

Original research

The Potential Role of Platelet Indices and Red Cell Distribution Width in Metabolic Dysfunction-Associated Fatty Liver Disease

Shimaa Moustafa Mansour¹, Rehab Badawi², Shaimaa Soliman³, Manal Saad Negm⁴, Fatma Ali Elgebaly⁵.

¹Lecturer of Tropical Medicine and Infectious Diseases, Faculty of Medicine, Tanta University.

²Assistant professor of Tropical Medicine and Infectious Diseases, Faculty of Medicine, Tanta University.

³Assistant Professor of Public Health and Community Medicine, Faculty of Medicine, Menoufia University.

⁴Assistant professor of Internal Medicine and Nephrology, Faculty of Medicine. Tanta University.

⁵Lecturer of Tropical Medicine and Infectious Diseases, Faculty of Medicine, Tanta University.

Corresponding to: Dr Shimaa Moustafa Mansour.

Lecturer, Department of Tropical Medicine and Infectious Diseases, Faculty of Medicine, Tanta University.

Telephone: +201003911123.

Email: shaimaa.mansour@med.tanta.edu.eg

ORCID: [0000-0002-3953-9244](https://orcid.org/0000-0002-3953-9244).

DOI: [10.21608/AJGH.2024.250315.1044](https://doi.org/10.21608/AJGH.2024.250315.1044).

Submission date: 21 November 2023.

Revision date: 1 January 2024.

Acceptance date: 9 January 2024.

Published online: 14 January 2024.

Original research

Abstract.**Background:**

Hepatic steatosis, nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and even hepatocellular carcinoma are all possible outcomes of metabolic dysfunction-associated fatty liver disease (MAFLD). Some platelet function measures are strongly correlated with the incidence of insulin resistance's intensity and its associated problems. Platelet indices, including platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), red cell distribution width (RDW), and red cell distribution width to platelet ratio (RPR), were found to be associated with the presence of many diseases. Hence, this research aimed to evaluate the significance of platelet indices and RDW in MAFLD and their possible association with the degree of liver steatosis and fibrosis.

Patients and methods:

This study was carried out on 220 patients who attended Tanta Tropical Medicine and fulfilled MAFLD criteria and CBC, including PC, MPV, PDW, PCT, RDW, and RPR, determined in all patients.

Results:

It was found that the PC was significantly decreased as the steatosis grade increased ($p < 0.00$). There was a significant increase in MPV as the steatosis grade increased ($p < 0.001$). PDW% also substantially increased as the steatosis grade increased ($p < 0.001$). It also found that RDW% showed a significant increase when the steatosis grade increased ($p < 0.001$), while PCT% showed no significant difference in its level about the steatosis grades, $p = 0.917$.

Conclusion: MPV, PDW, RDW, and RPR may be used as non-invasive indicators for liver fibrosis and steatosis in MAFLD.

Keywords: platelet indices, MAFLD, RDW, MPV, CAP.

Introduction

A group of international specialists has advocated replacing the pessimistic "non-alcoholic fatty liver disease" (NAFLD) with the more upbeat "metabolic dysfunction-associated fatty liver disease" (MAFLD). Those with metabolic syndrome and an abnormal buildup of fat in the liver, regardless of alcohol consumption, are diagnosed with MAFLD [1]. Hepatic steatosis alone is insufficient for diagnosing NAFLD [2].

Original research

Obesity, type 2 diabetes, or a metabolic imbalance are also required for a definitive diagnosis of NAFLD. NAFLD and MAFLD are on the rise in Egypt, and the country's high obesity rates are likely to be blamed. NAFLD and MAFLD were found to occur in 57.65% of the Egyptian sample population [3]. Hepatic steatosis, non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and even hepatocellular carcinoma are all disorders that fall under the umbrella of NAFLD [4].

For this purpose, a liver biopsy has been the highest standard for identifying liver pathology for many years; however, owing to its intrusive nature, expensive cost, and risk of severe consequences (bleeding in particular), non-invasive diagnostics were developed. Different scores are produced. The results of these tests can come from a wide range of noninvasive imaging modalities and combinations of serologic markers [5]. Transient elastography (TE) utilizing ultrasound and a variable attenuation parameter has developed as a promising imaging technology in the last decade. However, owing to the unavailability of the Controlled attenuation parameter (CAP) and the high cost of the device, there is an urgent need for a simple, cheap, available, and non-invasive precise test to detect the stages of liver fibrosis and steatosis [5].

