Current Science International
Volume: 12 | Issue: 01| Jan. - March| 2023

EISSN:2706-7920 ISSN: 2077-4435
DOI: 10.36632/csi/2023.12.1.2
Journal homepage: www.curresweb.com
Pages: 7-14

A High Red Cell Distribution Width-To-Platelet Ratio is a Good Marker of Liver fibrosis in Non-Alcoholic Fatty Liver Disease

Lobna A. EL-Sherif [1], Noha E. Esheba[1], Amira Y. Ahmed[2] and Laila M. S. Ahmed[1]

[1]Department of Internal Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt
[2]Department of Clinical Pathology, Faculty of Medicine, Tanta University, Tanta, Egypt

Received: 20 Nov. 2022 **Accepted:** 22 Dec. 2022 **Published:** 15 Jan. 2023

ABSTRACT

Background: Most patients with NAFLD are commonly asymptomatic and often identified incidentally, and the patients come to the clinician's attention usually because of the elevation of liver enzymes. Moreover, the platelet count itself and platelet-related indexes, such as the AP index, APRI index, and FIB4 index have been widely used to evaluate the severity of various liver diseases. **Aim of the work:** In our study, we have attempted to assess red cell distribution width-to-platelet ratio as a marker of liver fibrosis. Material and methods: This prospective study was carried out on a selected group of 50 patients, 25 of them who have a non-alcoholic fatty liver with liver fibrosis and 25 patients who have non-alcoholic fatty liver without liver fibrosis which Pelvi-abdominal U/S and fibroscan diagnose. All patients had RDW to platelet ratio (RPR) =RDW×100/ PLT (109/L) and Fib 4 score = (Age × AST) / (Platelet count × (square root of ALT). **Results:** There was a significant increase in RPR% in NAFLD patients with fibrosis in comparison to NAFLD patients without fibrosis. There was also a positive significant correlation between RPR% and BMI, RDW%, HbA1c, fibrosis, and FIB4, while there was a negative significant correlation between RPR and platelets. **Conclusion**: RPR has a good sensitivity of 88% so it can be employed as an excellent non-invasive marker for the prediction of fibrosis.

Keywords: Non-alcoholic fatty liver, NAFLD, RPR, FIB4, Fibroscan

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is a global health issue that affects more than 25% of the world's population. According to reports, the Middle East has the highest prevalence of NAFLD (31.79%) (Hassan *et al.,* 2020). While Africa has the lowest prevalence rate (13.48%) (Younossi *et al.,* 2016).

NAFLD is more common in men (31%) than in women (16%) in Egypt, and its prevalence rises with age, from less than 20% in those under 20 to more than 40% in those over 60 (Alkassabany *et al.,* 2014).

Aspartate-aminotransferase (AST) or alanine aminotransferase (ALT) elevations, which are typically noted during routine laboratory examinations or abnormal imaging studies done for other reasons, are the most common reasons that patients with NAFLD are brought to the clinician's attention (Chen *et al.,* 2008). Patients may also complain of fatigue and dull aching pain in the right upper abdomen (Ahmed *et al.,* 2017).

RBC distribution width (RDW) is an automated measure of red cell size (RBC) heterogeneity (eg, anisocytosis) and is routinely performed as part of a complete blood count. RDW is used in the differential diagnosis of anemia (Pascual-Figal *et al.,* 2009). Recently, a number of studies have shown that RDW can serve as a new independent predictor of prognosis in patients with cardiovascular disease (e.g., heart failure, stable coronary artery disease, acute myocardial infarction, stroke and pulmonary hypertension) (Förhécz *et al.,* 2009).

Corresponding Author: Lobna Ahmed EL-Sherif, Department of Internal Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt. E-mail: lobnaelsherif91@gmail.com

High RDW values have also been shown to be associated with an increased risk of mortality in the general population. However, the relationship between RDW and NAFLD is less certain. If confirmed in future follow-up studies, this association could justify the introduction of simple and inexpensive RDW into NAFLD risk prediction algorithms (Ani and Ovbiagele 2009).

