

# Evaluation Of Blood Platelet Indices, Platelet Aggregation And Coagulation Profile In The Activity State Of Inflammatory Bowel Disease Patients On Biological Treatment

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## Article

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# Abstract

## Background& aim:

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract associated with systemic complications. Platelets play a key role in both hemostasis and inflammation, and alterations in platelet indices may serve as biomarkers of disease activity. This study aimed to evaluate platelet indices and platelet aggregation in patients with IBD, investigate their correlation with disease activity, and assess the impact of biological therapy on these parameters.

## Methods

A cross-sectional study was conducted on adult patients diagnosed with IBD. Platelet indices, including neutrophil/lymphocyte ratio (NLR), mean platelet volume (MPV), platelet-to-lymphocyte ratio (PLR), and plateletcrit (PCT), were measured alongside platelet aggregation tests. Disease activity was assessed using standard clinical and laboratory indices.

## Results

Patients with active IBD exhibited significantly higher PLR, NLR, with lower MPV compared to those with inactive disease ( $p < 0.05$ ). Platelet aggregation was elevated in active disease). Biological therapy was associated with normalization of platelet indices and reduced platelet aggregation, reflecting decreased systemic inflammation. For predicting active disease; it was found that MPV had the best accuracy (83% at cutoff point  $< 7.89$  fl) followed by PLR (79% at cutoff point  $> 187.67$ ) and NLR (72% at cutoff point  $> 4.56$ ). Least accuracy was reported with platelets aggregation with 68% accuracy at cutoff point  $> 75.67\%$

## Conclusion

Altered platelet indices and increased platelet aggregation are associated with IBD activity and respond to biological therapy. PLR and MPV may serve as accessible, non-invasive biomarkers for monitoring disease activity and therapeutic response. Routine assessment of platelet indices may complement existing clinical and laboratory tools, aiding early detection of flares and optimizing treatment strategies in IBD patients. Further longitudinal studies are warranted to validate these markers and establish standardized reference ranges.

## Introduction

Platelets, traditionally recognized for their role in hemostasis, also act as mediators of inflammation. In inflammatory bowel disease (IBD), activated platelets release pro-inflammatory cytokines, express

adhesion molecules, and interact with leukocytes, thereby contributing to mucosal damage and systemic inflammatory responses (1).

Several platelet indices, including mean platelet volume (MPV), platelet-to-lymphocyte ratio (PLR), and platelet aggregation, have been proposed as accessible biomarkers for evaluating disease activity, predicting flares, and monitoring response to therapy (2).

Understanding these relationships may offer a cost-effective and minimally invasive method to monitor disease progression, optimize therapy, and identify patients at increased risk of complications (3). Therefore, the present study aimed to evaluate platelet indices and platelet aggregation in patients with IBD, assess their correlation with disease activity, and examine the effects of biological therapy on these hematologic parameters. The rationale is to establish reliable, easily measurable biomarkers that can complement existing clinical and laboratory tools for improved patient management.

## Patients & Methods

A case control study was conducted in IBD Clinic of Internal Medicine Department at Al-Rajhy University Hospital in period between 2024 and 2025.

## Selection criteria

Any patient who was above age of 18 years old and diagnosed to have IBD (UC and/or CD) was recruited in the study. Pregnant patients with IBD, previous thrombotic events or on anticoagulants or antiplatelet drugs and colonic malignancy or history of colonic surgeries were excluded from the study

## Sample size calculation

Based on previous reported estimated proportion of acute exacerbation in patients with IBD and that was 29.4% (4) in addition to probability error 5% and 80% power on a two-tailed test, a minimum of 120 patients with IBD are needed as an effective sample size for the current issue. Another 30 healthy subjects were enrolled in the study as control group.

## Methodology

All patients recruited in the current study underwent detailed history taking and comprehensive clinical evaluation. Laboratory investigations included a complete blood count (CBC) with recording of platelet indices, including mean platelet volume (MPV), platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), platelet distribution width (PDW), plateletcrit (PCT), and platelet-large cell ratio (P-LCR).

Coagulation assessment included prothrombin time (PT), prothrombin concentration (PC), international normalized ratio (INR), activated partial thromboplastin time (APTT), thrombin time (TT), fibrinogen level, and D-dimer level. Additional laboratory investigations comprised liver function tests (LFTs), kidney function tests (KFTs), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).

## Platelets aggregation test

It was done by Light Transmission Aggregometry (LTA) for assessing platelet aggregation and function. Venous blood is collected into sodium citrate (3.2%) anticoagulant tubes where platelet-rich plasma was obtained by low-speed centrifugation and was set as 0% light transmission baseline.

Stimulation with agonists as ADP (adenosine diphosphate), collagen, epinephrine, or arachidonic acid. Then measurement of aggregation as following where platelets aggregate → plasma becomes clearer. Aggregometer detects increase in light transmission (%) and aggregation curves are generated for each agonist.

## Endoscopic assessment and disease's activity

**In cases of UC;** evaluation of colonoscopic disease activity utilizing the Mayo Disease Activity Index as follows: inactive disease (remission) with score two point or less and active disease with score more than two points (5).

Meanwhile, **in patients with CD;** we used the Crohn's disease activity index was used for CD to assess severity of CD. Patients with scores lower than 150 were considered to be in remission, and those with scores equal to or higher than 150 to have active disease (6).

