Middle East Current Psychiatry

RESEARCH

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C-reactive protein as a biomarker for unipolar versus bipolar depression: a cross-sectional study

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Abstract

Background Differentiating unipolar depression from bipolar depression is clinically important. The identification of biomarkers that characterize the pathophysiology of each disorder may provide biological targets for treatment. The objective of the study was to demonstrate a relationship between CRP level and the severity of depressive symptoms and see if C-reactive protein (CRP) levels can be used as a biomarker to distinguish between unipolar and bipolar depression. A convenience sample of 90 individuals was consecutively recruited from the psychiatry outpatient clinic at Beni-Suef University Hospital, Egypt. They were divided into three equal groups: patients with major depressive disorder (MDD) (group 1), bipolar depression (group 2), and a healthy volunteer group (group 3). Patient groups were assessed using semi-structured interviews, and CRP levels were measured.

Results Patients with bipolar depression and MDD showed a significantly higher score on the Beck Depression Inventory scale than the control group (32.97 ± 2.4 vs. 31.93 ± 2.3 vs. 8.00 ± 2.3 in all groups respectively) (*P*-value < 0.001). Patients with bipolar depression and MDD showed a significantly higher serum CRP level than the control group (134.96 ± 16.45 vs. 133.86 ± 17.59 vs.56.04 ± 26.71 vs. in all groups respectively) (*P*-value < 0.001). In all studied groups, elevated plasma CRP levels have a significant linear correlation with the severity of depression as measured by the Beck Depression Inventory (BDI) ($r = 0.887$, *P*-value < 0.001).

Conclusions Serum CRP levels are significantly higher in MDD and BD patients when compared to controls. Individuals with higher CRP levels had more severe depression, and this finding was significantly higher in women than in men.

Keywords CRP, Bipolar depression, Unipolar depression

Background

Recent studies suggest that chronic inflammation may play a role in mental disorders. Circulating pro- and anti-inflammatory cytokine profiles are abnormal in patients with schizophrenia, MDD, and bipolar disorder [1]. Some meta-analyses have revealed an increase in the levels of inflammatory markers, such as C-reactive protein (CRP), homocysteine, tumour necrosis factor (TNF), and interleukin-6 (IL-6), in patients with depression. Specific genes may also cause both increased depression and

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inflammation, as some inflammation-related genes have been linked to major depression and bipolar disorder [2].

Tillett and Francis discovered C-reactive protein (CRP) in 1930. It is a pentraxin superfamily member. The discovery of a distinct third fraction in the sera of patients with pneumococcus infection that could precipitate the "C" polysaccharide derived from the pneumococcus cell wall was the first feature of this protein [3].

The liver primarily produces C-reactive protein because of a pentamer composed of five identical, non-covalently linked, 23-kD protomers that are folded into two antiparallel sheets using the "jelly roll" topology. For apoptotic cell membranes and bacterial cell walls, each protomer has a binding face with a PC-binding site [4].

The liver is what produces the vast majority of CRP. Although CRP production has been reported in a variety of other cell types, such as adipocytes, renal cells, neuronal cells, respiratory epithelial cells, and leukocytes, it is not believed that extrahepatic CRP production has a significant influence on plasma CRP concentrations [5, 6].

C-reactive protein levels in the blood rise during inflammatory conditions like rheumatoid arthritis, certain cardiovascular diseases, and infection. Within 24–72 h of severe tissue damage, such as trauma or progressive cancer, CRP plasma levels rise from around 1 µg/mL to over 500 µg. Age, gender, smoking status, weight, lipid levels, and blood pressure are all factors that can affect baseline CRP levels [7]. Thus, in obese patients, a calorie-restricted diet may reduce chronic inflammation and C-reactive protein (CRP) [8]. Active smokers with a C-allele at rs3093068 of 12 CRP single-nucleotide polymorphisms are more likely to have elevated CRP concentrations; smoking as a behaviour contributes to increased inflammation levels [9, 10].

Several studies have found that inflammatory markers can help distinguish between mood disorders and illness stages, as well as predict treatment response [10, 11].

