate the prognosis, riskor a number of illnesses severity unrelated to anaemia, including cardiovascular conditions, liver conditions linked to the HBV, autoimmune diseases, in addition to stroke[9].

AIM OF THE STUDY

This study aim was to estimate the RDW-lymphocyte ratio (RLR) and RDW utilization in diagnosing HBV-related hepatic cirrhosis.

PATIENTS AND METHODS

This was case control study involving hepatitis B cases, who were attending or hospitalized to the Hepatology unit, at Ain Shams University Hospital. The two parameters (RLR and RDW) diagnostic potential was validated in this study through the enrollment of patients. This study had three groups, two groups of cases and one group as control.

Group 1 cases: 30 CHB and CHC cases, group 2 cases: 30 HBV and HCV-related liver cirrhosis (HCV-LC) cases were registered in our study, control group: as controls 30 healthy individuals joined.

Upon enrollment in the research, laboratory and demographic records were obtained for every subject. The following patient data was provided: RDW, RLR, prothrombin time, FIB-4, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), white blood cell counts (WBC), AST, serum bilirubin, albumin, creatinine, APRI, ALT, blood urea nitrogen, PLT count, and international normalized ratio (INR). A quantitative grading standard for the liver reserve function assessment is the FIB-4 score. The following formulas were employed to estimate the FIB-4 and APRI scores for HBV-related liver diseases: APRI=[(AST)/(PLT s×40)]; FIB-4=age × (AST/PLT) × (ALT)1/2;multiplied by 100.

Inclusion Criteria:

1. Aged (above 18 years old).
2. All cirrhosis participants will be confirmed by a non-invasive method.
3. Chronic HBV Cases.

Exclusion Criteria:

1. Coronary heart disease treated with anticoagulants.
2. Co-infection with tuberculosis.
3. Coinfection with HCV.
4. Haematological disease.
5. Chronic kidney disease.
6. Non-alcoholic or alcoholic fatty liver disease diagnosis (excluded by Abdominal Ultrasound).
7. Hepatocellular Carcinoma (excluded by Abdominal Ultrasound and Alfa feto protein).
8. Diabetic Patients.
9. Chronic liver disease of other cause (Autoimmune hepatitis, Wilson disease, Haemochromatosis, Budd Chiari Syndrom and Primary biliary Cholangitis).
10. Patients with iron deficiency anaemia.
11. Thyroid disease.
12. Patients with the haemolytic disease as thalassemia and sickle cell disease.

METHODS

Clinical examination and full history taking.Liver cirrhosis diagnosed by clinical symptoms and signs like Jaundice, ascites, Splenomegaly, shrinked liver, haematemesis, lower limb edema), Lab (total bilirubin, S. Albumin, PT and INR, PTT and radiological by Abdominal Ultrasound).Other laboratory examinations involving iron profile: total iron binding capacity, serum iron, and ferritin, kidney functions(Urea and Creatinine), Thyroid functions

(TSH, Free T3, Free T4), Fasting blood sugar, HbA1C, blood test (haptoglobin,Retics, CBC. Coombs test, RDW, NLR, viral markers for hepatitis pattern (HBsAg – HbeAg, HCV Ab), LMR, White blood cell counts (WBC), Hepatic function tests (SGOT, SGPT, and ɣ-glutamyltransferase GGT), haemoglobin Electrophoresis, alpha-Feto protein to exclude HCC, Antinuclear antibody (ANA), ASMA, AMA test to exclude Autoimmune hepatitis and Primary biliary cholangitis, (to exclude α1-antitrypsin deficiency, Wilson's disease) serological markers was done like (S.Ceruloplasmin, S.Alfa one antitrypsin enzyme level, Scoring systems: Non-alcoholic fatty liver disease (NAFLD) fibrosis score, FIB-4 (fibrosis-4) index: It includes diverse variables including (AST, ALT, age, and PLT). Abdominal ultrasonography: with the following characteristics (1) echogenic diffusely, but it is particularly essential to observe the luminosity within the first 2-3 cm of depth. (2) attenuation of image quickly within 4-5 cm of depth, making deeper structures difficult to decipher; (3) liver uniformly heterogeneous; (4) thick subcutaneous depth (> 2 cm), (5) liver fills entire field with no edges visible. Anthropometric measurements: including Body Mass Index (BMI), ECG and echocardiography were done to exclude Coronary heart disease, S.PCR for TB and TB gold quantiferon to exclude Tuberculosis.

Statistical Analysis:

IBM Corp. announced the release of IBM SPSS software version 25.0 in 2017. This software was employed to analyze the data that was inputted into the computer. "IBM SPSS Statistics for Windows, Version 25.0." IBM Corp., Armonk, NY. Quantitative data were described using the IQR, median, mean, standard deviation (SD), and range (minimum and maximum). Qualitative data were explained in terms of percentage and count. In order to verify the distribution's normality, the Shapiro-Wilk test was implemented. The results were evaluated at a significance level of 5%.

RESULTS

This study was conducted on 60 hepatitis B cases, who were attending or admitted to the Hepatology unit, at Ain Shams University Hospital. They were classified into three groups; group I (control): involved 30 apparently healthy individuals, group II (Hepatitis group): having 30 (CHB) and CHC cases, group III (Cirrhosis group): having 30 HBV and HCV-related liver cirrhosis (HBV-LC) cases.

Table 1: Demographic characteristics among the studied groups.

		Group I Control group (No.= 30)	Group II Hepatitis group (No.= 30)	Group III Cirrhotic group (No.= 30)	Test value	*P-value*
Age (years)	Mean±SD	52.53± 13.65	55.37± 17.34	51.17± 15.01	F=	0.562 (NS)
	Range	29- 75	30- 86	24- 76	0.580	
Gender	Male	11 (36.7%)	14 (46.7%)	12 (40.0%)	X^2= 0.643	0.725 (NS)
	Female	19 (63.3%)	16 (53.3%)	18 (60.0%)		
Residence	Rural	16 (53.3%)	10 (33.3%)	14 (46.7%)	X^2= 2.520	0.284 (NS)
	Urban	14 (46.7%)	20 (66.7%)	16 (53.3%)		

P >0.05: Not significant (NS); *P* <0.05 is significant (S); *p*<0.01 is highly significant (HS).
F: One-Way ANOVA Test; X^2: Chi-Square test; SD: standard deviation.

The mean age in control group was 52.53± 13.65 years, 63.3% cases were females with 53.3% were from rural areas. 55.37± 17.34 years was the mean age in hepatitis group 53.3% cases were females with 66.7% were from urban areas. 51.17± 15.01 years as the mean age in cirrhotic group, 60% cases were females with 53.3% were from urban areas. According to age, gender and residence there was insignificant difference among the three groups (*p*>0.05). (Table 1).