## Ethical consideration

The current study was applied be in accordance with Code of Good Practice and the guidelines of Declaration of Helsinki, 7th revision, 2013 and after being approved by the Medical Ethics Committee of the Faculty of Medicine at Assiut University. The study was registered on ClinicalTrials.gov with NCT05406934. Also, a written informed consent was obtained from all participants before being enrolled in the study.

## Statistical analysis

Data was collected in a pre-formed data collection form prior to being entered in the spread-sheet. Statistical analysis was going to be performed using the statistical package for social sciences (SPSS) version 20.0 for Windows (SPSS-Inc ®, Chicago, IL, USA). Continuous variables expressed as mean and standard deviation while categorical data expressed as numbers and percentages.

Diagnostic accuracy of different used parameters in the study in prediction of active IBD was determined by receiver operator characteristics (ROC) curve. Correlation different continuous variables was determined by Pearson coefficient correlation. Level of confidence was kept at 95% hence, P value is significant if  $< 0.05$ .

## Results

### Baseline data of the studied groups (Table 1):

Different studied groups had comparable baseline data. CD group had significantly higher frequency of abdominal pain (76.7% vs. 30%;  $p < 0.001$ ) meanwhile, UC group had higher frequency of rectal bleeding (88.3% vs. 23.3%;  $p < 0.001$ ). Other clinical presentations were comparable between both groups

Table 1  
Baseline data of the studied groups

| Age (years)                | UC group<br>(n = 60) | CD group<br>(n = 30) | Control group<br>(n = 30) | P value |
|----------------------------|----------------------|----------------------|---------------------------|---------|
|                            | 42.01 ± 7.01         | 38.11 ± 4.58         | 39.34 ± 4.70              | 0.51    |
| Sex                        |                      |                      |                           |         |
| Male                       | 40 (66.7%)           | 21 (70%)             | 20 (66.7%)                | 0.91    |
| Female                     | 20 (33.3%)           | 9 (30%)              | 10 (33.3%)                |         |
| Residence                  |                      |                      |                           | 0.59    |
| Rural                      | 38 (63.3%)           | 17 (56.7%)           | 16 (53.3%)                |         |
| Urban                      | 22 (36.7%)           | 13 (43.3%)           | 14 (46.7%)                |         |
| BMI (kg/m <sup>2</sup> )   | 22.15 ± 2.45         | 22.19 ± 3.19         | 21.01 ± 2.09              | 0.12    |
| Smoking                    | 6 (10%)              | 3 (10%)              | 5 (16.7%)                 | 0.40    |
| Family history of IBD      | 2 (3.3%)             | 1 (1.1%)             | 1 (1.1%)                  | 0.08    |
| Comorbidities              |                      |                      |                           |         |
| DM                         | 4 (6.6%)             | 2 (6.7%)             | 0                         | 0.56    |
| HTN                        | 3 (5%)               | 2 (6.7%)             | 0                         | 0.34    |
| IHD                        | 1 (1.6%)             | 1 (3.3%)             | 0                         | 0.87    |
| CKD                        | 0                    | 2 (6.7%)             | 0                         | 0.55    |
| Chest diseases             | 1 (1.6%)             | 2 (6.7%)             | 0                         | 0.07    |
| Others                     | 2 (3.3%)             | 0                    | 0                         | 0.34    |
| Duration of disease (year) | 8.50 ± 1.30          | 6.09 ± 1.29          |                           | 0.87    |
| Manifestations             |                      |                      |                           |         |
| Bowel motion               | 5.11 ± 2.33          | 4.01 ± 1.6           |                           | 0.45    |
| Diarrhea                   | 43 (71.6%)           | 21 (70%)             |                           | 0.11    |
| Rectal bleeding            | 53 (88.3%)           | 7 (23.3%)            |                           | < 0.001 |
| Abdominal pain             | 18 (30%)             | 23 (76.7%)           |                           | < 0.001 |
| Fever                      | 10 (16.7%)           | 6 (20%)              |                           | 0.09    |

Data expressed as frequency (percentage), mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; BMI: body mass index; IBD: inflammatory bowel disease; DM: diabetes mellitus; HTN: hypertension; IHD: ischemic heart disease; CKD: chronic kidney disease

| <b>Age (years)</b>                                                                                                                                                                                                                                                                                    | <b>UC group<br/>(n = 60)</b> | <b>CD group<br/>(n = 30)</b> | <b>Control group<br/>(n = 30)</b> | <b>P value</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------------------------|-----------------------------------|----------------|
|                                                                                                                                                                                                                                                                                                       | <b>42.01 ± 7.01</b>          | <b>38.11 ± 4.58</b>          | <b>39.34 ± 4.70</b>               | <b>0.51</b>    |
| EIMs                                                                                                                                                                                                                                                                                                  | 8 (13.3%)                    | 5 (16.7%)                    |                                   | 0.51           |
| <b>Therapy</b>                                                                                                                                                                                                                                                                                        |                              |                              |                                   | ---            |
| Conventional therapy                                                                                                                                                                                                                                                                                  | 30 (50%)                     | 15 (30%)                     |                                   |                |
| Biological therapy                                                                                                                                                                                                                                                                                    | 30 (50%)                     | 15 (30%)                     |                                   |                |
| <b>Disease activity</b>                                                                                                                                                                                                                                                                               |                              |                              |                                   | ----           |
| In active disease                                                                                                                                                                                                                                                                                     | 30 (50%)                     | 15 (30%)                     |                                   |                |
| Active disease                                                                                                                                                                                                                                                                                        | 30 (50%)                     | 15 (30%)                     |                                   |                |
| Data expressed as frequency (percentage), mean (SD). <i>P</i> value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; BMI: body mass index; IBD: inflammatory bowel disease; DM: diabetes mellitus; HTN: hypertension; IHD: ischemic heart disease; CKD: chronic kidney disease |                              |                              |                                   |                |