Platelets are best known for their role in blood clotting; Platelets have dual physiologic roles as both cellular mediators of thrombosis and immune modulatory cells [6]. The inflammatory state created in MAFLD associated with diminished thrombopoiesis results in an increase in MPV. This altered platelet is called the pro-inflammatory phenotype that enhances sinusoidal endothelial leucocyte recruitment, leading to the propagation of the inflammatory process in MAFLD. They play an essential part in the liver's inflammatory response. Leukocytes are recruited through the hepatic sinusoids after activating effector cells [7]. Several research studies suggest that changes in platelet function and shape may occur in diabetic patients and metabolic syndrome patients [8]. The mean platelet volume (MPV), the platelet distribution width (PDW), and the plateletcrit (PCT) are used to measure platelet health and activity. Platelet indices have been hypothesized to be closely connected to the prevalence and severity of insulin resistance [9,10].

When assessing erythrocyte size variation (i.e., anisocytosis), the red cell distribution width (RDW) is a valuable metric to use [11]. RDW has recently gained importance

Original research

as a prognostic marker for a wide range of diseases and conditions, including sepsis, acute myocardial infarction, heart failure, autoimmune diseases, liver diseases, and various cancers [12-17]. Also, RPR has gained substantial attention as a prognostic marker of various medical conditions such as severe burn injury, primary biliary cholangitis, patent ductus arteriosus, predicting hepatic fibrosis and cirrhosis in chronic hepatitis B, diagnosis of premature ovarian insufficiency; myocardial infarction; acute pancreatitis in pregnancy [18] because it is simple, easy to measure and handle, cost-effective, and accurate for predicting the severity of fibrosis.

There was an association between increased RDW and platelet indices and fibrosis progression and the severity of inflammation. So MPV, PDW, RDW, and RPR may be used as non-invasive indicators for liver fibrosis and steatosis in MAFLD.

Evidence shows they had a high sensitivity and specificity for diagnosing NASH [19]. So, this study aimed to evaluate the significance of platelet indices and RDW in MAFLD and its possible association with the severity of liver steatosis and fibrosis.

Patients and Methods:

Two hundred twenty patients with MAFLD were recruited from the Tropical Medicine department at Tanta University for this cross-sectional study. From September 2021 until August 2022. Just after obtaining ethical approval from the Ethical Committee of the Faculty of Medicine, Tanta University (approval code: 34908/ 9 /21).

This research included 220 patients, 86 males and 134 females, more than 18 years old who were diagnosed with MAFLD when hepatic steatosis was present in addition to the presence of three or more of the following risk determinants: 1) increased waist circumference (>102 cm [>40 in] for men, >88 cm [>35 in] for women); 2) elevated triglycerides (≥ 150 mg/dl); 3) low HDL cholesterol (<40 mg/dl in men, <50 mg/dl in women); 4) hypertension ($\geq 130/\geq 85$ mmHg) or taking the antihypertensive drug; and 5) impaired fasting glucose (≥ 110 mg/dl) or taking antidiabetic drug [20].

We excluded patients who had one or more of the following conditions: age < 18 years, alcohol consumption (more than 40g of alcohol per day), a history of viral hepatitis, chronic liver disease due to drug administration, autoimmune hepatitis, history of

Original research

blood diseases (e.g., ITP), history of myocardial infarction, and stroke, history of receiving drugs which cause steatosis (e.g., amiodarone) or drugs that interact with normal platelet functions (aspirin), anemia either microcytic hypochromic (iron deficiency anemia) or macrocytic due to vit B12 deficiency, history of blood transfusion during the last four months, or patients who refused to participate in this study.

All the patients were subjected to a complete history and examination. The examination which included body mass index and waist circumference, and laboratory investigation, which included liver functions, blood urea, serum creatinine, lipid profiles, and iron profile to exclude iron deficiency anemia) complete blood picture, which included platelet indices and RDW.

Venous blood samples were collected into sterile standard tubes with a consistent anticoagulant dose. After obtaining blood samples, laboratory tests were conducted a few minutes later in the Clinical Pathology department. The automated analyzer was used to perform the complete blood count analyses.

Ultrasound on the abdomen and pelvis and Transient Elastography (Fibroscan) were done for all the patients for evaluation of the liver condition. Transient elastography was used to assess the staging of liver fibrosis and steatosis by measuring the velocity of a low-frequency (50 Hz) elastic shear wave propagating through the liver. This velocity has a direct relation to the stiffness of the tissue. The CAP score (Controlled attenuation parameter) is measured in decibels per meter (dB/m) and ranges from 100-400 as follows: S0:<237.7, S1: 237.7- 259.4, S3(severe steatosis) :>292.3.

Fibrosis was classified according to the following cutoff levels (F): F0 = no fibrosis (5.5 kPa), F1 = mild fibrosis (5.5 to 8.0 kPa), F2 = moderate fibrosis (8.0 to 10.0 kPa), F3 = severe fibrosis (11 to 16.0 kPa), and F4 = cirrhosis (>16.0 kPa) [21].

