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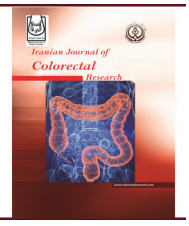

A Comprehensive Review of the Role of Hemogram-derived Inflammatory Markers in Gastrointestinal Conditions

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Abstract

Context: Inflammation, whether overt or subtle, has an important role in the pathogenesis of various diseases. Hemogram-derived markers are novel inflammatory predictors and have been studied in different settings, including gastrointestinal conditions. The main indices are mean platelet volume (MPV), red cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio. Besides the well-established roles of these markers in various hematological issues like differentiating anemia, platelet activation, and infections, recent literature suggests that they could be associated with the inflammatory burden in gastrointestinal conditions from inflammatory bowel disease to functional disorders and malignancies. In the present work, we aimed to review the literature to reveal the association between these markers and gastrointestinal diseases, thereby establishing their diagnostic and prognostic roles in disorders of the gastrointestinal system.
Evidence Acquisition: An extensive literature search was done to select articles that studied hemogram parameters in gastrointestinal disorders.
Results: Literature data suggest that MPV, RDW, NLR, PLR, and MLR are associated with various gastrointestinal disorders. They also have a prognostic role in certain diseases.
Conclusion: Due to their inexpensive and easy-to-assess nature, MPV, RDW, NLR, PLR, and MLR could be considered diagnostic or prognostic tools in gastrointestinal disorders.

Keywords: Hemogram indices, Inflammation, Gastrointestinal diseases

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Introduction

Gastrointestinal disorders are usually associated with some degree of inflammation. Overt inflammation is a hallmark feature of some of them, such as pancreatitis, hepatitis, inflammatory bowel disease (IBD), and cholangitis. On the other hand, other conditions, such as irritable bowel syndrome, hepatosteatosis, and gastrointestinal malignancies, are characterized by subtle inflammation.

Novel inflammatory markers derived from routine hemogram tests have been introduced in recent years. Mean platelet volume (MPV), red cell distribution width (RDW), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and monocyte/lymphocyte ratio (MLR) are among such

hemogram markers. MPV has been suggested as an inflammatory marker in various inflammatory diseases, including nasal polyposis (1), rheumatoid arthritis (2), obesity (3), type 2 diabetes mellitus (4), infections (5), and vertebral disc hernia (6). RDW is also linked with inflammation in thyroiditis (7), autoimmune hepatitis (8), hypothyroidism (9), and chronic kidney disease (10). Recent literature has revealed a significant association between NLR and inflammatory diseases such as cardiac arrhythmia (11), Hashimoto's disease (12), type 2 diabetes mellitus (13), thyroid conditions (14), and COVID-19 (15). Similarly, PLR was suggested as a marker of inflammation in type 2 diabetes mellitus (16) and cancer (17). Finally, MLR is considered an inflammatory predictor in diabetic nephropathy (18), frailty (19), and malignancy (20).

In the present study, we aimed to comprehensively review the role of these hemogram-derived inflammatory markers in gastrointestinal diseases.

Role of Mean Platelet Volume (MPV) in Gastrointestinal Disorders

As a measure of the mean size of platelets, the MPV is a critical hematological indicator of platelet production (21). Platelets, which act as a bridge between the inflammatory response and the activation of coagulation, may play an essential role in the onset of acute pancreatitis and the development of complications. A study found decreased MPV values in the initial phase of acute pancreatitis (22), while some authors reported that MPV values increase during the remission period after treatment (22-25). On the other hand, Kefeli et al. found no notable difference in MPV values during the onset and remission periods (26). MPV has a significant value in determining the severity of the disease (22), despite Yarkaç et al. informing that MPV could not reach statistical significance in distinguishing mild and severe acute pancreatitis cases (27).

Recently, the role of MPV in various liver diseases such as steatosis, cirrhosis, and hepatitis has also been investigated, and elevated values have been observed (28-30). It is thought that due to the expansion in inflammatory cytokine levels in hepatitis, which is characterized by chronic inflammation, the entry of young platelets from the bone marrow to the circulation may increase, and thus the MPV levels rise (31). MPV, a simple, non-invasive, and independent routine laboratory parameter, has shown promise in diagnosing cirrhosis in hepatitis B patients (32).

