Asian Journal of Research and Reports in Gastroenterology

5(2): 1-9, 2021; Article no.AJRRGA.66302

Mean Platelet Volume as a Complementary Non-Invasive Biomarker for Disease Activity in Inflammatory Bowel Disease: A Single Centre Study

Soon Liang Lee[1*], Chiun Yann Ng[1], Jasminder Sidhu[1], Lai Teck Gew[1] and Kian Boon Law[2]

[1]Department of Medicine, Gastroenterology and Hepatology Unit, Kuala Lumpur General Hospital, Malaysia.
[2]National Clinical Research Centre, Malaysia.

Authors' contributions

This work was carried out in collaboration among all authors. Author SLL designed the study, wrote the protocol and wrote the first draft of the manuscript. Author KBL performed the statistical analyses. Authors SLL and CYN managed the analyses of the study and managed the literature searches. Authors JS and LTG supervised the conduct of the study. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. P. Veera Muthumari, V. V. Vanniaperumal College for Women, India.
Reviewers:
(1) Alan Kelbis Oliveira Lima, University of Brasília, Brazil.
(2) Roberto de Paula do Nascimento, University of Campinas, Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/66302

Original Research Article

Received 28 December 2020
Accepted 02 March 2021
Published 16 March 2021

ABSTRACT

Aims: Mean platelet volume (MPV) has been a potential biomarker for disease activity of inflammatory bowel disease (IBD), with an observed inverse relationship between MPV and disease activity. The study aims to investigate MPV as a complementary biomarker for disease activity in IBD.
Study Design: This was a retrospective study.
Place and Duration of Study: Kuala Lumpur, between January 2019 and December 2019.
Methodology: We retrospectively enrolled and evaluated 88 patients with ulcerative colitis (UC) and 52 patients with Crohn's disease (CD). Various disease scores, such as Modified Trulove Witt's Severity Index (MTWSI) and Mayo Endoscopic Sub-score (MES) in UC, and Crohn's Disease Activity Index (CDAI) and Simple Endoscopic Score for Crohn's Disease (SES-CD) in CD were analyzed with various blood parameters to identify potential associations and correlations.

**Corresponding author: Email: soonliang13@gmail.com;*

Results: There was no statistically significant association found between mean MPV and MTWSI or MES in UC. Clinically moderate to severe UC has higher total white cell count than those with mild disease *(P*=0.0162). No significant correlation was found between MPV and CDAI or SES-CD in CD (*P*>0.05). Clinically active disease in CD had significantly higher C-reactive protein (CRP) (*P*=0.0450), platelet albumin ratio (PAR) (*P*=0.0369), and lower albumin (*P*=0.0011) than those in asymptomatic remission. The study identified a significant correlation between SES-CD with CRP (*r*=0.5101, *P*=0.0003), erythrocyte sedimentation rate (ESR) (*r*=0.3243, *P*=0.0386), albumin (*r*=–0.4798, *P*=0.0008), and PAR (*r*=0.3379, *P*=0.0232).
Conclusion: We do not recommend MPV as a complementary biomarker for IBD disease activity. More prospective large cohort studies are needed to examine its reliability. The PAR should be considered as a predictor of IBD disease activity in future prospective studies.

Keywords: Ulcerative colitis, Crohn's disease, platelet albumin ratio, C-reactive protein.

ABBREVIATIONS

CRP: C-reactive Protein
ESR: Erythrocyte Sedimentation Rate
TWC: Total White Cell
HB: Haemoglobin
PLT: Platelet
MPV: Mean Platelet Volume
ALB: Albumin
PAR: Platelet Albumin Ratio

1. INTRODUCTION

Inflammatory bowel diseases (IBD), such as ulcerative colitis (UC) and Crohn's Disease (CD), have a strong association with the interaction of genetic, environmental, and immunological factors [1]. Platelet plays a vital role in most inflammatory processes as thrombocytosis correlates well to disease severity in IBD. The mechanism of thrombocytosis in IBD is still unclear to date. However, an increased plasma level of thrombopoietin and interleukin-6 (IL-6) in IBD affecting thrombopoiesis could be the possible cause of thrombocytosis [2].

