

Comparison of Monocyte to Lymphocyte and Platelet to Lymphocyte Ratio between Patients with Depression according to Severity of Disease

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Abstract

Background: Depression is one of the most common psychiatric disorders with global public health concern that is linked to systemic inflammation. The monocyte to lymphocyte (MLR) and platelet to lymphocyte ratio (PLR) are partially new markers which may be evaluated with simple blood test and which are shown to be highly informative in showing chronic low grade inflammation associated with pathophysiology of depressive disorder.

Objective: To evaluate the relation of MLR and PLR between patients with depression according to severity of disease.

Methods: This observational study was conducted in the Department of Psychiatry of Jahurul Islam Medical College Hospital (JIMCH), Bajitpur, Kishoregonj between November 2012 and April 2013. Subjects between the age group of 25 and 55 were included in the study that involved 253 subjects with diagnosed depressive disorder according to the criteria of Diagnostic and Statistical Manual of Mental Disorders, Revised Text (DSM IV-TR) who received no pharmacological therapy of depression within the past 01 month. A sociodemographic information form and the Hamilton Rating Scale for depression (HAM-D) were administered. Patients were classified into four groups according to their HAM-D score such as mild, moderate, severe and very severe depression. Blood sample were taken for biochemical analysis and complete blood parameters were evaluated in the hematology laboratory of JIMCH. All data were expressed as mean±SD. For statistical analysis, Chi-square test (χ^2) was used to compare categorical variables, frequencies, and ratios. An independent sample 't' test was used to compare normally distributed variables between two groups.

Results: In the present study, it was found significant differences in the MLR, PLR, monocyte, leukocyte values of the patient group with depression according to severity of disease. Severe and very severe depression had significantly higher MLR levels compared to patients with

mild and moderate depression. On the other hand, mild and moderate depression had significantly higher PLR levels compared to patients with severe and very severe depression.

Conclusion: The findings of the study reveal that higher HAM-D scores are associated with higher MLR and lower PLR levels in patients with depressive illness compared to patients with lower HAM-D scores. Moreover, a high MLR values supports the view that inflammation is a critical factor in the etiology of depression.

Keywords: Depression, Lymphocyte, Monocyte, Platelet, Inflammation.

Introduction

Depression is a mental disease with worldwide public health concern, especially in developing countries and it is associated with imminent disability, social burden and reduced quality of life.^{1,2} It affects more than 168 million people globally and is one of the major causes of disease burden, accounting for the fifth highest global years lived with disability; this rate rises to the third highest in high income countries given the higher rate of prevalence.³ It also disrupts the ordinary flow of daily life and can manifest across all ages including the young and old.⁴ The white blood cell (WBC) count, a non-specific inflammatory marker is usually measured as part of the complete blood count (CBC) panel. Moreover, a few reports suggest that depression and stress are accompanied by disturbances in total white blood cell counts (i.e., leukocytosis) and leukocyte subset [i.e., neutrophilia, monocytosis as well as decreased lymphocytes (lymphopenia) counts^{5,6}], hypertension, diabetes mellitus and atherosclerotic cardiovascular disease.⁷

Previous studies demonstrated that depression is associated with elevated inflammatory markers including C-reactive protein (CRP), interleukin-6 (IL-6), and interleukin-1 (IL-1) that may play role in the etiopathogenesis of depression.⁸ A recent study showed that elevated level of CRP is associated

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with increased risk of depression and psychological distress.⁹ Patients with depressive illness have elevated levels of peripheral and central proinflammatory cytokines and proinflammatory agents have been shown to facilitate the progression of depressive symptoms.⁸ Importantly the activation of neutrophils can cause oxidative stress by releasing reactive oxygen species which may contribute to the pathogenesis of depression.¹⁰ Platelets and lymphocytes also can release proinflammatory cytokines which are involved in the development and progress of inflammatory diseases. The platelet to lymphocyte ratio (PLR) was calculated by combining the ratio of both.¹¹ A number of studies have shown that monocyte to lymphocyte (MLR) and PLR is likely to be higher in severe and chronic mental illness when compared with healthy subjects.¹² Neutrophil and leukocyte subsets play an important role in inflammatory processes to decrease and normalize high pretherapeutic serum proinflammatory cytokine levels.¹³ The purpose of the present study is to evaluate the relation of MLR and PLR between patients with depression according to severity of disease.

Materials and Methods

This observational study was conducted in the Department of Psychiatry of Jahurul Islam Medical College Hospital (JIMCH), Bajitpur, Kishoregonj from November 2012 to April 2013. Study subjects between the age group of 25 and 55 were included in the study that involved 253 subjects with diagnosed depressive disorder according to the criteria of Diagnostic and Statistical Manual of Mental Disorders, Revised Text (DSM IV-TR) who reported at the Out Patient Department (OPD) of Department of Psychiatry of JIMCH, Bajitpur, Kishoregonj and had undergone no pharmacological therapy within the previous month. The Sociodemographic characteristics of the patients and controls were similar and age, sex, body mass index (BMI), level of education, socioeconomic status, occupation and marital status were adjusted to prevent any effect on the hemogram variables.

