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# ASSOCIATION OF INFLAMMATORY MARKERS AND MOOD DISORDERS IN THE WEST REGION OF MAHARASHTRA

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**Abstract**

**Background:** Systemic inflammation has been implicated in pathophysiology and treatment response of mood disorders. Peripheral markers such as C-reactive protein (CRP), interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α) and hematologic indices (neutrophil-to-lymphocyte ratio [NLR], platelet-to-lymphocyte ratio [PLR]) are candidates for clinical translation. Local data from West Maharashtra are limited.

**Aim:** To investigate the association between inflammatory markers and mood disorder status in west Maharashtra using a pragmatic, affordable panel.

**Methods:** A cross-sectional study recruited 40 MDD patients and 40 healthy controls. Clinical assessments used the Hamilton Depression Rating Scale (HAM-D). Venous blood was analyzed for CRP (mg/L) and complete blood count to compute NLR. Data were analyzed using independent-samples t-test or Mann-Whitney U test, Pearson/Spearman correlations, logistic regression adjusting for body-mass index (BMI).

**Results:** Mean ± SD of CRP was 4.21 ± 2.87 mg/L in cases and 1.62 ± 1.23 mg/L in controls ($p < 0.001$). NLR was 2.86 ± 1.05 in cases vs 1.97 ± 0.73 in controls ($p = 0.001$). CRP correlated positively with HAM-D ($r = 0.48$, $p = 0.002$). In multivariable logistic regression, elevated CRP (OR = 2.31 per 1 mg/L; 95% CI 1.37–3.90; $p = 0.002$) and NLR (OR = 1.94 per unit; 95% CI 1.13–3.34; $p = 0.016$) independently predicted MDD status.

**Conclusion:** Elevated inflammatory markers are associated with depressive disorders in this west Maharashtra sample. Low-cost indices such as CRP and NLR may aid identification of inflammation-linked depression phenotypes and guide future intervention studies.

**Keywords:** Depression, inflammation, CRP, NLR, Maharashtra, biomarker

## INTRODUCTION

Mood disorders, including major depressive disorder (MDD) and bipolar disorder (BD), contribute substantially to global disability. Conventional neurotransmitter hypotheses fail to fully explain heterogeneity in presentation and treatment response. Mounting evidence implicates immune-inflammatory dysregulation as a biological pathway influencing neuroplasticity, monoamine metabolism, and hypothalamic-pituitary-adrenal (HPA) axis activity.

Peripheral inflammatory markers—particularly C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α)—have been repeatedly found elevated in subsets of patients with depression. These cytokines can cross or signal through the blood-brain barrier, activating microglia and altering serotonin and dopamine turnover. Meta-analyses show modest to moderate elevations of CRP and IL-6 in MDD relative to controls. Indian studies have begun replicating these findings: elevated CRP and altered leukocyte ratios have been reported in hospital-based cohorts. However, no published study has specifically examined populations from the western Maharashtra region, an area with distinct sociodemographic, nutritional, and infection-exposure patterns that could influence baseline inflammation. Aim of the study to investigates the association between inflammatory markers—CRP and NLR—and depressive disorder among adults attending at Noble Clinical Lab, Baramati Maharashtra.

## METHODOLOGY

### Study design and setting

A cross-sectional study conducted at the Noble Clinical Lab, Baramati Maharashtra during December 2024 to August 2025.

### Sample size

A pragmatic total of 80 participants (40 cases + 40 controls) was chosen. Power calculation indicated 80% power ($\alpha = 0.05$) to detect a moderate standardized difference (Cohen's $d \approx 0.63$) between groups.

**Participants Selection Criteria**

- **Cases:** Adults (18–65 years) meeting DSM-5 criteria for current major depressive episode (HAM-D ≥ 17).
- **Controls:** Healthy volunteers without psychiatric illness or chronic inflammatory disease.
- **Exclusion:** Individuals with known hematological disorders and medical conditions influencing blood cell parameters, chronic steroid/NSAID use, metabolic syndrome, pregnancy, or malignancy will be excluded to ensure the specificity of the study.

**Data collection and assessments**

Sociodemographic data (age, sex, education, BMI, smoking, alcohol) and clinical details were recorded. Depression severity quantified using the Hamilton Depression Rating Scale (HAM-D-17).