The production of peripheral platelets is mainly regulated by thrombopoietin, which is a glycoprotein hormone mainly synthesized in the liver. Previously, several studies reported an inverse correlation between the degree of chronic hepatitis and the number of peripheral platelets (Fang *et al.,* 2018). In addition, platelet count itself and platelet index such as AP index, APRI index and FIB4 index have been widely used to assess the severity of various liver diseases, especially in patients with liver disease. chronic infection with hepatitis B or C virus (Murali *et al.,* 2015). However, the effect of NAFLD on platelet count is controversial. The results of numerous studies suggest that the platelet count could serve as an ideal biomarker of the severity of fibrosis in NAFLD patients (Riediger *et al.,* 2014).

The aim of this work was to study red cell distribution width-to-platelet ratio as a marker of liver fibrosis in non-alcoholic fatty liver disease.

2. Patients & Methods

2.1. Study Design: This was a cross-sectional study.

2.2. Study population

This prospective study was carried out on selected group of 50 patients from the inwards and outpatient clinic of the Internal Medicine Department, Tanta University Hospital. The study duration started from September 2020 to March 2021.

The study population was divided into 2 groups: NAFLD-F: 25 patients who have non-alcoholic fatty liver with liver fibrosis. And NAFLD: 25 patients who have non-alcoholic fatty liver without liver fibrosis. The approval of Tanta Medical Ethical Committee was obtained (approval number: 34057/8/20), and a written informed consent was signed by each participant.

2.3. Inclusion criteria

Patient ≥ 18 years diagnosed with non-alcoholic fatty liver disease by FibroScan device model 502 F01405 (Metavir cut-off).

2.4. Exclusion criteria

Patients with any of the following were excluded from the study: alcohol consumption >140 g/week for men and >70 g/week for women, patients with chronic liver disease, patients with viral hepatitis patients with renal impairment (serum creatinine > 2.5 mg/dl or estimated glomerular filtration rate <30 mL/min/1.73 m^2), patients with HCC, pregnant females and patients with recent infection.

2.5. Methods

Hepatic Fibrosis with nonalcoholic fatty liver disease was diagnosed based on: Pelvi-abdominal U/S and fibroscan. All the participants were subjected to: full history taking, complete clinical examination, body mass index, blood pressure, laboratory investigation: complete blood count (CBC), RDW to platelet ratio (RPR)=RDW×100/ PLT (10^9/L), fasting plasma glucose, complete liver function, renal function, CRP, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), fibrosis-4 (FIB-4) calculator score =(Age x AST) / (Platelet count x (square root of ALT)), radiological investigations: (Pelvi_abdominal U/S, Fibroscan)

3. Results

In current study when comparison between the studied groups NAFLD control group & NAFLD-F patients. There was a significant increase in all the following parameters in the NAFLD-F group: age, BMI, SBP, DBP, Hb, platelets, RDW%, RPR%, TC, HDL-C, AST, steatosis, fibrosis, FIB-4index. Only ALT was significantly lower in this group (Table 1).

Histopathological assessment is the current reference standard for diagnosis, risk stratification and therapeutic efficacy evaluation for NAFLD. Unfortunately, liver biopsy for histological assessment carries risks, including even rare mortality.

Histopathological assessment is also susceptible to sampling error and intra- and inter-reader variability. These drawbacks of liver biopsy have limited biopsy-based assessment in routine practice and pose challenges in clinical trial design and interpretation. Therefore, there is a need for reliable non-invasive tools for the diagnosis, risk stratification and monitoring of the course of NAFLD.

In the current study conducted on NAFLD population, we provided evidence that NAFLD with fibrosis had a higher RPR.

The results also indicated that RPR ratio was an independent risk factor for advanced fibrosis. Finally, we established a predictive model for NAFLD by utilizing RPR which had a large area under the curve (AUC) and good sensitivity. To our knowledge, our study is the first to demonstrate a significant association between RPR and NAFLD. NAFLD is reported to be associated with genetic, environmental, and metabolic factors. The underlying mechanism by which RPR interacts with NAFLD remained unclear.

In this study we assessed fibrosis in patients with NAFLD by using RPR % fibroscan and FIB4 in 50 Egyptian patients with NAFLD divided into two subgroups; NAFLD-F group: 25 patients who have non-alcoholic fatty liver with liver fibrosis. They were 18 males and 7 females, their age ranged from (42 – 68) years with mean (53.20 ± 7.40) years.

Table 1: Comparison between the studied groups NAFLD control group & NAFLD-F patients (Mean ± SD) regarding some studied parameters.