Patients were evaluated for severity of depressive symptoms by using Hamilton Rating Scale for Depression (HAM-D). HAM-D has proven useful for many years as a method of determining a patient's level of depression.¹⁴ HAM-D consists of 21 items but the scoring is based on the first 17 items. Eight items are scored on a 5-point scale, ranging from zero point (not present) to four points (severe). Nine items are scored from 0 to 2. Total score is evaluated as follows; 0-7=Normal, 8-13=Mild Depression, 14-18=Moderate Depression, 19-22=Severe Depression, ≥ 23 =Very Severe Depression.

Patients with psychiatric diseases having comorbidity according to the criteria of Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) inflammatory or

autoimmune diseases, severe systemic diseases and using of medical treatment to affect the white blood cell counts such as hematopoietic system disorders, active infections, hypertension, diabetes mellitus, epilepsy, myocardial infarction, heart failure and other cardiac disease, hepatic failure, renal failure, alcohol or other substance addiction, severe head injury, mental retardation, pregnancy, obesity (BMI>30 kg/m²), drug use for any reason, smoking habit were excluded from the study. All the selected patients were informed in detail about the aim, objectives and procedure of the study and were encouraged for their voluntary participation. An informed written consent was taken from each participant. Detail personal, medical, family, socio-economic, occupational and drug history were taken as well. Thorough physical examination of each patient was done and was documented. Blood was taken for biochemical analysis. After 12 hours of fasting, blood samples of study subjects were taken from antecubital vein and stored in hemogram tubes (08 am), after which complete blood parameters were evaluated in the hematology laboratory of JIMCH. The study was approved by the local ethics committee.

All data were expressed as mean \pm SD. For statistical analysis, Chi-square test (χ^2) was used to compare categorical variables, frequencies, and ratios. An independent sample 't' test was used to compare normally distributed variables between two groups. Statistical analyses were performed by using Statistical Package for the Social Sciences (SPSS; version 16.0). In the interpretation of results, p value of <0.05 was considered as statistically significant.

Results

In this study, baseline characteristics of study population in respect of age, sex, BMI, education, socioeconomic status, occupation and marital status were similar as their differences were statistically non-significant (Table-I).

Measurement of the complete blood count parameters of study subjects are expressed in Table-II and were compared regarding severity of depression with MLR and PLR between groups. All patients were divided into two groups according to scores of HAM-D such as mild and moderate or severe and very severe depression (HAM-D scores 8-18 or ≥ 19). In the present study, significant differences were found in the monocyte, leukocyte values of the patient group with depression according to severity of disease. Severe and very severe depression group had significantly higher MLR levels when compared to patients with mild and moderate depression. On the other hand, mild and moderate depression had significantly higher PLR levels compared to patients with severe and very severe depression.

Table-I: Sociodemographic characteristics of study subjects (n=253)

| Variables | Mild (n=44) | Moderate (n=39) | Severe (n=42) | Very severe (n=128) | P value |
|------------------------------|----------------------|----------------------|----------------------|------------------------|------------|
| Age (years) | 32.3±11.2 (25-55) | 33.4±12.1 (25-55) | 35.3±13.4 (25-55) | 38.6±12.7 (25-55) | 0.541 |
| Sex | | | | | |
| Male | 7(17%) | 9(23%) | 11(26.2%) | 30(23.4%) | 0.213 |
| Female | 37(83%) | 30(77%) | 31(73.8%) | 98(76.6%) | 0.312 |
| BMI (kg/m ²) | 19.8±3.1 | 23.8±4.1 | 21.8±3.9 | 22.1±3.2 | 0.756 |
| Education | | | | | |
| ≤5 years | 12(26.34%) | 10(25.2%) | 13(30.24%) | 31(24.41%) | 0.134 |
| 6-8 years | 16(37.2%) | 15(39.37%) | 16(37.32%) | 46(36.22%) | 0.221 |
| 9-11 years | 11(25.21%) | 9(23.2%) | 9(22.31%) | 26(20.13%) | 0.423 |
| >11 years | 5(11.31%) | 5(12.23%) | 4(10.13%) | 25(19.24%) | 0.342 |
| Socioeconomic status (score) | 1.60±0.80 (1-4) | 1.58±0.33 (1-4) | 1.62±0.60 (1-4) | 1.70±0.58 (1-4) | 0.859 |
| Occupation (score) | 2.02±1.10 (1-4) | 2.21±1.30 (1-4) | 2.09±1.02 (1-4) | 2.17±1.17 (1-4) | 0.975 |
| Married | 27(61.16%) | 23(58.11%) | 31(74.1%) | 90(70.61%) | 0.225 |