The objective of the study

The study demonstrated a relationship between the level of CRP and the severity of depressive symptoms among those with MDD and bipolar disorder (depressive type).

Methods

Study design

This comparative cross-sectional study had the objective of exploring the relationship between CRP level and severity of depressive symptoms and whether the risk of the CRP level may be used as a biomarker to distinguish between unipolar and bipolar depression.

The inclusion criteria for the participants in this study included age 18–45 years old and having no history of other medical condition that make them in no need of taking medications or vitamins, and persons in that age group do not take vitamins or supplements on a regular basis.

The exclusion criteria of the participants in this study included a young age of less than18 years or more than 45 years, suffering of any chronic diseases that can affect CRP and suffering from any psychiatric diseases or disorders, pregnancy, or lactation. Participants with illicit drugs, substance use disorders, or other psychiatric disorders have been excluded from the study.

Samples

A convenience sample of 90 individuals was recruited based on the inclusion and exclusion criteria. The sample was divided into three equal groups, involving MDD: patients (group 1), bipolar depression patients (group 2) recruited from the psychiatry outpatient clinic at Beni-Suef University Hospital, Egypt, and a healthy volunteer group (group 3) recruited from the nursing and administrative staff at Beni-Suef University Hospital. They were matched with the patient groups in terms of age, sex, and socio-demographic status. Epi Info, version 3.5.1, 2008, was used to calculate the sample size. The patients who participated in the study were divided based on a confidence level of 95%, a power of 80%, and a 50% prevalence: 30 patients with MDD, 30 patients with BD, and 30 control subjects (sample size calculations: $n = [DEFF^*Np(1-p)]/[(d2/Z21-\alpha/2^*(N-1)+p^*(1-p)])$.

Data collection procedure

Individuals of both sexes, aged 18–45 years, were invited to participate in this study from February 2019 to August 2019. A total of 47 patients with MDD (previously diagnosed), 45 patients with bipolar depression (previously diagnosed), and 40 healthy volunteers were invited to participate in the study. However, 17 patients with MDD, 15 patients with bipolar depression, and 10 healthy volunteers were excluded if they had a chronic medical illness, comorbid substance use disorders or other psychiatric disorders, severe agitation, acute inflammation, were pregnant or lactating, or refused to participate.

Patients who were recruited from the psychiatry outpatient clinic at Beni-Suef University were diagnosed using a semi-structured interview derived from the DSM-5 (*Diagnostic and Statistical Manual of Psychiatric Disorders-5th Edition* — text revised criteria in the DSM-5 for the diagnosis of major depressive disorder and bipolar depression). The Beck Depression Inventory (BDI) was used to assess the severity of depression in the patient group. The assessment procedure lasted for an average of 60–90 min and included obtaining venous blood samples (5 ml) that were withdrawn.

Tools

I. Brief Semi-Structured Clinical Sheet, Psychiatry Clinic, Beni-Suef University Hospital

Clinical data were obtained (including socio-demographics, onset of illness, previous episodes, family history, medical history, previous treatments, adherence to medications).

II. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Arabic version

To apply the diagnostic criteria for MDD and bipolar disorder (depressive type) and to rule out other psychiatric disorders, the Structured Clinical Interview for DSM-IV (SCID-I) was used. The SCID-I is classified into separate modules according to the categories of diagnoses. Most of sections begin with an entry question that allows the interviewer to skip the related questions if they were not met. For all diagnoses, symptoms are coded as present, subthreshold, or absent [12].

III. Beck Depression Inventory (BDI), Arabic version

The Beck Depression Inventory (BDI) is a self-report scale used to track depressive symptoms such as sadness, guilt, loss of interest, social withdrawal, increase and decrease in appetite or sleep, suicidal ideation, and other behavioural manifestations of depression over time to monitor symptoms and assess response to therapeutic interventions among patients with depressive illnesses. It has an acceptable level of validity because it assesses a wide range of symptoms and attitudes related to depression. The inventory consists of 21 statements on a 4-point scale, with the subject choosing the one that best describes his or her current situation. Each statement refers to a distinct behavioural manifestation. Responses are graded on a 0–3 scale, with 0 indicating no disturbance, mild, moderate, or severe disturbance. The scale runs from 0 to 63, with a higher score indicating greater depression severity [13].