Table 2: Comparison between the studied groups regarding Liver lab evaluations.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
ALT (U/L)	Group I: Control group	12.03	±4.55	11.0	8.0	-16.0	6.0	-24.0	59.38	<0.001 (HS) *p*1<0.001 *p*2<0.001 *p*3= 0.389
	Group II: Hepatitis group	391.90	±146.5	370.0	303.0	-496.0	124.0	-713.0		
	Group III: Cirrhotic group	285.83	±207.93	205.5	104.0	-494.0	10.0	-626.0		
AST (U/L)	Group I: Control group	16.43	±1.55	16.0	15.0	-17.0	14.0	-20.0	58.59	<0.001 (HS) *p*1<0.001 *p*2<0.001 *p*3= 0.847
	Group II: Hepatitis group	388.57	±204.78	360.0	267.0	-517.0	25.0	-918.0		
	Group III: Cirrhotic group	378.97	±261.52	308.5	181.0	-645.0	18.0	-732.0		
GGT (U/L)	Group I: Control group	40.01	±1.26	40.15	39.1	-40.8	37.75	-43.08	74.43	<0.001 (HS) *p*1<0.001 *p*2<0.001 *p*3<0.001
	Group II: Hepatitis group	62.97	±6.74	63.88	56.5	-68.12	53.31	-75.75		
	Group III: Cirrhotic group	115.60	±33.01	110.63	92.27	-145.7	59.31	-163.8		
T. Bilirubin (mg/dL)	Group I: Control group	0.86	±0.23	0.85	0.64	-0.98	0.53	-1.33	24.75	<0.001 (HS) *p*1= 0.705 *p*2<0.001 *p*3<0.001
	Group II: Hepatitis group	0.92	±0.30	0.80	0.73	-1.08	0.56	-1.66		
	Group III: Cirrhotic group	1.85	±0.82	1.77	1.21	-2.56	0.57	-3.03		

P >0.05: Not significant (NS); *P* <0.05 is significant (S); *p*<0.01 is highly significant (HS).
KW: Kruskal Wallis test; SD: standard deviation; IQR: Inter-quartile range; AST: Aspartate aminotransferase; ALT: alanine aminotransferase; GGT: Gamma-glutamyl transferase.
p1: Comparison between group I & group II; p2: Comparison between group I & group III; p3: Comparison between group II & group III

ALT & AST exhibted significant differences among the studied groups (*P*<0.001), being higher in cirrhosis group and hepatitis group than controls while both groups were insignificantly different from each other. In terms of total bilirubin, it was significantly different among the groups (*P*<0.001) showing a significant elevation in LC group than hepatitis & control groups. Between the groups GGT was significantly different (*P*<0.001), being elevated in cirrhosis group comparing them to hepatitis group while it was greater in cirrhosis group & hepatitis group than controls. (Table 2).

Table 3: Comparison between the studied groups regarding serum proteins.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
Albumin (g/dL)	Group II: Hepatitis group	4.46	±0.11	4.50	4.42	-4.54	4.22	-4.60	71.93	<0.001 (HS)
										*p*1<0.001
	Group III: Cirrhotic group	3.99	±0. 16	3.97	3.89	-4.15	3.71	-4.20		*p*2<0.001
		3.21	±0.56	3.33	2.65	-3.73	2.41	-4.02		*p*3=0.001
Ferritin, (ng/mL)	Group I: Control group	1683.73 ± 337.57		1551.43	1487.53 -1768.61		1306.11 -2534.37		24.73	<0.001 (HS)
	Group II: Hepatitis group	1816.67 ± 245.48		1873.45	1590.02 -2016.49		1390.57 -2191.43			*p*1= 0.209
										*p*2<0.001
	Group III: Cirrhotic group	3035.67 ± 1280.36		2737.23	1717.61 -343.43		1328.65 -4780.76			*p*3= 0.006

P >0.05: Not significant (NS); *p*<0.01 is highly significant (HS); *P* <0.05 is significant (S).
KW: Kruskal Wallis test; SD: standard deviation; IQR: Inter-quartile range
*p*1: Comparison between group I & group II; *p*2: Comparison between group I & group III; *p*3: Comparison between group II & group III

A statistically significant difference was noted among the three groups regarding albumin level (*P*<0.001) as it reduced significantly in cirrhosis group in comparison to hepatitis group while it was significantly lesser in cirrhosis group & hepatitis group than controls. As regards ferritin level, group III had significantly higher ferritin level than group I & group II. (Table 3)

Table 4: Comparison between the studied groups regarding CBC.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
Hgb (g/dl)	Group I: Control group	14.82	±0.12	14.82	14.73	-14.94	14.55	-15.0	77.22	<0.001 (HS)
										p1<0.001
	Group II: Hepatitis group	13.32	±0.28	13.40	13.10	-13.5	12.90	-13.8		p2<0.001
	Group III: Cirrhotic group	11.00	±1.37	11.05	9.80	-12.0	9.30	-13.1		p3<0.001
RBCs (10^9/L)	Group I: Control group	5.54	±0.09	5.55	5.51	-5.59	5.25	-5.63	79.16	<0.001 (HS)
	Group II: Hepatitis group	4.89	±0.06	4.89	4.84	-4.94	4.76	-4.98		p1<0.001
	Group III: Cirrhotic group	4.33	±0.31	4.40	4.07	-4.64	3.89	-4.75		p2<0.001
										p3<0.001
RDW (%)	Group I: Control group	12.98	±0.70	12.96	12.42	-13.5	11.98	-14.8	52.84	<0.001 (HS)
										p1= 0.136
	Group II: Hepatitis group	12.59	±0.62	12.65	12.0	-13.1	11.6	-13.9		p2<0.001
	Group III: Cirrhotic group	19.34	±4.35	18.1	15.5	-23.0	12.9	-26.1		p3<0.001
Platelet count (10^9/L)	Group I: Control group	163.47	±15.98	160.0	150.0	-170.0	133.0	-200.0	71.54	<0.001 (HS)
										p1<0.001
	Group II: Hepatitis group	92.43	±42.49	77.0	55.0	-125.0	42.00	-182.0		p2<0.001
	Group III: Cirrhotic group	25.80	±14.66	23.0	19.0	-30.0	11.00	-91.0		p3<0.001

P >0.05: Not significant (NS); *P* <0.05 is significant (S); *P*<0.01 is highly significant (HS).
KW: Kruskal Wallis test; SD: standard deviation; IQR: Inter-quartile range; RDW: red blood cell distribution width
P1: Comparison between group I & group II; P2: Comparison between group I & group III; P3: Comparison between group II & group III