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages. For continuous data, they were tested for normality by the Kolmogorov- Smirnov. Quantitative data were expressed as a range (minimum and

Original research

maximum), mean, standard deviation, and median, usually distributed quantitative variables. At the same time, the ANOVA test was used to compare the different studied groups, followed by the post hoc test (Tukey) for pairwise comparison. The significance of the obtained results was judged at the 5% level.

Results

The study population consisted of 220 subjects, which included 86(39.1%) males and 134(60.9%) females. Their ages were 47.2 ± 7.8 . There were 86(39.1%) patients had diabetes mellitus and 104 (47.3%) patients had hypertension, according to body mass index (BMI), it was 35.5 ± 5.1 and waist circumference was 110.4 ± 10.3 cm as demonstrated in table (1).

Regarding the grade of steatosis, there were 148 (67.3%) patients in grade 1, 32 (14.5%) patients in grade 2 and 40 (18.2%) patients grade 3, while regarding the fibrosis stages there were 20 (9.1%) patients in' stage 0, 72 (32.7%) patients' stage 1, 80 (36.4%) stage 2, 28(12.7%) stage 3 and 20 (9.1%) patients' stage 4 as demonstrated in table (2).

It was found that the platelet count was significantly decreased as the steatosis grade increased; the platelet counts was $198.0 \times 10^3 \pm 11.11$ in S1, $190.0 \times 10^3 \pm 29.08$ in and $145.7.0 \times 10^3 \pm 11.76$ in S3, with $p < 0.001$ as shown in table (3).

Regarding MPV value, there was a significant increase in MPV as the steatosis grade increased. It was 10.87 ± 0.92 in S1, 10.98 ± 1.72 in S2, and 11.77 ± 0.62 in S3, with $p < 0.001$. PDW% also showed a significant increase as the steatosis grade increased as it was 61.09 ± 7.12 in S1, 61.25 ± 13.07 in S2, and 68.45 ± 3.69 in S3, with $p < 0.001$. Also, we found that RDW% showed a significant increase when the steatosis grade increased, as it was $15.91\% \pm 1.51$ in S1, 17.71 ± 3.87 in S2, and 19.95 ± 2.86 in S3 with $p < 0.001$. Also, RPR was higher when the steatosis grade increased, while PCT% showed no significant difference in its level about the steatosis grades; the p-value was 0.266, as shown in Table (3).

As regards the stages of fibrosis, there was a significant decrease in platelet count as the fibrosis stages increased ($p < 0.001$) as well as MPV, PDW%, RDW%, and RPR significantly increased as the fibrosis stage increased ($p < 0.001$). At the same time, PCT showed no significant difference in fibrosis stages, as shown in Table (4).

Original research

There was a significant positive relationship between MPV, PDW%, RDW%, RPR, LDL, TG, and waist circumference ($P < 0.001$). Still, there was a significant inverse relationship between them and HDL ($p < 0.001$), as shown in Table (5).

There was a significant inverse relationship between platelet count and LDL, triglycerides, and waist circumference ($p < 0.001$), but there was a significant positive relationship between it and HDL. There was no significant relationship between PCT and HDL, LDL, TG, and waist circumference, as shown in Tab (5).

Tab 1. Distribution of the studied cases according to demographic and biochemical data.

	No. (%)
Age(y)	
Mean \pm SD.	47.2 \pm 7.8
Sex	
Male	86 (39.1%)
Female	134 (60.9%)
Diabetic	86 (39.1%)
Hypertensive	104 (47.3%)
BMI	
Mean \pm SD.	35.5 \pm 5.1
Waist circumference(cm)	
Mean \pm SD.	110.4 \pm 10.3
Hb (g/dl)	
Mean \pm SD.	13.0 \pm 1.8
RDW%	
Mean \pm SD.	16.9 \pm 2.8
PDW%	
Mean \pm SD.	62.5 \pm 8.3
PCT%	
Mean \pm SD.	0.3 \pm 0.1
MPV (fl)	
Mean \pm SD.	11.1 \pm 1.1
Platelet (x10³/ul)	
Mean \pm SD.	187.3 \pm 25.0
RPR	
Mean \pm SD.	0.09 \pm 0.03
ALT (IU/L)	
Median (Min. – Max.)	42.5 (29.0 – 102.0)
AST (IU/L)	
Median (Min. – Max.)	41.0 (16.0 – 100.0)
Albumin(g/dl)	
Median (Min. – Max.)	3.8 (3.2 – 4.7)
Bilirubin(mg/dL)	
Mean \pm SD.	0.8 \pm 0.2
LDL (mg/dL)	

Original research

Mean ± SD.	133.5 ± 7.7
HDL (mg/dL)	
Mean ± SD.	36.1 ± 4.9
Triglycerides (mg/dL)	
Mean ± SD.	168.0 ± 31.5

BMI: body mass index, **Hb:** hemoglobin, **RDW:** red cell distribution width, **PDW:** platelet distribution width, **PCT:** plateletcrit, **MPV:** mean platelet volume, **RPR:** red cell distribution width platelet ratio, **ALT:** Alanine aminotransferase **Min:** minimum, **Max:** maximum, **SD:** Standard deviation, **HDL:** high-density lipoproteins, **LDL:** low-density Lipoproteins.