Statistical analysis

Data were coded and entered using the Statistical Package for the Social Sciences (SPSS v. 25). The data were summarized using the minimum, maximum, mean, and standard deviation for quantitative data and the frequency distribution for qualitative data for a descriptive analysis of the results. To compare the means of two groups of quantitative variables, the Student's *t*-test was used. The chi-square test was used to compare the frequency of events or two groups of categorical data. For the correlation coefficient (r), which describes the degree of relationship between two variables, the Pearson correlation test was used. The significant predictors were identified using ROC, AUC [14], and regression analysis. *P* 0.05 was deemed significant.

Result

Ninety participants were equally divided into three groups for the current study: 30 MDD patients, 30 bipolar depression patients, and 30 healthy controls. Regarding socio-demographic data and clinical characteristics of the studied groups, their ages ranged from 18 to 43 years, with a mean of 30.04 ± 5.7. A total of 54.4% were males. Among the participants, 63.3% were rural residents. Concerning occupation, 42.2% of the participants worked as manual workers, and 37.8% were unemployed. Approximately one-fifth of them read and write about their educational level and had a primary education. Of them, 51.1% were married. Half of the participants were non-smokers, while 36.7% smoked more than 10 cigarettes per day. A positive family history of psychiatric diseases was significantly more prevalent among the study groups ($P=0.02$), as was a statistically significant duration of current episodes ($P=0.03$). The BMI means 24.77 ± 3.4 between the studied groups in Table 1.

The difference between the bipolar and MDD groups was not statistically significant. Comparing mean values pairwise revealed a statistically significant difference between the control and bipolar groups (56.04, 26.71 vs. 134.96, 16.45 in both groups respectively), (*P*-value 0.001), a statistically significant difference between the control and MDD groups (56.04, 26.71 vs. 133.86, 17.59 in both groups respectively), (*P*-value 0.001), but a non-statistically significant difference was detected between the bipolar and MDD (Table 2).

In the BD group, there was a significant positive linear correlation between CRP and depression severity ($r=0.834$, *P*-value <0.001), and there was a significant positive linear correlation between CRP and depression severity in the MDD group ($r=0.642$ *P*-value <0.001) (Table 3).

In Table 4, higher CRP levels were significantly associated with the severity of depressive symptoms, according to the linear regression analysis.

The ROC curve analysis results demonstrated the CRP's diagnostic ability; the CRP had the best sensitivity/specificity balance (93.3% sensitivity and 96.7% specificity at the cut-off point of 106.50), *P*-value 0.001, indicating a statistically significant level of CRP serum diagnosis of MDD disease state with a 93.3% sensitivity (true-positive cases) and 96.7% specificity (true-negative cases). This suggests that CRP could be a biological marker for MDD diagnosis (Table 5).

An analysis of the ROC curve was utilized to assess the diagnostic accuracy of C-reactive protein (CRP)

