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Original Article

Association between the Blood-Inflammatory Index with Depression and Anxiety in a Large Population

*#Mina Nosrati [1,2], #Hossein Hatamzadeh [2], Amin Mansoori [3,4,5], Mahsa Tousi [2], Shakiba Najjar Khalilabad [6], Fateme Rojoee [6], Fatemeh Mohammadyari [7], Gordon A. Ferns [8], *Habibollah Esmaily [4,9], *Majid Ghayour-Mobarhan [1,2]*

1. *International UNESCO Center for Health-Related Basic Sciences and Human Nutrition, Mashhad University of Medical Sciences, Mashhad, Iran*
2. *Department of Nutrition, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
3. *Department of Applied Mathematics, Ferdowsi University of Mashhad, Mashhad, Iran*
4. *Social Determinants of Health Research Center, Mashhad University of Medical Sciences, Mashhad, Iran*
5. *Mathematical Biology Research Laboratory (MBRL), Faculty of Mathematical Sciences, Ferdowsi University of Mashhad, Mashhad, Iran*
6. *Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
7. *School of Medicine, Guilan University of Medical Sciences, Rasht, Iran*
8. *Department of Medical Education, Brighton and Sussex Medical School, Brighton, United Kingdom*
9. *Department of Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran*

***Corresponding Authors:** Emails: esmailyh@mums.ac.ir, ghayourm@mums.ac.ir
#Equally contributed authors

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Abstract

Background: Inflammatory indices have been linked to mood disorders. We aimed to examine whether these inflammatory indices are associated with the severity of depression and anxiety as measured by Beck scores.

Methods: This cross-sectional analysis included 9,704 participants aged 35–65 years from the Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) cohort study. Depression and anxiety were assessed using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Inflammatory indices were calculated based on hematological and biochemical parameters. Multinomial logistic regression was applied to evaluate the associations between inflammatory markers and mood disorder severity.

Results: In cases of severe depression, the neutrophil-to-lymphocyte ratio (NLR), white blood cell (WBC) count, and serum high-sensitivity C-reactive protein (hs-CRP) levels were significantly higher (OR = 1.29, 1.08, and 1.01, respectively; $P < 0.05$) than in individuals with minimal depression. Serum hs-CRP levels were also significantly higher (OR = 0.98; 95% CI: 0.95–0.99) in participants with moderate anxiety compared with those with minimal anxiety.

Conclusion: Higher levels of depression were associated with increased inflammatory hematological indices, and that the severity of depression was related to elevated levels of NLR, WBC, and hs-CRP.

Keywords: Depression; Anxiety; C-Reactive protein; Inflammation; Blood

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Introduction

The WHO has estimated that the number of individuals suffering from depression and other mental disorders is increasing globally (https://www.who.int/news-room/fact-sheets/detail/depression). Mental health disorders are generally classified into two major subgroups: depressive disorders and anxiety disorders. These conditions may manifest through various symptoms that can persist for months or even years. The recurrence of such symptoms can profoundly affect patients' quality of life and functional capacity (1). Anxiety disorders include generalized anxiety disorder, panic disorder, social anxiety disorder, agoraphobia, and specific phobias, which together affect approximately 374 million people worldwide. Depressive disorders are characterized by low mood, impaired cognitive function, and diminished volitional activity, and are estimated to affect around 221 million people globally (2). Depression will become one of the major global health problems by 2030; however, the underlying mechanisms of depression and other mental disorders have not yet been fully understood (3). Psychiatric illnesses, such as depression and anxiety, are closely correlated with an inflammatory process (4). Pro-inflammatory markers increase the risk of occurrence and progression of mental disorders (5, 6). Some inflammatory biomarkers such as high-sensitivity C-Reactive Protein (hs-CRP) (7), cytokines, and oxidative stress indicators have been investigated in relation to depression using various parameters (6).

The platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and monocyte-to-lymphocyte ratio (MLR) are inflammatory indices that can be calculated using a routine blood count test. Due to their high sensitivity and easy availability, these indices can be used as systemic inflammation markers in infections, autoimmune diseases, and metabolic disorders (6). The role of PLR, NLR, and MLR suggests that inflammation plays a potential role in the pathophysiology of psychiatric disorders, including depression (6). The comorbidity of depression and anxiety has been well documented; however, investigations into the relationship between inflammation and anxiety symptoms remain infrequent (7).

Despite numerous studies conducted in this field, the relationship between hematological inflammatory indicators and depression and anxiety remains controversial (6). Therefore, we conducted a study to investigate the association between blood inflammatory indices and depression and anxiety.

Materials and Methods

Data from the Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) cohort study were analyzed. The cohort study began in 2006 with 9,704 participants, aiming to evaluate the risk factors for cardiovascular diseases in individuals aged 35–65 years in Mashhad, all of whom were free of chronic diseases at baseline (8).

Demographic, socioeconomic, anthropometric, blood pressure, medical history, nutritional assessment, and physical activity level (PAL) data were collected from all participants (8). We excluded participants with incomplete depression and anxiety questionnaires. The final analysis was performed on 9,686 participants. All participants provided informed consent.

The study was approved by the Human Research Ethics Committee of Mashhad University of Medical Sciences (MUMS) (8).

Blood sample analysis

Fasting blood specimens (10–12 hours fasting) were drawn and collected in vacuum tubes from each participant at baseline according to a standard protocol. Blood samples for serum parameters were centrifuged within 30–45 minutes at room temperature, sent to the Bu Ali Research Institute in Mashhad, and stored in a –80 °C refrigerator for future analysis (8). The hematological parameters such as hemoglobin (Hb), platelets (PLT), white blood cells (WBC), neutrophils, lymphocytes, and biochemical parameters including triglycerides (TG), total cholesterol (TC), high-density

lipoprotein (HDL), low-density lipoprotein (LDL), fasting blood glucose (FBG), hs-CRP, and uric acid were measured as described previously (8-11).

Study definitions

The primary objective in the current study was to evaluate whether there was a relationship between the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), serum uric acid to HDL ratio (UHR), systemic immune-inflammation index (SII), and hemoglobin-to-platelet ratio (HPR) with depression and anxiety, and the secondary objective was to assess the changes in these indices with the progression of depression and anxiety.

The definition of the indices was as follows: NLR (neutrophil to lymphocyte ratio), PLR (platelet to lymphocyte ratio), UHR (uric acid to HDL ratio), SII ([neutrophil * platelet] / lymphocyte), HPR (Hb to platelet ratio).

Depression and anxiety diagnosis

To assess depression and anxiety, we used the Beck questionnaires. All participants completed the Beck questionnaires through interviews conducted by professional healthcare staff at baseline. The Beck Anxiety Inventory (BAI) was used to assess anxiety levels as follows: 0–7, minimal; 8–15, mild; 16–25, moderate; and 26–63, severe. The Beck Depression Inventory-II (BDI-II) was used to assess depression levels as follows: 0–13, none or minimal; 14–19, mild; 20–28, moderate; and 29–63, severe. These questionnaires have been validated in the Iranian population (12, 13).

Statistical analysis

The statistical analysis was performed using IBM SPSS version 25 (IBM Corp., Armonk, NY, USA) and MedCalc version 19.3 (Ostend, Belgium). The Kolmogorov–Smirnov test was used to evaluate the normality of data. Descriptive statistics were reported as the mean and standard deviation (SD) for quantitative variables with normal distribution. The chi-square test was used to compare qualitative variables. To explore the correlations between indicators and depression, a simple *t*-test was used. A multinomial regression test was employed to evaluate changes in the indicators compared with minimal scores as the reference group. Receiver operating characteristic (ROC) curve analysis was used to set the cut-off level of NLR, PLR, UHR, SII, and HPR to evaluate sensitivity and specificity of indicators to prediction of depression and anxiety. A $P<0.05$ was considered statistically significant.