Tab 2. Distribution of the studied cases according to fibrosis and steatosis grades (n=220).

	No (%)
Fibrosis	
F 0	20 (9.1%)
F 1	72 (32.7%)
F 2	80 (36.4%)
F 3	28 (12.7%)
F 4	20 (9.1%)
Steatosis	
S 1	148 (67.3%)
S 2	32 (14.5%)
S 3	40 (18.2%)

Tab 3. Relationship between steatosis grades, platelet indices, and RDW % (n = 220).

	Steatosis grades			P
	S 1(n = 148)	S 2(n = 32)	S 3(n = 40)	
RDW %				
Mean ± SD.	15.91 ± 1.51	17.71 ± 3.87	19.95 ± 2.86	<0.001*
Sig. bet. Grps	p ₁ <0.001*, p ₂ <0.001*, p ₃ <0.001*			
PDW %				
Mean ± SD.	61.09 ± 7.12	61.25 ± 13.07	68.45 ± 3.69	<0.001*
Sig. bet. Grps	p ₁ =0.994, p ₂ <0.001*, p ₃ <0.001*			
PCT %				
Mean ± SD.	0.30 ± 0.06	0.32 ± 0.08	0.30 ± 0.08	0.266
MPV				
Mean ± SD.	10.87 ± 0.92	10.98 ± 1.72	11.77 ± 0.62	<0.001*
Sig. bet. Grps	p ₁ =0.850, p ₂ <0.001*, p ₃ =0.004*			
Platelet x10³				
Mean ± SD.	198.0 ± 11.11	190.0 ± 29.08	145.7 ± 11.76	<0.001*
Sig. bet. Grps	p ₁ =0.020*, p ₂ <0.001*, p ₃ <0.001*			
RPR				
Mean ± SD.	0.08 ± 0.01	0.10 ± 0.03	0.14 ± 0.02	<0.001*
Sig. bet. Grps	p₁<0.001*, p₂<0.001*, p₃<0.001*			

SD: Standard deviation, **RDW:** red cell distribution width, **PDW:** platelet distribution width, **PCT:** plateletcrit, **MPV:** mean platelet volume, **RPR:** red cell distribution width platelet ratio **grps:** groups. **p:** p-value for comparing between

Original research

different categories. p_1 : p-value for comparing **Grade 1**, and **Grade 2**, p_2 : p-value for comparing **Grade 1** and **Grade 3**, p_3 : p-value for comparing **Grade 2** and **Grade 3**, *: Statistically significant at $p \leq 0.05$.

Tab 4. Relationship between Fibrosis staged and platelet indices and RDW% (n = 220).

	Fibrosis stages					p
	F 0 (n = 20)	F 1 (n = 72)	F 2 (n = 80)	F 3 (n = 28)	Grade 4 (n = 20)	
RDW %						
Mean ± SD.	12.0 ± 0.7	15.7 ± 0.6	17.5 ± 1.8	18.7 ± 1.8	21.4 ± 2.9	<0.001*
p_0		<0.001*	<0.001*	<0.001*	<0.001*	
p_1			<0.001*	<0.001*	<0.001*	
Sig. bet. Grps			$p_2=0.007^*$, $p_3<0.001^*$, $p_4<0.001^*$			
PDW %						
Mean ± SD.	41.7 ± 1.8	61.2 ± 5.2	65.1 ± 4.2	68.3 ± 3.9	69.2 ± 2.5	<0.001*
p_0		<0.001*	<0.001*	<0.001*	<0.001*	
p_1			<0.001*	<0.001*	<0.001*	
Sig. bet. Grps			$p_2=0.006^*$, $p_3=0.001^*$, $p_4=0.948$			
PCT %						
Mean ± SD.	0.32 ± 0.09	0.32 ± 0.05	0.30 ± 0.07	0.29 ± 0.09	0.31 ± 0.07	0.211
MPV						
Mean ± SD.	8.5 ± 0.3	10.9 ± 0.7	11.4 ± 0.7	11.9 ± 0.7	11.7 ± 0.5	<0.001*
p_0		<0.001*	<0.001*	<0.001*	<0.001*	
p_1			<0.001*	<0.001*	<0.001*	
Sig. bet. Grps			$p_2=0.002^*$, $p_3=0.146$, $p_4=0.910$			
Platelet $\times 10^3$						
Mean ± SD.	226.3 ± 16.4	201.2 ± 7.4	188.2 ± 7.2	157.2 ± 6.5	137.1 ± 10.5	<0.001*
p_0		<0.001*	<0.001*	<0.001*	<0.001*	
p_1			<0.001*	<0.001*	<0.001*	
Sig. bet. Grps			$p_2<0.001^*$, $p_3<0.001^*$, $p_4<0.001^*$			
RPR						
Mean ± SD.	0.05 ± 0.004	0.08 ± 0.005	0.09 ± 0.01	0.12 ± 0.0	0.15 ± 0.0	<0.001*
p_0		<0.001*	<0.001*	<0.001*	<0.001*	
p_1			<0.001*	<0.001*	<0.001*	
Sig. bet. Grps			$p_2<0.001^*$, $p_3<0.001^*$, $p_4<0.001^*$			