Table 1 Socio-demographic and clinical characteristics of the studied groups

	Group			**Total** ***n*** **= 90** ***n*** **(%)**	***P-value***
	BD ***n*** **= 30** ***n*** **(%)**	**MDD** ***n*** **= 30** ***n*** **(%)**	**Controls** ***n*** **= 30** ***n*** **(%)**		
Age (years)					
Mean ± SD	29.87 ± 5.4	29.67 ± 6.8	30.60 ± 4.8	30.04 ± 5.7	0.80
Minimum	18	18	21	18	
Maximum	39	43	40	43	
Sex					
Male	16 (53.3)	18 (60.0)	15 (50.0)	49 (54.4)	0.73
Female	14 (46.7)	12 (40.0)	15 (50.0)	41 (45.6)	
Residence					
Rural	22 (73.3)	17 (56.7)	18 (60.0)	57 (63.3)	0.37
Urban	8 (26.7)	13 (43.3)	12 (40.0)	33 (36.7)	
Occupation					
Not work	15 (50.0)	13 (43.3)	6 (20.0)	34 (37.8)	0.31
Manual work	11 (36.7)	14 (46.7)	13 (43.3)	38 (42.2)	
Employee	4 (13.3)	3 (10.0)	11 (36.7)	18 (20.0)	
Education					
Illiterate	4 (13.3)	7 (23.3)	3 (10.00)	14 (15.6)	0.49
Read and write	9 (30.0)	7 (23.3)	3 (10.00)	19 (21.1)	
Primary education	7 (23.3)	9 (30.0)	4 (13.4)	20 (22.2)	
Secondary education	5 (16.7)	4(13.4)	7 (23.3)	16 (17.8)	
University graduate	5 (16.7)	3 (10.0)	13 (43.3)	21(23.3)	
Marital status					
Single	15 (50.0)	13 (43.3)	4 (13.3)	32 (35.6)	0.21
Married	11 (36.7)	12 (40.0)	23 (77.7)	46 (51.1)	
Divorced	3 (10.0)	5 (17.7)	3 (10.0)	11 (12.2)	
Widow	1 (3.3)	0 (0.0)	0 (0.0)	1 (1.1)	
Smoking					
No smoking	17 (56.7)	13 (43.4)	15 (50.0)	45 (50.0)	0.27
1–10 cigarettes/day	1 (3.3)	7 (23.3)	4 (13.3)	12 (13.3)	
> 10 cigarettes/day	12 (40.0)	10 (33.3)	11 (36.7)	33 (36.7)	
Family history of psychiatric disease					
Positive	11 (36.7)	3 (10.0)	-	14 (23.3	0.02*
Negative	19 (63.3)	27 (90.0)	-	46 (76.7)	
Duration of current episode					
2–4 weeks	15 (50.0)	7 (23.3)	-	22 (36.7)	0.03*
> 4 weeks	15 (50.0)	23 (76.7)	-	38 (63.3)	
Adherence to treatment					
Adherent	10 (33.3)	13 (43.3)	-	23 (38.3)	0.55
Not adherent	19 (63.4)	15 (50.0)	-	34 (56.7)	
No treatment	1 (3.3)	2 (6.7)	-	3 (5.0)	
BMI (kg/m^2)					
Mean ± SD	24.97 ± 3.4	24.13 ± 3.1	25.20 ± 3.7	24.77 ± 3.4	0.45
Minimum	19	18	18	18	
Maximum	30	31	30	31	

BD Bipolar depression, *MDD* Major depressive disorder

* *P*-value < 0.05 is considered statistically significant

Table 2 Comparative analysis of studied groups of patients with BD and MDD

	BD $N=30$	MDD $N=30$	Controls $N=30$	*P*-value
Total scores of BDI				
Mean ± SD	32.97 ± 2.4a	31.93 ± 2.3a		0.090
Minimum	28	28		
Maximum	37	36		
CRP				
Mean ± SD	134.96 ± 16.45	133.86 ± 17.59	56.04 ± 26.71	< 0.001*
Minimum	95.00	88.00	7.00	
Maximum	152.40	149.80	108.00	
CRP (patients' groups)				
Mean ± SD	134.96 ± 16.45	133.86 ± 17.59	-	0.838
Minimum	95.00	88.00	-	
Maximum	152.40	149.80	-	

Table 3 Correlation between C-reactive protein (CRP) and depression severity as assessed by Beck Depression Inventory (BDI)

	C-reactive protein (CRP)	
	BD	MDD
Beck Depression Inventory (BDI)		
R	0.834	0.642
***P*-value**	< 0.001*	< 0.001*

Statistical analysis was carried out using Pearson correlation analysis. *r* Pearson correlation coefficient, **P*-value < 0.05 is considered significant

Table 4 Linear regression analysis identified an association between an increase in CRP levels and a higher risk of depression

	Unstandardized Coefficient		*R*	*R*-square	*P-value*
	B	Std. error			
Constant	− 2.471	1.591			
CRP	0.247	0.014	0.887	0.788	< 0.001*