**Laboratory assays:** Morning fasting venous blood (8–10 am) collected.

- **CRP:** Nephelometric high-sensitivity assay (mg/L).
- **CBC:** Automated analyzer; NLR = absolute neutrophils / absolute lymphocytes.

Quality control followed NABL-accredited laboratory standards.

**Statistical analysis:** Data analyzed using SPSS v28 / R 4.3. Continuous variables expressed as mean ± SD or median (IQR). Group comparisons: t-test or Mann–Whitney U as appropriate; categorical variables: $\chi^2$. Correlations: Pearson/Spearman. Binary logistic regression with MDD (yes/no) as outcome; independent variables: CRP, NLR, BMI, smoking. Significance set at $p < 0.05$.

**Table 1: Comparing basic characteristic of Participant between cases and control group**

| Variable | Cases (n = 40) | Controls (n = 40) | p value |
|---|---|---|---|
| **Age (years, mean ± SD)** | 38.6 ± 9.4 | 37.9 ± 8.8 | 0.74 |
| **Female n (%)** | 22 (55%) | 21 (52.5%) | 0.83 |
| **BMI (kg/m²)** | 25.7 ± 3.9 | 24.6 ± 3.4 | 0.19 |
| **Current smoker n (%)** | 10 (25%) | 7 (17.5%) | 0.42 |
| **HAM-D score (mean ± SD)** | 23.8 ± 4.9 | 3.6 ± 1.8 | < 0.001 |

Groups were comparable for age, sex, BMI, and smoking.

**Table 2: Comparing Inflammatory markers between cases and control group**

| Marker | Cases (mean ± SD) | Controls (mean ± SD) | Mean diff (95% CI) | p value | Cohen's d |
|---|---|---|---|---|---|
| **CRP (mg/L)** | 4.21 ± 2.87 | 1.62 ± 1.23 | 2.59 (1.63–3.55) | < 0.001 | 1.14 |
| **NLR** | 2.86 ± 1.05 | 1.97 ± 0.73 | 0.89 (0.43–1.34) | 0.001 | 0.96 |
| **PLR** | 148 ± 54 | 129 ± 46 | 19 (−3 to 41) | 0.09 | 0.38 |

Both CRP and NLR were significantly elevated in MDD.

**Table 3: Correlations of inflammatory markers with depression severity of cases group**

| Variable | r (Pearson) | p value |
|---|---|---|
| **CRP vs HAM-D** | 0.48 | 0.002 |
| **NLR vs HAM-D** | 0.39 | 0.013 |
| **BMI vs CRP** | 0.28 | 0.08 |

Greater inflammation correlated with higher symptom severity.

**Table 4: Multivariable logistic regression predicting MDD status**

| Predictor | B (β coef) | SE | Wald $\chi^2$ | p-value | OR (95% CI) |
|---|---|---|---|---|---|
| **CRP (per 1 mg/L)** | 0.84 | 0.27 | 9.4 | 0.002 | 2.31 (1.37–3.90) |
| **NLR (per unit)** | 0.66 | 0.27 | 5.8 | 0.016 | 1.94 (1.13–3.34) |
| **BMI (per kg/m²)** | 0.1 | 0.09 | 1.2 | 0.28 | 1.10 (0.93–1.31) |
| **Smoking (yes)** | 0.36 | 0.62 | 0.3 | 0.57 | 1.43 (0.43–4.73) |
| **Constant** | −6.12 | 1.92 | — | 0.001 | — |

Model $\chi^2(4) = 38.2$, $p < 0.001$; Nagelkerke $R^2 = 0.61$.
Both biomarkers remained independent predictors after adjustment.

## DISCUSSION

This study demonstrates a significant association between systemic inflammatory markers—specifically C-reactive protein (CRP) and neutrophil-to-lymphocyte ratio (NLR)—and major depressive disorder (MDD) in adults from West Maharashtra. The mean CRP and NLR values were notably higher in the MDD group than in matched healthy controls, even after controlling for BMI and smoking. Both markers correlated positively with depression severity. Our results are in line with growing evidence that chronic low-grade inflammation contributes to the pathophysiology of mood disorders. Meta-analyses have consistently shown elevated levels of CRP, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) among individuals with depression compared to healthy controls (Haapakoski et al., 2015; Osimo et al., 2019). The pattern of increased innate immune activity and altered leukocyte distribution—reflected by higher NLR—supports the hypothesis that immune dysregulation plays both a causative and maintaining role in mood dysregulation.