SD: Standard deviation, RDW: red cell distribution width, PDW: platelet distribution width, PCT: plateletcrit, MPV: mean platelet volume, RPR: red cell distribution width platelet ratio, grps: groups, p: p-value for comparing between different categories. p_0 : p-value for comparing **Grade 0** and **each group**. p_1 : p-value for comparing **Grade 1** and **each group**. p_2 : p-value for comparing **Grade 2** and **Grade 3**. p_3 : p-value for comparing **Grade 2** and **Grade 4**. p_4 : p-value for comparing **Grade 3** and **Grade 4**. *: Statistically significant at $p \leq 0.05$.

Tab 5. Correlation between Lipid profile, Waist circumference platelet indices, and RDW% (n = 220).

LDL	HDL	Triglycerides	Waist circumference
-----	-----	---------------	---------------------

Original research								
	R	P	R	p	R	P	R	p
RDW %	0.672*	<0.001*	-0.642*	<0.001*	0.496*	<0.001*	0.675	<0.001*
PDW %	0.806*	<0.001*	-0.716*	<0.001*	0.529*	<0.001*	0.506	<0.001*
PCT %	0.049	0.467	-0.012	0.861	-0.002	0.975	0.060	0.374
MPV	0.833*	<0.001*	-0.703*	<0.001*	0.589*	<0.001*	0.504	<0.001*
Platelet x103	-0.806*	<0.001*	0.736*	<0.001*	-0.592*	<0.001*	-0.470	<0.001*
RPR	0.788	<0.001*	-0.727	<0.001*	0.573	<0.001*	0.604	<0.001*

*RDW: red cell distribution width, PDW: platelet distribution width, PCT: plateletcrit, MPV: mean platelet volume, RPR: red cell distribution width platelet ratio, HDL: high-density lipoproteins, LDL: low-density Lipoproteins, r: Pearson coefficient, *: Statistically significant at $p \leq 0.05$.*

Discussion

MAFLD is a new term that changed from NAFLD. MAFLD is a common chronic liver disease globally, associated with the growing obesity epidemic today [22,23]. The clinic pathological spectrum of MAFLD covers a mild-to-severe range from simple steatosis (SS) to NASH and then to NASH-related fibrosis or cirrhosis.

The capacity to assess the extent of steatosis and fibrosis of the liver and to estimate the course of the disease is essential in managing patients with MAFLD. For many years, the gold standard for this purpose was liver biopsy. However, its invasive nature, high cost, and risk of developing severe complications. New reliable blood markers required in the evaluation of liver fibrosis and clinical prognosis of cirrhosis are permanently in the interest of scientists. Several years ago, primary hematological indices used in everyday life were proposed as potential candidates in this area, e.g., MPV, PCT, and RDW, and the creation of noninvasive diagnostic tools. These tools are composed of many scores obtained from multiple combinations of serologic markers and noninvasive imaging techniques [24]. When a promising imaging modality emerged, ultrasound-based TE with CAP minimized sampling errors noticed with liver biopsy [25]. This research aimed to evaluate the significance of platelet indices and RDW in MAFLD and their possible association with the severity of steatosis and fibrosis of the liver.

Original research

Gülali et al. imply that platelets contribute to the process of liver fibrosis by reducing the expression of the main fibrogenic cytokine TGF- β and upregulating the expression of matrix metalloproteinase [26].

Saremi et al. revealed that lower PC (platelet count) is associated with more advanced fibrosis and found an inverse relationship between the progression of liver fibrosis and platelets; taking this into account, PC is presented in many prognostic scores for fibrosis and cirrhosis of the liver, this agrees our study there was a significant decrease in PC as the fibrosis stages and steatosis grade increased [27].