* *P*-value < 0.05 is considered significant

serum levels in distinguishing MDD and BD disease from the normal population. The best sensitivity/specificity balance was observed for the CRP (93.3% sensitivity and 96.7% specificity at cut-off point ≥ 106.50), *P*-value < 0.001; therefore, the CRP serum level diagnosed the MDD disease state at a statistically significant level with a 93.3% sensitivity (true positive cases) and 96.7% specificity (true negative cases), while the best sensitivity/specificity balance was observed for the CRP (93.3% sensitivity and 96.7% specificity at cut-off point ≥ 106.50), *P*-value < 0.001, so the CRP serum level diagnosed the BD disease state at a statistically significant level with a 93.3% sensitivity (true-positive cases) and 96.7% specificity (true-negative cases) (Figs. 1 and 2).

There is no diagnostic value between MDD and BD disorders, as shown by Table 6 and Fig. 3, which also showed that there was no statistical significance ($P=0.790$) with an area under the curve (AUC) of 0.480 (95% confidence interval: 0.331–0.629). We conducted a ROC analysis in the two groups to determine whether CRP levels could serve as a distinct biomarker for MDD and BD disorders during a major depressive episode. The results revealed that CRP levels were not statistically significant (*P*-value = 0.790), with an area under the curve (AUC) of 0.480 (95% confidence interval: 0.331–0.629).

Discussion

Socio-demographic data

The demographic data of the sample showed that there was no statistically significant difference between the studied groups as regards age, sex, residence, education, occupation, and marital status. The mean age ± SD was 29.87 ± 5.4, 29.67 ± 6.8, and 30.60 ± 4.8 for the BD, MDD, and control groups. This is consistent with studies showing that the age range of patients with BD was 20–24 years [15], and for patients with MDD, it was 18–29 years [16]. As regards the gender of the studied population, the BD group showed that 53.3% were men and 46.7% were women, and it is established that BD affects men and women equally [17]. On the other hand, 60% of the MDD group were men and 40% were women, and this was contradictory to various previous findings

Table 5 ROC curve analysis of sensitivity and specificity of C-reactive protein (CRP) serum level in diagnosis of MDD

	AUC	SE[a]	95% *CI*	Sensitivity	Specificity	Cutoff value	*P*-value[b]
CRP in patients with MDD	0.988	0.006	0.969– > 0.999	86.7%	96.7%	≥ 107.30	< 0.001*
CRP in patients with BD	0.994	0.006	0.984– > 0.999	93.3%	96.7%	≥ 106.50	< 0.001*

AUC Area under the curve, *SE* Standard error, *CI* Confidence interval of AUC

[a] Under the nonparametric assumption

[b] Null hypothesis: true area = 0.5

* *P*-value < 0.05 is considered significant

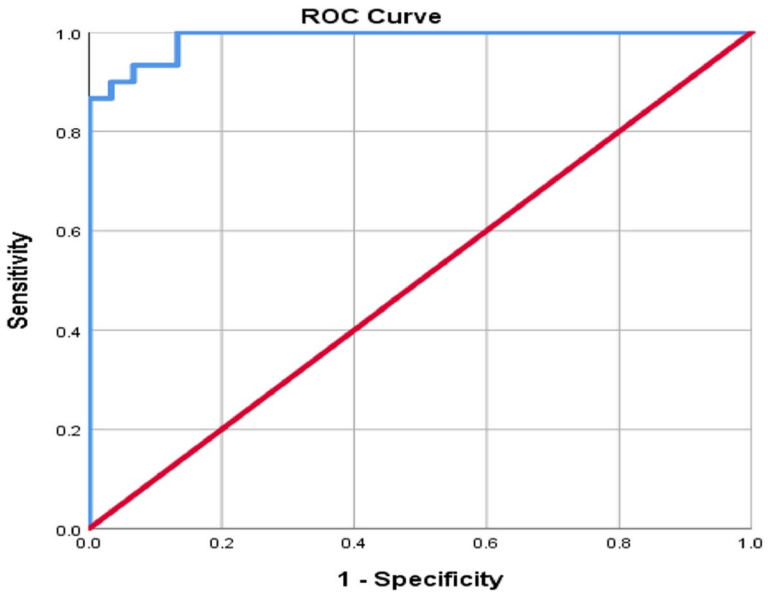

Fig. 1 The results of ROC curve analysis of sensitivity and specificity of C-reactive protein (CRP) serum level in diagnosis of MDD