Reduced mean platelet volume (MPV) has also been recognized as a characteristic of platelet dysfunction in IBD and may result from a disturbed thrombopoiesis [2]. With the increased use of non-invasive biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fecal calprotectin in diagnosis and evaluation of IBD disease severity, MPV may be considered as a potential non-invasive biomarker. Several investigations have shown that MPV is a potential marker of disease severity in IBD and has an inverse relationship to other clinical biomarkers such as CRP and ESR. [1-3]

A study by Kapsoritakis et al. [1] showed that the mean platelet count increased in patients with active IBD, while a significant reduction of MPV occurred in active UC (*P*<0.002) and CD (*P*<0.0005), as compared to inactive diseases or healthy controls. The study also found that the extent of reduction of MPV correlated to the extent of bowel involvement extent in both UC and CD. Patients with ulcerative pancolitis had a much lower MPV than left-sided or ulcerative proctitis and the MPV of patients with ileocolonic CD was lower than the MPV of CD with only colonic or terminal ileum involvement [1]. However, there were also studies showing no association between MPV and IBD activity and other inflammatory biomarkers [4,5].

The MPV with red cell distribution width shows an added value to established inflammatory parameters in predicting disease severity in UC [6]. One retrospective study conducted by Sobolewska et al. [7] showed that the change of MPV at baseline and week 14 could predict sustained response to infliximab with a sensitivity of 87% and specificity of 93% [7]. As MPV is negatively correlated to disease severity in IBD as shown in several studies, its use as a biomarker of treatment response should be taken into consideration as well. [1,2,7]

The study aims to investigate MPV in patients with IBD on whether it can be a useful, affordable, and complementary non-invasive biomarker to other established inflammatory

laboratory parameters to evaluate clinical and endoscopic disease severity.

2. MATERIALS AND METHODS

This retrospective study enrolled 88 patients with UC and 52 patients with CD diagnosed until 2019. The diagnosis of UC and CD was established based on history, clinical examination, blood parameters, imaging investigations, endoscopy, and histopathology assessment. Relevant data of these patients were extracted from the National Gastrointestinal Registry and their clinic progression notes. The study included patients above 12 years old with an established diagnosis of IBD and under active follow-up with the Gastroenterology clinic. Patients who had the following criteria such as heart failure, stage 2 chronic kidney disease and beyond, cancer, deranged liver function, receiving anticoagulants, contraceptives, non-steroidal anti-inflammatory drugs, recent trauma or surgery in the last six months of follow up, pregnant, and lost to follow-up were excluded from the study.

The blood sample results, such as C-reactive protein (CRP), mean platelet volume (MPV), erythrocyte sedimentation rate (ESR), and total white blood cell count (TWC), were recorded simultaneously with clinical severity indices for IBD and endoscopic activity. Platelet albumin ratio (PAR) was calculated by dividing the platelet count (10^9/L) with the value of serum albumin (g/L).

All patients with UC and CD were classified based on the Montreal Classification. For CD, categories of disease location included ileal (L1), colon (L2), ileocolon (L3), and upper gastrointestinal location (L4). Disease behaviors for CD include non-stricturing, non-penetrating (B1), stricturing (B2), penetrating (B3), as well as perianal involvement (PA). The extent of UC was classified into proctitis (E1), left sided (E2), and extensive (E3).

The clinical disease severity was assessed with Modified Trulove Witt's Severity Index (MTWSI) in UC and Crohn's Disease Activity Index (CDAI) in CD. Categories for MTWSI were severe disease for score ≥ 12, mild to moderate for score 5-11, and in remission for score ≤ 4. For CDAI, a score less than 150 was categorized as mild disease, 150-450 as moderately severe disease, and more than 450 for severe disease. Patients with UC who had score 5 and above in MTWSI were categorized as active disease. As for patients with CD, a score of 150 and above in the CDAI were categorized as active disease.