Groups				**Unpaired t-test**	
		NAFLD (NO=25)	**NAFL-F (NO=25)**	**T**	**P-value**
Sex	**Male**	14(56%)	18(72%)	1.39	0.239
	Female	11(44%)	7(28%)		
Age (years)		47.20±8.50	53.20±7.40	2.673	0.01*
BMI		28.52±3.53	31.78±3.39	3.431	0.001*
SBP (mmHg)		118.40±15.70	129.00±14.50	2.483	0.016*
DBP (mmHg)		67.40±8.10	75.60±10.40	2.959	0.005*
Hb (gm%)		12.36±1.43	13.79±1.71	3.211	**0.002***
WBCs (x10^3)		7.38±2.03	7.00±1.98	0.667	**0.52**
Platelets(x10^3)		320.90±44.74	237.50±57.28	5.737	**<0.001***
RDW%		12.54±2.016	13.42±4.22	2.740	**0.009***
RPR%		3.99±0.73	5.98±1.53	5.874	**<0.001***
TG (mg/dl)		148.70±66.24	181.10±87.64	1.476	**0.146**
TC (mg/dl)		193.30±42.49	218.3±28.49	2.44	**0.018***
LDL-C (mg/dl)		132.4± 45.69	130.80±27.94	0.149	**0.887**
HDL-C (mg/dl)		54.68±13.30	47.80± 11.48	1.958	**0.056**
ALT(U/L)		42.32±12.20	34.00±12.41	2.391	**0.021***
AST(U/L)		32.52±14.15	41.00± 12.60	2.237	**0.031***
Steatosis(CAP)		263.30±20.49	307.60±33.27	5.671	**<0.001***
Fibrosis(KPa)		4.22±0.898	9.65±1.637	14.53	**<0.001***
FIB-4index		0.682±0.225	1.67±0.399	10.7	**<0.001***

ALT: Alanine transaminase. AST: aspartate aminotransferase. BMI: body mass index. DBP: diastolic blood pressure. Hb: hemoglobin. RDW: red cell distribution width. RPR: red cell distribution width-to-platelet ratio. SBP: systolic blood pressure. WBC: white blood cells. TG: triglycerides. TC: total cholesterol. HDL-C: high-density lipoprotein cholesterol. LDL-C: low-density lipoprotein cholesterol.

RPR% showed significant positive correlation with the following: BMI, RDW%, HbA1c%, fibrosis and FIB4. On the other hand, there was a significant negative correlation between RPR% and platelet count. There was non- significant correlation between RPR% and the remaining studied parameters (Table 2)

Table 2: Correlation Matrix between RPR% and other parameters

Parameter	RPR%	
	R	p-Value
AGE(y)	0.306	0.137
BMI	0.600	<0.01*
SBP(mmHg)	0.092	0.661
DBP(mmHg)	0.035	0.868
Hb (gm %)	0.321	0.118
RDW%	0.603	<0.01*
Platelet (×10^3)	-0.937	<0.01*
WBCs (×10^3)	0.035	0.867
HbA1c%	0.527	<0.01*
FBG(mg/dl)	-0.365	0.073
CRP(mg/dl)	0.115	0.583
TAG(mg/dl)	0.256	0.216
HDL-C(mg/dl)	-0.323	0.115
LDL-C(mg/dl)	0.201	0.336
TC(mg/dl)	-0.127	0.544
ALT(U/L)	0.079	0.708
AST(U/L)	-0.129	0.538
Uric Acid(mg/dl)	0.1397	0.505
S. Creatinine (mg/dl)	-0.091	0.664
Steatosis (CAP)	0.332	0.105
Fibrosis (KPa)	0.497	<0.05*
FIB4	0.603	<0.01*

On performing the univariate analysis, we found that FIB-4, RPR%, BMI, RDW%, HbA1c% and steatosis were effectors on fibrosis. When we performed the multivariate analysis on them, only FIB-4, BMI and RDW% were effectors (Table 3).