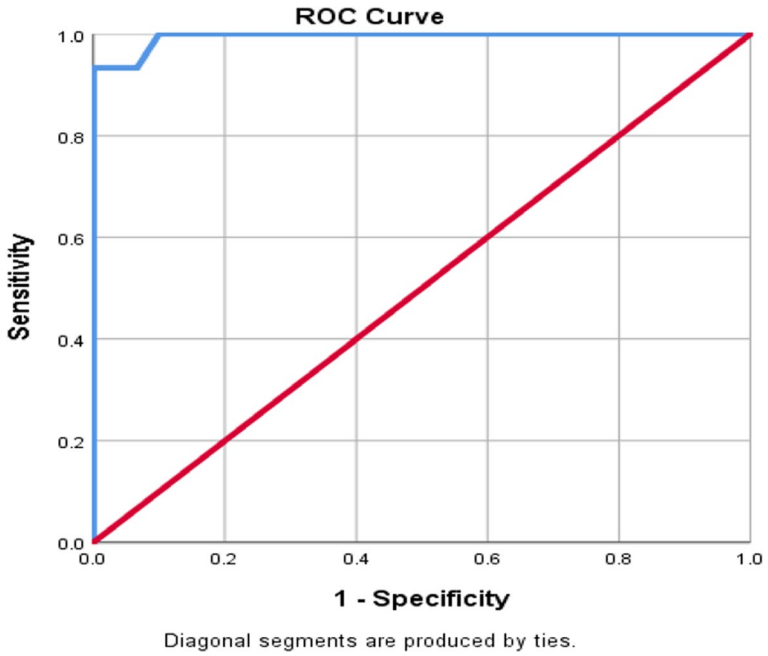

Fig. 2 The results of ROC curve analysis of sensitivity and specificity of C-reactive protein (CRP) serum level in diagnosis of BD

where depression was found to be more common in females [18]. Concerning residence, occupation, education, and marital status, there were no statistically significant differences among the three groups ($P=0.37$, 0.31, 0.49, and 0.21, respectively). First-degree relatives of people with bipolar disorder are seven times more likely to develop the disorder than the general population, and the offspring of a bipolar parent has a 50% chance of developing another major psychiatric disorder [15].

Duration of current episode

The duration of the current episode was significantly longer ($P=0.030$) among the studied patients with MDD as compared with patients with BD. Studies suggest that

Table 6 The results of ROC curve analysis of sensitivity and specificity of C-reactive protein (CRP) serum level to differentiate between both diagnoses

AUC	SE[a]	*P*-value[b]	Asymptotic 95% *CI*	
			Lower bound	Upper bound
0.480	0.076	0.790	0.331	0.629

AUC Area under the curve, *SE* Standard error, *CI* Confidence interval of AUC

[a] Under the nonparametric assumption

[b] Null hypothesis: true area = 0.5

episodes of bipolar depression have a shorter duration than those of unipolar depression, but it is difficult to distinguish between BD and UD [19, 20].

Adherence to treatment

In this study, more than half of the population was not adherent to treatment (56.7% of patients with MDD and bipolar disorder). This was consistent with the results of many studies that reported a higher non-adherence percent to antidepressant therapy. The reasons for non-adherence to antidepressants were forgetting to take drugs, side effects of antidepressants, a stigma among individuals with mental illness, and the higher cost of the medication [21, 22]. It was recently discovered that one-quarter of depressed patients has excessive immune system activation [23]. Thus, depressed patients could be classified as inflammatory or non-inflammatory [19]. Treatment-resistant depression, which is far more likely to have raised inflammatory markers than treatment-responsive depression, already exists as a subcategory of depression. Chronic, low-level inflammation appears to cause depression through a variety of mechanisms. These include the kynurenine pathway and microglial cell activation, which result in a decrease in hippocampal volume. Elevated inflammatory cytokines also disrupt monoaminergic signalling, which may explain the prevalence of treatment resistance in inflammatory depression patients. As a result, if treatment-resistant depression and inflammatory depression are semi-synonymous, anti-inflammatory drugs will display high efficiency in both subtypes [23–25].