CBC exhibted significantly different in the three groups (P<0.001) as there was a significant decline in Hgb, RBCs and PLT count in cirrhosis group than hepatitis group than controls. Regarding RDW, it was significantly elevated in cirrhosis group in comparison to hepatitis group & controls. (Table 4)

Table 5: Comparison between the studied groups regarding WBCs count.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
Neutrophils (10^9/L)	Group I: Control group	2.78	±0.60	2.75	2.40	-3.20	1.70	-4.5	7.144	0.028 (S)
	Group II: Hepatitis group	4.44	±2.31	4.20	2.30	-6.10	1.40	-8.8		p1=0.019
	Group III: Cirrhotic group	4.61	±2.77	4.60	2.20	-6.0	1.30	-12.6		p2=0.023
										p3=0.945
Lymphocytes (10^9/L)	Group I: Control group	2.59	±0.44	2.50	2.30	-3.0	1.90	-3.5	60.33	<0.001 (HS)
	Group II: Hepatitis group	2.10	±0.56	2.15	1.70	-2.5	1.20	-3.1		p1= 0.061
	Group III: Cirrhotic group	0.52	±0.48	0.30	0.30	-0.5	0.20	-2.1		p2<0.001
										p3<0.001
Monocyte (10^9/L)	Group I: Control group	1.20	±0.51	1.12	0.72	-1.53	0.49	-2.38	37.75	<0.001 (HS)
	Group II: Hepatitis group	1.15	±0.58	0.97	0.68	-1.69	0.37	-2.30		p1= 0.689
	Group III: Cirrhotic group	0.30	±0.57	0.05	0.02	-0.19	0.01	-2.31		p2<0.001
										p3<0.001

P >0.05: Not significant (NS); P <0.05 is significant (S); p<0.01 is highly significant (HS).
KW: Kruskal Wallis test; SD: standard deviation; IQR: Inter-quartile range; AST: Aspartate aminotransferase; ALT: alanine aminotransferase; GGT: Gamma-glutamyl transferase.
p1: Comparison between group I & group II; p2: Comparison between group I & group III; p3: Comparison between group II & group III

Across the groups WBCs counts were significantly different (P<0.05) as there was a significant drop of lymphocytes and monocytes in cirrhosis group compared to hepatitis individuals and controls. Meanwhile, A significant elevation was detectedin neutrophils in cirrhosis group and hepatitis group compared to controls. (Table 5)

Table 6: Comparison between the studied groups regarding kidney function tests.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
Urea (mmol/L)	Group I: Control group	3.70	±0.24	3.62	3.50	-3.89	3.39	-4.20	52.67	<0.001 (HS)
	Group II: Hepatitis group	3.92	±0.22	3.84	3.74	-4.02	3.65	-4.51		p1= 0.018
	Group III: Cirrhotic group	5.55	±1.13	5.57	4.44	-6.71	3.79	-6.91		p2<0.001
										p3<0.001
Creatinine (mg/dL)	Group I: Control group	7.13	±.25	7.06	6.91	-7.33	6.77	-7.63	75.53	<0.001 (HS)
	Group II: Hepatitis group	65.13	± 1.89	65.17	63.85	-66.41	62.09	-69.0		p1<0.001
	Group III: Cirrhotic group	78.21 ±10.29		76.47	68.48 -85.38		65.81 -95.76			p2<0.001
										p3<0.001

P >0.05: Not significant (NS); P <0.05 is significant (S); p<0.01 is highly significant (HS).
KW: Kruskal Wallis test; SD: standard deviation; IQR: Inter-quartile range.
p1: Comparison between group I & group II; p2: Comparison between group I & group III; p3: Comparison between group II & group III

The groups exhibited in kidney function tests differed significantly (P<0.001), with in serum creatinine and blood urea a significant elevation in the cirrhosis group contarsted to the hepatitis group and controls, and a substantially higher level in the hepatitis group in comparison to the controls. (Table 6)

Table 7: Comparison between the studied groups regarding coagulation factors, tumor and inflammatory markers.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
PT (seconds)	Group I:	11.12	±0.58	11.20	10.59	-11.48	10.20	-12.31	61.54	<0.001 (HS)
	Control group									p1<0.001
	Group II:	12.50	±0.84	12.39	11.96	-13.15	11.01	-14.18		p2<0.001
	Hepatitis group									p3= 0.001
	Group III:	16.94	±3.97	16.01	13.06	-20.98	11.95	-22.60		
	Cirrhotic group									
INR	Group I:	0.96	±0.08	0.97	0.92	-1.03	0.80	-1.10	68.59	<0.001 (HS)
	Control group									p1<0.001
	Group II:	1.40	±0.05	1.39	1.37	-1.43	1.31	-1.52		p2<0.001
	Hepatitis group									p3=0.007
	Group III:	1.75	±0.28	1.76	1.53	-2.00	1.32	-2.12		
	Cirrhotic group									
AFP, (ng/mL)	Group I:	14.64	±6.06	11.88	9.56	-19.50	8.30	-27.0	37.47	<0.001 (HS)
	Control group									p1= 0.844
	Group II:	16.15	±5.45	15.89	11.23	-19.05	9.02	-29.23		p2<0.001
	Hepatitis group									p3<0.001
	Group III:	48.74	±25.70	46.52	27.07	-69.48	10.65	-89.88		
	Cirrhotic group									
NLR	Group I:	1.10	±0.31	1.00	.82	-1.37	0.68	-1.88	62.02	<0.001 (HS)
	Control group									p1= 0.003
	Group II:	2.13	±1.09	2.06	1.21	-2.50	0.48	-5.18		p2<0.001
	Hepatitis group									p3<0.001
	Group III:	13.44	±10.04	10.01	4.20	-20.67	1.33	-30.50		
	Cirrhotic group									
LMR	Group I:	2.45	±0.78	2.31	1.73	-3.11	1.22	-3.88	24.5	<0.001 (HS)
	Control group									p1= 0.529
	Group II:	2.08	±0.59	2.06	1.54	-2.40	1.16	-3.51		p2= 0.002
	Hepatitis group									p3<0.001
	Group III: Cirrhotic group	9.50	±7.22	7.08	2.63	-15.0	0.40	-20.0		

P >0.05: Not significant (NS), P <0.05 is significant (S), p<0.01 is highly significant (HS). KW: Kruskal Wallis test, SD: standard deviation, IQR: Inter-quartile range, PT: Prothrombin Time, INR: International Normalized Ratio, AFP: Alpha Fetoprotein, NLR: Neutrophil to Lymphocyte Ratio, LMR: Lymphocyte to monocyte ratio,
P1: Comparison between group I & group II, P2: Comparison between group I & group III, P3: Comparison between group II & group III

Significantly different was detected regarding PT, INR, and NLR were among the studied groups (P<0.001), being greater in cirrhosis group than hepatitis group and controls while they were significantly higher in hepatitis group contrasted to controls. AFP and LMR differed significantly between the three groups (P<0.001), being elevated in cirrhosis group than hepatitis group and controls. (Table 7)

Table 8: Comparison between the studied groups regarding liver function indices.