Results

The final analysis was performed on 9,686 participants. The characteristics of these participants are shown in Table 1. Negative depression and anxiety were defined as minimal and mild, while positive depression and anxiety were defined as moderate and severe based on the BDI and BAI scores. The number of individuals with positive depression and anxiety was 1,998 and 2,412, respectively. For both groups, the percentage of women was higher than that of men (71.18% for depression and 72.64% for anxiety). The mean age of the positive and negative depression and anxiety groups was similar, and there were no significant differences between the groups in terms of age.

According to the BDI-II score, to evaluate the severity of depression, participants were divided into four groups as follows: none or minimal (n = 5,999), mild (n = 1,692), moderate (n = 1,295), and severe (n = 700) for both genders (Table 2). The percentage of females with depression was significantly higher than that of males across all severity levels of depression ($P < 0.001$). The NLR, SII, and WBC levels in severe depression were significantly higher than in minimal depression ($P < 0.05$). Patients with severe depression had significantly higher serum hs-CRP levels compared to those with minimal and mild depression ($P < 0.001$), and HPR in severe depression was significantly lower than in minimal and mild depression ($P < 0.001$) (Table 2).

Table 1: Clinical characteristics of the participants

Variable	Depression+ (n=1998) (Mean±SD)	Depression- (n=7691) (Mean±SD)	*P*-value	Anxiety+ (n=2412) (Mean±SD)	Anxiety- (n=7281) (Mean±SD)	*P*-value
Age (year)	47.91±8.37	48.12±8.23	0.304	47.91±8.31	48.13±8.24	0.304
Male	576 (28.82 %)	3303 (42.95 %)	0.001	660 (27.36 %)	3220 (44.22 %)	0.001
Female	1422 (71.18 %)	4388 (57.05 %)		1752 (72.64 %)	4061 (55.78 %)	
NLR	1.70±2.28	1.62±1.09	0.029	1.67±2.08	1.62±1.11	0.029
PLR	114.90±43.13	113.72±62.85	0.335	115.09±41.73	113.59±64.05	0.335
SII	399.64±471.40	377.21±340.00	0.021	393.24±429.73	378.14±349.38	0.021
HPR	0.063±0.02	0.065±0.02	<0.001	0.063±0.029	0.065±0.025	<0.001
UHR	0.345±0.125	0.341±0.122	0.221	0.345±0.111	0.341±0.126	0.221
WBC (µl)	6.17±1.64	6.06±1.54	0.005	6.11±1.58	6.07±1.56	0.005
MPV (fl)	10.07±0.98	10.09±2.22	0.480	10.04±0.96	10.10±2.27	0.480
Hs-CRP (mg/dl)	5.34±11.31	3.84±8.03	<0.001	5.25±11.10	3.79±7.90	<0.001
BMI (kg/m²)	28.39±5.10	27.75±4.62	<0.001	28.66±5.03	27.62±4.60	<0.001
PAL	1.62±0.29	1.58±0.28	<0.001	1.62±0.28	1.58±0.28	<0.001
SBP (mmHg)	120.64±19.89	122.05±18.13	0.002	121.25±19.31	121.93±18.24	0.002
DBP (mmHg)	78.37±11.78	79.26±11.08	0.002	78.66±11.53	79.22±11.13	0.002
WC (cm)	94.88±12.60	95.29±11.90	0.172	95.64±12.48	95.07±11.90	0.172
Glucose (mg/dl)	94.11±42.57	92.33±38.46	0.072	93.72±41.88	92.35±38.46	0.072
HDL (mg/dl)	42.52±9.80	42.91±9.96	0.115	42.93±9.84	42.81±9.97	0.115
LDL (mg/dl)	115.46±35.75	116.85±35.10	0.120	115.64±36.55	116.88±34.77	0.120
Cholesterol(mg/dl)	191.10±39.38	191.37±39.08	0.781	191.95±40.06	191.12±38.84	0.781
TG (mg/dl)	143.30±91.94	142.43±92.86	0.710	144.67±91.04	141.84±93.00	0.710
Diabetes Mellitus	328 (16.76 %)	1041 (13.70 %)	0.001	390 (16.46 %)	979 (13.63 %)	0.001