In another study, MPV values went from highest to lowest across patients with severe chronic hepatitis B, chronic hepatitis B, acute hepatitis B, and healthy controls (33). While Purnak et al. declared high MPV values in inactive hepatitis B carriers (34), another study observed lower MPV values in patients with severe fibrosis than in patients with moderate fibrosis (35). It is well-known that MPV differs in inflammatory diseases (31, 36, 37). Irritable bowel syndrome (IBS) is a common condition that affects the digestive system causing symptoms like stomach cramps, bloating, diarrhea, and constipation. In a study by Aktas et al., in which they examined the MPV values of patients with constipation-type IBS and diarrhea and mixed-type IBS compared to healthy controls, MPV scaled independently (38). Likewise, Arhan et al. showed a rise in MPV values in their study comparing IBS patients with a healthy group (36). These outcomes align with the studies in which some authors express that subclinical inflammation plays a role in the pathogenesis of IBS (39-42). However, in another study, MPV values were statistically low in IBS patients. These analyses indicate that the relationship between IBS and MPV requires further investigation with larger sample groups. MPV tends to increase or decrease depending on the severity of inflammation and disease-related reasons, and it has been suggested that while it typically falls in high-grade inflammatory diseases, it grows in low-grade inflammatory disorders (31).

Tahtacı et al. stated that MPV could replace liver biopsy as it is a new cheap, and easy prognostic indicator in determining the severity of primary biliary cholangitis (PBC), which is one of the gastrointestinal disorders. The study they completed revealed that MPV diminished significantly in patients with early-stage PBC. They elucidated that low MPV values in the early stage of PBC are due to significant inflammation, while they remarked that elevated MPV levels might be associated with liver damage and diminished inflammation in late-stage PBC (43).

Crohn's disease (CD) and Ulcerative colitis (UC) represent the two types of IBD, both known to alter platelet count and morphology secondary to chronic inflammation (44, 45). In a study that included patients with active and inactive CD, active CD patients had remarkably lower MPV values (46). Similarly, Zubcevic et al. revealed that MPV values varied dramatically with the severity of CD (47). Besides, active UC patients had lower MPV values than inactive UC patients and healthy controls (48-50). Contrary to these studies, Saler et al. explored both CD and UC patients under active and inactive disease categories and did not encounter statistically meaningful differences in MPV values (51). More research is needed to clinch whether MPV will be a valid parameter for evaluating IBD.

Non-alcoholic fatty liver disease (NAFLD) or hepatic steatosis, generally seen in overweight or obese people, denotes a range of conditions induced by a build-up of fat in the liver. Hepatic steatosis is a significant disease affecting 30% of the global population. Ectopic adipose tissues gathered in the liver trigger the inflammatory process, resulting in a series of metabolic processes (52-55). Aktas et al. reckoned high MPV values in hepatic steatosis (56) in agreement with other studies in the literature

(30, 57). Another study also indicated that MPV is relatively elevated in patients with NAFLD, and platelet activity is advanced in these patients (58).

The MPV may be a warning sign for gastrointestinal cancer due to increased platelet count. The MPV level has been known to be a marker of inflammation in hepatocellular carcinoma (HCC) and pancreatic adenocarcinoma. A study proved that worse survival outcomes in pancreatic cancer patients with liver metastases are related to high MPV values (59). For diagnosis and screening of colorectal cancers, blood tests (such as blood count, iron parameters, and tumor markers), endoscopy/biopsy (colonoscopy/rectosigmoidoscopy/rectoscopy), and radiological examinations are utilized. Unlike the routine tests, Tuncel et al. showed that increased MPV could be used as a prognostic parameter in metastatic colorectal cancer patients (60). These studies demonstrate the importance of activated platelets in tumor growth and metastasis.

It is possible to benefit from MPV in diagnosing HCC. Kurt et al. reported higher MPV values in patients with chronic liver disease (CLD) compared to control subjects, and those with HCC had higher MPV values than patients with CLD. Therefore, MPV can be a potential marker of HCC (61).

In a study examining whether MPV could be a useful inflammatory marker in detecting gastric cancer patients at an early stage, patients with hypertension, hematologic and kidney disease, heart failure, chronic infection, liver disorder, and other cancers were excluded from the study, and preoperative MPV values were higher in gastric cancer patients than in controls (62).

Role of Red Cell Distribution Width (RDW) in Gastrointestinal Disorders

The RDW is a parameter frequently used in laboratories to measure the degree of erythrocyte anisocytosis, which reflects the variability of the size of circulating red blood cells. Although it is a laboratory value generally used to determine the type of anemia, it has recently been used as an independent marker of the degree of inflammation and may determine the prognosis of many diseases (63, 64).