The endoscopic activity of CD and UC were assessed with the Simple Endoscopic Score for Crohn's Disease (SES-CD) and Mayo Endoscopic Sub-score (MES). The SES-CD encompasses a few categories: remission for score 0-2, mild endoscopic activity for score 3-6, moderate endoscopic activity for score 7-15, and severe endoscopic activity for score 15 above. MES scores for UC included 0 for normal, 1 for mild, 2 for moderate, and 3 for severe disease activity.

For the analysis of blood samples, 2 ml of venous blood was taken from patients and placed into standardized tubes containing ethylenediaminetetraacetic acid (EDTA). The adult normal reference range for MPV, WBC, and PLT were 7.4–10.4 fL, 4-10 x10^9/L, and 150-410 x10^9/L, respectively.

For ESR and CRP, 2 ml of venous blood was collected from the patients into the serum tube before analysis with an automated device. Normal adult range of ESR and CRP were 0-20 mm/hr and < 5 mg/L, respectively.

2.1 Statistical Analysis

Descriptive analysis was performed to describe clinical and social demographics of patients. We reported mean and standard deviation (SD) for numerical variables and count (n) and proportion (%) for categorical variables. Population estimates were captured using 95% confidence interval (95% CI) for mean and proportion. Correlations of MPV with other blood parameters were analyzed using either Pearson's correlation coefficient (*r*) or Spearman's correlation coefficient (*rho*) depending on the data. Correlation coefficients with its 95% CI were reported. Two variables were regarded as highly correlated if the correlation coefficient was more than 0.5 with Cohen's criteria for correlation coefficient. A correlation is regarded statistically significant if its p-value (*P*) was smaller than 0.05 (2-sided). Data were organized in Microsoft Excel, and analyzed using R version 3.5.3 with validated packages such as 'gmodels', 'car', and so on.

3. RESULTS

Baseline characteristics from patients who were included in this retrospective study are shown in Table 1. In the UC cohort, 44.3% of the patients

were Malay in ethnic origin followed by 38.6% Indian and 17.1% Chinese. About 23.9% of the patients with UC had proctitis, 29.5% of patients had left sided disease, and 46.6% had extensive disease. About 46.2% of patients with CD were Indian followed by 32.7% Malay, 19.2% Chinese, and 1.9% Others. About 5.8% of the CD patients had ileal disease, 40.4% had colonic disease, 51.9% had ileocolonic disease, and 1.9% had upper gastrointestinal disease. About 46.2% of CD patients had non-stricturing and non-penetrating disease, 23% had stricturing disease, 15.4% had fistulising disease, and 15.4% had both fistulising and stricturing disease. About 21% of CD patients had perianal involvement. Patients with UC had higher mean age (41.7 years) compared to patients with CD (32.6 years). Median disease duration for both UC and CD were 8 and 7 years, respectively. Table 2 showed the summary of laboratory parameters for patients with UC and CD. The mean MPV for both UC and CD were comparable at 9.57±1.69 fL and 9.51±1.59 fL, respectively.

3.1 Modified Truelove and Witt's Severity Index (MTWSI) in Ulcerative Colitis

With regards to MTWSI, 88.5% of patients with UC was categorized as mild disease (<4), 6.9% as moderate disease (4-6) and 4.6% as severe disease (>6). About 11.5% of patients with UC in this study had active disease and 88.5% had inactive disease based on MTWSI. The mean MPV of active UC (8.64 ± 3.14 fL) based on MTWSI was lower than those with inactive disease (9.70 ± 1.39 fL). However, the Wilcoxon rank sum test showed no statistically significant association between MPV and MTWSI (*P*=0.284). Patients with active UC had TWC (10.83 ± 3.89 $x10^9$/L) higher than those with inactive UC (7.80 ± 2.67 $x10^9$/L), and this was statistically significant (*P*=0.0162). The mean PAR was higher in those with active UC (8.61 ±1.71 $x10^9$) compared to inactive UC (8.25 ± 2.51 $x10^9$), but not statistically significant (Table 3).