Abbreviations: NLR: Neutrophil Lymphocyte Ratio; PLR: Platelet Lymphocyte Ratio; SII: Systemic Immune Inflammation index ; HPR: Hemoglobin Platelet Ratio; UHR: Uric Acid Hemoglobin Ratio; WBC: Withe Blood Cell; MPV: Mean Platelet Volume; Hs-CRP: high-sensitivity C-Reactive Protein; BMI: Body Mass Index; PAL: Physical Activity Level; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; WC: Waist Circumference; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; TG: Tri-Glyceride;

Table 2: Comparison between BDI-II scores and inflammatory indices

Variables	Minimal (Mean±SD)	Mild (Mean±SD)	Moderate (Mean±SD)	Severe (Mean±SD)	*P*-value
Age(yr)	48.05±8.26	48.38±8.11	47.87±8.52	47.98±8.09	0.359
Male	2715	588[a]	406[a,b]	170[a,b,c]	<0.001
Female	3284	1104[a]	889[a,b]	530[a,b,c]	
NLR	1.61±1.13	1.64±0.89	1.66±0.82	1.78±3.70[a]	0.038
SII	376.34±366.14	380.34±221.94	388.73±238.78	420.17±730.06[a]	0.038
HPR	0.066±0.02	0.065±0.027	0.064±0.026	0.061±0.025[a,b]	<0.001
PLR	114.11±67.85	112.34±40.32	114.61±44.01	115.44±41.48	0.609
UHR	0.34±0.12	0.34±0.10	0.34±0.13	0.35±0.10	0.542
WBC (µl)	6.03±1.52	6.15±1.59[a]	6.14±1.61	6.22±1.70[a]	0.001
PDW (%)	12.76±2.63	12.81±2.02	12.79±2.02	12.84±1.92	0.817
MPV (fl)	10.10±2.46	10.07±0.92	10.05±1.01	10.09±0.93	0.899
Hs-CRP (mg/dl)	3.72±7.75	4.26±8.94	5.18±11.42[a,b]	5.64±11.13[a,b]	<0.001

a: Group 1 vs. Groups 2, 3, 4
b: Group 2 vs. Groups 3, 4
c: Group 3 vs. Groups 4
Group 1: dep 1; Group 2: dep 2; Group 3: dep 3; Group 4: dep 4.
Abbreviations: NLR: Neutrophil Lymphocyte Ratio; SII: Systemic Immune Inflammation index ; HPR: Hemoglobin Platelet Ratio; PLR: Platelet Lymphocyte Ratio; UHR: Uric Acid Hemoglobin Ratio; WBC: Withe Blood Cell; PDW: Platelet Distribution Width; MPV: Mean Platelet Volume; Hs-CRP: high-sensitivity C-Reactive Protein.

According to the BAI score, the participants were divided into four groups as follows: minimal (n = 4,665), mild (n = 2,616), moderate (n = 1,478), and severe (n = 934) for both genders (Table 3). The number of females with anxiety was significantly higher than that of males across all anxiety levels ($P < 0.001$). Serum hs-CRP levels in mild, moderate, and severe anxiety were significantly higher than in the minimal group ($P < 0.001$).