	Groups	Mean	± SD	Median	IQR		Min.- Max.		Test value (Kw)	*P-value*
FIB-4	Group I:	0.78	±0.27	0.73	0.60	-0.90	0.40	-1.35	70.28	<0.001 (HS)
	Control group									p1<0.001
	Group II:	3.45	±1.88	3.42	1.69	-4.59	0.66	-8.34		p2<0.001
	Hepatitis group									p3<0.001
	Group III:	61.61	±42.23	51.92	31.33	-95.73	0.91	-125.58		
	Cirrhotic group									
APRI	Group I:	0.10	±0.0	0.10	0.10	-0.10	0.09	-0.12	66.96	<0.001 (HS)
	Control group									p1<0.001
	Group II:	4.85	±2.87	4.03	2.69	-7.34	0.56	-9.94		p2<0.001
	Hepatitis group									p3=0.043
	Group III:	20.16	±17.19	14.90	4.23	-32.00	0.21	-52.29		
	Cirrhotic group									

P >0.05: Not significant (NS); *P* <0.05 is significant (S); *p*<0.01 is highly significant (HS).
KW: Kruskal Wallis test; SD: standard deviation; IQR: Inter-quartile range; FIB-4: Fibrosis-4 score; APRI: AST to Platelet Ratio Index
P1: Comparison between group I & group II; P2: Comparison between group I & group III; P3: Comparison between group II & group III

According to liver function indices, FIB-4 and APRI were significantly different between the studied groups (*P*<0.001), being higher in cirrhosis group than hepatitis group and controls while they were significantly elevated in hepatitis group contrasted to controls. PLR was significantly different between the three groups (*P*<0.001), being higher in the cirrhosis group than hepatitis group and controls. (Table 8)

Table 9: Comparison between the studied groups regarding RDW/ lymphocytes ratio.

			Group I Control group (No.= 30)	Group II Hepatitis group (No.= 30)	Group III Cirrhotic group (No.= 30)	Test value	*P-value*
RDW/ lymphocytes ratio		Mean ± SD	5.17± 1.03	6.49± 1.98	61.51± 40.21	KW=	<0.001 (HS)
		Median (IQR)	5.36(4.17- 5.85)	5.91 (4.88- 7.76)	60.33 (31.0- 76.67)	59.02	p1= 0.199
		Range	3.74- 7.42	3.81- 10.5	6.84- 130.5		p2<0.001
							p3<0.001

P >0.05: Not significant (NS), *P* <0.05 is significant (S), *p*<0.01 is highly significant (HS).
KW: Kruskal Wallis test, SD: standard deviation, IQR: Inter-quartile range
P1: Comparison between group I & group II, P2: Comparison between group I & group III, P3: Comparison between group II & group III

RLR differed significantly across the groups (*P*<0.001), being higher in cirrhosis group and hepatitis group compared to controls. (Table 9)

Table 10: Correlation between serum RDW/ lymphocytes ratio and different parameters.

	RDW/ lymphocytes ratio	
	r	*p- value*
Age (years)	0.013	0.905
ALT (U/L)	0.538	<0.001
AST (U/L)	0.647	<0.001
GGT (U/L)	0.873	<0.001
T. Bilirubin (mg/dL)	0.656	<0.001
Albumin (g/dL)	0.434	<0.001
Ferritin (ng/mL)	0.741	<0.001
Hb (g/dL)	-0.860	<0.001
RBCs (10^9/L)	-0.859	<0.001
RDW (%)	0.815	<0.001
Platelets count (×109/L)	-0.740	<0.001
Neutrophil (10^9/L)	0.125	0.241
LYM (10^9/L)	-0.989	<0.001
Monocyte (10^9/L)	-0.880	<0.001
Blood urea (mmol/L)	0.863	<0.001
S. creatinine (mg/dL)	0.852	<0.001
PT (seconds)	0.799	<0.001
INR	0.758	<0.001
AFP (ng/mL)	0.775	<0.001
NLR	0.810	<0.001
LMR	0.681	<0.001
FIB-4	0.878	<0.001
APRI	0.779	<0.001

P value≤ 0.05 is significant; *P value*> 0.05 is not significant; r: Spearman correlation; AST: Aspartate aminotransferase; ALT: alanine aminotransferase; GGT: Gamma-glutamyl transferase; PT: Prothrombin Time; INR: International Normalized Ratio; AFP: Alpha Fetoprotein; NLR: Neutrophil to Lymphocyte Ratio; LMR: Lymphocyte to monocyte ratio; FIB-4: Fibrosis-4 score; APRI: AST to Platelet Ratio Index

A significant positive correlation was detected between RLR ratio and each of ALT (*P*=<0.001, r=0.538), AST (r=0.647, *P*=<0.001), GGT (*P*=<0.001, r=0.873), T. bilirubin (*P*=<0.001, r=0.656), albumin (r=0.434, *P*=<0.001), ferritin (*P*=<0.001, r=0.741), RDW (*P*=<0.001, r=0.815), urea (r=0.863, *P*=<0.001), creatinine (*P*=<0.001, r=0.852), PT (r=0.799, *P*=<0.001), INR (r=0.758, *P*=<0.001), AFP (r=0.775, *P*=<0.001), NLR (*P*=<0.001, r=0.810), LMR (r=0.681, *P*=<0.001), FIB-4 (r=0.878, *P*=<0.001) and APRI (r=0.779, *P*<0.001). However, an inverse correlation of a significant value was noted between RLR and each of Hb (r=-0.860, *P*<0.001), RBCs (*P*<0.001, r=-0.859), PLT s count (r=-0.740, *P*<0.001), lymphocytes (r=-0.989, *P*<0.001), and monocytes (*P*<0.001, r=-0.880). (Table 10)

Table 11: Univariate logistic regression analysis for factors predicting post hepatic cirrhosis.