3.2 Mayo Endoscopic Sub-Score (MES) in Ulcerative Colitis

32.9% of patients with UC were found to have MES of 0, 42% had MES 1, 23.5% had MES 2, and 1.18% had MES 3. Interestingly, patients with UC with moderate endoscopic disease activity had higher mean MPV (9.85 ± 0.87 fL) compared to those with normal endoscopic disease activity (9.64 ± 2.08 fL) and mild disease activity (9.36 ± 1.83 fL). There was however no statistically significant association between MPV and MES. Mean serum albumin was noted to be lower in UC patients (35.9 ± 3.83 g/L) with moderate endoscopic disease activity group compared to those with normal (39.0 ± 2.58 g/L) and mild endoscopic disease activity (38 ± 3.47 g/L). A statistically significant association between serum albumin (*P*=0.0149) and MES was found in this study. There was also a statistically significant association of PAR with MES (*P*=0.0436), with mean PAR (9.00 ± 2.90 $x10^9$) highest in those with the worst MES score (Table 4).

3.3 Crohn's Disease Activity Index (CDAI) in Crohn's Disease

There was statistically significant positive correlation between CDAI and blood parameters, such as CRP (*r*=0.40, *P*=0.031), TWC (*r*=0.2769, *P*=0.0469), and PLT (*r*=0.420, *P*=0.0068) as shown in Table 5. However, there was no correlation seen between CDAI and serum albumin but when PAR was used, a significant correlation was found with CDAI (*r*=0.5227, *P*=0.0005) in our study. However, there was no statistically significant inverse correlation between CDAI and MPV as hypothesized (*P*=0.5911). About 80.7% of patients with CD had a CDAI score of <150, 5.8% had a score between 150 and 220, 13.5% had a score between 221 and 450. When categorized according to the clinical disease activity, 19.3% of patients with CD in our study have active disease and 80.7% were in asymptomatic remission based on the CDAI score. As summarised in Table 6, patients with active CD had higher mean CRP (19.28 ± 19.2 mg/L) compared to CD patients in asymptomatic remission (7.64 ± 10.07 mg/L), and a statistically significant difference was found (*P*=0.0450). Serum albumin had a statistically significant association with CD severity (*P*=0.001), and mean serum albumin in active CD was found to be lower (30.5 ± 5.52 g/L) than those with asymptomatic remission (36.9 ± 4.33 g/L). The PAR was found to be higher in those with active CD (14.17 ± 7.85 $x10^9$) than those in asymptomatic remission (8.52 ± 3.47 $x10^9$), and the association was statistically significant (*P*=0.036). The MPV however did not show statistically significant association with CD activity based on CDAI score.

Table 1. Characteristics of patients with ulcerative colitis and Crohn's disease

Ulcerative colitis (N=88)			Crohn's disease (N=52)		
Characteristics	**N**	**(%)**	**Characteristics**	**N**	**(%)**
Gender			Gender		
Female	34	(38.6)	Female	20	(38.5)
Male	54	(61.4)	Male	32	(61.5)
Age, year			Age, year		
Mean (SD)	41.7	(14.8)	Mean (SD)	32.6	(13.8)
Ethnicity			Ethnicity		
Indian	34	(38.6)	Indian	24	(46.2)
Malay	39	(44.3)	Malay	17	(32.7)
Chinese	15	(17.1)	Chinese	10	(19.2)
			Other	1	(1.9)
Disease duration, year			Disease duration, year		
Median	8		Median	7	
Min, Max	(0,35)		Min, Max	(1,50)	
Location			Location		
Proctitis (E1)	21	(23.9)	Ileal (L1)	3	(5.8)
Left sided (E2)	26	(29.5)	Colon (L2)	21	(40.4)
Extensive (E3)	41	(46.6)	Ileo-colon (L3)	27	(51.9)
			Upper GI (L4)	1	(1.9)
			PA	11	(21.1)
			Disease behaviors		
			B1	24	(46.2)
			B2	12	(23.0)
			B2, B3	8	(15.4)
			B3	8	(15.4)

**PA: Perianal Disease; B1: Non-Penetrating, Non-Stricturing ; B2: Stricturing ; B3: Penetrating*

Table 2. Summary of blood investigation results for ulcerative colitis and Crohn's disease