Table 3: Univariate and Multivariate Regression Analysis between RPR% and other parameters in NAFLD-F cases

RPR%	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.417 (0.317 – 2.607)	0.057		
Sex	1.524 (0.854 – 6.531)	0.381		
BMI	0.362 (0.250 – 0.859)	0.007*	0.627 (0.241 – 0.895)	0.038*
SBP	0.637 (0.224 – 2.527)	0.210		
DBP	0.452 (0.237 – 2.568)	0.735		
HB	0.329 (0.125 – 6.527)	0.163		
RDW	0.329 (0.117 – 0.527)	0.005*	0.548 (0.305 – 0.658)	0.045*
Platelets	0.411 (0.162 – 0.658)	0.001*	0.351 (0.285 – 0.857)	0.012*
WBCs	0.257 (0.146 – 0.854)	0.040*	0.596 (0.269 – 1.856)	0.103
HbA1c	0.368 (0.248 – 0.853)	0.009*	0.267 (0.291 – 0.564)	0.041*
FBS	2.327 (1.127 – 10.528)	0.018*	3.697 (0.695 – 16.307)	0.254
CRP	0.517 (0.454 – 2.631)	0.078		
TAG	0.449 (0.216 – 2.635)	0.080		
HDL-C	1.697 (0.584 – 8.637)	0.277		
LDL-C	0.637 (0.468 – 3.635)	0.556		
TC	1.690 (0.859 – 2.634)	0.903		
ALT	2.251 (0.598 – 7.653)	0.887		
AST	1.637 (0.659 – 5.634)	0.898		
Uric acid	0.354 (0.291 – 8.521)	0.542		
S. Cr	2.526 (0.457 – 5.294)	0.026*	5.327 (0.876 – 14.632)	0.365
Steatosis	0.784 (0.543 – 2.657)	0.845		
Fibrosis	0.557 (0.116 – 0.873)	0.021*	0.638 (0.287 – 4.531)	0.149
FIB_4	0.394 (0.149 – 0.759)	0.022*	0.491 (0.308 – 3.627)	0.187

ALT: Alanine transaminase. AST: aspartate aminotransferase. BMI: body mass index. DBP: diastolic blood pressure. Hb: hemoglobin. RDW: red cell distribution width. RPR: red cell distribution width-to-platelet ratio. SBP: systolic blood pressure. WBC: white blood cells. TG: triglycerides. TC: total cholesterol. HDL-C: high-density lipoprotein cholesterol. LDL-C: low-density lipoprotein cholesterol. FIB-4 index: fibrosis index. S.Cr: serum creatinine.

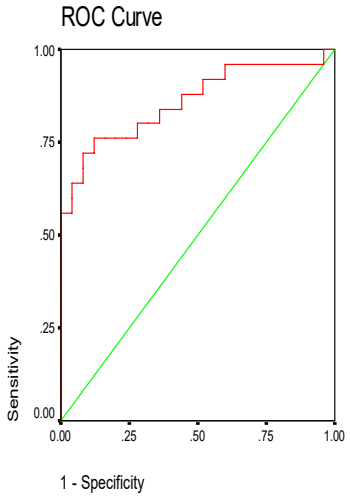

Fig. 1: Roc curve of RPR% showing area under the curve was 0.86, 88% Sensitivity and 52% specificity with a cut off value 4%. The positive predictive value was 65%, while the negative predictive value was 81% with 70% accuracy.

4. Discussion

Non-alcoholic fatty liver disease (NAFLD) affects approximately one-quarter of the global adult population (Younossi *et al.,* 2019). A subset of affected individuals worldwide has non-alcoholic steato-hepatitis (NASH), a more progressive form of the disease that has a higher risk of advancing to cirrhosis and end-stage liver disease (ESLD). Given the enormous number of affected patients, identification of the subset at risk of disease progression is critically important for efficient therapy allocation.

NASH patients with fibrosis stage 2 or higher have elevated all-cause and liver-related mortality (Younossi *et al.,* 2019), and those with high disease activity scores are at greater risk of fibrosis progression (20).

NAFLD group: 25 patients who have non-alcoholic fatty liver without liver fibrosis. They were 14 males and 11 females, their age ranged from (29–62) years with mean (47.20 ± 8.50) years. Age was significantly higher in NAFLD-F group (P= 0.01). This agreed with (Cengiz *et al.,* 2015) who reported that age was significantly different between their studied groups (P= 0.002), on the other hand in the study performed by Yusuf *et al.* (2019), the mean age was (49±12) in NAFLD patients (35.3%) of them were diagnosed with advanced fibrosis.