Table 3: Comparison between BAI scores and inflammatory indicators

Variables	minimal	mild	moderate	severe	*P*-value
Age(yr)	48.05±8.26	48.38±8.11	47.87±8.52	47.98±8.09	0.150
Male	2272	948[a]	422[a,b]	238[a,b,c]	<0.001
Female	2393	1668[a]	1056[a,b]	696[a,b,c]	
NLR	1.62±1.27	1.63±0.75	1.69±2.59	1.64±0.75	0.430
SII	378.24±407.84	377.98±206.96	396.07±522.32	388.80±215.37	0.402
HPR	0.062±0.025	0.064±0.024	0.064±0.031	0.062±0.026[a]	0.001
PLR	113.83±74.14	113.18±40.47	115.36±41.90	114.68±41.48	0.710
UHR	0.33±0.13	0.34±0.12	0.35±0.12	0.34±0.09	0.027
WBC (µl)	6.06±1.54	6.10±1.59[a]	6.06±1.56	6.18±1.61[a]	0.174
PDW (%)	12.78±2.77	12.82±2.06	12.75±1.94	12.71±2.02	0.666
MPV (fl)	10.07±1.75	10.15±2.97	10.05±0.95	10.04±0.97	0.315
Hs-CRP (mg/dl)	3.56±7.46	4.20±8.61[a]	5.04±10.93[a,b]	5.60±11.36[a,b]	<0.001

a: Group 1 vs. Groups 2, 3, 4
b: Group 2 vs. Groups 3, 4
c: Group 3 vs. Groups 4
Group 1: anx 1; Group 2: anx 2; Group 3: anx 3; Group 4: anx 4.
Abbreviations: NLR: Neutrophil Lymphocyte Ratio; SII: Systemic Immune Inflammation index; HPR: Hemoglobin Platelet Ratio; PLR: Platelet Lymphocyte Ratio; UHR: Uric Acid Hemoglobin Ratio; WBC: Withe Blood Cell; PDW: Platelet Distribution Width; MPV: Mean Platelet Volume; Hs-CRP: high-sensitivity C-Reactive Protein

The multinomial analysis showed that in severe depression, the levels of NLR, WBC, and hs-CRP increased significantly (OR: 1.29, 1.08, and 1.01; $P < 0.05$, respectively) compared with minimal depression. Accordingly, NLR, WBC, and hs-CRP had 29%, 8%, and 1% greater odds, respectively, in the severe group compared with the minimal group, and these indicators were independent predictors of depression severity. In the moderate anxiety group, hs-CRP levels increased significantly (OR: 0.98; 95% CI: 0.95–0.99) compared with the minimal group (Table 4).

As shown in Table 5, the serum hs-CRP cut-off values for depression and anxiety were 2.46 and 1.6 ($P = 0.001$), respectively. The sensitivity and specificity of the test for predicting mood disorders were 40.31% and 66.89% for depression, and 55.61% and 51.31% for anxiety, respectively. The area under the curve (AUC) values for the hs-CRP cut-offs were 0.54 (95% CI: 0.53–0.55) and 0.54 (95% CI: 0.53–0.55) for depression and anxiety, respectively.

Table 4: Multi-nominal Regression in depression and anxiety scales

Variable	Depression (ref: minimal)		Anxiety (ref: minimal)	
	OR (95 % CI)	*P*-value	OR (95 % CI)	*P*-value
Mild				
NLR	1.157 (0.976, 1.371)	0.092	0.865 (0.681, 1.100)	0.237
SII	1.000 (0.959, 1.030)	0.178	1.011 (0.978, 1.067)	0.261
PLR	0.999 (0.957, 1.012)	0.633	0.989 (0.945, 1.009)	0.739
UHR	0.925 (0.526, 1.128)	0.788	0.467 (0.227, 0.961)	0.039
WBC (µl)	1.053 (1.034, 1.206)	0.035	0.941 (0.876, 1.011)	0.096
Hs-CRP (mg/dl)	1.016 (0.938, 1.103)	0.111	0.980 (0.973, 0.988)	<0.001
Moderate				
NLR	1.189 (0.980, 1.441)	0.079	1.055 (0.818, 1.361)	0.680
SII	0.997 (0.967, 1.002)	0.161	1.000 (0.956, 1.016)	0.683
PLR	1.001 (0.978, 1.053)	0.562	1.001 (0.917, 1.015)	0.642
UHR	1.389 (0.789, 1.645)	0.254	1.177 (0.967, 1.443)	0.661
WBC (µl)	1.055 (0.997, 1.117)	0.062	0.989 (0.918, 1.067)	0.782
Hs-CRP (mg/dl)	1.016 (1.003, 1.122)	<0.001	0.988 (0.958, 0.995)	0.001
Severe				
NLR	1.298 (1.009, 1.670)	0.042	0.971 (0.751, 1.255)	0.822
SII	0.959 (0.908, 1.67)	0.151	1.007 (0.955, 1.015)	0.687
PLR	1.000 (0.957, 1.084)	0.983	1.012 (0.981, 1.027)	0.935
UHR	1.172 (0.926, 1.390)	0.084	1.141 (0.712, 1.335)	0.272
WBC (µl)	1.084 (1.007, 1.166)	0.031	0.972 (0.899, 1.051)	0.477
Hs-CRP (mg/dl)	1.015 (1.007, 1.124)	<0.001	0.966 (0.938, 1.014)	0.314