## Laboratory blood tests among the studied groups (Table 2):

Patients' groups of UC and CD had significantly lower haemoglobin, and serum albumin compared to the control group. Meanwhile, CRP and ESR were significantly higher among CD and UC groups compared to the control group

Table 2  
Laboratory blood tests among the studied groups

|                                                                                                                                                                                                                                                                                                                                                                               | UC group<br>(n = 60) | CD group<br>(n = 30) | Control group (n = 30) | P value           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|------------------------|-------------------|
| <b>Complete blood count</b>                                                                                                                                                                                                                                                                                                                                                   |                      |                      |                        |                   |
| Leucocytes (10 <sup>3</sup> /ul)                                                                                                                                                                                                                                                                                                                                              | 7.22 ± 4.07          | 9.01 ± 6.45          | 7.98 ± 2.22            | 0.10              |
| Hemoglobin (g/dl)                                                                                                                                                                                                                                                                                                                                                             | 11.10 ± 2.01         | 10.93 ± 2.98         | 12.51 ± 2.29           | <b>0.01</b>       |
| Platelets (10 <sup>3</sup> /ul)                                                                                                                                                                                                                                                                                                                                               | 250.98 ± 120.45      | 284.14 ± 118.9       | 289.98 ± 123.5         | 0.17              |
| Neutrophil/ lymphocyte ratio                                                                                                                                                                                                                                                                                                                                                  | 4.12 ± 1.87          | 5.09 ± 2.45          | 2.14 ± 0.56            | <b>&lt; 0.001</b> |
| Platelets/ lymphocyte ratio                                                                                                                                                                                                                                                                                                                                                   | 187.11 ± 34.87       | 189.11 ± 23.89       | 101.45 ± 23.65         | <b>&lt; 0.001</b> |
| <b>Coagulation profile</b>                                                                                                                                                                                                                                                                                                                                                    |                      |                      |                        |                   |
| INR                                                                                                                                                                                                                                                                                                                                                                           | 1.02 ± 0.04          | 1.10 ± 0.01          | 1.01 ± 0.09            | 0.89              |
| Prothrombin time (sec)                                                                                                                                                                                                                                                                                                                                                        | 12.11 ± 1.22         | 12.06 ± 1.11         | 12.01 ± 1.09           | 0.37              |
| PC (%)                                                                                                                                                                                                                                                                                                                                                                        | 97.17 ± 2.18         | 98.01 ± 0.98         | 98.97 ± 1.98           | 0.76              |
| aPTT (sec)                                                                                                                                                                                                                                                                                                                                                                    | 30.34 ± 4.56         | 29.90 ± 2.89         | 31.78 ± 4.19           | 0.87              |
| Thrombin time (sec)                                                                                                                                                                                                                                                                                                                                                           | 17.56 ± 3.21         | 18.01 ± 1.24         | 17.01 ± 2.01           | 0.22              |
| <b>Kidney function tests</b>                                                                                                                                                                                                                                                                                                                                                  |                      |                      |                        |                   |
| Urea (mmol/l)                                                                                                                                                                                                                                                                                                                                                                 | 8.88 ± 2.19          | 10.14 ± 4.33         | 12.01 ± 2.57           | 0.11              |
| Creatinine (mmol/l)                                                                                                                                                                                                                                                                                                                                                           | 110.34 ± 21.13       | 115.98 ± 24.11       | 118.34 ± 25.54         | 0.34              |
| <b>Liver function tests</b>                                                                                                                                                                                                                                                                                                                                                   |                      |                      |                        |                   |
| Albumin (mg/dl)                                                                                                                                                                                                                                                                                                                                                               | 38.19 ± 3.11         | 33.09 ± 5.09         | 33.22 ± 5.11           | <b>0.01</b>       |
| Bilirubin (umol/l)                                                                                                                                                                                                                                                                                                                                                            | 12.11 ± 2.19         | 15.58 ± 2.67         | 13.29 ± 3.67           | 0.52              |
| ALT (u/L)                                                                                                                                                                                                                                                                                                                                                                     | 23.10 ± 2.19         | 22.88 ± 18.54        | 31.90 ± 9.09           | 0.31              |
| AST (u/L)                                                                                                                                                                                                                                                                                                                                                                     | 28.189 ± 4.48        | 24.04 ± 11.56        | 32.09 ± 2.18           | 0.67              |
| <b>Inflammatory markers</b>                                                                                                                                                                                                                                                                                                                                                   |                      |                      |                        |                   |
| ESR (ml/hr)                                                                                                                                                                                                                                                                                                                                                                   | 23.18 ± 3.98         | 20.10 ± 4.56         | 8.19 ± 2.22            | <b>0.001</b>      |
| Data expressed as mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; EIMs: extraintestinal manifestations; INR: international randomized ratio; PC: prothrombin concentration; PTT: partial thromboplastin time; ALT: alanine transaminase; AST: aspartate transaminase; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein |                      |                      |                        |                   |