In recent studies, RDW has been recommended as an inflammatory marker in patients with acute pancreatitis. Studies reported a link between mortality risk and RDW levels in subjects with acute pancreatitis (65, 66). Early diagnosis and treatment are particularly important in acute pancreatitis to achieve a better prognosis. For this purpose, many criteria have been developed, including the Ranson criteria, Glasgow-Imrie score, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score. However, these scores are not cost-effective in comparison to a simple RDW measurement (67). RDW is a well-recognized predictor of acute pancreatitis at the first presentation to the hospital and in the first 24 hours (64, 65). Moreover, RDW is a valuable marker in differentiating and predicting severe and mild acute pancreatitis (68). RDW was assigned as a predictor of mortality in patients with acute pancreatitis in a Portuguese study (69). RDW gradually decreased after hospital admission in patients who survived acute pancreatitis (70). Thus, it can be considered a laboratory sign of decreasing pancreatic inflammation. The prognostic yield of RDW has been found to be superior to APACHE-II and SOFA scores, which are frequently used prognostic tools in acute pancreatitis (71). All these studies show that RDW can be used as an inexpensive, simple, easy to assess and repeat, noninvasive, and high-quality marker in assessing the severity and mortality of acute pancreatitis.

Chronic hepatitis is a progressive destructive inflammatory disease of the liver parenchyma, causing fibrosis and cirrhosis. The role of RDW in hepatitis B is well established (72, 73). The severity of hepatitis B is associated with blood RDW levels (74). Moreover, it has been proposed as a reliable marker of fibrosis and risk of cirrhosis (73). This finding was supported by other studies in the literature (75). In a comparison of RDW levels of inactive hepatitis B virus carriers and chronic hepatitis B subjects, the latter had greater RDW values (76).

Blood levels of RDW are also considered a marker of treatment efficacy in hepatitis subjects. One study found that effective treatment of chronic hepatitis B caused a reduction in RDW values (76). Conflicting studies in the literature reported that RDW was associated with the inflammatory burden but not with fibrosis grade in patients with chronic hepatitis (77). However, RDW reflects the degree of inflammatory reaction by affecting the disease course or changing with the condition's progression.

The two forms of IBD are associated with high inflammatory burden, especially in activation periods during the disease course. Hemoglobin level, platelet count, C-reactive protein, and erythrocyte sedimentation rate are among the inflammatory markers commonly used in these patients. Endoscopic procedures to determine disease activity are invasive and expensive (78). The sensitivity and specificity of RDW in detecting IBD activity have been studied and found to be superior to CRP and ESR (79). In addition, Song et al. reported that the association between RDW and IBD was significant regardless of the presence of anemia (80). These findings show that RDW increases due to underlying inflammation rather than as a consequence of anemia in IBD patients. Finally, Yesil et al. reported that the RDW of IBD subjects was higher than that of the healthy controls, and this increment was even more prominent in IBD subjects with active disease (37). Thus, RDW could be a reliable and cost-effective disease marker in patients with IBD.

Irritable bowel syndrome (IBS) is a gastrointestinal disease that changes bowel habits, causes chronic

abdominal pain, and presents with discomfort and bloating. RDW has been studied in IBS subjects, and higher RDW was reported in these patients compared to controls (38). Although IBS is considered a functional bowel condition, some authors suggest an association between inflammation and IBS (42). Similar findings have been reported by Atak et al. (81) and Kahveci et al. (82). These findings support a relationship between inflammation and IBS; thus, elevated RDW is a predictable consequence of the inflammatory burden in this syndrome.

Non-alcoholic fatty liver disease (NAFLD) is a common cause of hepatosteatosis. It can also progress to steatohepatitis, fibrosis, and cirrhosis (83), and represents the most common chronic liver condition in different parts of the world (84, 85). Chronic inflammation is well-established in NAFLD. A study revealed the role of RDW in determining fibrosis and inflammation in NAFLD subjects (86). Another study with a population of more than 24,000 showed that high RDW values were correlated with the degree of fibrosis in patients with hepatosteatosis (87). Aktas et al. suggested that increased RDW is a laboratory feature of liver steatosis (56). Subsequently, other studies confirmed the results of the previous works (87, 88). These data suggest that RDW could be considered a predictor of inflammatory burden in patients with liver steatosis.

Elevated RDW could be associated with different types of gastrointestinal cancers. Montagnana et al. reported that RDW was increased in patients with gastric tumors (89). This finding was subsequently supported by Saito et al.'s study (90). On the other hand, increased RDW levels have been associated with decreased survival in HCC (91). In addition, RDW was suggested to be related to the prognosis of HCC (92).

