Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Serum BDNF and IL-1β, but not ApoE levels, may be associated with obsessive-compulsive disorder: A case-control study

Samia Zerin
University of Asia Pacific
Ahmad Niaz Rahman
University of Asia Pacific
Md. Hamiduzzaman
University of Asia Pacific
Md. Asaduzzaman
University of Asia Pacific
Mohammad Shahriar
University of Asia Pacific
Md. Rabiul Islam
robi.ayaan@gmail.com

BRAC University
Zabun Nahar
University of Asia Pacific

Research Article

Keywords: obsessive-compulsive disorder, brain-derived neurotrophic factor, interleukin-1 beta, apolipoprotein E, mental health, psychiatry

Posted Date: June 15th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9633673/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Obsessive-compulsive disorder (OCD) is a psychiatric disorder associated with dysregulation of neurotrophic, inflammatory, and metabolic pathways. Brain-derived neurotrophic factor (BDNF), interleukin-1 beta (IL-1β), and apolipoprotein E (ApoE) have been implicated in neuroplasticity, immune activation, and lipid-related neuronal function, respectively. However, evidence regarding these biomarkers in OCD remains limited, particularly in Bangladeshi populations. In this study the objective is to investigate BDNF, IL-1β, and ApoE serum levels in Bangladeshi OCD patients and healthy individuals and to examine their associations with symptom severity.

Methods

This study was comprised of 104 patients with OCD and 104 healthy controls. Sociodemographic, clinical, and laboratory data were collected. OCD symptom severity was assessed using the Yale-Brown obsessive-compulsive scale (Y-BOCS). BDNF, IL-1β, and ApoE serum levels were measured and analyzed across groups. Spearman's correlation analysis was utilized to assess relationships among clinical and biomarker variables. The receiver operating characteristic curve was analyzed to evaluate the variations of performances of significant biomarkers.

Results

We observed OCD patients with significantly higher Y-BOCS scores than healthy controls (21.16 ± 7.59 vs. 4.79 ± 2.18, $p < 0.001$). Serum BDNF levels were significantly elevated in OCD patients compared with controls (43.27 ± 38.28 vs. 25.94 ± 22.56 ng/mL, $p < 0.001$), as were serum IL-1β levels (10.73 ± 4.65 vs. 5.60 ± 3.97 pg/mL, $p < 0.001$). Serum ApoE levels did not differ notably across groups ($p = 0.860$). Among OCD patients, Y-BOCS scores were positively correlated with BDNF and IL-1β levels, and BDNF was positively correlated with IL-1β. ROC analysis showed fair discriminatory ability for BDNF and good discriminatory ability for IL-1β.

Conclusion

Elevated serum BDNF and IL-1β levels may be associated with the pathophysiology and development of OCD. The present study urges evaluation of these findings for their potential to be used as predictive markers of OCD.

1. Introduction

Obsessive-compulsive disorder is a chronic, common neuropsychiatric condition that has many debilitating effects and severely deteriorates patients' quality of life [1]. Obsessions are persistent, unwelcome thoughts, figures, or urges that torment individuals with anxiety and discomfort [2]. Common obsessional patterns in OCD include worries about harming others, being a bad person, or contaminating

one another. The obsessions become persistent, followed by repetitive actions or mental exercises (compulsion) [3]. However, these actions offer transient relief; the ongoing obsessive thoughts perpetuate the cycle, making the lives of individuals with OCD progressively uncomfortable and unbearable. The persistence of obsessions and compulsions can be so pervasive that they occupy substantial amounts of time, leading to marked distress and significant impairment in daily functioning [4].