In our study, there were 32 male patients who constituted about 64% of studied groups and 18 females who constituted about 36% of studied groups. Sex had no statistical significant difference among studied groups (P=0.239). This was in agreement with the result of (Zhou *et al.,* 2019), about 77.5% of studied groups were male (P=0.456). On the other hand, (Van den Berg *et al.,* 2017), Reported that sex had significant difference between the studied groups (P<0.0001), about 62.1% of the studied groups were female.

As regard body mass index (BMI), It was significantly higher in NAFLD-F (P=0.001) as compared to NAFLD, this disagreed with (Zhou *et al.,* 2019), who reported no significant difference between his studied patients regarding BMI (p> 0.659).

Regarding the systolic blood pressure, it was significantly higher in NAFLD-F (P=0.016) in comparison to NAFLD, mean ± SD 129 ± 14.5 mmHg and 118.4 ± 15.7 mmHg respectively. That agreed with the results of (Alempijevic *et al.,* 2017), who reported that systolic blood pressure was significantly higher in NAFLD patients, mean ± SD 130 ± 8.9 mmHg while mean ± SD was 124± 6.6 mmHg in control group(P<0.01).

Regarding the diastolic blood pressure, it was significantly higher in NAFLD-F (P=0.005) in comparison to NAFLD, (65-95) mmHg and (55-90) mmHg respectively, but the results of (Alempijevic *et al.,* 2017), reported non-significant difference between the studied groups regarding diastolic blood pressure (82.6 ± 6.4) in NAFLD, (81.5 ± 4.4) in controlled group (P>0.05).

Regarding Hb, it was significantly higher in NAFLD-F (P=0.002) in comparison to NAFLD, mean ± SD 13.79 ± 1.71 gm% and 12.36 ± 1.43 gm% respectively. This agreed with results of (Van den Berg *et al.,* 2017), who reported that Hb showed significant difference between the studied groups (P<0.0001). But disagreed with the result of (Zhou *et al.,* 2019), who reported non-significant difference between the studied groups regarding to hemoglobin (P = 0.524).

Regarding WBC, there was no significant difference between the studied groups (P= 0.52). That agreed with the result of (Chen *et al.,* 2013) as they reported that there was no significant difference between the studied groups regarding to WBC (P =0.014). Our result also agreed with that of (Van den Berg *et al.,* 2017), who reported no significant difference between the studied groups regarding to WBC (P = 0.847).

Regarding platelet count, it was high statistical significant as (P=0.001) in comparison NAFLD-F to NAFLD, mean ± SD 237 ± 57.28×103 and 320 ± 44.74 ×103) respectively. That agreed with the result of (Zhou *et al.,* 2019), as they documented that platelet count was significantly higher in NAFLD without advanced fibrosis (P <0.001) in comparison to NAFLD with advanced fibrosis, mean ± SD 240±47and 186±44 respectively. On the other hand, the result of (Chen *et al.,* 2013) found non-significant difference between the studied groups regarding to platelet count (P = 0.207).

Regarding RDW%, it was significantly higher in NAFLD-F (P =0.009) in comparison to NAFLD, mean ± SD 13.42± 4.22% and 12.54 ± 2.016% respectively. That agreed with the result of Zhou *et al.,* 2019(155), they reported that RDW%, was significantly higher in NAFLD with advanced fibrosis (P <0.05) in comparison to NAFLD without advanced fibrosis, mean ± SD (13.24±0.73) and mean ± SD (13.04±0.71) respectively. On the other hand, the result of Chen *et al.,* 2013 (18) found non-significant difference between the studied groups regarding to RDW% (P =0.069).

Regarding RPR%, it was significantly higher in NAFLD-F (P <0.001) in comparison to NAFLD, mean ± SD 5.98 ± 1.53 % and 3.99 ±0.73% respectively. That agreed with the result of (Zhou *et al.,* 2019) documented that RPR% was significantly higher in NAFLD with advanced fibrosis in comparison to NAFLD without advanced fibrosis (P <0.001). On the other hand, the result of (Chen *et al.,* 2013) non-significant difference between the studied groups regarding to RPR (P = 0.627).

As for FBG, HbA1c and CRP, there was no significant difference between the studied groups regarding those parameters (P > 0.05).