Parameters	P-value	Odds	95%CI	
		ratio (OR)	Lower limit	Upper limit
Age (years)	0.416	0.988	0.960	1.017
Gender (male)	0.895	1.062	0.434	2.600
Residence (Rural)	0.771	0.877	0.363	2.120
ALT (U/L)	0.086	1.002	1.000	1.004
AST (U/L)	0.003	1.003	1.001	1.005
GGT (U/L)	0.000	1.168	1.071	1.274
T. Bilirubin (mg/dL)	0.000	20.849	5.545	78.386
Albumin (g/dL)	0.917	1.000	0.996	1.004
Ferritin (ng/mL)	0.000	1.002	1.001	1.003
Hb (g/dL)	0.082	1.090	0.989	1.200
RBCs (10^9/L)	0.781	1.149	0.433	3.049
RDW (%)	0.000	7.306	2.392	22.317
Platelets count (×109/L)	0.000	0.874	0.812	0.942
Neutrophil (10^9/L)	0.053	1.217	0.997	1.485
Lymphocytes (10^9/L)	0.000	0.014	0.002	0.097
Monocyte (10^9/L)	0.000	0.032	0.007	0.134
Blood urea (mmol/L)	0.000	125.965	9.353	1696.55
S. creatinine (mg/dL)	0.002	2.392	1.364	4.195
PT (seconds)	0.996	0.997	0.310	3.200
INR	0.489	0.945	0.804	1.110
AFP, ng/mL	0.228	1.079	0.953	1.222
NLR	0.000	3.553	1.929	6.544
LMR	0.002	1.937	1.276	2.940
FIB-4	0.006	1.753	1.174	2.616
APRI	0.000	1.288	1.132	1.466
RDW/ lymphocytes ratio	0.008	2.081	1.207	3.590

B: Regression coefficient; S.E.: Standard error, CI: Confidence interval

Univariate analyses were accomplished to investigate the possible predictive factors for post hepatic cirrhosis. In univariate analysis: AST, GGT, total bilirubin, ferritin, RDW, lymphocytes, monocytes, urea, Creatinine, Uric acid, NLR. LMR, FIB-4, APRI and RLR ratio were significantly correlated with of post hepatic cirrhosis enhanced risk. (Table 11)

Table 12: Multivariate logistic regression analysis for factors related with post hepatic cirrhosis

Parameters	P-value	Odds ratio (OR)	95%CI	
			Lower limit	Upper limit
AST, U/L	0.315	0.996	0.989	1.004
GGT, U/L	0.000	6.831	2.363	19.745
T. Bilirubin (mg/dL)	0.524	0.103	0.000	111.941
Ferritin (ng/mL)	0.112	0.976	0.947	1.006
RDW (%)	0.000	6.831	2.363	19.745
Platelets count (×109/L)	0.509	0.974	0.899	1.054
Lymphocytes (10^9/L)	0.045	0.002	0.000	0.876
Monocyte (10^9/L)	0.127	6.690	0.584	76.598
Blood urea (mmol/L)	0.326	6.538	0.154	276.941
S. creatinine (mg/dL)	0.030	2.028	1.072	3.837
NLR	0.000	4.780	2.112	10.817
LMR	0.152	0.534	0.226	1.261
FIB-4	0.187	13.510	0.282	647.110
APRI	0.095	0.008	0.000	2.314
RDW/ lymphocytes ratio	0.042	3.741	1.050	13.331

B: Regression coefficient; S.E.: Standard error; CI: Confidence interval.

In multivariate analysis, using model adjusted for previously mentioned parameters, it was found that GGT, RDW, lymphocytes, creatinine, NLR and RLR ratio were independent predictors for post hepatic cirrhosis.(Table 12)

Table 13: Validity (AUC, sensitivity, specificity) for RDW/ lymphocytes ratio in prediction of post hepatic cirrhosis.

	Best cut off	Sensitivity	Specificity	PPV	NPV	AUC	*P-value*
Cirrhotic group Vs hepatitis group	6.93	43.3%	96.7%	92.9%	63%	0.695	0.005
Cirrhotic group Vs controls	10.5	100%	93.3%	93.7%	100%	0.972	<0.001

AUC: Area Under a Curve; *p value*: Probability value; NPV: Negative predictive value; PPV: Positive predictive value;
*: Statistically significant at $p \leq 0.05$

To verify the RLR value in of post hepatic cirrhosis detection. Receiver operating characteristic (ROC) analysis was accomplished. RLR had 43.3% sensitivity and 96.7% specificity at a threshold value of 6.93 with AUC = 0.695 and was highly significant (*P*=0.005) in differentiation between cirrhotic group and hepatitis group. Meanwhile it had 93.3% specificity and 100% sensitivity at a threshold value of 10.5 with AUC = 0.972 and was highly significant (*P*<0.001) in differentiation between cirrhotic group and control group. (Table 13), (Figure 1 and Figure 2).

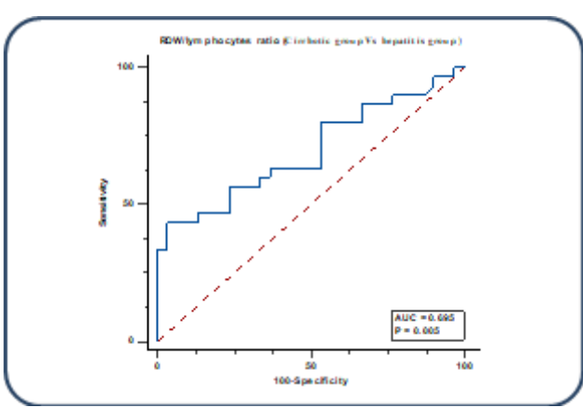

Fig. 1: ROC curve of RDW/ lymphocytes ratio in differentiation between cirrhotic group and hepatitis.

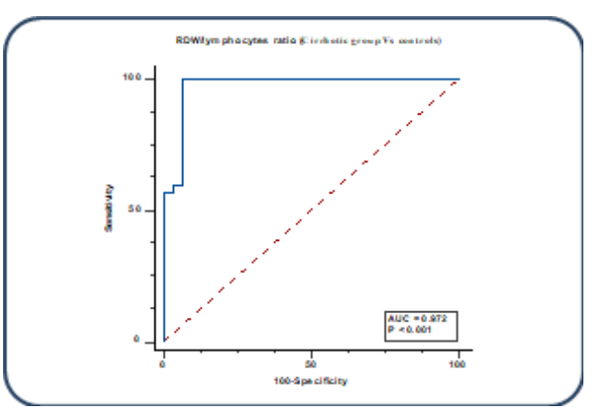

Fig. 2: ROC curve of RDW/ lymphocytes ratio in differentiation between cirrhotic group and control.