	Ulcerative colitis			Crohn's disease		
Parameters	**N**	**mean**	**(SD)**	**N**	**mean**	**(SD)**
CRP	84	6.77	(9.93)	51	9.92	(13.01)
ESR	73	27.23	(17.94)	48	32.29	(24.29)
TWC	87	8.14	(2.95)	52	8.02	(3.50)
HB	88	13.51	(3.48)	52	12.85	(3.69)
PLT	72	313.90	(88.27)	40	329.2	(136.89)
MPV	84	9.57	(1.69)	49	9.51	(1.59)
ALB	87	38.03	(3.47)	52	35.73	(5.21)
PAR	71	8.2	(2.5)	40	9.5	(4.9)

CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; TWC: Total White Cell; HB: Haemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; ALB: Albumin; PAR: Platelet Albumin Ratio

Table 3. Association of blood parameters to MTWSI

Parameters	**Mild**		**Moderate - Severe**		**Wilcoxon rank sum test *P*-value**
	Mean	**(SD)**	**Mean**	**(SD)**	
CRP	6.98	(10.43)	5.47	(6.06)	0.5381
ESR	27.26	(18.15)	28.86	(17.69)	0.7178
TWC	7.80	(2.67)	10.83	(3.89)	0.0162
HB	13.53	(3.54)	13.04	(3.01)	0.8417
PLT	308.70	(81.84)	372.50	(112.46)	0.0690
MPV	9.70	(1.39)	8.64	(3.14)	0.2840
ALB	37.94	(3.42)	38.44	(3.97)	0.9098
PAR	8.25	(2.51)	8.62	(1.71)	0.5570

CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; TWC: Total White Cell; HB: Haemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; ALB: Albumin; PAR: Platelet Albumin Ratio

3.4 Simple Endoscopic Score (SES-CD) in Crohn's disease

Correlation of SES-CD with the blood parameters were shown in Table 7. In our study, CRP (*r*=0.501, *P*=0.0003), ESR *(r*=0.324, *P*=0.038), ALB (*r*=-0.4798, *P*=0.0008), and PAR (*r*=0.3379, *P*=0.0232) had statistically significant correlation with SES-CD in CD patients. However, there was no statistically significant inverse correlation found between MPV and SES-CD on Spearman analysis (*r*=-0.132, *P*=0.4037).

4. DISCUSSION

In our study, we found no association between mean platelet volume (MPV) and Mayo Endoscopic Score (MES) or disease activity based on Modified Trulove Witt's Severity Index (MTWSI) in patients with UC, despite certain studies proving otherwise [1,8]. In the study by Yuksel et al. [8] MPV of active UC was significantly lower than that of inactive UC. However, that study included a small cohort of patients with UC, and the disease activity was only evaluated with Rachmilewitz Endoscopic Activity Index, and no clinical disease severity index such as Mayo disease activity score or MTWSI were utilized. The study also found no correlation between MPV and other inflammatory markers, such as ESR, CRP, and TWC [8].

Similar result of significant reduction of MPV found in active UC in which inverse correlation with other inflammatory markers was also revealed in the study by Kapsoritakis et al. [1] The UC disease activity with its relation to MPV in the study was however evaluated using Clinical Colitis Activity Index without the utilization of endoscopic assessment of disease activity. With the paradigm shift of deep remission being the optimal treatment target in IBD, the role of endoscopic assessment cannot be emphasized enough. We found no association of MTWSI with other inflammatory parameters such as ESR, CRP, PLT and PAR. This could be explained by the fact that symptoms of IBD are subjective and endoscopic activity may be independent of the clinical symptoms. Patients who reported symptoms may have a quiescent disease, while those in supposedly clinical remission may be having active endoscopic disease [9]. Contrary to findings seen in other studies, we failed to prove an association between MES and CRP in our UC cohort and this is likely attributed to the under representation of the UC patients in the severe category of MES [10,11].