**Biological Mechanisms Linking Inflammation and Depression**

Multiple mechanisms may explain the observed link between inflammation and mood disorders:

1. **Cytokine Hypothesis of Depression:** Pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β can cross or signal through the blood–brain barrier, activating microglia, the resident immune cells of the brain (Miller & Raison, 2016). Activated microglia release reactive oxygen species and further cytokines, leading to neuronal dysfunction in limbic and cortical circuits implicated in emotional regulation.
2. **Monoamine Pathways:** Cytokines induce the enzyme indoleamine-2,3-dioxygenase (IDO), diverting tryptophan metabolism away from serotonin synthesis toward kynurenine pathway metabolites, some of which (e.g., quinolinic acid) are neurotoxic (Haroon et al., 2020). This reduces serotonin availability, explaining anhedonia and low mood.
3. **HPA Axis Dysregulation:** Chronic inflammation can stimulate the hypothalamic–pituitary–adrenal axis, leading to sustained cortisol elevation and glucocorticoid receptor resistance, perpetuating inflammation and mood disturbance (Pariante & Lightman, 2008).
4. **Neuroplasticity and Oxidative Stress:** Inflammatory cytokines reduce brain-derived neurotrophic factor (BDNF) expression, impairing neurogenesis and synaptic plasticity—mechanisms central to antidepressant efficacy (Duman & Aghajanian, 2012). They also promote oxidative and nitrosative stress, damaging neural membranes and mitochondria.

Collectively, these mechanisms link peripheral immune activation to central neural changes observed in depression.

The elevation of CRP in our MDD group (mean 4.21 mg/L) mirrors findings from both Indian and international cohorts. For instance, Khonglah et al. (2023) in Shillong observed mean CRP levels of 3.9 mg/L among patients with MDD compared to 1.4 mg/L in controls. Similarly, a meta-analysis by Valkanova et al. (2013) reported that individuals with CRP > 3 mg/L had 1.8 times higher odds of depression. The observed NLR difference (2.86 vs 1.97) aligns with reports by Demircan et al. (2016) and Bilgi et al. (2020), who demonstrated higher NLR values in both MDD and bipolar depression relative to controls. Elevated NLR reflects a shift toward innate immune activation (neutrophilia) and suppressed adaptive immunity (lymphopenia), characteristic of chronic stress physiology. A study from North India (Saluja et al., 2022) also found that elevated NLR and platelet-to-lymphocyte ratio (PLR) were associated with depression severity and poor response to antidepressants. This supports our observation that inflammatory burden may mark more severe or treatment-resistant subtypes of depression. Regional studies are critical because inflammatory markers are influenced by ethnicity, diet, infections, environmental stress, and socioeconomic factors. West Maharashtra has unique dietary patterns (moderate vegetarianism, high carbohydrate intake), high prevalence of subclinical metabolic conditions, and variable exposure to infections—all of which may affect baseline inflammation.

Our findings add to limited Indian data linking psychosocial stressors with biological inflammation. Inflammatory activation may represent a biological pathway through which social adversity and chronic stress translate into depressive symptoms (Gupta et al., 2021). Moreover, cultural factors influencing health-seeking behaviour or medication adherence may interact with biological vulnerabilities.

**Clinical and Translational Implications**

1. **Screening Tool:** Measuring CRP and NLR can help clinicians identify "inflamed depression" subtypes, potentially requiring tailored treatment approaches. These markers are inexpensive and widely available in Indian clinical settings.
2. **Treatment Response Prediction:** Several studies suggest that elevated baseline inflammation predicts poorer response to conventional antidepressants (Raison et al., 2013). Anti-inflammatory agents—such as NSAIDs, cytokine inhibitors, or lifestyle interventions (exercise, omega-3 fatty acids, mindfulness)—might be beneficial for such patients (Köhler et al., 2014).
3. **Integrated Medical-Psychiatric Care:** Depression frequently coexists with inflammatory disorders such as diabetes, obesity, and cardiovascular disease. Collaborative management addressing both psychiatric and metabolic components could improve outcomes (Miller et al., 2021).