DISCUSSION

The gold standard for the LC diagnosis is the liver biopsy application. Nevertheless, the invasive character of the procedure had been reported to be associated with a number of problematic issues[10].

Additionally, regular liver fibrosis surveillance is necessary for CHB patients to identify the potential development of HCC and the likelihood of complications, including mortality, linked to CHB. As a result, numerous investigations concentrate on the noninvasive procedures utilization to diagnose LC. Three noninvasive methods are currently in use, each with its own advantages and disadvantages. The initial method is imaging, that is widely employed to evaluate liver fibrosis[11].

In general, the results of liver histology exhibit a substantial correlation with those obtained through imaging. Nevertheless, these imaging methods necessitate the use of specialized instruments and the expertise of interpretation specialists. Laboratory investigations for collagen, laminin, and hyaluronic acid comprise the second approach. Nevertheless, these biochemical assays are not regularly accessible. Composite diagnostic panels are also employed and can be computed utilizing regular laboratory records. The AAR is the term for AAR and the APRI are examples of such indicators[12].

The APRI and fibrosis index based on four factors (FIB-4) are specifically beneficial for the LC diagnosis among the current measures in use. ***Xiao et al.*** conducted a study that utilized a combination of blood marker measurements and imaging modalities to comprehensively illustrate the LC diagnosis. The study also posited that a single noninvasive approch for diagnosis needed to be improved in the optimal scenario[13].

Some new techniques have been devised to indirectly diagnose LC and evaluate prognosis. An independent biomarker that predicts mortality in patients with HCC following curative resection is the low LMR[14].

RDW has the possibility to evaluate HBV-related liver disease severity[15].

In HBV-related decompensated cirrhosis cases, the NLR is an early mortality predictor[16].

Nevertheless, there are a few reseches that compare the LMR, NLR, FIB-4, APRI, and RDWfor CHB-LC diagnostic value. The LC risk is increased by the HBV incompetent immune clearance, which results in CHB[17].

During HBV infection, liver injury is induced by the immune system. A study demonstrated that the number of lymphocytes decreased during CHB and cirrhosis. Numerous studies demonstrated a rise in RDW during LC[18].

This study aim was to estimate and contrast RDW and RLR utiliation in diagnosing HBV-related LC .

This study was conducted on 60 hepatitis B cases, who were attending or admitted to the Hepatology unit of Ain Shams University Hospitals.

Our results revealed that the three groups exhibted statistically insignificant difference regarding age, gender and residence ($p>0.05$).

Our results are consistent with those of another study that specifically examines the diagnostic potential of red cell distribution RLR for HBV-LC[19]. Four hundered and ten HBV-LC patients, 327 CHB patients, and 750 healthy controls were included in this study. There was no significant difference between the three categories in terms of age, gender, and residence ($p>0.05$).

ALT and AST levels were signifecntly different between the studied groups ($P<0.001$), with AST and ALT levels being greater in the cirrhosis and hepatitis groups than in the controls. However, the two groups differed insignificantly from one another. The cirrhosis group experienced a substantially higher GGT than the hepatitis group ($P<0.001$), while the cirrhosis and hepatitis groups experienced a greater GGT than the controls. The three groups substantially differed on the basis of total bilirubin ($P<0.001$), with a significant elevation in the cirrhosis group in comparison with the hepatitis and control groups.

In agreement with another study, our findings indicate that individuals with HBV-LC exhibited substantial disparities in ALT, neutrophil, RLR, AST, lymphocyte, NLR, RDW, FIB-4, PLT, LMR, ALB, and APRI when contrasted with healthy controls. Similarly, we observed substantial variations in these parameters between the HBV-LC and CHB teams. Relative to the control and CHB groups, patients with HBV-LC exhibited a lower LMR and greater RDW, RLR, APRI, FIB-4, and NLR.

In addition to concurring with a separate study that focused on a total of 130 cases, including 41 healthy individuals, 69 CHB individuals, and 61 HBV-LC cases[20,21] The mean ages of the healthy controls, HBV-LC and CHB patients were 49.98±10.78 years, 52.33±13.54, and 48.10±12.85 years, respectively. Significant elevations in serum ALT, total bilirubin, and AST.

Our findings indicated that the three groups exhibited a statistically significant difference in albumin levels ($P<0.001$). The cirrhosis group exhibited a significantly lower level than the hepatitis group, and the cirrhosis and

hepatitis groups had a significantly lower level than the controls. In terms of ferritin levels, group III exhibited a significantly greater ferritin level than group I and group II.

In patients with HBV-LC, significant reduction in PLT count, and hemoglobin, albumin concentration were detected, which also aligns with an earlier study[18]. CHB patients exhibited elevated ALT levels in comparison to those with HBV-LC (335.65±452.92 vs 141.99±322.92 U/L, $P<0.05$). In 22 of the 61 HBV-LC cases and 21 of the 69 CHB cases serum hepatitis B e-antigen (HBeAg) was detected ($P>0.05$).

Our findings contradict a study that determined that cases were categorized into three categories based on their NLR levels: group A (NLR ≤ 2.0), group B (>2.0, but <5.0), and group C (≥5.0)[19]. There were no discernible variations in the levels of ALT, total bilirubin, AST, gender, INR, or age. Additionally, than those in groups A and B the white cell and neutrophil counts of patients in group C were considerably higher. Conversely, in group C than in groups A and B the lymphocyte count was lower. These data indicate that a higher NLR in patients may be predominantly due to a decrease in lymphocyte counts and an increase in neutrophil counts.

Our findings indicated that the three groups CBC differed significantly ($P<0.001$), with a significant decline in Hgb, RBCs, and PLT count in the cirrhosis group in contrast to the hepatitis group and controls. In comparison to the hepatitis group and controls, the cirrhosis group exhibited a substantially higher RDW.

A study revealed a correlation between HBV-infected patients and RDW values of varying disease states. The study discovered that RDW values were significantly elevated in hepatitis B cases and linked to its severity.

Our findings are consistent with those of an additional study that examined the correlation across RDW values and HBV-related liver diseases, such as CHB and HBV-LC[19]. The RDW values of HBV-LC cases were significantly elevated in comparison to those of CHB patients and healthy controls. Additionally, CHB individuals exhibited elevated RDW values. This is in accordance with the findings of[8].

The cirrhosis group exhibited a substantial decrease in lymphocytes and monocytes in comparison to the hepatitis group and controls, resulting in a significant difference in WBC counts ($P<0.05$). Meanwhile, the cirrhosis and hepatitis groups exhibited a substantial increase in neutrophils in comparison to the control group.

In contrast to healthy controls, CHB patients exhibited a lower number of lymphocytes, which was further reduced during cirrhosis. In patients with cirrhosis, hypersplenism results in a reduction in white blood cell count[20,21].