Data were expressed as mean±SD. Figures in parentheses indicate ranges. Statistical analysis was done with independent sample 't' test and Chi-square test

Table-II: Comparison of complete blood count parameters of the study subjects (n=253)

| Variables | Mild (n=44) | Moderate (n=39) | Severe (n=42) | Very severe (n=128) | P value |
|---|----------------|--------------------|------------------|------------------------|------------|
| Lymphocyte count (10 ⁹ /L) | 2.11±0.7 | 2.45±0.5 | 2.42±0.8 | 2.37±0.7 | 0.02 |
| Lymphocyte (%) | 30.14±6.1 | 35.01±7.2 | 34.6±7.1 | 33.02±7.8 | 0.02 |
| Monocyte count (10 ⁹ /L) | 0.54±0.18 | 0.57±0.17 | 0.59±0.18 | 0.64±0.19 | 0.01 |
| Monocyte (%) | 6.02±2.12 | 6.33±2.14 | 6.61±2.19 | 7.11±2.18 | 0.01 |
| Leukocyte count (10 ⁹ /L) | 6.58±2.12 | 7.22±1.43 | 8.22±1.94 | 9.22±2.13 | 0.03 |
| Platelet count (10 ⁹ /L) | 249±55.2 | 231.14±60.4 | 219.12±51.2 | 205.44±62.1 | 0.04 |
| RBC count (10 ³ /mm ³) | 4.51±0.47 | 4.46±0.57 | 4.80±0.62 | 4.62±0.51 | 0.072 |
| Hemoglobin (gm/dl) | 12.8±1.2 | 13.5±1.4 | 13.2±1.2 | 13.3±1.5 | 0.084 |
| Hct (%) | 39.9±3.2 | 40.1±3.7 | 39.4±3.8 | 39.2±4.1 | 0.963 |
| MLR | 0.25±0.7 | 0.26±0.03 | 0.28±0.13 | 0.30±0.4 | <0.001 |
| PLR | 118.11±52.4 | 98.8±39.4 | 93.25±40.31 | 87.25±31.4 | 0.01 |

Data were expressed as mean±SD. Figures in parentheses indicate ranges. Statistical analysis was done with independent sample 't' test and Chi-square test

Discussion

In this study, we evaluated leukocyte, monocyte, lymphocyte, platelet counts, MLR and PLR in patients expressing a depressive episode and found that higher HAM-D scores were associated with higher monocyte, leukocyte values in the patient group with depression according to severity of disease, while lymphocyte percentages were decreased in the group of severe and very severe patient in comparison to the moderate depression group. Similar observation were also reported by several investigators.^{15,16}

With this result, it can be pointed out that inflammation plays very important role in the pathogenesis of depression.¹⁷ Elevated monocyte counts and alterations in their functionality have been observed in depression. Platelets get involved in the first-line inflammatory response to modulate the recruitment of neutrophils, macrophages and their effectors as well as endothelial permeability. The lymphocyte is a specific inflammatory mediator that serves as regulator in the adaptive immune response.¹⁸ The study evaluated the inflammatory ratios, e.g. MLR and according to this result severe and very severe depression had significantly higher MLR levels when

compared to patients with mild and moderate depression. These results are consistent with results from other studies that reported increased MLR in patients with depression.¹⁹

PLR is a relatively novel marker that gives information about inflammation and thrombosis and has been widely used as a prognostic indicator in cardiovascular disease.²⁰ In this study, Platelet number was decreased gradually in patients with depression according to their severity and we found that mild as well as moderate depression had significantly higher PLR levels when compared to patients with severe and very severe depression. Similar observation was also reported by several investigators.²¹ However, many other studies presented contradictory results regarding PLR; namely, a meta-analysis reported a higher PLR value in depressive illness patients when compared with healthy controls²² while other studies showed a lower PLR value²³ or no differences in PLR between patients with depression and healthy controls.²⁴ In this study, the RBC, Hct and hemoglobin values in the male and female patients were within normal ranges and they were in accordance with the usual differences observed between the two sexes.

This study has several limitations. It would be better if we followed the patients and explored the relation between course of depression and MLR as well as PLR levels. We didn't evaluate the prognostic value of the MLR and PLR and its relation with cardiovascular and other systemic disease risk factors in these patients. Since we could not determine the subtype of depression, we could not assess the varieties related to this issue and further studies may determine the association between MLR, PLR and subtype of depression.

Conclusion

Findings of the study reveal that higher HAM-D scores are associated with higher MLR and lower PLR levels in patients with depressive illness when compared to patients with lower HAM-D scores. Moreover, a high MLR values support the view that inflammation is a critical factor in the etiology of depression.

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