|                                                                                                                                                                                                                                                                                                                                                                               | UC group<br>(n = 60) | CD group<br>(n = 30) | Control group (n = 30) | P value      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|------------------------|--------------|
| <b>Complete blood count</b>                                                                                                                                                                                                                                                                                                                                                   |                      |                      |                        |              |
| CRP (ml/hr)                                                                                                                                                                                                                                                                                                                                                                   | 33.12 ± 6.78         | 30.22 ± 3.10         | 2.18 ± 1.09            | <b>0.001</b> |
| Fibrinogen (g/dl)                                                                                                                                                                                                                                                                                                                                                             | 2.11 ± 0.85          | 2.01 ± 0.45          | 1.99 ± 0.11            | 0.98         |
| D-dimer (µg/ml)                                                                                                                                                                                                                                                                                                                                                               | 0.24 ± 0.08          | 0.27 ± 0.09          | 0.22 ± 0.01            | 0.33         |
| Data expressed as mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; EIMs: extraintestinal manifestations; INR: international randomized ratio; PC: prothrombin concentration; PTT: partial thromboplastin time; ALT: alanine transaminase; AST: aspartate transaminase; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein |                      |                      |                        |              |

## Blood and platelets indices among studied groups (Tables 3–5):

Patients' groups of UC and CD had significantly higher NLR, PLR, and platelets aggregation with significantly lower MPV compared to the control group. At the same time, all these parameters were comparable between CD and UC groups.

Table 3  
Blood and platelets indices among studied groups

| NLR                                                                                                                                                                                                                 | UC group<br>(n = 60) | CD group<br>(n = 30) | Control group (n = 30) | P value           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|------------------------|-------------------|
|                                                                                                                                                                                                                     | <b>4.12 ± 1.87</b>   | <b>5.09 ± 2.45</b>   | <b>2.14 ± 0.56</b>     | <b>&lt; 0.001</b> |
| PLR                                                                                                                                                                                                                 | 187.11 ± 34.87       | 189.11 ± 23.89       | 101.45 ± 23.65         | <b>&lt; 0.001</b> |
| MPV (fl)                                                                                                                                                                                                            | 8.78 ± 2.19          | 8.17 ± 3.10          | 11.23 ± 4.11           | <b>&lt; 0.001</b> |
| PDW (%)                                                                                                                                                                                                             | 11.89 ± 3.46         | 10.09 ± 5.19         | 10.99 ± 2.11           | 0.25              |
| Plateletcrit (%)                                                                                                                                                                                                    | 0.30 ± 0.09          | 0.29 ± 0.10          | 0.33 ± 0.15            | 0.16              |
| P-LCR (%)                                                                                                                                                                                                           | 29.56 ± 9.18         | 30.34 ± 10.76        | 35.87 ± 15.67          | 0.99              |
| Platelets aggregation (%)                                                                                                                                                                                           | 87.17 ± 16.78        | 88.17 ± 18.91        | 66.01 ± 14.89          | <b>&lt; 0.001</b> |
| Data expressed as mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio |                      |                      |                        |                   |

Table 4  
Blood and platelets indices among patients with inactive disease

| <b>NLR</b>                                                                                                                                                                                                          | <b>Inactive UC group<br/>(n = 30)</b> | <b>Inactive CD group<br/>(n = 15)</b> | <b>Control group (n = 30)</b> | <b>P value</b> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|---------------------------------------|-------------------------------|----------------|
|                                                                                                                                                                                                                     | <b>3.18 ± 0.78</b>                    | <b>2.29 ± 0.34</b>                    | <b>2.14 ± 0.56</b>            | <b>0.45</b>    |
| PLR                                                                                                                                                                                                                 | 121.10 ± 12.76                        | 109.31 ± 18.34                        | 101.45 ± 23.65                | 0.32           |
| MPV (fl)                                                                                                                                                                                                            | 10.28 ± 1.65                          | 10.34 ± 2.99                          | 11.23 ± 4.11                  | 0.17           |
| PDW (%)                                                                                                                                                                                                             | 11.09 ± 2.12                          | 10.01 ± 3.16                          | 10.99 ± 2.11                  | 0.30           |
| Plateletcrit (%)                                                                                                                                                                                                    | 0.28 ± 0.15                           | 0.31 ± 0.09                           | 0.33 ± 0.15                   | 0.78           |
| P-LCR (%)                                                                                                                                                                                                           | 30.56 ± 6.22                          | 31.21 ± 8.67                          | 35.87 ± 15.67                 | 0.07           |
| Platelets aggregation (%)                                                                                                                                                                                           | 71.17 ± 8.79                          | 70.45 ± 17.87                         | 66.01 ± 14.89                 | 0.22           |
| Data expressed as mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio |                                       |                                       |                               |                |