Abbreviations: NLR: Neutrophil Lymphocyte Ratio; SII: Systemic Immune Inflammation index; PLR: Platelet Lymphocyte Ratio; UHR: Uric Acid Hemoglobin Ratio; WBC: Withe Blood Cell; Hs-CRP: high-sensitivity C-Reactive Protein.

Table 5: ROC analysis of the predictive value of inflammation indices on prevalence of depression and anxiety

Variable	Cut-off value	Sensitivity (%)	Specificity (%)	+LR	-LR	AUC (95%CI)	P-value
Depression							
NLR	2.15	17.87	84.72	1.17	0.97	0.513 (0.503, 0.524)	0.076
SII	424.89	32.79	70.82	1.12	0.95	0.519 (0.509, 0.530)	0.011
HPR	0.05	40.56	65.45	1.17	0.91	0.537 (0.527, 0.547)	<0.001
PLR	126.11	34.26	68.69	1.09	0.96	0.510 (0.500, 0.520)	0.176
UHR	0.51	6.21	95.55	1.40	0.98	0.506 (0.496, 0.516)	0.423
WBC (µl)	6.5	35.66	68.10	1.12	0.94	0.518 (0.508, 0.528)	0.015
Hs-CRP (mg/dl)	2.46	40.31	66.89	1.22	0.89	0.541 (0.530, 0.550)	<0.001
Anxiety							
NLR	1.76	33.29	69.14	1.08	0.96	0.509 (0.499, 0.520)	0.185
SII	326.45	55.22	48.35	1.07	0.93	0.518 (0.508, 0.529)	0.010
HPR	0.05	39.42	65.41	1.14	0.93	0.536 (0.526, 0.546)	<0.001
PLR	98.26	64.79	38.99	1.06	0.90	0.517 (0.507, 0.527)	0.014
UHR	0.25	83.42	18.69	1.03	0.89	0.512 (0.502, 0.522)	0.069
WBC (µl)	6.4	36.84	65.60	1.07	0.96	0.506 (0.495, 0.516)	0.418
Hs-CRP (mg/dl)	1.6	55.61	51.31	1.14	0.87	0.543 (0.533, 0.553)	<0.001

Abbreviations: NLR: Neutrophil Lymphocyte Ratio; SII: Systemic Immune Inflammation index; HPR: Hemoglobin Platelet Ratio; PLR: Platelet Lymphocyte Ratio; UHR: Uric Acid Hemoglobin Ratio; WBC: Withe Blood Cell; Hs-CRP: high-sensitivity C-Reactive Protein.

Discussion

We explored the relationship between BDI-II scores and inflammatory indicators, including WBC, NLR, and hs-CRP values, in depressive patients. However, higher BDI-II scores were correlated with lower HPR values. Moreover, WBC, NLR, and hs-CRP were identified as independent predictors of depression.

