*Research Article / Araştırma Makalesi*

# Are There any Associations Between RDW and MPV and Noninvasive Fibrosis Scores in Primary Biliary Cirrhosis?

## Primer Biliyer Sirozda RDW ve MPV'nin Noninvaziv Fibrozis Skorları ile İlişkisi Var mıdır?

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**Abstract**

**Background:** Primary Biliary Cholangitis (PBC) is a progressive autoimmune disease of unclear etiology that causes destructive inflammation in the intrahepatic bile ducts. Predicting liver fibrosis in these patients is important for the early identification of those who may require transplantation. Our aim is to investigate the role of routinely measured complete blood count parameters—specifically red cell distribution width (RDW) and mean platelet volume (MPV) in predicting liver fibrosis.
**Materials and Methods:** Data from 39 patients diagnosed with PBC, including demographic, hematological, biochemical, and imaging parameters, were retrospectively analyzed. The presence of anti-mitochondrial antibodies was recorded for diagnostic purposes. To assess the severity of fibrosis, Fibrosis 4 score (FIB-4) and Aspartate Aminotransferase to Platelet Ratio Index (APRI) scores were calculated. Patients were divided into three groups based on FIB-4 (<1.45, 1.45-3.25, and >3.25) and APRI (<0.5, 0.5-1.5, and >1.5) scores, and laboratory parameters were compared.
**Results:** Of the patients included in the study, 37 (94.9%) were female. The mean age was 51.6± 15.5 years. The average FIB-4 score was 1.7 ± 1.3 (range: 0.4–6.2), and the APRI score was 1.0 ± 0.5 (range: 0.1–8.8). Six patients (15.3%) had a FIB-4 score above 3.25 and 5 patients (12.8%) had an APRI score above 1.5. In the comparison based on FIB-4 score, significant differences were found between the groups in age (p=0.041), aspartate transferase (AST) (p=0.005), alanine transferase (ALT) (p=0.004), bilirubin level (p=0.002), and platelet count (p<0.001). However, no significant differences were found in MPV (p=0.159) and RDW (p=0.357). In the comparison based on APRI score, significant differences were found between the groups in AST (p<0.001), ALT (p<0.001), ALP (p=0.009), GGT (p=0.030), and total bilirubin (p<0.001). Similarly, no significant differences were found between the groups in MPV (0.195) and RDW (p=0.369).
**Conclusions:** As a result of our study, we determined that MPV and RDW values are not useful parameters for predicting fibrosis or progression to cirrhosis in patients with PBC.

**Keywords:** Primary Biliary Cholangitis, Mean Platelet Volume, Red Cell Distribution Width, FIB-4 Score

**Öz**

**Amaç:** Primer Biliyer kolanjit (PBK), intrahepatik safra yollarında destrüktif tipte bir inflamasyona neden olan, progresif ve etiyolojisi tam olarak aydınlatılamamış bir otoimmün hastalıktır. Bu hastalarda karaciğerde fibrozisi önceden tahmin etmek transplantasyon ihtiyacı olan hastaları erken belirlemek adına önemlidir. Amacımız tam kan parametrelerinde rutin olarak bakılan Eritrosit dağılım indeksi (RDW) ve ortalama trombosit hacmi (MPV) değerlerinin fibrozisi tahmin etmedeki rolünü araştırmaktır.
**Materyal ve Metod:** PBK tanısı olan 39 hastanın demografik, hematolojik, biyokimyasal ve görüntüleme parametrelerini içeren verileri retrospektif olarak analiz edilmiştir. Anti-mitokondriyal antikorların varlığı tanısal açıdan kaydedilmiştir. Fibrozis şiddetini değerlendirmek için Fibrozis 4 indeksi (FIB-4) ve AST Trombosit oranı indeksi (APRI) skorları kullanıldı. Hastalar FIB-4 (<1.45 olanlar, 1.45-3.25 arası olanlar ve >3.25 olanlar) ve APRI (<0.5 olanlar, 0.5-1.5 arasında olanlar ve >1.5 olalar) skorlarına göre 3 gruba ayrılarak laboratuvar parametreleri açısından karşılaştırmalar yapıldı.
**Bulgular:** Çalışmaya alınan hastaların 37'si (%94.9) kadındı. Hastaların yaş ortalaması 51.6± 15.5 idi. Hastaların ortalama FIB-4 skoru 1.7 ± 1.3 (0.4-6.2 arası), APRI skoru ise 1.0 ± 0.5 (0.1-8.8 arası) idi. Hastaların 6'sının (%15.3) FIB-4 skoru 3.25'in üzerinde, 5'inin de (%12.8) APRI skoru 1.5'in üzerinde idi.FIB-4 skoruna göre yapılan karşılaştırmada yaş (p=0.041), Aspartat Transferaz (AST) (p=0.005), Alanin Transferaz (ALT) (p=0.004), Bilirubin seviyesi (p=0.002) ve Trombosit sayısı (p<0.001) gruplar arasında anlamlı farklılık gösteriyordu. Ancak, MPV (p=0.159) ve RDW (p=0.357) açısından anlamlı bir farklılık saptanmadı. APRI skoruna göre yapılan karşılaştırmada ise; gruplar arasında AST (p<0.001), ALT (p<0.001), ALP (p=0.009), GGT (p=0.030) ve total bilirubin (p<0.001) açısından anlamlı farklılık saptandı. Benzer şekilde, MPV (0.195) ve RDW (p=0.369) açısından gruplar arasında anlamlı farklılık saptanmadı.
**Sonuç:** Araştırmamız sonucunda PBK hastalarında MPV ve RDW değerinin fibrozisi ve siroza gidişi öngörmede faydalı parametreler olmadığını belirledik.