According to lipid profile findings of NAFLD patients and NAFLD-F patients, only TC had p value less than 0.05 with significant difference, as it was higher in NAFLD –F group (p=0.018). But according to (Zhou *et al.,* 2019), all findings of lipid profile were no significant. And on the contrary for (Kim *et al.,* 2013) Found that all lipid profile findings were significant (p<005). On the other hand, the study of (Jaafar *et al.,* 2022) reported that both TG and HDL were non- significant (P= 0.15, 0.07) respectively, while LDL was significant (P=0.01).

When we measured live enzymes, ALT was significantly higher in NAFLD in comparison to NAFLD-F as it was (p =0.021) and for AST was (P=0.031) which was higher in NAFLD-F as it was 41.00± 12.60 and for NAFLD was 32.52±14.15. Similar results were found by (Xu *et al.,* 2015), ALT in their study showed significant difference (P<0.05) and AST was (P<0.001).

There was no significant difference between the studied groups regarding to renal function tests, uric acid and serum creatinine (P >0.05).

Regarding to steatosis, it was significantly higher in NAFLD-F (P<0.001) in comparison to NAFLD, mean ± SD 307.60 ± 33.27 and 363.30 ±20.49 respectively. On the other hand, the result of (Adams *et al.,* 2011), Reported that there was no significant difference between the studied groups regarding to steatosis (P=0.08). Similar results were reported by (Cengiz *et al.,* 2015), who reported no significant difference in their studied groups regarding steatosis (P=0.395).

Regarding to fibrosis, it was significantly higher in NAFLD-F in comparison to NAFLD, mean ± SD 9.56 ± 1.637 and 4.22±.898 respectively (P <0.001). This agreed with the result of (Adams *et al.,* 2011), who reported that there was significant difference between the studied groups regarding to fibrosis (P<0.001). Also it was in accordance with the results of Cengiz *et al.* (2015), who reported

similar results (P<0.001). Permutt *et al.* (2014) as well, reported similar result regarding to fibrosis (P=0.0197).

Regarding to FIB-4, it was significantly higher in NAFLD-F (P <0.001) in comparison to NAFLD, mean ± SD 1.67 ±0.399 and 0.682 ±0.22 respectively. This agreed the result of (Cengiz *et al.,* 2015) (P<0.001). Also this agreed the result of (Sven H. *et al.,* 2022), who reported that FIB-4 showed highly significant difference between the studied groups (P<0.0001). On the other hand, (Jaafa *et al.,* 2019), reported that FIB-4 was not statistically different in the studied groups (P=0.09).

Regarding to correlation between RPR% and other parameters in our study RPR% showed significant positive correlation with the following: BMI, RDW%, HbA1c%, fibrosis and FIB4. On the other hand, there was a significant negative correlation between RPR% and platelet count. There was non- significant correlation between RPR% and the remaining studied parameters. And according to (Zhou *et al.,* 2019), reported that RPR% showed significant positive correlation with the following: age, Creatinine, Hb and had significant negative correlation with the following: WBC, sex. There was non- significant correlation between RPR% and the remaining studied parameters.

Regarding to ROC curve for RPR%, at a cut-off value of 4, it showed 88% sensitivity and 52% specificity. On the other hand, when (Zhou *et al.,* 2019), performed ROC curve for RPR%, their cut-off value was 6.39, and it showed 74.3% sensitivity and 79.3% specificity.

5. Conclusion

RPR was significantly higher in NAFLD with fibrosis in comparison to NAFLD without fibrosis. There was a positive significant correlation between RPR% and FIB4, which is a known non-invasive marker of fibrosis. RPR has a good sensitivity of 88%, so it can be employed as a good non-invasive marker for prediction of fibrosis.

References

Adams, L.A., et al., 2011. "Complex non-invasive fibrosis models are more accurate than simple models in non-alcoholic fatty liver disease." Journal of gastroenterology and hepatology 26 (10): 1536-1543.

Ahmed, M.H., S.K. Noor, S.O. Bushara *et al.,* 2017. Non-alcoholic fatty liver disease in Africa and middle east: an attempt to predict the present and future implications on the healthcare system. Gastroenterol. Res., 10:271–279.

Alempijevic, T. M. *et al.,* 2017."Diagnostic accuracy of platelet count and platelet indices in noninvasive assessment of fibrosis in nonalcoholic fatty liver disease patients." Canadian Journal of Gastroenterology and Hepatology. Can J Gastroenterol Hepatol. 2017; 2017:6070135. doi: 10.1155/2017/6070135. Epub 2017 Dec 31.