Depression is a complex and prevalent disorder that often leads to a reduced quality of life, increased social burden, and, in some cases, death (14). Depression is correlated with the interaction between the nervous and immune systems (15). Chronic stress in depression leads to the suppression of the immune system (15). The main pathophysiological mechanism of depression involves alterations in the levels of interleukins (IL-1, IL-6) and tumor necrosis factor-alpha (TNF-α). However, although inflammatory cytokines are important and useful biomarkers for the diagnosis and treatment of diseases, their measurement is expensive and often limited in accessibility in developing countries (14).

Hematological tests, including WBC, RBC counts, and related indices, can be used as simple, cost-effective, and accessible inflammatory biomarkers (16). WBC and related indices including NLR, interact in inflammatory processes. Ongoing non-specific inflammation can be reflected by changes in neutrophil and lymphocyte counts, which may serve as markers of regulatory immune pathways (17). Higher levels of NLR lead to elevated cytokine production and oxidative stress, both of which are observed in depressive disorders (17-19). The role of inflammation in depression has been reported in several studies (4, 6, 20) and multiple studies have indicated an elevation in WBC and NLR levels in depressive patients (18, 21-23) that its consistent with our findings. Results from our study also showed that NLR, hs-CRP are correlated with the severity of depression.

Proinflammatory cytokines, including IL-1, IL-6, and TNF-α, play an important role in the pathophysiology of depression through alterations in neuroendocrine functions, neurotransmitter metabolism, monoamine metabolism, and synaptic plasticity (24, 25). IL-1 is secreted by endothelial cells, lymphocytes, monocytes and microglia (6). IL-6 is involved in the differentiation and stimulation of B-cells and the differentiation and activation of T-cells (26). TNF-α is known to cause elevated acute phase reactants and neutrophilia (6). IL-1, IL-6, and TNF-α lead to the upregulation of serotonin transporter mRNA and proteins. As a result, serotonin neurotransmission increases, and consequently, the levels of serotonin decline. The interaction between serotonin/serotonin transporter and inflammation may be a significant factor in the onset of depression (6, 25). hs-CRP, leucocytes, and neutrophils play a role in inflammation caused by cytokines in response to depression. It appears that an increased leucocyte/neutrophil ratio is followed by elevated IL-6 secretion from activated monocytes in depression (27). A reduced lymphocyte response to mitogen stimulation and disrupted neutrophil activity have been reported in patients with depression (6, 28). A decrease in the proliferation and serum levels of B-cells, T-cells, and lymphocytes (cellular immunity suppression) has been observed, whereas the serum concentrations of leucocytes and neutrophils increase in patients with major depressive disorder (MDD) (27, 29). Our study was also supported these findings.

We report that serum hs-CRP was correlated with the severity of depression and anxiety. The relationship between depression and anxiety and hs-CRP has also been demonstrated in previous studies (30, 31). However, both longitudinal and cross-sectional studies have shown that the relationship between higher levels of hs-CRP and depression is evident in populations with or without chronic disorders such as diabetes, cardiovascular disease, cancer, or renal disease (30, 20, 32). Nevertheless, hs-CRP is not only involved in immune-related molecular modifications; it has been suggested that hs-CRP increases secondary to the elevation of inflammatory cytokines, including IL-6, IL-10, and TNF-α, in patients with mood disorders (33). Also, serum hs-CRP levels are influenced by various factors such as sex, age, smoking status, eating

habits, medications, blood pressure, BMI, and lipid profile (30, 31).

The strength of our study lies in its large sample size and the observed increase in inflammatory indices with higher levels of depression and anxiety. However, our study has some limitations. First, data regarding medication use in depressive patients were not available.

Second, the assessment of depression and anxiety was based on self-rating scales rather than clinical diagnosis. Third, there were differences in the fundamental characteristics of the participants. Future studies should take into account medication use and variations in fundamental participant characteristics.

Conclusion

Higher levels of depression are correlated with increased inflammatory indices, and the severity of depression is associated with elevated levels of NLR, WBC, and hs-CRP. Furthermore, NLR, WBC, and hs-CRP levels greater than 29%, 8%, and 1%, respectively, were independent predictors of severe depression.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interests

The authors declare no conflict of interests.

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