Table 4. Association of blood parameters to Mayo Endoscopic Sub-score (MES)

Parameters	Normal		Mild		Moderate		Kruskal Wallis *P*-value
	Mean	(SD)	Mean	(SD)	Mean	(SD)	
CRP	4.49	(7.26)	8.26	(12.7)	7.86	(7.51)	0.0723
ESR	22.08	(16.17)	30.29	(17.40)	31.56	(19.95)	0.0999
TWC	8.39	(2.88)	8.21	(2.71)	7.49	(3.13)	0.5979
HB	13.75	(1.48)	12.99	(2.50)	13.96	(6.27)	0.3078
PLT	283.8	(76.84)	338.10	(94.17)	319.3	(86.3)	0.0574
MPV	9.64	(2.08)	9.36	(1.83)	9.85	(0.87)	0.4014
ALB	39.07	(2.58)	38.09	(3.47)	35.95	(3.83)	0.0149
PAR	7.35	(2.25)	8.64	(2.20)	9.00	(2.90)	0.0436

CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; TWC: Total White Cell; HB: Haemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; ALB: Albumin; PAR: Platelet Albumin Ratio

Table 5. Correlation of blood parameters with Crohn's Disease Activity Index (CDAI)

Parameter	Correlation, *r*	95% CI	*P*-value
CRP	0.4057	0.1465; 0.6128	0.0031
ESR	0.1810	-0.1087; 0.4424	0.2182
TWC	0.2769	0.0044; 0.5112	0.0469
HB	-0.1795	-0.4312; 0.0982	0.2030
PLT	0.4209	0.1259; 0.6475	0.0068
MPV	-0.0787	-0.3521; 0.2071	0.5911
ALB	-0.0697	-0.2775; 0.1443	0.5234
PAR	0.5227	0.2522; 0.7174	0.0005

CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; TWC: Total White Cell; HB: Haemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; ALB: Albumin; PAR: Platelet Albumin Ratio

Table 6. Association of blood parameters to Crohn's disease severity

Parameters	AR		Mild to Severe		Wilcoxon rank sum test *P*-value
	Mean	(SD)	Mean	(SD)	
CRP	7.64	(10.07)	19.28	(19.2)	0.0450
ESR	31.69	(25.38)	34.89	(19.94)	0.4278
TWC	7.59	(2.90)	9.82	(5.18)	0.5852
HB	13.12	(3.96)	11.72	(1.95)	0.1091
PLT	310.2	(116.41)	418.60	(195.54)	0.1687
MPV	9.52	(1.72)	9.47	(0.82)	0.3936
ALB	36.98	(4.33)	30.50	(5.52)	0.0011
PAR	8.52	(3.47)	14.17	(7.85)	0.0369

CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; TWC: Total White Cell; HB: Haemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; ALB: Albumin; PAR: Platelet Albumin Ratio

Table 7. Correlation of blood parameters with SES-CD

Parameter	Correlation, *rho**	*P*-value
CRP	0.5101	0.0003
ESR	0.3243	0.0386
TWC	0.2764	0.0660
HB	-0.2954	0.0488
PLT	0.2330	0.1280
MPV	-0.1323	0.4037
ALB	-0.4798	0.0008
PAR	0.3379	0.0232

**Spearman's Test: CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; TWC: Total White Cell; HB: Haemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; ALB: Albumin; PAR: Platelet Albumin Ratio*

Our findings showed that reduced serum albumin was evident in those with worse MES as revealed in previous studies. Ongoing active intestinal inflammation promoting leakage of albumin, reduced albumin synthesis in the liver, and malnutrition from reduced protein intake are the possible factors leading to a decreased level of albumin in active IBD [10]. Moreover, changes in serum albumin have been proven to predict the endoscopic activity and treatment response in UC [12]. Uchihara et al. [10] reported a good correlation between platelet count and endoscopic activity in UC, which was not shown in our data [10]. However, when using PAR in the analysis, a higher PAR value was evident in those with higher MES scores.