A recent meta-analysis reported that RDW was associated with overall and disease-free survival in colorectal carcinoma (93). Interestingly, some authors concluded that RDW level is associated with tumor localization in colorectal carcinoma (94). Moreover, decreased RDW levels were associated with better patient outcomes in subjects with gallbladder carcinoma (95). According to the accumulating data in the literature, RDW looks to have a close relationship with gastrointestinal tumors.

Neutrophil/Lymphocyte Ratio (NLR) in Gastrointestinal Disorders

The circulating neutrophil/lymphocyte ratio (NLR) has attracted great interest from researchers in recent years. Besides its role in various infectious (15) and inflammatory conditions (12), it has important diagnostic and prognostic value in gastrointestinal disorders.

The role of NLR has been studied in IBD. Elevated NLR is a laboratory feature of ulcerative colitis (96). In 2021, a meta-analysis revealed that NLR might be a promising marker of IBD due to its inexpensive, easy-to-assess, and widely available nature (97). Later studies confirmed its usefulness in the diagnosis of IBD (98). Besides NLR's role in the diagnosis of IBD, Metwally reported that it is also associated with the activity and severity of the disease (99). Indeed, a meta-analysis concluded that NLR could serve as a valuable biomarker for predicting the severity of IBD (100). Additionally, Tsunoda et al. reported that NLR was useful in predicting complications after surgery in subjects with CD (101). These valuable data in the literature show that NLR has an important diagnostic and prognostic role in the course of IBD.

The association between inflammatory markers and IBS has recently been investigated. NLR is one of these inflammatory markers, and researchers found that IBS is characterized by increased blood NLR levels (102). In support of this finding, another study reported higher NLR levels in patients with IBS compared with healthy volunteers (103). However, more data is needed to ascertain NLR's role in diagnosing IBS.

Non-alcoholic fatty liver disease (NAFLD) is another condition related to high NLR levels. Aktas et al. found higher blood NLR values in patients compared to controls in their work (104). In a more recent study, NLR levels correlated with inflammation and fibrosis in NAFLD patients (105). In support of these results, a study published in 2022 found that NLR was positively and significantly correlated with steatosis and fibrosis in a NAFLD population (106). Furthermore, increased NLR was reported to be related to HCC risk in subjects with NAFLD (107). Finally, decreased NLR has been introduced as a risk factor for fatty liver disease (108). Thus, high NLRs could be accepted as a marker of steatosis in NAFLD.

The association between NLR and acute pancreatitis has been investigated in different settings. For example, a study found that NLR was a reliable and early predictive marker of the severity of endoscopic retrograde cholangiopancreatography-induced pancreatitis (109). Hypertriglyceridemia-associated acute pancreatitis was also associated with high NLR in the blood, and additionally, increased NLR was an independent risk factor for organ failure development (110). NLR is also useful in assessing the severity of acute pancreatitis. In a study, authors reported higher NLR levels in severe pancreatitis compared to mild and moderate cases (111). NLR has also been a valuable predictor of treatment response in acute pancreatitis cases. Gupta et al. suggested that NLR can be a useful marker for treatment efficacy in acute necrotizing pancreatitis (112). Accumulating data in the literature shows that NLR could successfully predict disease severity and has a high diagnostic value in patients with acute pancreatitis.

Gastrointestinal cancers and NLR have been studied in numerous studies. Survival of patients with gastric cancer was reported to be associated with NLR (113). Likely, decreased NLR was related

to better survival in gastric cancer patients with advanced disease (114). Moreover, NLR has been useful in determining the treatment strategy (115). Other gastrointestinal cancers are also associated with NLR. In a meta-analysis, authors concluded that NLR had an excellent prognostic value in patients with colorectal carcinoma (116). These data were supported by a Chinese study that found high NLRs were associated with poor overall survival in colorectal carcinoma patients (117). Thus, NLR has a valuable prognostic role in gastrointestinal cancers.

Platelet-Lymphocyte Ratio (PLR) in Gastrointestinal Disorders

The PLR is a novel inflammatory marker calculated by platelet count divided by absolute lymphocyte count. The PLR indirectly reveals a patient's inflammatory state, yet several inflammatory conditions may influence it. Though there is platelet migration and destruction at the site of inflammation, simultaneous lymphocyte reduction will occur; thus, the PLR maintains its power to inform about inflammation.