Platelet size, density, other comorbidities, and age impact platelet functions. Platelet activation rises with more giant platelets because they have many granules and adhesion receptors, which increases [28]. PDW directly refers to platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology [29]. Our study showed a significant positive correlation between PDW and fibrosis score and steatosis grade, which agrees with Milovanovic et al., who found that PDW is higher in NAFLD patients than controls [30]. Still, the study of Cao et al. demonstrated a negative correlation between PC and PDW and the stage of fibrosis [31].

Ozhan et al. found that lower PC and higher MPV are independent indicators of MAFLD [32]. Several studies have demonstrated that liver steatosis has been linked to the elevation in MPV [33]. A major Korean study found a significant relationship between NAFLD and the increase of MPV values in 628 obese volunteers [34]. This agrees with our research that showed a significant positive correlation between MPV and fibrosis stages and steatosis grade.

Our study PCT showed no significant difference in its level about the steatosis grades; the p-value was 0.917, and there was no significant difference in fibrosis stages. This is by Milovanovic T et al., who didn't discover any significant difference in the values of PCT between NAFLD groups; however, they found substantial variations in the values of PCT between NAFLD patients and the controls [30].

RDW has been studied in inflammatory diseases. It is associated with disease activity in inflammatory bowel syndrome [35]. Some other reports showed that patients with inflammatory bowel disease had increased RDW compared to health controls. Li et al. reported that anti-TNF antibodies, potent suppressors of inflammation, caused

Original research

complete resolution in hepatic steatosis in a mice model. This report shows that hepatosteatosis may be an inflammatory process [36].

Aktas et al. also found an increase in RDW in patients with hepatosteatosis compared to healthy controls; this agrees with our study, as we found a significant positive correlation between RDW and fibrosis stages and steatosis grade [37]. Also, Michalak A observed that elevation in RDW can be assumed as a sign of the progression of simple steatosis to steatohepatitis and the progression of liver fibrosis during MAFLD [38].

The current study found that NAFLD with advanced fibrosis had a higher red cell distribution width-to-platelet ratio (RPR). This agrees with the Zhou et al. study; their results showed a significant relationship between RPR and advanced fibrosis in the NAFLD population [39], which indicated that the RPR ratio might be used as an independent risk factor for advanced fibrosis.

In our study, there was a significant positive relationship between MPV and LDL, triglycerides, and waist circumference ($P < 0.001$). Still, MPV and HDL had a significant inverse relationship ($p < 0.001$). This agrees with Li L, who found that MPV was positively correlated with TC, TG, and LDL-C while negatively correlated with HDL-C for NAFLD patients [40].

Conclusions: Certain aspects of a patient's complete blood count could be used to help in the diagnosis of MAFLD and NAFLD. MPV, PC, RDW, and RPR were all significant indicators for the grades of steatosis, suggesting that RDW, platelets, and platelet indices could be used as non-invasive markers for diagnosing MAFLD.

Abbreviations:

MAFLD: metabolic dysfunction-associated fatty liver disease

NAFLD: non-alcoholic fatty liver disease.

PC: Platelet count

RDW: red cell distribution width,

PDW: platelet distribution width,

PCT: plateletcrit,

MPV: mean platelet volume

RPR: red cell distribution width platelet ratio

BMI: body mass index.

Hb: hemoglobin.

ALT: Alanine aminotransferase.

Min: minimum,

Max: maximum,

SD: Standard deviation.

HDL: high-density lipoproteins

Original research

LDL: low-density Lipoproteins

TG: triglycerides

grps: groups

NASH: non-alcoholic steatohepatitis.

TE: transient elastography.

Footnotes.

Peer-Reviewers: Sara salem (lecturer of internal medicine), Marwa Shabana (Assistant professor of clinical pathology), Ola Elfaragey (professor of medical oncology).

E- Editor: Salem Youssef Mohamed, Osama Ahmed Khalil, Mohamed Hassan Ali Emara.

Copyright ©. This open-access article is distributed under the Creative Commons Attribution License (CC BY). The use, distribution, or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited. The original publication in this journal is cited by accepted academic practice. No use, distribution, or reproduction is permitted, complying with these terms.

Disclaimer: All claims expressed in this article are solely those of the authors and do not necessarily represent their affiliated organizations or those of the publisher, the editors, and the reviewers. Any product evaluated in this article or its manufacturer's claim is not guaranteed or endorsed by the publisher.

Ethics Approval and Consent to Participate: All procedures followed were by the ethical standards of the responsible committee on human experimentation (Institutional Review Board (IRB)) (34908/ 9 /21) of Tanta University and with the Helsinki Declaration of 1964 and later versions.

Consent for publication: All patients included in this research gave written informed permission to publish the data contained within this study.

Availability of data and materials: The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This study had no funding from any resource.

Authors' contributions

The study was conceptualized and designed by all authors. FAE, SM, RB, and SS collected and compiled data. SM and RB conducted the statistical analysis, while RB, SS, and MSN drafted the manuscript. SM, RB, SS, MSN, and FAE provided significant intellectual input throughout the project, contributing to comments and revisions. All authors reviewed and approved the final manuscript.