In the CD cohort, there was also no significant correlation found between MPV and disease activity based on CDAI. In one study by Song Liu et al. [4] MPV was lower in patients with CD than healthy patients but it failed to correlate with ESR, CRP, and TWC. Moreover, the study also revealed that MPV could not differentiate active CD from non-active CD as it did not prove a statistically discriminative value [4]. Our data and results are consistent with the study by Saler et al. [5] which did not show any significant association between MPV and disease activity but found higher CRP in those with active CD [5]. Significant association of CRP, TWC, and PLT with Simple Clinical Colitis Activity Index in UC was found in a study by Ricanek P et al. [13] This was demonstrated in our CD cohort where a direct correlation of CDAI with CRP, TWC, and PLT was found [13]. These biomarkers should be collectively assessed and complement CDAI to predict disease activity in CD [14]. Our study also showed higher CRP and lower serum albumin level in active CD and these two biomarkers along with faecal calprotectin had always been vital in evaluating disease activity, disease monitoring, and treatment response in CD [15].

There was no significant correlation found between SES-CD and MPV in our CD cohort. To our knowledge, there were no other studies that have investigated the correlation between them. Therefore, more prospective studies may be needed to investigate the relationship between SES-CD and MPV before drawing any conclusion. As shown in the validation study of SES-CD by Daperno et al. [16] our study also found a significant correlation between SES-CD and CRP with ALB [16]. ESR and PAR in our study showed a positive correlation with SES-CD though it was not as strong as compared to CRP and ALB. The PAR has been used in several studies to predict future surgery in UC and CD patients [17,18]. The PAR was found to be

elevated in active CD and endoscopically active UC in our study. Reactive thrombocytosis and hypoalbuminemia from protein losing enteropathy in IBD patients resulting from ongoing intestinal inflammation may have contributed to the high value of PAR in active IBD [2,19]. With the easier access of PAR as compared to faecal calprotectin, especially in resource-limited countries, it should be researched further to assess its reliability as a potential non-invasive biomarker in assessing disease activity and treatment response.

We acknowledge that there were a few limitations to our study. Firstly, this is a single-center retrospective study with a limited number of patients. A larger number of recruited patients involving multiple centers would have been ideal. Secondly, in the evaluation and analysis of the laboratory parameters, there was no control group of healthy volunteers for paired analysis, as seen in previous studies [1,4,5]. Thirdly, the low number of patients in the severe category of the MES and CDAI presents a limitation in affecting the analysis and comparative evaluation of MPV in active and non-active IBD patients.

5. CONCLUSION

In conclusion, MPV should not be recommended as a complementary biomarker to evaluate and assess disease activity in both UC and CD. More prospective studies with a larger cohort are needed to examine the reliability of MPV as a complementary biomarker in IBD. From our data, PAR measurement in IBD seems to be a promising non-invasive biomarker in determining disease activity, although future studies are needed to validate and prove its usefulness.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Ethical approval was obtained from Medical Research & Ethics Committee (MREC) and Ministry of Health (MOH) Malaysia. Study no: NMRR-9-2840-50086(IIR) Date: 18 November 2019.

ACKNOWLEDGEMENTS

We thank all the clinical staffs for their effort and contribution to this study. We would also like to thank the Director General of Health for his permission to publish this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kapsoritakis AN, Koukourakis MI, Sfiridaki Potamianos SP, Kosmadaki MG, Koutroubakis IE, Kouroumalis EA. Mean platelet volume: A useful marker of inflammatory bowel disease activity. Am J Gastroenterol. 2001;96(3):776-81
2. Danese S, Motte Cd Cde L, Fiocchi C. Platelets in inflammatory bowel disease: clinical, pathogenic, and therapeutic implications. Am J Gastroenterol. 2004;99 (5):938-945
3. Öztürk ZA, Dag MS, Kuyumcu ME, Cam H, Yesil Y, Yilmaz N, et al. Could platelet indices be new biomarkers for inflammatory bowel diseases? Eur Rev Med Pharmacol Sci. 2013;17(3):334-341.
4. Liu S, Ren J, Han G, Wang G, Gu G, Xia Q, et al. Mean platelet volume: a controversial marker of disease activity in Crohn's disease. Eur J Med Res. 2012;17(1):27.
5. Saler T, Keşkek So, Ergin C, Ahbab S, Sağlam Z. Mean platelet volume in patients with inflammatory bowel disease. Gen Int Med Clin Innov. 2016;1(3):40-43.
6. Manesh Nasim, Ostadrahimi Alireza , Abedymanesh Saeid ,Mohammad Asghari Jafarabadi, Mohammad Hossein Somi, Ali Akbar Movassaghpour et al. Added predictive ability of mean platelet volume and red cell distribution width to inflammatory parameters in disease activity of ulcerative colitis. Euroasian Journal of Hepato-Gastroenterology. 2013; 3(2):103-107.
7. Sobolewska A, Włodarczyk M, Stec-Michalska K, Fichna J, Wiśniewska-Jarosińska M. Mean platelet volume in crohn's disease patients predicts sustained response to a 52-week infliximab therapy: A pilot study. Dig Dis Sci. 2016;61(2):542-549.