**Anahtar Kelimeler:** Primer Biliyer Kolanjit, Ortalama Trombosit Hacmi, Kırmızı Hücre Dağılımı, FIB-4 Skoru

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## Introduction

Primary Biliary Cirrhosis (PBC) is a chronic and progressive autoimmune disease that primarily affects the liver. It involves the gradual and targeted destruction of small to medium-sized bile ducts. In PBC, the immune system mistakenly attacks the cells lining these bile ducts, leading to inflammation and scarring (fibrosis) over time. This results in a significant impairment of bile flow, eventually causing bile to accumulate in the liver, which can lead to further liver damage, cirrhosis, and complications such as liver failure. Patients may experience various symptoms, including fatigue, itching (pruritus), and jaundice, as the disease progresses. The exact cause of this autoimmune response remains unclear, but it may involve a combination of genetic, environmental, and hormonal factors (1). PBC is a chronic liver disease characterized by the destruction of small and medium-sized bile ducts. The diagnosis can typically be made when at least two of the following three criteria are present: (1) Elevated Alkaline Phosphatase (ALP) Levels: Increased ALP indicates cholestasis and liver dysfunction, (2) Anti-Mitochondrial Antibodies (AMA): The presence of these antibodies is a key marker of PBC, signifying an autoimmune process, and (3) Liver Biopsy Findings: While generally not needed for diagnosis, a biopsy may show destructive changes in bile ducts when conducted. In most cases, PBC can be diagnosed without a biopsy if the first two criteria—elevated ALP and positive AMA—are fulfilled, allowing for prompt management of the disease (2).

Mean Platelet Volume (MPV) is an important hematological parameter that reflects the average size of platelets in the blood and can provide valuable insights into various health conditions. Research indicates that MPV levels can fluctuate in response to different disease states and levels of disease activity, making it a potentially useful biomarker in clinical settings (3). One of the significant conditions associated with changes in MPV is non-alcoholic fatty liver disease (NAFLD). Numerous studies have demonstrated that patients with NAFLD often exhibit elevated MPV values (4). This increase may be linked to the inflammatory processes and metabolic disturbances that characterize the disease. As the liver struggles to process fats effectively, the resulting strain can influence platelet production and maturation, thereby affecting MPV levels. Understanding this relationship can aid not only in the diagnosis of NAFLD but also in monitoring disease progression and response to therapy (5). Red Cell Distribution Width (RDW) has similarly gained attention as a potential marker associated with poor prognostic outcomes in various liver diseases. Deviations in red blood cell size variability may reflect physiological changes tied to liver dysfunction (6). However, current studies on this topic involve relatively small patient cohorts. Thus, larger, more comprehensive research is needed to fully understand the implications of RDW in liver health and to establish definitive prognostic criteria (7).