References

1. **Eslam M, George J.** Reply to correspondence regarding "A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement." *J of Hepatol.* 2020; 73(6):1575-1581.

Original research

2. **Kaya E, Yilmaz Y.** Metabolic-associated Fatty Liver Disease (MAFLD): A Multi-systemic Disease Beyond the Liver. *J of Clinical and Translational Hepatol.* 2021; 19(2):329–338.
3. **Eletreby R, Abdellatif Z, Gaber Y, Ramadan A, Ahmad N, Khattab H, et al.** The validity of routine biochemical and ultrasound scores for predicting hepatic fibrosis and steatosis in NAFLD. *Egypt Liver J.* 2021; 11(1):44–54.
4. **Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al.** The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatol.* 2017; 67(1):328–357.
5. The Platelet Napoleon Complex—Small Cells, but Big Immune Regulatory Functions Craig N. Morrell, Daphne N. Pariser, Zachary T. Hilt, and Denisse Vega Ocasio *Annual Review of Immunology* 2019 37:1, 125-144.
6. **Wieckowska A, Feldstein A.** Diagnosis of nonalcoholic fatty liver disease: Invasive versus noninvasive. *Seminars in Liver Disease.* 2008; 28(4):386–395.
7. **Chauhan A, Adams DH, Watson SP, Lalor PF.** “Platelets: No longer bystanders in liver disease”. *Hepatol.* 2016; 64(5): 1774–1784.
8. **Adane, T., Asrie, F., Getaneh, Z. and Getawa, S.** (2021), White blood cells and platelet profiles of diabetic patients at University of Gondar specialized referral hospital: A comparative cross-sectional study. *J Clin Lab Anal*, 35: e23808.
9. **Budak YU, Polat M, Huysal K.** “The use of platelet indices, plateletcrit, and mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: a systematic review”. *Biochemia Medica.* 2016; 26(2): 178–193.
10. **Eminler AT, Uslan MI, Ayyildiz T, Irak K, Kiyıcı M, Gurel S, et al.,** “Mean platelet volume is an important predictor of hepatitis C but not hepatitis B liver damage.” *Journal of Research in Medical Sciences.* 2015; 20 (9): 865–870.
11. **Farkas N, Szabo A, Lorand V, Sarlós DP, Minier T, Prohászka Z, et al.** Clinical usefulness of measuring red blood cell distribution width in patients with systemic sclerosis. *Rheumatol.* 2014; 53(8):1439–1445.
12. **Han YQ, Zhang L, Yan L, Li P, Ouyang P, Lippi G, et al.** Red blood cell distribution width predicts long-term outcomes in sepsis patients admitted to the intensive care unit. *Clin Chim Acta.* 2018; 487(1):112–116.
13. **Ilhan E, Guvenc TS, Altay S, Çağdaş M, Çalik AN, Karaca M, et al.** Predictive value of red cell distribution width in intra-hospital mortality and post-intervention thrombolysis in myocardial infarction flow in patients with acute anterior myocardial infarction. *Coron Artery Dis* 2012; 23(7):450–454.
14. **Zeng T, Yu J, Tan L, Wu Y, Tian Y, Wu Q, et al.** Non-invasive indices for monitoring disease course in Chinese patients with autoimmune hepatitis. *Clin Chim Acta.* 2018; 486:135–141.
15. **Fan X, Deng H, Wang X, Fu S, Liu Z, Sang J, et al.** Association of red blood cell distribution width with severity of hepatitis B virus-related liver diseases. *Clin Chim Acta.* 2018; 482:155–160.
16. **Muhlestein JB, Lappe DL, Anderson JL, Muhlestein JB, Budge D, May HT, et al.** Both initial red cell distribution width (RDW) and change in RDW during heart