Table 5  
Blood and platelets indices among patients with active disease

| <b>NLR</b>                                                                                                                                                                                                          | <b>Active UC group<br/>(n = 30)</b> | <b>Active CD group<br/>(n = 15)</b> | <b>Control group (n = 30)</b> | <b>P value</b>    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------|-------------------|
|                                                                                                                                                                                                                     | <b>5.44 ± 1.29</b>                  | <b>6.21 ± 2.21</b>                  | <b>2.14 ± 0.56</b>            | <b>&lt; 0.001</b> |
| PLR                                                                                                                                                                                                                 | 190.22 ± 44.56                      | 192.09 ± 19.75                      | 101.45 ± 23.65                | <b>&lt; 0.001</b> |
| MPV (fl)                                                                                                                                                                                                            | 7.98 ± 2.81                         | 8.01 ± 2.87                         | 11.23 ± 4.11                  | <b>&lt; 0.001</b> |
| PDW (%)                                                                                                                                                                                                             | 11.96 ± 2.20                        | 10.32 ± 4.33                        | 10.99 ± 2.11                  | 0.87              |
| Plateletcrit (%)                                                                                                                                                                                                    | 0.31 ± 0.02                         | 0.28 ± 0.08                         | 0.33 ± 0.15                   | 0.46              |
| P-LCR (%)                                                                                                                                                                                                           | 28.16 ± 4.37                        | 29.21 ± 9.56                        | 35.87 ± 15.67                 | 0.71              |
| Platelets aggregation (%)                                                                                                                                                                                           | 90.27 ± 18.18                       | 89.07 ± 16.89                       | 66.01 ± 14.89                 | <b>&lt; 0.001</b> |
| Data expressed as mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio |                                     |                                     |                               |                   |

**Blood and platelets indices in studied patients based on activity (Table 6–7):**

Patients with active disease (either CD or UC) had significantly higher NLR, PLR, and platelets aggregation with significantly lower MPV compared to patients with inactive disease. Other parameters showed no significant value.

Table 6  
Blood and platelets indices among UC group based on activity

| <b>NLR</b>                                                                                                                                                                                     | <b>Inactive UC group<br/>(n = 30)</b> | <b>Active UC group (n = 30)</b> | <b>P value</b>    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|---------------------------------|-------------------|
|                                                                                                                                                                                                | <b>3.18 ± 0.78</b>                    | <b>5.44 ± 1.29</b>              | <b>&lt; 0.001</b> |
| PLR                                                                                                                                                                                            | 121.10 ± 12.76                        | 190.22 ± 44.56                  | <b>&lt; 0.001</b> |
| MPV (fl)                                                                                                                                                                                       | 10.28 ± 1.65                          | 7.98 ± 2.81                     | <b>&lt; 0.001</b> |
| PDW (%)                                                                                                                                                                                        | 11.09 ± 2.12                          | 11.96 ± 2.20                    | 0.67              |
| Plateletcrit (%)                                                                                                                                                                               | 0.28 ± 0.15                           | 0.31 ± 0.02                     | 0.09              |
| P-LCR (%)                                                                                                                                                                                      | 30.56 ± 6.22                          | 28.16 ± 4.37                    | 0.21              |
| Platelets aggregation (%)                                                                                                                                                                      | 71.17 ± 8.79                          | 90.27 ± 18.18                   | <b>&lt; 0.001</b> |
| Data expressed as mean (SD). P value was significant if < 0.05. UC: ulcerative colitis; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio |                                       |                                 |                   |

Table 7  
Blood and platelets indices among patients with CD based on activity

| <b>NLR</b>                                                                                                                                                                                  | <b>Inactive CD group<br/>(n = 15)</b> | <b>Active CD group (n = 15)</b> | <b>P value</b>    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|---------------------------------|-------------------|
|                                                                                                                                                                                             | <b>2.29 ± 0.34</b>                    | <b>6.21 ± 2.21</b>              | <b>&lt; 0.001</b> |
| PLR                                                                                                                                                                                         | 109.31 ± 18.34                        | 192.09 ± 19.75                  | <b>&lt; 0.001</b> |
| MPV (fl)                                                                                                                                                                                    | 10.34 ± 2.99                          | 8.01 ± 2.87                     | <b>&lt; 0.001</b> |
| PDW (%)                                                                                                                                                                                     | 10.01 ± 3.16                          | 10.32 ± 4.33                    | 0.09              |
| Plateletcrit (%)                                                                                                                                                                            | 0.31 ± 0.09                           | 0.28 ± 0.08                     | 0.23              |
| P-LCR (%)                                                                                                                                                                                   | 31.21 ± 8.67                          | 29.21 ± 9.56                    | 0.18              |
| Platelets aggregation (%)                                                                                                                                                                   | 70.45 ± 17.87                         | 89.07 ± 16.89                   | <b>&lt; 0.001</b> |
| Data expressed as mean (SD). P value was significant if < 0.05. CD: Crohn's disease; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio |                                       |                                 |                   |

**Baseline and follow up indices in patients with active disease (Table 8):**

In both groups of patients with active disease (either UC or CD), there were significant reduction in NLR, PLR, MPV and platelets aggregation three months after biological therapy.