The immunity is significantly monitored by lymphocytes. The progressive reduction in the variety of lymphocytes may be associated with apoptosis and immune cell dysfunction, and the advanced cirrhosis onset may be tied to this phenomenon[20,21].

Additionally, the LC threat is elevated due to the inefficient HBVimmune elimination, which results in CHB. A reduction in lymphocetic cells count was facilitated by HBV, which in turn promoted recurrent infection, and immune-mediated liver impairment arose throughout HBV infection. Consequently, the LC progression is facilitated by the persistent HBV and the reduction in lymphocytes[22].

In our study, individuals with a higher NLR lymphocyte counts were lower than in those with lower NRLs. A possible reason for the diminished lymphocytes number in bloodstream is that lymphocytes were extensively consumed by liver for necroinflammation[23].

Our results also agree with another study targeting the RLR diagnostic ability for HBV-LC[23]. The study included 410 HBV-LC individuals, 327 CHB individuals, and 775 healthy individuals as the control group. A significant increase in blood urea and serum creatinine was exhibted in the cirrhosis group with regard to the hepatitis group and controls, while they were significantly greater in the hepatitis group than in the controls.

Our findings indicated that the PT, INR, and NLR differed signifecantly between the studied groups ($P<0.001$). The cirrhosis group exhibited higher values than the hepatitis cases and controls, while the hepatitis group exhibited values that were significantly higher than the controls. The AFP and LMR values were substantially different among the three groups ($P<0.001$), with the cirrhosis cohort exhibiting a higher level than the hepatitis cohort and controls.

Our findings are consistent with those of another study that reported a correlation between RLR and other liver function measures[19]. RLR demonstrated a negative correlation with serum PLT (all $P<.05$) and a positive correlation with APRI and FIB-4 (all $P<.05$) in all three groups. In the CHB group, RLR exhibited a positive correlation with ALT; however, this correlation did not reach statistical significance ($P=.203$). In the HBV-LC cohort, RLR exhibited a negative correlation with ALT. Our findings indicate that RLR exhibits a high degree of concordance with FIB-4, PLT, and APRI parameters in both the HBV-LC and CHB groups.

There are only a few studies available that compare the diagnostic value of utilizing RDW, LMR, NLR, APRI, and FIB-4 in addition to CHB for CHB-LC 1

CONCLUSION

This study has determined significant insight into the noninvasive methods utility for HBV-LC diagnosis. This study demonstrated that both RDW and RLR are significantly linked with HBV-LC, showing a clear distinction in values between cirrhotic cases, hepatitis B cases, and healthy controls.

The RLR emerged as a potent diagnostic marker with a strong correlation to various liver function parameters and substantial predictive value for cirrhosis. These findings underscore the utility of RDW and RLR as non-invasive, accessible markers for diagnosing and monitoring HBV-LC.

ETHICAL CONSIDERATION

This is to certify that the Research Ethics Committee at the Faculty of Medicine, Ain Shams University FMASU MS 563/ 2023 has reviewed your study protocol from the ethical point of view and approves it requiring the following:

1. A progress report every 3 months.
2. A final pre-publication report to inform the Committee of the study results
3. Regular monitoring of the project will be done by a monitoring board described by the FMASU REC
4. This approval is valid for one year till 8/10 /2024

The FMASU REC is organized and operated according to guidelines of the International Council on Harmonization (ICH) Anesthesiology and the Islamic Organization for Medical Sciences (IOMS), the United States Office for Human Research Protections and the United States Code of Federal Regulations and operates under Federal Wide Assurance No. FWA 000017585.

The REC does not declare the names of its members according to the University and the REC's Standard operating Procedures.

CONFLICT OF INTERESTS

All authors declare they have no conflict of interest nor personal benefit that influenced the work reported in this paper.

AUTHORS' CONTRIBUTION

Massoud S.S. collected and followed up on the patients, carrying out the requested investigations. Hilal E.M. developed the ideas for research and reviewed the work done. El-Gaaly S.A. wrote the discussion and analyzed the collected data. Al-Ashram M.N. assisted in writing the literature and editing the paper. All authors authorized the manuscript.

REFERENCES

1. **Locarnini, S., Hatzakis, A., Chen, D. S., & Lok, A. (2015).** Strategies to control hepatitis B: Public policy, epidemiology, vaccine and drugs. Journal of hepatology, 62(1), S76-S86.

2. **Neuberger, J., & Cain, O. (2021).** The need for alternatives to liver biopsies: non-invasive analytics and diagnostics. Hepatic Medicine: Evidence and Research, 59-69.

3. **Ji, D., Chen, Y., Bi, J., Shang, Q., Liu, H., Wang, J. B.,. & Yang, Y. (2022).** Entecavir plus Biejia-Ruangan compound reduces the risk of hepatocellular carcinoma in Chinese patients with chronic hepatitis B. Journal of Hepatology, 77(6), 1515-1524.

4. **Forlano, R., Mullish, B. H., Giannakeas, N., Maurice, J. B., Angkathunyakul, N., Lloyd, J., & Manousou, P. (2020).** High-throughput, machine learning–based quantification of steatosis, inflammation, ballooning, and fibrosis in biopsies from patients with nonalcoholic fatty liver disease. Clinical Gastroenterology and Hepatology, 18(9), 2081-2090.

5. **Friedman, L.S. (2004).** Controversies in liver biopsy: who, where, when, how, why?. Current gastroenterology reports, 6(1), 30-36.

6. **Fernández-Ruiz, M., López-Medrano, F., Romo, E.M., Allende, L. M., Meneu, J.C., Fundora-Suárez, Y., & Aguado, J.M. (2009).** Pretransplant lymphocyte count predicts the incidence of infection during the first two years after liver transplantation. Liver transplantation, 15(10), 1209-1216.

7. **Panel, C. P. G., Berzigotti, A., Tsochatzis, E., Boursier, J., Castera, L., Cazzagon, N.,. & European Association for the Study of the Liver. (2021).** EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis–2021 update. Journal of hepatology, 75(3), 659-689.

8. **Fukui, H., Saito, H., Ueno, Y., Uto, H., Obara, K., Sakaida, I.,. & Shimosegawa, T. (2016).** Evidence-based clinical practice guidelines for liver cirrhosis 2015. Journal of gastroenterology, 51, 629-650.

9. **Kwon, J. H., Jang, J. W., Kim, Y. W., Lee, S. W., Nam, S. W., Jaegal, D.,. & Bae, S. H. (2015).** The usefulness of C-reactive protein and neutrophil-to-lymphocyte ratio for predicting the outcome in hospitalized patients with liver cirrhosis. BMC gastroenterology, 15, 1-7.