In the case of Primary Biliary Cholangitis, performing a biopsy is not a standard practice. Instead, healthcare professionals often rely on various non-invasive methods to assess the degree of fibrosis present in the liver (8). Key among these methods are laboratory tests that measure liver enzymes, specifically aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT). Additionally, scores such as the AST to Platelet Ratio Index (APRI) and the Fibrosis-4 (FIB-4) score play a crucial role in evaluating liver health. These tools provide valuable insights into the extent of liver damage without the need for more invasive procedures (9).

The primary aim of this study was to thoroughly investigate the relationship between MPVand RDW values and their potential impact on FIB-4 and APRI scores in patients diagnosed with primary biliary cirrhosis. This research was conducted at our medical center, where we closely monitored these patients to gain deeper insights into how variations in MPV and RDW might correlate with liver fibrosis progression. Understanding these associations could provide valuable information for better management and treatment strategies for those afflicted by this chronic liver disease.

## Materials and Methods

This study included 39 patients diagnosed with PBC who were under follow-up at the Internal Medicine and Gastroenterology Clinics of our hospital between 2018-2024. Patient data were retrospectively retrieved from our hospital's Nucleus system, ensuring comprehensive data collection.

### *Patient Data Collection*

Demographic, laboratory, and clinical data were systematically recorded to evaluate potential associations with disease progression. The collected data included:

- **Demographic Parameters**: Age and gender.
- **Laboratory Parameters:**
- Hematological markers: WBC count, Neutrophil count, Hemoglobin level, Platelet count, Lymphocyte count, RDW, and MPV.
- Liver function and fibrosis markers: Total Bilirubin, AST, ALT, GGT, and Albumin.
- Coagulation marker: INR.

### *Additional Diagnostic Evaluations*

- **Autoimmune Marker**: The presence of AMA, a key serological marker for PBC, was recorded to make the diagnosis of PBC.

PBC was diagnosed based on persistent cholestatic liver enzyme elevation, positivity for AMA, and/or compatible liver histology, according to current international guidelines (European Association for the Study of the Liver [EASL], 2017) (20).

### *Ethical Considerations*

This study was conducted in full compliance with the principles of the Declaration of Helsinki for ethical medical research. This study received approval from the Clinical Research Ethics Committee of Health Sciences University Gazi Yasargil Training and Research Hospital (date: 25.11.2022; decision number 244). Because the study was retrospective, participants were not asked to provide written informed consent when enrolled.

### *1. FIB-4 Score Calculation*

FIB-4 index is a non-invasive scoring system used to estimate liver fibrosis in patients with chronic liver disease, particularly in hepatitis C and NAFLD. It is calculated using the following formula: FIB-4=Age (years) ×AST (U/L)Platelet count ($10^9$/L)× ALT (U/L)\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count ($10^9$/L)} \times \sqrt{\text{ALT(U/L)}}}FIB-4=Platelet count ($10^9$/L)×ALT (U/L)Age (years)×AST (U/L) (10).

### *Reference Values for FIB-4 Interpretation:*

- **< 1.45:** Low risk of advanced fibrosis
- **1.45 - 3.25**: Indeterminate
- **>3.25:** High risk of advanced fibrosis

### *2. APRI Score Calculation*

The APRI is another non-invasive score used to assess liver fibrosis, especially in chronic hepatitis C. It is calculated as follows: APRI=(AST (U/L)Upper Limit of Normal AST (U/L)) ×100÷Platelet count ($10^9$/L)\text{APRI} = \left( \frac{\text{AST (U/L)}}{\text{Upper Limit of Normal AST (U/L)}} \right) \times 100 \div \text{Platelet count ($10^9$/L)}APRI=(Upper Limit of Normal AST (U/L)AST (U/L))×100÷Platelet count ($10^9$/L) (11).

### *Reference Values for APRI Interpretation:*

- **< 0.5**: Low risk of significant fibrosis
- **0.5 - 1.5**: Indeterminate
- **>1.5**: High likelihood of significant fibrosis
- **>2.0**: Suggestive of cirrhosis

### *Statistics*

To control the normal distribution of patient data, the Kolmogorov-Smirnov, Shapiro-Wilk test, coefficient of variation, skewness, and kurtosis methods were used. While the average and standard deviation values were indicated as continuous variables, the categorical variables were indicated as percentages. The ANOVA test for the parameters whose variations are distributed homogeneously and Kruskal Wallis tests were applied for the parameters whose distribution is not normal and whose variances are not homogenous. A p-value of less than 0.05 was established as the threshold for statistical significance. Statistical Package for Social Sciences (SPSS) Ver.26.0 commercial software was used for the described statistical analyses.