Despite extensive research, pathophysiological mechanisms of OCD remain inadequately explained. Emerging evidence indicates that OCD stems from a complicated interplay of diverse factors, namely biological, genetic, environmental, and immunological determinants [5–7]. OCD pathogenesis is thought to involve dysregulation of neurotrophic signaling, heightened proinflammatory cytokine activity contributing to neuroimmune imbalance, and disturbances in lipid and fat metabolism pathways that may influence neurotransmitter function and brain energy homeostasis [8]. Neurobiological studies suggest that the pathogenesis of OCD is primarily linked with abnormalities in cortico-striato-thalamo-cortical (CSTC) circuits, while emerging evidence highlights the contribution of additional networks, including the fronto-limbic, fronto-parietal, and cerebellar circuits [9]. Dysfunction in corticostriatal circuits, characterized by excessive striatal excitability, may result from altered regulation of neurotrophins, with brain-derived neurotrophic factor (BDNF) playing a key regulatory role [10]. BDNF is a type of growth factor in the nervous system that plays a vital part in the survival of neurons, differentiation, growth, and synaptic plasticity, especially in ventromedial striatum and hypothalamic circuits [11]. In these neuronal circuits BDNF regulates inhibitory signaling and behavioral outcomes. In the ventromedial hypothalamus (VMH), endogenous BDNF regulates GABAergic inhibitory transmission, with exogenous BDNF increasing spontaneous inhibitory postsynaptic potential frequency and decreasing neuronal excitability [12]. Thus, the impaired BDNF function promotes the intrusive thoughts and compulsive behaviors characteristic of OCD [13]. Additionally, early trauma and perceived stress mediate BDNF metabolism disruption, with stress playing a complete mediating role between childhood trauma and BDNF levels in OCD patients [14].

Neuroinflammatory and autoimmune processes play a wider role in OCD pathogenesis [15]. Elevated rates of OCD in autoimmune diseases as well as associations with developmental disorders like Tourette syndrome support this autoimmune mechanism [16, 17]. Imaging studies, including TSPO-PET, have reported increased microglial activation and inflammatory changes in brain regions affected in OCD [18]. Experimental models further demonstrate that neuroinflammation, driven by microglial activation and proinflammatory cytokines, can cause anxiety-related behaviors [19]. Several studies have demonstrated elevated levels of these proinflammatory cytokines, particularly IL-1β, in OCD patients [20]. Interleukin-1 beta (IL-1β) is a proinflammatory cytokine that mediates neuroimmune signaling, modulates microglial activity, and orchestrates both innate and adaptive immunity, with key relations in autoimmunity and autoinflammation [21]. IL-1β can penetrate the central nervous system, activate resident microglia or astrocytes, and trigger cascades of neuroinflammation. This will have a major impact on serotonergic or dopaminergic pathways by damaging neurocircuits, which can potentially cause hyperexcitability [22]. This exacerbates neuroinflammation in neurodegenerative and obsessive-compulsive-related disorders

[20]. Immune-modulating agents, such as anti-cytokine medications, have been utilized as adjunct therapy to further signify the role of IL-1β in OCD [23]. TRAPS patients presenting with tics and OCD-like symptoms demonstrated significant symptom amelioration following treatment with the IL-1β antagonist anakinra [24].

Lipid metabolism has emerged as a critical component in the pathogenesis of diverse neuropsychiatric disorders [25]. Lipids, which make up 50–60% of neuronal cell membranes, are essential for processes such as myelin formation, neurotransmission, synaptic plasticity, metabolism, and inflammation [26]. Accumulating evidence implies alterations in phospholipid composition, cholesterol balance, and fatty acid signaling in the disruption of neuronal membrane integrity, neurotransmitter receptor dynamics, and synaptic plasticity within CSTC circuits [27]. Within this biochemical framework, apolipoprotein E (ApoE) plays a crucial role as the primary lipid transport protein in the brain. ApoE-enriched high-density lipoproteins (HDL-like) redistribute cholesterol and phospholipids to support membrane repair, synaptogenesis, and neuronal plasticity. mediating cholesterol and phospholipid redistribution across neurons, astrocytes, and microglia. ApoE interacts with the microglial receptor TREM2 and the lipid transporter ABCA1, together forming a regulatory axis that governs lipid efflux, microglial lipid clearance, and the balance between pro-inflammatory (M1) and reparative (M2) microglial states [28]. Dysfunction of this pathway. Impaired ABCA1 activity, or defective TREM2 signaling, results in lipid accumulation within microglia [29]. This, in turn, drives a chronic pro-inflammatory phenotype accompanied by excessive production of reactive oxygen species. Such processes not only propagate neuroinflammation but also disturb synaptic pruning and remodeling, thereby destabilizing CSTC connectivity central to OCD symptomatology [30]. Thus, ApoE and its associated pathways provide a potential mechanistic link between lipid dysregulation, oxidative injury, and circuit dysfunction, positioning ApoE isoforms as promising yet underexplored candidates for stratifying risk of OCD [31].