10. **Liu, L., Cao, J., Zhong, Z., Guo, Z., Jiang, Y., Bai, Y., & Xu, J. (2019).** Noninvasive indicators predict advanced liver fibrosis in autoimmune hepatitis patients. Journal of Clinical Laboratory Analysis, 33(7), e22922.

11. **Henry, B. M., Benoit, J. L., Benoit, S., Pulvino, C., Berger, B. A., Olivera, M. H. S. D.,. & Lippi, G. (2020).** Red blood cell distribution width (RDW) predicts COVID-19 severity: a prospective, observational study from the Cincinnati SARS-CoV-2 emergency department cohort. Diagnostics, 10(9), 618.

12. **Hu, Z., Sun, Y., Wang, Q., Han, Z., Huang, Y., Liu, X.,. & Deng, A. (2013).** Red blood cell distribution width is a potential prognostic index for liver disease. Clinical Chemistry and Laboratory Medicine, 51(7), 1403-1408.

13. **Khallafi, H., & Qureshi, K. (2015).** Imaging based methods of liver fibrosis assessment in viral hepatitis: a practical approach. Interdisciplinary Perspectives on Infectious Diseases, 2015.0–1:.

14. **Deng, H., Qi, X., & Guo, X. (2015).** Diagnostic accuracy of APRI, AAR, FIB-4, FI, King, Lok, Forns, and FibroIndex scores in predicting the presence of esophageal varices in liver cirrhosis: a systematic review and meta-analysis. Medicine, 94(42), e1795.

15. **Xiao, G., Yang, J., & Yan, L. (2015).** Comparison of diagnostic accuracy of aspartate aminotransferase to platelet ratio index and fibrosis-4 index for detecting liver fibrosis in adult patients with chronic hepatitis B virus infection: a systemic review and meta-analysis. Hepatology, 61(1), 292-302.

16. **Lin, Z. X., Ruan, D. Y., Li, Y., Wu, D. H., Ma, X. K., Chen, J.,. & Wu, X. Y. (2015).** Lymphocyte-to-monocyte ratio predicts survival of patients with hepatocellular carcinoma after curative resection. World journal of gastroenterology: WJG, 21(38), 10898.906–.

17. **Huang, R., Yang, C., Wu, K., Cao, S., Liu, Y., Su, R.,. & Wu, C. (2014).** Red cell distribution width as a potential index to assess the severity of hepatitis B virus-related liver diseases. Hepatology Research, 44(14), E464-E470.

18. **Zhang, H., Sun, Q., Mao, W., Fan, J., & Ye, B. (2016).** Neutrophil-to-lymphocyte ratio predicts early mortality in patients with HBV-related decompensated cirrhosis. Gastroenterology research and practice, 2016.5–1 .

19. **Cheng, L. S., Liu, Y., & Jiang, W. (2015).** Restoring homeostasis of CD4+ T cells in hepatitis-B-virus-related liver fibrosis. World Journal of Gastroenterology: WJG, 21(38), 10721.31-.

20. **Xu, R., Zhang, Z., & Wang, F. S. (2012).** Liver fibrosis: mechanisms of immune-mediated liver injury. Cellular & molecular immunology, 9(4), 296-301.

21. **Meng, J., Xu, H., Liu, X., Wu, R., & Niu, J. (2018).** Increased red cell width distribution to lymphocyte ratio is a predictor of histologic severity in primary biliary cholangitis. Medicine, 97(48), e13431.

22. **Lou, Y., Wang, M., & Mao, W. (2012).** Clinical usefulness of measuring red blood cell distribution width in patients with hepatitis B. PloS one, 7(5), e37644.

23. **Zhang, X., Wang, D., Chen, Z., Guo, N., Wang, W., Xiong, C.,. & Sun, M. (2020).** Red cell distribution width-to-lymphocyte ratio: A novel predictor for HBV-related liver cirrhosis. Medicine, 99(23), e20638.

القيمة التنبؤية لنسبة عرض توزيع خلايا الدم الحمراء إلى نسبة الخلايا اللمفاوية في تشخيص التليف الكبدي ما بعد الكبدي

سونيا أحمد علي الجعلي، عصام محمد بيومي هلال، شيماء شاذلي مسعود و محمد نبيل بدوي الأشرم

قسم أمراض الجهاز الهضمي والكبد، كلية الطب، جامعة عين شمس

الخلفية: ظهرت نسبة عرض توزيع خلايا الدم الحمراء إلى نسبة الخلايا اللمفاوية (RDW-to-LR) كعلامة حيوية واعدة غير جراحية لتشخيص أمراض الكبد المزمنة، بما في ذلك التليف الكبدي ما بعد الكبدي. تعتبر هذه الأمراض من التحديات الصحية الكبيرة على مستوى العالم، مما يبرز الحاجة إلى أساليب تشخيصية غير جراحية بديلة عن خزعة الكبد التقليدية.

الهدف: تهدف هذه الدراسة إلى تقييم القيمة التنبؤية لـ RDW-to-LR في تشخيص التليف الكبدي ما بعد الكبدي واستكشاف الآليات التي تعكس التغيرات الفسيولوجية المرضية المرتبطة بالتليف الكبدي.

الطرق: شملت الدراسة ٦٠ مريضًا مصابًا بالتهاب الكبد الوبائي (B) من مستشفى جامعة عين شمس، تم تقسيمهم إلى ثلاث مجموعات: ٣٠ شخصًا سليمًا (المجموعة الضابطة)، ٣٠ مريضًا بالتهاب الكبد المزمن، و٣٠ مريضًا بالتليف الكبدي المرتبط بالفيروس (HBV). تم قياس إنزيمات الكبد (GGT)، (AST)، (ALT)، البيليروبين الكلي، والكولينستيراز في المصل.

النتائج: أظهرت النتائج اختلافات كبيرة في مستويات إنزيمات الكبد بين المجموعات، حيث كانت مرتفعة في مجموعات التهاب الكبد والتليف الكبدي. أظهرت التحليلات الارتباطية أن RDW-to-LR مرتبط بشكل إيجابي مع معايير وظيفة الكبد وعكسيًا مع مؤشرات صحة الدم. كما أظهرت تحليلات الانحدار اللوجستي أن RDW-to-LR يعد مؤشرًا هامًا للتليف الكبدي.

الاستنتاج: تدعم هذه الدراسة استخدام RDW-to-LR كعلامة حيوية غير جراحية موثوقة لتشخيص التليف الكبدي المرتبط بالتهاب الكبد الوبائي (HBV).