The value of PLR as a prognostic indicator in acute pancreatitis has been examined, and its relationship with ICU admission, hospital stay, and mortality has been elucidated (118). In a study evaluating 243 biliary acute pancreatitis patients, the predictive value of PLR was significantly higher than that of CRP (119), while Karabuga et al., studying with larger samples, concluded that CRP is more dependable (111). Liu et al. reported that the sensitivity of PLR was 95.84% in demonstrating organ damage due to acute pancreatitis, measured higher compared to the sensitivity of BISAP (70.83%) as the traditional method. The specificity of PLR was 44.71% (120). Although prognostic markers have their own advantages and disadvantages, PLR is easy, simple, and inexpensive to use, and it is a valuable marker in terms of providing information about mortality and prognosis.

It is essential to make an early and accurate diagnosis of hepatitis B and hepatitis C, which impact large portions of society among gastrointestinal system diseases, as they initiate with inflammation and end with HCC. PLR has been shown to be thriving in grading fibrosis in hepatitis B patients, in line with previous studies (121). It was previously known that PLR provides practical information regarding the prognosis and progression of hepatitis B (122, 123), as it successfully reveals large-scale changes in the immune system during disease (124). Avanzas et al. confirmed the usability of PLR as predictive for fibrosis and cirrhosis in 457 patients diagnosed with hepatitis B by liver biopsy (125). In another study in which 120 patients infected with the hepatitis C virus and 40 healthy individuals were appraised together, the existence of a prominent aspect of PLR was mentioned. As in hepatitis B patients, PLR was closely affiliated and markedly lowered in patients who developed HCV-related cirrhosis and HCC in hepatitis C patients. Therefore, PLR can be deemed a substantial marker in demonstrating disease progression in patients with HCV-associated liver disease. However, more surprisingly, the PLR gradually raised in patients with virus clearance, giving information about PLR virus removal (126). Regular follow-up of PLR will contribute to the prognosis, progression, and virological response outcome for HBV infection-related and HCV-infection-related diseases.

Inflammatory bowel disease (IBD) impairs the gastrointestinal system via prolonged inflammation, causing symptoms like diarrhea, abdominal pain, and rectal bleeding. In the study conducted by Yujin et al., NLR and PLR values were interpreted together in UC patients, their superiority over each other was confronted, and it was stated that the levels of both were increased. While NLR was a more predictive biomarker in distinguishing patients with UC from healthy ones, PLR was superior in differentiating severe UC from mild and moderate (127). PLR and NLR were examined together after raised PLR values were pursued in patients with active UC, and NLR and PLR combination had more precision in predicting UC than either NLR or PLR alone (128). When questioning how it advances in UC patients, active UC PLR values were observed to be more elevated than those in remission (129). Crohn's disease (CD), another IBD, is chronic and recurrent and can influence any part of the gastrointestinal tract. As in UC, elevations in PLR and NLR parameters have been reported in CD (130). The low lymphocyte (131) and high neutrophil values previously reported in CD patients (132) support these results. Instead of evaluating PLR alone in UC and CD patients, evaluating NLR and PLR together may be more accurate in terms of diagnosis and severity prediction (133, 134).

Albeit ultrasonography is the gold standard for diagnosing acute cholecystitis, which is primarily an inflammation reasoned by an obstruction in the gallbladder stones, bedside tests are also needed. Complete blood count parameters have become progressively utilized in this sense. Although PLR is more inadequate than NLR in terms of sensitivity and specificity in diagnosing acute cholecystitis, it has been shown that its levels are promoted in patients with acute pancreatitis and can be used for diagnostic purposes (135).

Routine hemogram tests are useful in evaluating IBS. Even though it was previously assumed to be a somatosensory disease, infection and inflammation are involved in its etiology (136). Aktas et al. noted high PLR values in IBS patients and stated that they expected this as a result of elevated platelet production and reduced lymphocyte counts due to inflammation (102). Further studies must be made to signify how PLR and IBS correlate.

Fatty liver and NAFLD are expanding in developed

countries, leading to liver failure by destroying the liver cells. While NAFLD refers to a spectrum of liver disorders of varying severity, it can range from less severe nonalcoholic fatty liver (NAFL) to more severe nonalcoholic steatohepatitis (NASH). In a study conducted, it was determined that NAFLD and PLR were negatively associated when the PLR was higher than 42.29. No correlation was seen with NAFLD at lower values (108). Consistent with this, Emma et al. declared that PLR in non-obese patients was inversely linked (137), and Agata et al. reported that PLR values did not demonstrate any noteworthy change in NAFLD patients (138). These analyses explain that PLR is a poor parameter for demonstrating fatty liver.