Research on brain-derived neurotrophic factor (BDNF) has produced inconsistent results: three studies reported significantly reduced BDNF levels in patients with or without previous pharmacological treatment [32–34]. However, a longitudinal study demonstrated notably higher serum BDNF levels in Japanese OCD patients [35]. While some studies found elevated levels of IL-1β in OCD patients compared to HCs, other studies revealed the opposite [36–38]. In comparing symptom severity, elevated IL-1β levels in OCD patients were found to have positive correlations to Y-BOCS scores [20]. To date, no studies have examined apolipoprotein E serum levels in OCD cohorts. Nonetheless, dysregulation of ApoE has been repeatedly implicated not only in major neurodegenerative conditions like Alzheimer's and Parkinson's disease but also in psychiatric pathologies, including anxiety spectrum disorders, suggesting that ApoE may represent a promising yet unexplored biomarker in OCD [29, 31–40].

Although there have been a few studies aiming to find potential serum biomarkers for cost-effective and efficient diagnosis of OCD, most of them cannot sufficiently do so. And the search for the diagnostic and prognostic biomarkers for OCD continues. According to current literature, BDNF and interleukin-1β were both reported to have elevated and reduced levels, with inconsistent associations to symptom severity. Apolipoprotein E, despite its established role in neurodegeneration and psychiatric disorders, remains

unexplored in OCD. There is a clear lack of information about a potentially serious pathophysiological mechanism regarding apolipoprotein E and its potential role in lipid metabolism and OCD onset. These gaps highlight the need for further investigation, particularly in diverse populations. To address this, our study examines the serum levels of BDNF, IL-1β, and ApoE in Bangladeshi OCD patients, aiming to clarify their potential contributions to disease pathophysiology and identify population-specific biomarker patterns.

2. Methodology

2.1 Study population

This study was designed as a case–control investigation with a Bangladeshi cohort. A total of 208 individuals were recruited, comprising 104 patients diagnosed with OCD and 104 healthy controls. The study population was drawn from both clinical and community settings to ensure appropriate representation of cases and controls. Serum samples from OCD patients were collected between April 15, 2025, and July 15, 2025, at the National Institute of Neurosciences and Hospital, Dhaka. To minimize the influence of confounding factors, cases and controls were carefully matched on key demographic and socioeconomic variables, including age, sex, educational attainment, socioeconomic status, and place of residence. The cases were diagnosed according to the DSM-5 criteria, ensuring standardized and internationally recognized diagnostic accuracy. In addition, the Y-BOC scale was utilized (both English and Bengali versions) to assess the severity of symptoms. Patients were diagnosed and healthy controls were evaluated by a psychiatrist. Although we screened 120 patients initially, 16 were declined due to strict inclusion criteria. We recruited subjects aged between 18 and 60 years. Inclusion criteria for the control group were also strictly followed. Only the individuals with sound health and no personal or familial history of psychiatric illness were recruited from the general community. Age-sex matched healthy participants were selected from areas close to the residence of the selected patients. Exclusion criteria included any comorbid major psychiatric disorder, neurodevelopmental conditions, or chronic systemic illness that could act as potential confounders. Participants were tested for the above-mentioned diseases, as well as any participants with chronic illnesses such as rheumatoid arthritis, hypertension, ulcerative colitis, asthma, etc. were excluded from the study. Before participation, information regarding the study goals and procedures was elaborated to all participants, and informed consent in black and white was obtained in compliance with standard ethical guidelines.

2.2 Diagnosis criteria

All patients were evaluated by professional psychiatrists, and the diagnosis was established using the DSM-5. The Y-BOCS was used to evaluate symptom severity. According to DSM-5 criteria, patients must present with obsessions and compulsions, or both, which are frequent, persistent, and cause distress [41]. The Y-BOCS incorporates a comprehensive symptom inventory together with a 10-item scale designed to quantify symptom severity. Each item is rated on a 0–4 scale, giving a total score ranging from 0 to 40, where higher scores indicate greater severity [42]. In clinical practice, the Y-BOCS is

administered through a structured interview in which patients are guided to describe their intrusive thoughts and repetitive behaviors in detail. This allows the clinician to systematically quantify the burden of OCD symptoms, monitor treatment response, and establish standardized diagnostic criteria for inclusion in research studies. The Bengali as well as the English adaptations of the Y-BOCS questionnaire were employed for the diagnosis of OCD.

2.3 Sample collection and serum storage

From each participant, 5 ml of venous blood was syringed out from the upper arm for biochemical analysis of serum. Blood was collected into special tubes free of anticoagulant and was set at room temperature to clot for an hour. After clotting, blood samples were centrifuged at 3,000 rpm for 15 minutes at 25°C. Separated serum was subsequently conveyed into Eppendorf tubes and stored at -80°C to preserve it till the next analysis.