Alkassabany, Y.M., A.G. Farghaly, E.M. El-Ghitany *et al.,* 2014. Prevalence, risk factors, and predictors of nonalcoholic fatty liver disease among schoolchildren: a hospital-based study in Alexandria, Egypt. Arab J. Gastroenterol. 15:76–81.

Ani, C., and B. Ovbiagele, 2009. Elevated red blood cell distribution width predicts mortality in persons with known stroke. J. Neurol. Sci., 277:103–108.

Chen, B., B. Ye, J. Zhang, *et al.,* 2013. RDW to platelet ratio: a novel noninvasive index for predicting hepatic fibrosis and cirrhosis in chronic hepatitis B. PLoS One, 8: e68780.

Chen, Z.W., L.Y. Chen, H.L. Dai, *et al.,* 2008. Relationship between alanine aminotransferase levels and metabolic syndrome in nonalcoholic fatty liver disease. J. Zhejiang Univ. Sci., B. 9:616–622.

Dabbah, S., H. Hammerman, W. Markiewicz, *et al.,* 2010. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction. Am. J. Cardiol. 105:312–317.

Fang, L., Z. Hui, C. Lei *et al.,* 2018. Risk of reduced platelet counts in patients with nonalcoholic fatty liver disease (NAFLD): a prospective cohort study: Lipids in Health and Disease, 17: 221.

Förhécz, Z., T. Gombos, G. Borgulya, *et al.,* 2009. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. Am. Heart J., 158:659–666.

Hassan, A., M. Elhaw, A. Ahmed, *et al.,* 2020. Value of screening for nonalcoholic fatty liver disease in hyperuricemic patients with normal body mass index by two-dimensional ultrasound: Upper Egypt experience Al azhar internal medicine journal, 18:104-109.

Jaafar, R.F., et al., 2019. "Fibroscan and low-density lipoprotein as determinants of severe liver fibrosis in diabetic patients with nonalcoholic fatty liver disease." European journal of gastroenterology & hepatology, 31(12): 1540-1544.

Kim, H.M., B.S. Kim, Y.K. Cho, *et al.,* 2013. Elevated red cell distribution width is associated with advanced fibrosis in NAFLD. Clin. Mol. Hepatol., 19:258–65.

Loosen, S.H., et al., 2022."An elevated FIB-4 score predicts liver cancer development: A longitudinal analysis from 29,999 patients with NAFLD." Journal of Hepatology 76(1): 247-248.

Murali, A.R., B.M. Attar, A. Katz, *et al.,* 2015. Utility of platelet count for predicting cirrhosis in alcoholic liver disease: model for identifying cirrhosis in a US population. J. Gen. Intern. Med., 30:1112–7.

Pascual-Figal, D.A., J.C. Bonaque, B. Redondo, *et al.,* 2009. Red blood cell distribution width predicts long-term outcome regardless of anaemia status in acute heart failure patients. Eur. J. Heart Fail., 11:840–846.

Riediger, C., *et al.,* 2014. Low postoperative platelet count is associated with negative outcome after liver resection for hepatocellular carcinoma. Hepato-Gastroenterology, 61:1313–20.

Van den, B., H. Eline, *et al.,* 2017. "Prevalence and determinants of non-alcoholic fatty liver disease in lifelines: A large Dutch population cohort." PLoS One, 12(2): e0171502.

Xu, W.-S., et al., 2015. "Red blood cell distribution width levels correlate with liver fibrosis and inflammation: a noninvasive serum marker panel to predict the severity of fibrosis and inflammation in patients with hepatitis B." Medicine, 94(10).

Younossi, Z., F. Tacke, M. Arrese, S.B. Chander, I. Mostafa, E. Bugianesi, *et al.,* 2019. Global perspectives on nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Hepatology, 69:2672–2682.

Younossi, Z.M., A.B. Koenig, D. Abdelatif *et al.,* 2016. Global epidemiology of nonalcoholic fatty liver disease: metaanalytic assessment of prevalence, incidence, and outcomes. Hepatology; 64:73–84.

Zhou, W. J., *et al.,* 2019. "Association between red cell distribution width-to-platelet ratio and hepatic fibrosis in nonalcoholic fatty liver disease: A cross-sectional study." Medicine 98(3).