## Results

The study included 39 patients, with 94.9% being female, and a mean age of 51.6 ± 15.5 years. FIB-4 scores were less than 1.45 in 53.8% of patients, 1.45–3.25 in 30.8%, and greater than 3.25 in 15.4%. APRI scores were less than 0.5 in 46.1%, 0.5–1.5 in 41.1%, and greater than 1.5 in 12.8%. Hematologic parameters included a mean WBC count of 7500 ± 1800/µL, a platelet count of 255.8 ± 80.8 × $10^3$/µL (range: 71–416), a hemoglobin level of 13.1 ± 1.4 g/dL, RDW of 14.0 ± 1.6%, and MPV of 10.5 ± 1.2 fL. The mean fibrosis indices were FIB-4 at 1.7 ± 1.3 (range: 0.4–6.2) and APRI at 1.0 ± 0.5 (range: 0.1–8.8). Other results are summarized in Table 1.

**Table 1.** Descriptive analysis of patients demographic and laboratory data

| Parameter | (Mean+SD or Median) |
|---|---|
| **Age (Years)** | 51.6±15.5 |
| **Gender (n/%)** | |
| **Female** | 37 (%94.9) |
| **Male** | 2 (%5.1) |
| **FIB-4 stage (n/%)** | |
| **< 1.45** | 21 (%53.8) |
| **1.45 - 3.25** | 12 (%30.8) |
| **> 3.25** | 6 (%15.4) |
| **APRI stage** | |
| **< 0.5** | 18 (%46.1) |
| **0.5 - 1.5** | 16 (%41.1) |
| **> 1.5** | 5 (%12.8) |
| **WBC** | 7500±1800 |
| **Platelets** | 255.8±80.8 (71-416) |
| **Hemoglobin** | 13.1±1.4 |
| **RDW** | 14.0±1.6 |
| **MPV** | 10.5±1.2 |
| **T.bilirubin** | 0.7±0.5 |
| **AST** | 68.9±100.1 (12-624) |
| **ALT** | 77.1±124.3 (7-783) |
| **ALP** | 207±182 (41-785) |
| **GGT** | 187±87 (13-1277) |
| **Albumin** | 4.1±0.4 |
| **INR** | 1.0±0.08 |
| **FIB-4** | 1.7±1.3 (0.4-6.2) |
| **APRI** | 1.0±0.5 (0.1-8.8) |

***WBC:*** *White Blood Cell,* ***RDW:*** *Red Cell Distribution Width,* ***MPV:*** *Mean Platelet Volume,* ***AST:*** *Aspartate Transaminase,* ***ALT:*** *Alanine Transaminase,* ***ALP:*** *Alkaline Phosphatase,* ***GGT:*** *Gamma-Glutamyl Transferase,* ***INR:*** *International Normalized Ratio,* ***FIB-4:*** *Fibrosis-4 Index,* ***APRI:*** *Aspartate Aminotransferase to Platelet Ratio Index*

### *Results Based on FIB-4 Score Categories*

Patients were stratified into three groups based on FIB-4 scores: <1.45, 1.45–3.25, and >3.25. Age increased significantly with FIB-4 score (p = 0.041). WBC counts showed a significant decline with increasing APRI scores (8.43 ± 1.53 vs. 7.12 ± 1.45 vs. 5.20 ± 1.29, $p < 0.001$). Platelet counts also decreased significantly across the groups (297 ± 68 vs. 229 ± 72 vs. 174 ± 60 ×$10^3$/µL, $p = 0.001$). RDW values were 14.01 ± 1.85, 13.70 ± 0.76, and 14.9 ± 1.72, while MPV values were 10.1 ± 1.14, 11.0 ± 1.1, and 10.9 ± 1.79 across the groups, with no significant differences (p = 0.151 and p = 0.099, respectively). And also, hemoglobin levels did not differ significantly among the APRI groups (13.25 ± 1.59 vs. 13.34 ± 1.24 vs. 12.63 ± 1.59, $p = 0.613$).AST and ALT levels

rose significantly with higher FIB-4 scores (p = 0.005 and p = 0.004, respectively). Total bilirubin also increased significantly across groups (p = 0.002). Platelet count showed a significant inverse relationship with FIB-4 (p< 0.001). Albumin levels trended lower with increasing FIB-4 (p = 0.365). INR and GGT showed no statistically significant differences across groups (p = 0.081 and p = 0.737, respectively). ALP levels were not significantly different across fibrosis stages (p = 0.223) (Table 2).