Original research

- failure hospitalization are associated with length of hospital stay and 30-day outcomes. *Int J Lab Hematol*. 2016; 38 (3):328–337.
17. **Jiang X, Wang Y, Su Z, Yang F, Lv H, Lin L, et al.** Red blood cell distribution width to platelet ratio levels in the assessment of histologic severity in patients with primary biliary cholangitis. *Scand J Clin Lab Invest* 2018; 78:258–63.
 18. **Ai L, Mu S, Hu Y.** Prognostic role of RDW in hematological malignancies: a systematic review and meta-analysis. *Cancer Cell Int* 2018; 18:61.
 19. **Kim HM, Kim BS, Cho YK, Kim BI, Sohn CI, Jeon WK, et al.** Elevated red cell distribution width is associated with advanced fibrosis in NAFLD. *Clin Mol Hepatol*. 2013; 19(3):258–265.
 20. **Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults:** Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 285: 2486 –2497,2001
 21. **Adibi A, Kamali L, Ebrahimian S, Jafari F, Sharifi M.** Diagnostic Performance of Ultrasonography in Detecting Fatty Liver Disease in Comparison with Fibroscan in People Suspected of Fatty Liver. *Advanced Biomedical Research*. 2019;8(1):69.
 22. **Lazarus JV, Mark HE, Villota-Rivas M, Palayew A, Carrieri P, Colombo M, et al.** The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge? *J Hepatol* 2022; 76:771-80.
 23. **Horn CL, Morales AL, Savard C, Farrell G and Ioannou G.** Role of Cholesterol-Associated Steatohepatitis in the Development of NASH. *Hepatol Commun* 2022; 6:12-35
 24. **Wieckowska A and Feldstein A.**Diagnosis of nonalcoholic fatty liver disease: Invasive versus noninvasive. *Seminars in Liver Disease*.2008;28(4):386–395.
 25. **Foucher J., Chanteloup E., Vergniol J, Castéra L, Bail B, Adhoute X.**Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut*.2006 ;55(3):403–408
 26. **Gülali A., Aytekin A., Buket K.** Mean Platelet Volume and Red Cell distribution width in Hepatosteatois. *National Journal of Medical Research*.2013 ;3(3):264–266.
 27. **Saremi Z., Rastgoo M., Mohammadifard M., Bijari B., Akbari E.** Comparison of platelet number and function between nonalcoholic fatty liver disease and normal individuals. *Journal of Research in Medical Sciences*. 2017 ,22(1): p.
 28. **Kim C, Kim S, Lee M, Kwon Y, Kim Y, Park K.** An increase in mean platelet volume from baseline is associated with mortality in patients with severe sepsis or septic shock. *PLoS ONE*.2015 ;10(3)
 29. **Chauhan A., Adams D, Watson S, Lalor P.** Platelets: No longer bystanders in liver disease. *Hepatology*.2016;64(5):1774–1784.
 30. **Milovanovic AT, Stojkovic LM, Dumic I, Jovic N, Pavlovic MA, Dragasevic S, et al.,** **Diagnostic accuracy of platelet count and platelet indices in the noninvasive assessment of fibrosis in nonalcoholic fatty liver disease patients.** *Can J Gastroenterol Hepatol* ;2017?

Original research

31. **Cao W., Zhao C., Shen C., Wang Y.** Cytokeratin 18, alanine aminotransferase, platelets, and triglycerides predict the presence of nonalcoholic steatohepatitis. *PLoS ONE*. 2013;8(12)
32. **Ozhan H, Aydin M, Yazici M, Yazgan O, Basar C, Gungor A, et al.** Mean platelet volume in patients with non-alcoholic fatty liver disease. *Platelets*; 2010; 21(1):29.
33. **Madan SA, John F, Pitchumoni CS.** Nonalcoholic Fatty Liver Disease and Mean Platelet Volume: A Systemic Review and Meta-analysis. *J Clin Gastroenterol* 2016; 50:69-74.
34. **Shin W., Jung D., Shim J., Lee H.** The association between non-alcoholic hepatic steatosis and mean platelet volume in an obese Korean population. *Platelets*. 2011;22(6):442–446.
35. **Song C, Park D, Yoon M, Seok H, Park J, Kim H, et al.** Association Between Red Cell Distribution Width and Disease Activity in Patients with Inflammatory Bowel Disease. *Digest Dis Sci*.2012;57(4):1033-8.
36. **Li Z, Yang S, Lin H, Huang J, Watkins P, Moser A, et al.** Probiotics and antibodies to TNF inhibit inflammatory activity and improve nonalcoholic fatty liver disease. *Hepatology*. 2003;37(2):343-50
37. **Aktas G, Alcelik A, Tekce BK, Savlı H, Uyeturk U, Kurt M, et al.** Mean platelet volume and red cell distribution width in hepatosteatosis. *Natl J Med Res* 2013 ;3(3):264-6.
38. **Michalak A, Guz M, Kozicka J, Cybulski M, Jeleniewicz W, Lach T.** Red blood cell distribution width derivatives in alcohol-related liver cirrhosis and metabolic-associated fatty liver disease *World J Gastroenterol* 2022 October 14; 28(38): 5636-5647.
39. **Zhou W, Yang J, Zhang G, Hu Z, Jiang and Yu F.** Association between red cell distribution width-to-platelet ratio and hepatic fibrosis in nonalcoholic fatty liver disease. *Medicine (Baltimore)*. 2019 Jul; 98(30).
40. **Li L, Jianxiu Y, Zhongwei Z,** Association between platelet indices and non-alcoholic fatty liver disease: a systematic review and meta-analysis *Rev Esp Enferm Dig* 2022.