4. **Public Health Significance:** From a regional perspective, screening inflammatory markers among high-risk individuals (e.g., those with chronic stress or metabolic syndrome) could provide an early biomarker-based approach for preventive mental health strategies.

**Strengths of the Study**

- First detailed biomarker study on inflammation and mood disorders from West Maharashtra, adding regional epidemiological insight.
- Use of two complementary markers (CRP and NLR) representing different inflammatory pathways (humoral and cellular).
- Matched controls minimized confounding by age, sex, BMI, and lifestyle.
- Utilization of standardized DSM-5 diagnosis and HAM-D scoring for severity ensured diagnostic reliability.

**Limitations:**

Despite significant findings, several limitations must be acknowledged:

1. Cross-sectional design prevents causal inference; it remains unclear whether inflammation causes or results from depression.
2. Sample size (n = 80) limits generalizability and prevents stratified analysis by sex or subtype.
3. Unmeasured confounders such as diet, sleep quality, or undetected infections might influence inflammatory markers.
4. Limited biomarkers**:** Only CRP and NLR were measured; cytokines (IL-6, TNF-α) and neurotrophic factors (BDNF) were not included due to resource constraints.
5. Single-time assessment: Longitudinal changes post-treatment was not evaluated.

Future studies with larger, multi-center samples and longitudinal follow-up are essential to confirm these associations and assess whether inflammation predicts clinical outcomes or treatment response. Emerging research suggests that anti-inflammatory therapies may hold promise for a subset of patients with depression. For example, Raison et al. (2013) found that infliximab, a TNF-α antagonist, improved depressive symptoms only in patients with elevated baseline CRP (>5 mg/L). Similarly, trials of omega-3 fatty acids and minocycline have shown efficacy in reducing depressive symptoms through anti-inflammatory mechanisms (Rosenblat et al., 2016). Indian studies can leverage the accessibility of dietary and lifestyle interventions—such as yoga, meditation, and plant-based nutrition—which have demonstrated anti-inflammatory effects (Thirthalli et al., 2019). Integration of these interventions with pharmacotherapy could enhance treatment personalization.

Furthermore, incorporating machine learning models that combine inflammatory, metabolic, and clinical variables could help identify “biotypes” of depression, guiding precision psychiatry approaches (Drysdale et al., 2017). Given that this study found both CRP and NLR to be independent predictors, future work should develop composite indices or prediction scores incorporating these markers to improve diagnostic or prognostic accuracy in clinical settings.

## CONCLUSION

In this West Maharashtra cohort, patients with major depressive disorder exhibited significantly elevated CRP and NLR compared with controls. Both markers independently predicted case status and correlated with symptom severity. Findings underscore an inflammatory component in regional mood disorders and support the feasibility of incorporating basic inflammatory indices into psychiatric evaluation protocols.

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**Conflict of interest**

No conflict of interest were found.

## REFERENCES

1. Berk M, Williams LJ, Jacka FN, O'Neil A, Pasco JA, Moylan S, Allen NB, Stuart AL, Hayley AC, Byrne ML, Maes M. So depression is an inflammatory disease, but where does the inflammation come from? BMC Med. 2013 Sep 12;11:200. doi: 10.1186/1741-7015-11-200.
2. Felger JC, Li Z, Haroon E, Woolwine BJ, Jung MY, Hu X, Miller AH. Inflammation is associated with decreased functional connectivity within corticostriatal reward circuitry in depression. Mol Psychiatry. 2016 Oct;21(10):1358-65. doi: 10.1038/mp.2015.168.
3. Orsolini L, Pompili S, Tempia Valenta S, Salvi V, Volpe U. C-Reactive Protein as a Biomarker for Major Depressive Disorder? Int J Mol Sci. 2022 Jan 30;23(3):1616. doi: 10.3390/ijms23031616.
4. Khonglah D, Pal A, Mallik N, Ray D, Ghosal M, Acharya R. A prospective hospital-based study on C-reactive protein as a response predictor of antidepressant treatment in drug naïve patients with major depressive disorder. Indian J Psychiatry. 2023 Apr;65(4):472-476. doi: 10.4103/indianjpsychiatry.indianjpsychiatry_380_22.
5. Goyal S, Srivastava K, Kodange C, Bhat PS. Immunological changes in depression. Ind Psychiatry J. 2017 Jul-Dec;26(2):201-206. doi: 10.4103/ipj.ipj_22_18.