**Table 2.** Relationship between liver disease stage and laboratory parameters according to FIB-4 score

| Parameter/FİB-4 score | < 1.45 | 1.45-3.25 | > 3.25 | p* |
|---|---|---|---|---|
| **Age** | 46.0±13.4 | 59.2±15.0 | 56.1±17.7 | **0.041** |
| **WBC** | 8.43±1.53 | 7.12±1.45 | 5.20±1.29 | **<0.001** |
| **Hemoglobin** | 13.25±1.59 | 13.34±1.24 | 12.63±1.59 | 0.613 |
| **Platelets** | 297±68 | 229±72 | 174±60 | **0.001** |
| **RDW** | 14.01±1.85 | 13.70±0.76 | 14.9±1.72 | 0.357 |
| **MPV** | 10.1±1.14 | 11.0±1.1 | 10.9±1.79 | 0.159 |
| **AST** | 36.6±21.6 | 69.1±40.5 | 181.6±125.9 | **0.005** |
| **ALT** | 46.1±32.0 | 75.0±60.3 | 189.6±190.3 | **0.004** |
| **ALP** | 180.0±172.7 | 287.0±210.6 | 156.0±134.3 | 0.223 |
| **GGT** | 196.8±293.4 | 209.4±190.4 | 116.0±114.9 | 0.737 |
| **Albumin** | 4.1±0.3 | 4.1±0.3 | 3.8±0.4 | 0.365 |
| **T.Bilirubin** | 0.5±0.2 | 0.8±0.3 | 1.4±1.0 | **0.002** |
| **Platelet** | 297.6±67.6 | 250.2±55.0 | 138.4±68.1 | **<0.001** |
| **INR** | 1.0±0.1 | 1.0±0.1 | 1.1±0.1 | **0.081** |

***WBC** – White Blood Cell (count), **RDW** – Red Cell Distribution Width, **MPV** – Mean Platelet Volume, **AST** – Aspartate Aminotransferase, **ALT** – Alanine Aminotransferase, **ALP** – Alkaline Phosphatase, **GGT** – Gamma-Glutamyl Transferase, **INR** – International Normalized Ratio * One-way ANOVA or Kruskal Wallis tests were applied.*

### *Results Based on APRI Score Categories*

Patients were categorized into three groups by APRI score: <0.5, 0.5–1.5, and >1.5. White blood cell counts decreased across the groups (7.93 ± 1.54, 7.24 ± 2.11, and 5.09 ± 0.57; p = 0.088), while hemoglobin levels remained similar (13.32 ± 1.59, 13.03 ± 1.33, and 12.85 ± 1.90; p = 0.808). Platelet counts showed a significant decline (286 ± 69, 220 ± 84, and 187 ± 67; p = 0.021). RDW and MPV values exhibited no significant differences between the groups (p = 0.369 and p = 0.195, respectively). AST and ALT levels showed a significant increase with higher APRI scores (p < 0.001). Total bilirubin levels also significantly increased across APRI groups (p < 0.001). ALP and GGT levels were significantly elevated in the intermediate group (0.5–1.5) compared to the other two groups (p = 0.009 and p = 0.030, respectively). Platelet count decreased with rising APRI scores, though the trend did not reach statistical significance (p = 0.095). Albumin and INR levels remained stable across groups (p = 0.871 and p = 0.772, respectively). Age showed no significant difference among the groups (p = 0.800) (Table 3).