High C-reactive protein (CRP) level in both BD and MDD groups

Serum C-reactive protein level was significantly higher in both the BD and MDD groups as compared with controls ($P=0.001$). However, there was no significant difference in serum CRP levels between unipolar and bipolar depression ($P=0.838$). Huang et al. discovered that depressive patients had higher serum CRP levels than non-depressive patients, and other research has discovered that the relationship between depression and inflammation is influenced by severity, type of depression, and somatic symptoms [26, 27]. Low-grade, increased CRP levels may indicate depression,

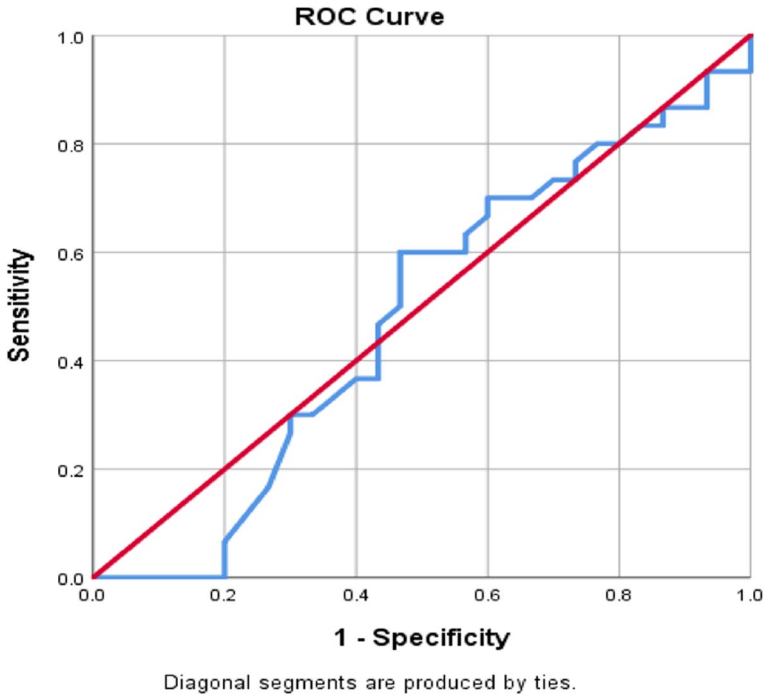

Fig. 3 ROC curve analysis of sensitivity and specificity of C-reactive protein (CRP) serum level in diagnosis of MDD and BD

independent of geographic area, age, or medications. After controlling for socio-demographic, lifestyle, and disease covariates, studies found no association between depression and elevated serum CRP, and two studies found a negative association. However, other studies reported no significant differences between controls and patients with BD [23, 28].

Correlation between C-reactive protein (CRP) and depression severity as assessed by Beck Depression Inventory

In the total population studied, elevated plasma CRP levels had a significant positive linear correlation with depression severity as measured by the Beck Depression Inventory ($r=0.887$, $P=0.001$). CRP levels in atypical depression were found to be higher than in melancholic depression, but no association was found between depression and markers of inflammation [29]. Inflammation and depression have a bidirectional relationship, with proinflammatory cytokines acting directly on emotion-regulating brain structures involved in depression. Recent Mendelian randomization analyses suggest that IL-6 and CRP are likely to be causally linked with depression [22, 30]. CRP does not cross the blood–brain barrier, but it may increase permeability to molecules such as proinflammatory cytokines, which could be an indicator of inflammatory status in the brain. Proinflammatory cytokines can influence neurotransmitter signalling by increasing the number and function of serotonin, norepinephrine, and dopamine reuptake pumps, resulting in diminished levels of these neurotransmitters within the synaptic cleft. Interferon-a treatment has been shown to increase cortisol and glucocorticoid resistance, which correlates with an increase in depressive symptoms [31, 32].