Table 8  
Baseline and follow up indices in patients with active disease

| Ulcerative colitis group     | Before biological therapy | After biological therapy | P value |
|------------------------------|---------------------------|--------------------------|---------|
| NLR                          | 5.44 ± 1.29               | 2.21 ± 0.67              | < 0.001 |
| PLR                          | 190.22 ± 44.56            | 122.11 ± 19.11           | < 0.001 |
| MPV (fl)                     | 7.98 ± 2.81               | 9.45 ± 1.87              | 0.01    |
| PDW (%)                      | 11.96 ± 2.20              | 11.08 ± 4.44             | 0.45    |
| Plateletcrit (%)             | 0.31 ± 0.02               | 0.30 ± 0.03              | 0.30    |
| P-LCR (%)                    | 28.16 ± 4.37              | 23.21 ± 4.59             | 0.17    |
| Platelets aggregation (%)    | 90.27 ± 18.18             | 50.57 ± 23.19            | 0.001   |
| <b>Crohn's disease group</b> |                           |                          |         |
| NLR                          | 6.21 ± 2.21               | 3.45 ± 1.01              | < 0.001 |
| PLR                          | 192.09 ± 19.75            | 130.57 ± 2.22            | < 0.001 |
| MPV (fl)                     | 8.01 ± 2.87               | 10.11 ± 3.49             | 0.03    |
| PDW (%)                      | 10.32 ± 4.33              | 10.77 ± 3.19             | 0.87    |
| Plateletcrit (%)             | 0.28 ± 0.08               | 0.27 ± 0.02              | 0.46    |
| P-LCR (%)                    | 29.21 ± 9.56              | 25.77 ± 4.44             | 0.71    |
| Platelets aggregation (%)    | 89.07 ± 16.89             | 55.58 ± 12.22            | < 0.001 |

Data expressed as mean (SD). *P* value was significant if < 0.05. UC: ulcerative colitis; CD: Crohn's disease; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio.

#### Correlation between different indices with thrombosis activity (Table 9);

It was found that different blood indices and platelets indices had insignificant differences with different parameters of thrombotic and coagulation activities as PT, TT, PTT, d-dimer and fibrinogen (*p* > 0.05).

Table 9  
Blood and platelets indices among patients with CD based on activity

| NLR                                                                                                                                                                                                                         | PT                      | TT                      | PTT                | D-dimer            | Fibrinogen         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|-------------------------|--------------------|--------------------|--------------------|
|                                                                                                                                                                                                                             | <b>-0.05<br/>(0.62)</b> | <b>-0.08<br/>(0.47)</b> | <b>0.09 (0.55)</b> | <b>0.01 (0.07)</b> | <b>0.13 (0.44)</b> |
| PLR                                                                                                                                                                                                                         | -0.19 (0.09)            | -0.09 (0.39)            | 0.12 (0.26)        | -0.07<br>(0.09)    | -0.04 (0.55)       |
| MPV (fl)                                                                                                                                                                                                                    | -0.06 (0.56)            | -0.02 (0.84)            | 0.03 (0.78)        | 0.21 (0.61)        | -0.11 (0.10)       |
| PDW (%)                                                                                                                                                                                                                     | 0.11 (0.56)             | 0.13 (0.49)             | 0.01 (0.49)        | 0.14 (0.20)        | -0.08 (0.43)       |
| Plateletcrit (%)                                                                                                                                                                                                            | 0.09 (0.20)             | -0.10 (0.51)            | 0.09 (0.18)        | 0.24 (0.40)        | -0.03 (0.79)       |
| P-LCR (%)                                                                                                                                                                                                                   | -0.1 (0.93)             | 0.03 (0.76)             | -0.04<br>(0.69)    | 0.01 (0.99)        | 0.17 (0.12)        |
| Platelets aggregation<br>(%)                                                                                                                                                                                                | 0.10 (0.19)             | 0.09 (0.19)             | 0.18 (0.20)        | 0.01 (0.07)        | 0.13 (0.44)        |
| <i>P</i> value was significant if < 0.05. PT: prothrombin time; TT: thrombin time; PTT: partial thromboplastin time; NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; P-LCR: Platelet –large cell ratio |                         |                         |                    |                    |                    |

## Accuracy of different indices in predicting active disease (Table 10, Fig. 1):

For predicting active disease; it was found that MPV had the best accuracy (83% at cutoff point < 7.89 fl) followed by PLR (79% at cutoff point > 187.67) and NLR (72% at cutoff point > 4.56). Least accuracy was reported with platelets aggregation with 68% accuracy at cutoff point > 75.67%

Table 10  
Accuracy of different indices in predicting active disease

| <b>Sensitivity</b>                                                                                                                                                                                                               | <b>MPV</b> | <b>PLR</b> | <b>NLR</b> | <b>Platelets aggregation</b> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|------------|------------|------------------------------|
|                                                                                                                                                                                                                                  | <b>81%</b> | <b>77%</b> | <b>75%</b> | <b>70%</b>                   |
| Specificity                                                                                                                                                                                                                      | 84%        | 80%        | 71%        | 68%                          |
| PPV                                                                                                                                                                                                                              | 67%        | 61%        | 51%        | 47%                          |
| NPV                                                                                                                                                                                                                              | 92%        | 90%        | 87%        | 84%                          |
| <b>Accuracy</b>                                                                                                                                                                                                                  | <b>83%</b> | <b>79%</b> | <b>72%</b> | <b>68%</b>                   |
| Prevalence                                                                                                                                                                                                                       | 29%        | 29%        | 29%        | 29%                          |
| Cutoff                                                                                                                                                                                                                           | 7.89       | 187.67     | 4.56       | 75.67                        |
| AUC                                                                                                                                                                                                                              | 0.82       | 0.72       | 0.69       | 0.58                         |
| <i>P</i> value                                                                                                                                                                                                                   | < 0.001    | 0.01       | 0.04       | 0.56                         |
| <i>P</i> value was significant if < 0.05. NLR: Neutrophil/ lymphocyte ratio; PLR: Platelets/ lymphocyte ratio; MPV: mean platelets volume, PPV: positive predictive value; NPV: negative predictive value; AUC: area under curve |            |            |            |                              |

## Discussion

Recent advances in hematologic research have identified several platelet-derived indices measurable by automated analyzers, such as MPV, PDW, plateletcrit (PCT), platelet–large cell ratio (P-LCR), and platelet–lymphocyte ratio (PLR) (7). Similarly, functional platelet tests such as light transmission aggregometry can directly quantify platelet reactivity and aggregation capacity (8).