8. Yüksel O, Helvaci K, Başar O, Köklü S, Caner S, Helvaci N et al. An overlooked indicator of disease activity in ulcerative colitis: mean platelet volume. Platelets. 2009;20(4):277-281.
9. Christensen B, Rubin DT. Understanding endoscopic disease activity in IBD: How to incorporate it into practice. Curr Gastroenterol Rep. 2016;18(1):5.
10. Uchihara M, Kato J, Tsuda S, Yoshida T, Maekita T, Iguchi M et al. Blood biomarkers reflect integration of severity and extent of endoscopic inflammation in ulcerative colitis. JGH Open. 2017;1(3):98-104.
11. Rosenberg L, Lawlor GO, Zenlea T, Goldsmith JD, Gifford A, Falchuk KR, et al. Predictors of endoscopic inflammation in patients with ulcerative colitis in clinical remission. Inflamm Bowel Dis. 2013;19 (4):779-784.
12. Lee SH, Walshe M, Oh EH, Hwang SW, Park SH, Yang DH et al. Early changes in serum albumin predict clinical and endoscopic outcomes in patients with ulcerative colitis starting anti-tnf treatment. Inflamm Bowel Dis. 2020;309.
DOI: 10.1093/ibd/izaa309.
[Epub ahead of print]
13. Ricanek P, Brackmann S, Perminow G, Lyckander LG, Sponheim J, Holme O et al. Evaluation of disease activity in IBD at the time of diagnosis by the use of clinical, biochemical, and fecal markers. Scand J Gastroenterol. 2011;46(9):1081-1091.
14. Nakarai A, Kato J, Hiraoka S, Inokuchi T, Takei D, Morito Y et al. Slight increases in the disease activity index and platelet count imply the presence of active intestinal lesions in C-reactive protein-negative Crohn's disease patients. Intern Med. 2014;53(17):1905–1911.
15. Shiga H, Abe I, Onodera M, Moroi R, Kuroha M, Kanazawa Y et al. Serum C-reactive protein and albumin are useful biomarkers for tight control management of Crohn's disease in Japan. Sci Rep. 2020; 10(1):511.
16. Daperno M, D'Haens G, Van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. Gastrointest Endosc. 2004;60(4):505-512.
17. Turkeltaub Joshua A, Waljee Akbar K, Govani Shail M, Limsrivilai Julajak, Higgins Peter, Stidham Ryan W. Platelet-to-albumin ratio is a predictor of colectomy within 90 days in patients hospitalized for severe ulcerative colitis, American Journal of Gastroenterology. 2016;111: S315
18. Stidham RW, Guentner AS, Ruma JL, Govani SM, Waljee AK, Higgins PD. Intestinal dilation and platelet:albumin ratio are predictors of surgery in stricturing small bowel crohn's disease. Clin Gastroenterol Hepatol. 2016;14(8):1112-1119.
19. Furfaro F, Bezzio C, Maconi G. Protein-losing enteropathy in inflammatory bowel diseases. Minerva Gastroenterol Dietol. 2015;61(4):261-265.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/66302