**Table 3.** Relationship between liver disease stage and laboratory parameters according to APRI score

| Parameter/APRI score | < 0.5 | 0.5 - 1.5 | >1.5 | p |
|---|---|---|---|---|
| **Age** | 53.3±14.1 | 49.7±17.1 | 51.8±17.8 | 0.800 |
| **WBC** | 7.93±1.54 | 7.24±2.11 | 5.09±0.57 | 0.088 |
| **Hemoglobin** | 13.32±1.59 | 13.03±1.33 | 12.85±1.90 | 0.808 |
| **Platelets** | 286±69 | 220±84 | 187±67 | **0.021** |
| **RDW** | 14.2±1.79 | 13.6±1.33 | 14.8±2.61 | 0.369 |
| **MPV** | 10.28±1.20 | 10.77±1.36 | 11.2±1.55 | 0.195 |
| **AST** | 26.0±7.5 | 66.4±28.6 | 227.8±127.4 | **<0.001** |
| **ALT** | 30.0±16.7 | 71.1±33.8 | 261.6±198.4 | **<0.001** |
| **ALP** | 131.5±93.5 | 314.8±224.5 | 157.2±148.9 | **0.009** |
| **GGT** | 97.1±95.3 | 313.5±232.3 | 136.2±118.8 | **0.030** |
| **Albumin** | 4.1±0.3 | 4.1±0.4 | 4.0±0.5 | 0.871 |
| **T.Bilirubin** | 0.5±0.2 | 0.7±0.3 | 1.6±1.0 | **<0.001** |
| **Platelet** | 284.6±71.1 | 255.5±85.6 | 182.7±91.2 | 0.095 |
| **INR** | 1.0±0.1 | 1.0±0.1 | 1.0±0.1 | 0.772 |

** One-way ANOVA or Kruskal Wallis tests were applied.*

### *RDW and MPV Across Fibrosis Stages*

For FIB-4 stages, RDW values were 14.0 in the <1.45 group and 14.9 in the >3.25 group (p = 0.357), while MPV values were 10.1, 11.0, and 10.9 across the respective groups (p = 0.159). For APRI stages, RDW values were 13.6 in the intermediate group and 14.8 in the >1.5 group (p = 0.369), and MPV values showed a gradual increase from 10.2 to 11.2 across groups (p = 0.195) (Figure 1).

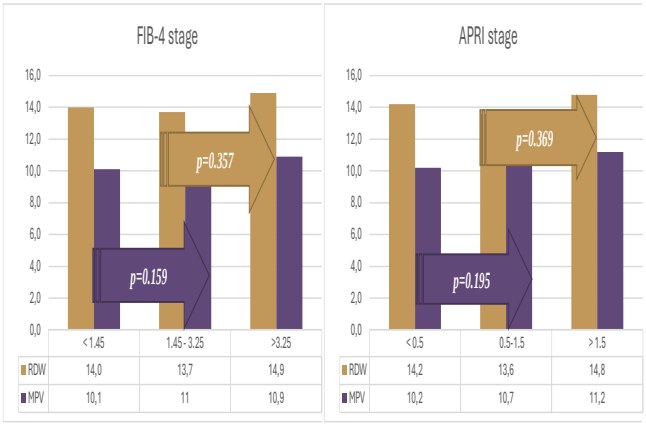


**Figure 1.** Changes in RDW and MPV values in patients grouped according to FIB-4 and APRI scores
*(* One-way ANOVA test were applied.)*

## Discussion

In this study, we conducted a detailed laboratory analysis of 39 patients diagnosed with Primary Biliary Cholangitis, all of whom were receiving ongoing care at our medical center. The investigation focused on the complex relationship between two hematological parameters: MPV and RDW. We also examined the association of these variables with the FIB-4 index, a widely utilized non-invasive marker for estimating liver fibrosis severity. By evaluating these relationships, we aimed to gain deeper insights into how fluctuations in MPV and RDW may reflect the progression of liver fibrosis in individuals with this chronic condition. The findings of this research may contribute to the advancement of diagnostic

approaches and the enhancement of clinical management strategies in patients with Primary Biliary Cholangitis.

PBC is a chronic autoimmune liver disease characterized by progressive destruction of the bile ducts within the liver, leading to a buildup of bile and subsequent liver damage. One of the primary indicators of this condition is the elevation of ALP, a liver enzyme that plays a crucial role in breaking down proteins and promoting bile flow. In patients with PBC, ALP levels can rise significantly, often between 2 to 10 times the normal range (12). In our study, we observed that the ALP level in the affected individual was measured at 207 ± 182 U/L, which is markedly elevated compared to the normal value of 87.5 IU/L. This substantial increase underscores the severity of bile duct damage associated with PBC. Additionally, liver function test (LFT) results indicated elevated levels of other enzymes: AST registered at 68.9 ± 100.1 U/L, and ALT measured at 77.1 ± 124.3 U/L, both of which suggest ongoing liver injury and inflammation. Furthermore, the total bilirubin level was found to be 0.7 ± 0.5 mg/dL, well within the normal range, which may indicate that while the liver is under stress from biliary obstruction or damage, it has not yet reached a stage of significant bilirubin accumulation. Together, these laboratory results provide vital insight into the liver's altered functioning in the context of Primary Biliary Cholangitis.