The current study included 120 participants—90 IBD patients (UC and CD) and 30 healthy controls—matched for age and sex, with no statistically significant differences between groups. The mean age of IBD patients was approximately mid-30s, with a slight female predominance.

The demographic distribution aligns with prior studies showing peak IBD onset between 20 and 40 years (9). A modest female predominance observed in this cohort is consistent with global epidemiological trends indicating slightly higher UC incidence in females (10).

Duration of disease in the current study is comparable with previous reports from Middle Eastern and Mediterranean populations (11, 12). Previous study found that the mean age of onset was  $35.1 \pm 12.5$  years ranging from 5 to 88 years with mean duration of illness at inclusion of  $13.6 \pm 16.7$  years (11).

Our study found that IBD patients demonstrated significantly elevated fibrinogen and D-dimer levels compared with controls ( $p < 0.001$ ), whereas PT, PTT, and TT remained within normal ranges but were

slightly prolonged. The magnitude of fibrinogen and D-dimer elevation was greater among patients with active disease.

Fibrinogen not only increases plasma viscosity but also facilitates platelet aggregation and fibrin formation, thereby exacerbating thrombotic risk. D-dimer elevation indicates ongoing subclinical coagulation and fibrinolysis, signifying the presence of microthrombi within inflamed intestinal or systemic vasculature (13, 14).

One of the main findings in the current study was that compared to healthy controls, IBD patients exhibited significantly lower MPV, but higher platelet count, PDW, PCT, PLR, and NLR ( $p < 0.05$  for all). MPV values were inversely correlated with disease activity, whereas PDW, PCT, and PLR increased progressively with disease severity.

Similarly, previous study assessed the correlation between decreased MPV value and severity of IBD activity, **Kapsoritakis et al (2001)** proposed the use of MPV as an effective marker of activity in IBD (15). Many reported studies confirmed such results (16–18).

In our study, patients with IBD either UC or CD had significantly higher NLR and PLR compared to healthy control group. At the same time, these parameters PLR and NLR in active disease were significantly higher compared their value in patients with inactive disease. We found that both markers had good diagnostic accuracy; PLR (79% at cutoff point  $> 187.67$ ) and NLR (72% at cutoff point  $> 4.56$ ); in predicting the activity of IBD.

Many reported studies confirmed the predictive value of NLR and PLR in IBD activity (19–22). The retrospective study, which included UC patients with active disease or patients in remission, found that an optimum cut-off value of 2.16 indicated the presence of active disease, with a sensitivity of 81.8% and a specificity of 80.5% (23).

The NLR values of the active UC group were elevated compared with those of the patients with inactive UC and the controls ( $2.59 \pm 1.47$ ,  $2.03 \pm 1.07$ , and  $1.98 \pm 0.85$ , respectively;  $p = 0.005$ ). The receiver operating characteristic revealed that the optimum NLR cut-off point for active UC was 2.39 (24).

**Feng et al (2022)** PLR and NLR were elevated in active IBD patients than those inactive disease/control group. The receiver-operating characteristic (ROC) analysis revealed the optimal cutoff of NLR for active UC was 2.19, with sensitivity and specificity of 78.8 and 65%, respectively. For PLR, the best cut-off value was 147.96, with sensitivity and specificity of 58.3 and 75%, respectively (21).

Also, in previous study, for identifying disease activity, the optimal cutoff of 179.8 for PLR had a sensitivity of 35.4% and a specificity of 90.6% (positive likelihood ratio 3.778, 95% CI 1.821–7.838; AUC 0.654, 95% CI 0.556–0.753) (25).

The present analysis highlights the pivotal role of platelet indices—particularly the platelet–large cell ratio (P-LCR) and plateletcrit (PCT)—in reflecting the inflammatory and thrombotic dynamics of

inflammatory bowel disease. A significant decrease in P-LCR suggests enhanced platelet utilization and destruction within the inflamed intestinal microvasculature.

In contrast, PCT levels were markedly elevated, reflecting reactive thrombocytosis and increased total platelet mass as a response to cytokine-driven megakaryopoiesis, particularly under the influence of interleukin-6 (26). Although many previous studies proved role of P-LCR and PCT in patients with IBD with raised PCT and decreased PCT associated with disease's activity (2, 26).

Yet, our study revealed comparable values between IBD vs. control group and active IBD vs. inactive IBD as regard PCT and L-LCR. Those could be explained by study design, selection bias, studied population and different sample size.

Lastly, we found that platelet aggregation percentage was significantly higher in IBD patients than in controls (mean ~ 85% vs. 70%,  $p < 0.01$ ). Moreover, patients with active disease had higher aggregation values than those in remission, suggesting disease activity-dependent platelet hyperreactivity.

This observation underscores the role of platelet hyperaggregation as a pathophysiologic hallmark of IBD-associated thrombosis. Activated platelets adhere to inflamed endothelium, release prothrombotic mediators, and form aggregates with leukocytes, contributing to microvascular occlusion and mucosal ischemia (3).