Sensitivity and specificity of C-reactive protein (CRP) serum level in diagnosis of MDD

In this study, ROC analysis was done for the MDD and control groups, and the results showed the diagnostic ability of the CRP. The best sensitivity/specificity balance was observed for the CRP (93.3% sensitivity and 96.7% specificity at the cut-off point ≥ 106.50), and the P-value was <0.001. This means that CRP might be a biological marker for the diagnosis of MDD [33].

C-reactive protein (CRP) serum level sensitivity and specificity in the diagnosis of bipolar depression

Similarly, ROC analysis was done for the BD and control groups, and the results showed the diagnostic ability of the CRP; the best sensitivity/specificity balance was observed for the CRP (93.3% sensitivity and 96.7% specificity at the cut-off point ≥ 106.50) and a P-value <0.001. This means that CRP may be a biological marker for BD, associated with inflammation and mood states [34].

Sensitivity and specificity of C-reactive protein (CRP) serum levels to differentiate between unipolar and bipolar depression

The results of the ROC analysis conducted in the MDD and BD groups in this research indicated that there is no diagnostic value between MDD and BD disorder, with a non-statistically significant $P=0.790$ and an area under the curve (AUC) of 0.480 (95% confidence interval = 0.331–0.629). In contrast to these findings, earlier research found that CRP levels could be used as a biomarker to distinguish between MDD and bipolar disorder in both their depressed and euthymic states [35, 36]. The relatively small sample size of this study may be the cause of its statistical insignificance.

Linear regression analysis showing the association of high levels of CRP with BDI scores

As in previous GENDEP studies, simple linear regression analysis revealed that CRP level was the mean predictor of Beck Depression Inventory (BDI) scale score (R-square = 0.788 and $P=0.001$) [37]. On the other hand, Lamers et al. [38] found that CRP neither predicted depression nor predicted subsequent CRP levels.

Limitations of the study

- The sample size is relatively small; hence, additional studies with a larger randomized sample would help provide more precise data representing the study group.
- Confounders other than metabolic syndrome parameters, such as diet, caffeine intake, and smoking, were not controlled for.
- The current study assessed the current episode of the mood disorder and not its lifetime prevalence. So, follow-up studies may be needed after remission of episodes to explore the relationship between CRP and MDD and BD.
- Participants with illicit drugs, substance use disorders, or other psychiatric disorders have been excluded from the study.

Conclusion

CRP is significantly increased in MDD and BD compared with controls. A non-statistically significant difference was detected between the MDD and BD groups

regarding the severity of depression and CRP levels. On assessing the CRP levels of the sample, it was found that individuals with higher CRP levels had depression that was more severe. This association was more pronounced in women than in men. CRP has a positive linear correlation with MDD and BD, but the study was unable to establish CRP as a distinguishing marker between BD and MDD because the sample was small.

Abbreviations

CRP	C-reactive protein
MDD	Major depressive disorder
BD	Bipolar disorder
BDI	Beck Depression Inventory
TNF	Tumour necrosis factor
IL-6	Interleukin-6
DSM-5	*Diagnostic and Statistical Manual of Psychiatric Disorders-5th Edition*
SCID	Structured Clinical Interview for DSM-5 Disorders

Acknowledgements
We would like to thank all the participants in the research.

Authors' contributions
HD, contributed to the idea, study design, questionnaire design, and writing; RK, data collection and writing; WM, data collection and curation, software, editing, and writing; AA, conceptualization, methodology, software, and writing; AL, conducted the statistical analysis, original draft preparation, and reviewing and editing; and HS, writing, original draft preparation, and reviewing. All authors reviewed and approved the final version of the article.

Funding
This research was not funded by the authors.

Availability of data and materials
On reasonable request, the datasets used and/or analysed during the current study are available from the corresponding author.

Declarations

Ethics approval and consent to participate
The study was approved by the Medical Research Committee (FWA00015574) Faculty of Medicine, Beni-Suef University, and participants were informed that participation is voluntary and does not imply a direct benefit. The results of the study could be used as a scientific publication, but the identity of the participant will be kept confidential.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 17 April 2023 Accepted: 13 June 2023
Published online: 28 August 2023

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