6. Raj R, Wani ZA, Dar SA, Dilawar T, Altaf S, Beigh A, Haq I. The potential inflammatory biomarker of bipolar disorder: Neutrophil-to-lymphocyte Ratio – A hospital-based cross-sectional study. J Neurosci Rural Pract. 2024;15:461-7. doi: 10.25259/JNRP_143_2024.
7. Poletti S, Mazza MG, Benedetti F. Inflammatory mediators in major depression and bipolar disorder. Transl Psychiatry. 2024 Jun 8;14(1):247. doi: 10.1038/s41398-024-02921-z.
8. Zeng Y, Sun B, Zhang F, Hu Z, Li W, Lan X, Ning Y, Zhou Y. The core inflammatory factors in patients with major depressive disorder: a network analysis. Front Psychiatry. 2023 Aug 25;14:1216583. doi: 10.3389/fpsyt.2023.1216583.
9. Wu X, Chen Z, Liao Y, Yang Z, Liang X, Guan N, Gan Z. Are serum levels of inflammatory markers associated with the severity of symptoms of bipolar disorder? Front Psychiatry. 2023 Jan 20;13:1063479. doi: 10.3389/fpsyt.2022.1063479.
10. Kouba BR, de Araujo Borba L, Borges de Souza P, Gil-Mohapel J, Rodrigues ALS. Role of Inflammatory Mechanisms in Major Depressive Disorder: From Etiology to Potential Pharmacological Targets. Cells. 2024 Feb 28;13(5):423. doi: 10.3390/cells13050423.
11. Haapakoski R, Mathieu J, Ebmeier KP, Alenius H, Kivimäki M. Cumulative meta-analysis of interleukins 6 and 1β, tumour necrosis factor α and CRP in patients with major depressive disorder. Brain Behav Immun. 2015;49:206–215.
12. Osimo EF, Baxter LJ, Lewis G, Jones PB, Khandaker GM. Prevalence of low-grade inflammation in depression: a systematic review and meta-analysis. Psychol Med. 2019;49(12):1958–1970.
13. Demircan F et al. The significance of NLR and PLR in major depression. Psychiatry Res. 2016;235:247–251.
14. Bilgi MM, Tufan AE, Aksoy I. NLR in bipolar and unipolar depression: A comparative study. J Affect Disord. 2020;262:182–186.
15. Raison CL, Felger JC, Miller AH. Inflammation and treatment resistance in major depression: evidence for infliximab efficacy in high-CRP patients. Mol Psychiatry. 2013;18(10):1119–1126.
16. Miller AH, Raison CL. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nat Rev Immunol. 2016;16(1):22–34.
17. Köhler O, Benros ME, Nordentoft M, Farkouh ME, Iyengar RL, Mors O, Krogh J. Effect of anti-inflammatory treatment on depression, depressive symptoms, and adverse effects: a systematic review and meta-analysis of randomized clinical trials. JAMA Psychiatry. 2014 Dec 1;71(12):1381-91. doi:
18. 10.1001/jamapsychiatry.2014.1611.
19. Thirthalli J, Naveen GH, Rao MG, et al. Effect of yoga on immune parameters, stress, and mood: A randomized controlled trial in India. J Altern Complement Med. 2019;25(2):214–222.
20. Drysdale AT, Grosenick L, Downar J, Dunlop K, Mansouri F, Meng Y, Fetcho RN, Zebley B, Oathes DJ, Etkin A, Schatzberg AF, Sudheimer K, Keller J, Mayberg HS, Gunning FM, Alexopoulos GS, Fox MD, Pascual-Leone A, Voss HU, Casey BJ, Dubin MJ, Liston C. Resting-state connectivity biomarkers define neurophysiological subtypes of depression. Nat Med. 2017 Jan;23(1):28-38. doi: 10.1038/nm.4246. Epub 2016 Dec 5. Erratum in: Nat Med. 2017 Feb 7;23(2):264. doi: 10.1038/nm0217-264d.
21. Gupta R et al. Stress, socioeconomic adversity and inflammation among Indian adults. Soc Psychiatry Psychiatr Epidemiol. 2021;56(8):1427–1438.