The mechanism involves increased levels of inflammatory cytokines such as IL-6 and TNF- $\alpha$ , which enhance platelet sensitivity to ADP and collagen, thus promoting aggregation. Additionally, endothelial dysfunction and increased von Willebrand factor release further potentiate platelet activation (2, 27).

This study comprehensively evaluated both morphological and functional platelet parameters—including P-LCR, PCT, MPV, PDW, PLR, and platelet aggregation—together with coagulation markers (fibrinogen and D-dimer). This multidimensional approach provides a holistic understanding of the interplay between inflammation, thrombosis, and platelet activation in IBD.

Yet, the current study had some limitations as relatively small sample size and being conducted in single-center design. Cross-sectional nature where the study design did not allow longitudinal follow-up, making it difficult to evaluate dynamic changes in platelet indices before and after therapy or across disease remission and relapse phases.

## Conclusions

The study found that patients with active inflammatory bowel disease (IBD) show significant changes in platelet indices and aggregation. Specifically, NLR, PLR, and platelet aggregation were elevated, while MPV was reduced compared to inactive patients and healthy controls, suggesting platelet activation as a potential biomarker of disease activity. Further studies are needed to confirm these findings.

## Declarations

## Competing interest:

Not applicable

## Funding:

Not applicable

## Author Contribution

M.H. and S.H. data collection, analysis, preliminary draft, prepared the draft, analyzed it, design the proposal, review literature M.Z. final revision, study design, assist in final drafting All authors reviewed the manuscript.

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Not applicable

## Data Availability

"The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request."

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## Figures

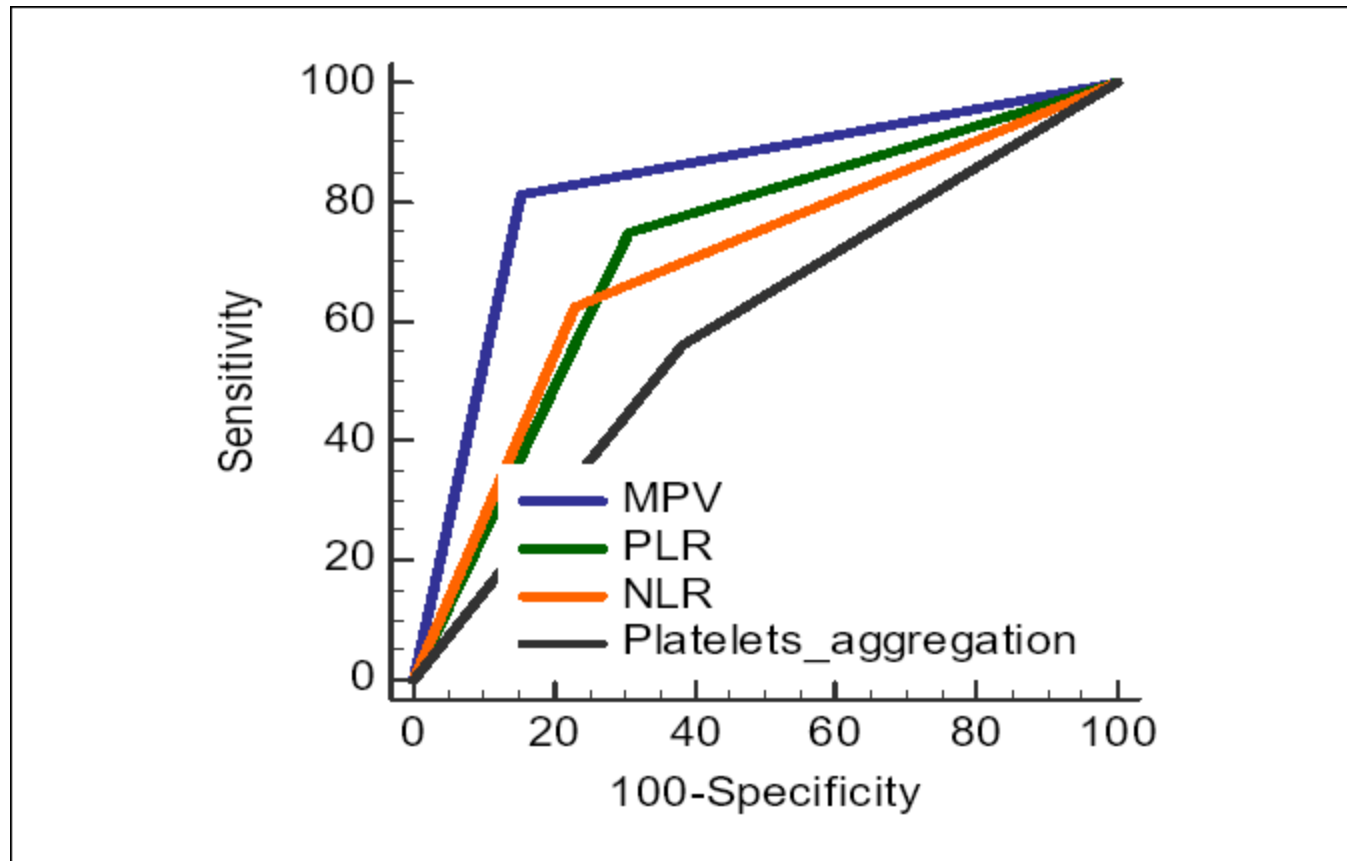


Figure 1