This study stratified patients by FIB-4 score to evaluate liver fibrosis non-invasively. The results align with established associations between FIB-4 components and fibrosis severity. Age, an integral part of FIB-4, increased significantly with score elevation ($p = 0.041$), reflecting its known link with fibrosis progression (13,14). AST and ALT levels also rose with increasing scores ($p = 0.005$ and $p = 0.004$), consistent with hepatocellular injury (15). Total bilirubin was higher in advanced fibrosis ($p = 0.002$), indicating impaired liver function (16). Platelet count showed a strong inverse correlation with FIB-4 ($p < 0.001$), reflecting portal hypertension and splenic sequestration in cirrhosis (17). In contrast, albumin, INR, GGT, and ALP did not differ significantly, possibly due to compensated liver function or non-cholestatic etiology (13). Overall, these findings affirm the clinical utility of FIB-4 as a practical tool for liver fibrosis assessment, especially when interpreted alongside other markers of liver function and damage.

This study categorized patients by APRI score (<0.5, 0.5–1.5, >1.5) to assess liver fibrosis non-invasively. The results support known associations between APRI and liver disease severity. AST and ALT levels increased significantly with APRI, reflecting progressive hepatocellular damage (15). Total bilirubin also rose with higher scores ($p < 0.001$), indicating worsening liver function (16). ALP and GGT were significantly elevated in the intermediate group, potentially reflecting transient cholestasis. Platelet count declined with higher APRI, though not significantly ($p = 0.095$), aligning with trends seen in portal hypertension (17). Albumin, INR, and age showed no significant variation, possibly due to preserved liver function or sample heterogeneity (13). These findings affirm APRI's utility as a simple, cost-effective fibrosis marker, especially when combined with other biochemical indicators for a more comprehensive evaluation.

MPV / RDW as standalone predictors show limited correlation with FIB-4 or APRI scores in chronic hepatitis B (18). In the same CHB population, MPV did not correlate significantly with fibrosis stage ($p > 0.05$), indicating limited utility on its own as a fibrosis marker. Therefore There are other parameters developed to understand fibrosis in patients with chronic liver disease such as (RDW to platelets ratio) RPR (19). In our study, the analysis of RDW and MPV across FIB-4 and APRI categories showed no statistically significant differences, suggesting limited value of these markers alone in staging liver fibrosis. RDW was slightly higher in advanced fibrosis (FIB-4 >3.25: 14.9 vs. <1.45: 14.0; $p = 0.357$), and MPV showed minimal variation across FIB-4 and APRI groups ($p > 0.05$ for all). Similar nonsignificant trends were observed for RDW and MPV within APRI strata. These findings are consistent with prior studies indicating that RDW and MPV, while reflecting systemic inflammation, are not reliable standalone markers of fibrosis. Composite indices like the RDW-to-platelet ratio (RPR) may offer greater diagnostic accuracy (21, 22).

One of the primary limitations of our study is its retrospective nature, which inherently introduces biases and restricts the ability to establish causality. Additionally, the overall sample size is quite limited, with only a few patients undergoing biopsy procedures. This small cohort significantly weakens the robustness of our biopsy-supported data, making it challenging to draw definitive conclusions. Consequently, the findings may not fully reflect the broader patient population, limiting the generalizability of our results.

## Conclusion

This study underscores the utility of FIB-4 and APRI in evaluating liver fibrosis in PBC. AST, ALT, ALP, and platelet count correlated with fibrosis severity, supporting their diagnostic value. RDW and MPV showed no significant associations, limiting their independent usefulness. A combined biomarker approach may provide a more accurate assessment of disease progression in primary biliary cholangitis.

***Ethical Approval:*** *This study received approval from the Clinical Research Ethics Committee of Health Sciences University Gazi Yasargil Training and Research Hospital (date: 25.11.2022; decision number 244).*

***Author Contributions:***
*Concept: J.K.*
*Literature Review: J.K.*
*Design : J.K.*
*Data acquisition: M.Z.A.*
*Analysis and interpretation: M.Z.A.*
*Writing manuscript: J.K.*
*Critical revision of manuscript: B.E.*

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