Pancreatic cancers have an abysmal prognosis among gastrointestinal cancers and are known to progress quite aggressively. The matter of quicker and more accurate diagnosis is obvious at this point. PLR, one of the hematological markers, was examined in a meta-analysis involving 3,028 patients, where rising values had an inverse relationship with overall survival (139). By binding to tumor cells, secreting tumor growth factor, and helping tumor cells to escape from the immune system, platelets may play a role in tumorigenesis, angiogenesis, and metastasis (140, 141). While reduced lymphocytes contribute to the development of malignancy (142), increased platelet counts also contribute to tumor maturation (143). Lymphocytopenia and thrombocytosis are adverse prognostic factors in many cancers; PLR was high in gastric cancer patients with poor prognoses (144, 145). In a meta-analysis study that included 28,929 gastric cancer patients, elevated PLR values were prognostic for poor overall and disease-free survival and were associated with poor clinicopathological parameters (146). This study finalized the link of PLR with gastric cancer, as established with pancreatic ductal adenocarcinoma, HCC, and colorectal cancer. Although some authors (147) point out that the relationship between PLR and gastric cancer is weak, this comprehensive study by Zhang et al. and the literature imply that PLR and gastric cancer are related.

Monocyte-to-Lymphocyte Ratio (MLR) in Gastrointestinal Disorders

The MLR is another hemogram-derived marker studied in various inflammatory conditions. MLR could serve as a marker to distinguish complicated appendicitis from uncomplicated cases (148, 149). It is also a good diagnostic tool for cirrhosis. Salehi et al. reported that MLR negatively correlates with the Model for End-stage Liver Disease score in cirrhotic subjects (150).

Another gastrointestinal disease in which the role of MLR has been observed is UC. Recent reports suggest its role in predicting treatment outcomes. A study from Japan revealed that MLR was associated with treatment failure in subjects with UC (151). Similarly, increased MLR levels were considered a reliable marker of disease activity in patients with UC in a study by Cherfane et al. (152). Subsequent works corroborated the conclusions of the previous studies that reported an association between MLR and disease activity of UC (153). These reports reveal the role of MLR in active inflammation in patients with IBD.

The role of MLR has also been studied in gastrointestinal cancers. Elevated levels of this marker were considered a predictor of survival in gastric cancer subjects (154). The role of MLR in response to cancer treatment has attracted much attention. A recent meta-analysis showed that MLR in the pretreatment period was correlated with tumor response to neoadjuvant chemoradiotherapy in a rectal cancer population (155). Moreover, a study from China reported that elevated MLR levels were related to unfavorable outcomes in patients with hepatocellular carcinoma receiving regional therapy (156). In addition, elevated MLR in the pretreatment period was suggested to be a predictor of a short interval to disease progression in HCC patients (157). Thus, MLR is valuable in predicting the treatment response in gastrointestinal cancer subjects.

High MLR is also associated with the prognosis of gastrointestinal cancers. Kubota et al. concluded that MLR was an independent predictor of disease-free and overall survival of the subjects who had undergone surgery for pancreatic ductal adenocarcinoma (158). Similar findings were reported in subjects with colon cancer by Gawinski et al., who found that lower MLRs were associated with longer five-year survival in that population (159). However, there are also controversial studies in the literature. A recent study from India reported no association between MLR and overall survival in patients with pancreatic cancer (160). Nevertheless, these studies are few, while studies reporting an association between MLR and survival of gastrointestinal tumors are many. Therefore, it can be concluded that high MLR levels are associated with poor prognosis in patients with gastrointestinal cancers.

Conclusion

Each gastrointestinal disease has its pathological features, inflammatory processes, diagnostic methods, and prognostic factors. Studies are being conducted on new diagnostic techniques that are less invasive, inexpensive, simple, applicable, and understandable, which can benefit patients and physicians in a near-ideal order. In this sense, hemogram parameters provide valuable information about the patient with a single blood tube. The hemogram parameters we investigated in this study, MPV, RDW, NLR, PLR, and MLR, sometimes helped achieve a more accurate and quick diagnosis than traditional methods. They were even evaluated in combination and were more valuable

than when they were alone in some cases. Although the lack of sufficient studies on some hemogram parameters has prevented more objective results from being obtained, it is obvious that more studies will be carried out in line with the increasing needs, facilitating an in-depth understanding of the value of these parameters .

Authors' Contribution

All authors contributed the study significantly and agree in the content of the manuscript.

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