2.4 Quantification of serum BDNF, IL-1β and ApoE levels

Enzyme-linked immunosorbent assays (ELISA) for IL-1β, BDNF, and ApoE were performed strictly following the manufacturer's guidelines. A hundred microliters of standards, samples, and controls were added in duplicate to pre-coated wells and kept under incubation for 90 minutes at 37°C or for 120 minutes under room temperature. After washing, 100 µl of the respective biotinylated goat anti-human polyclonal antibody (IL-1β, BDNF, or ApoE) was added and incubated for 90 minutes, followed by three washes with PBS. A hundred microliters of Avidin-Biotin-Peroxidase Complex was applied for 40 minutes, and the plates were washed five times with PBS-T. Color development was carried out using 90 µl of substrate reagent kept under incubation in the dark for 30 minutes, then stopped with 100 µl of stop solution. Values of absorbance were recorded at a wavelength of 450 nm within 30 minutes.

2.5 Statistical analysis

Data was presented using MS Excel and GraphPad Prism (v8.0.1), while statistical analyses were performed with SPSS (v27). Socio-demographic and clinical variables were summarized using descriptive statistics, and the mean along with standard deviation was calculated. We performed data normality tests and found that the data distribution pattern was normal. For continuous/quantitative variables, mean differences between OCD patients and healthy controls were assessed using an independent sample t-test (two-tailed), while categorical/qualitative variables were compared with chi-square tests. Box plots were generated to visually compare biomarker levels between groups. Correlation analyses, including Spearman's correlation, were conducted to explore associations among parameters. How well serum BDNF, IL-1β, and ApoE could distinguish OCD patients from healthy controls, receiver operating characteristic curves were constructed and subjected to further statistical analysis. Any p-value falling below 0.05 was considered statistically significant.

3. Results

3.1 Socio-demographic characteristics of study population

Socio-demographic characteristics of the study population are presented in Table 1. Both groups were predominantly young adults aged 18–25 years, with a slight male predominance, similar BMI distributions, and nearly identical marital status profiles. Economic standing was nearly identical between groups, with medium-to-low economic status characterizing the majority of participants in both groups. Residential distribution and smoking history followed a similar pattern. Most participants resided in urban areas, and the overwhelming majority were non-smokers, with neither variable differing significantly between cases and controls. Two sociodemographic variables, however, diverged significantly between cases and controls. Education level differed between groups ($p = 0.014$), with OCD cases showing greater representation at lower educational strata, including a small proportion who were illiterate or had only primary-level schooling. However, in the control group, none were illiterate, and the number of individuals with only primary education was fewer. Occupational distribution showed the most striking between-group difference ($p < 0.001$), with unemployment being the leading occupational category among cases, a substantially higher proportion of students among cases than controls, and no business participants in the control group whatsoever. Two clinical variables, as expected in a case-control design, differed most sharply of all. A prior personal history of OCD was present in nearly half of all cases and in none of the controls ($p < 0.001$), while a positive family history of OCD was reported by more than a third of cases compared with fewer than one in seventeen controls ($p < 0.001$).

Table 1
Sociodemographic profile of the study population.

Characteristics	Cases, N = 104		Controls, N = 104		
	n	%	n	%	p-value
Age in years					0.743
18–25	52	50.00	51	49.04	
26–35	33	31.73	28	26.92	
36–45	12	11.54	16	15.38	
46–65	7	6.73	9	8.66	
Sex					0.674
Male	58	55.77	61	58.65	
Female	46	44.23	43	41.35	
BMI (kg/m^2)					0.256
Underweight (below 18.5)	14	13.46	7	6.73	
Normal (18.5–25.0)	59	56.73	66	63.46	
Overweight (Above 25.0)	31	29.81	31	29.81	
Marital status					0.889
Married	48	46.15	47	45.19	
Unmarried	56	53.85	57	54.81	
Education level					**0.014**
Illiterate	1	0.96	0	0.00	
Primary	16	15.38	4	3.85	
Secondary	46	44.23	62	59.61	
Graduate and above	41	39.43	38	36.54	
Occupation					**< 0.001**
Business	9	8.65	0	0.00	
Housewife	20	19.23	10	9.62	
Service	15	14.42	24	23.08	

Abbreviations: OCD, obsessive-compulsive disorder; BMI, body mass index. p-value < 0.05 indicates statistically significant (bold).

Characteristics	Cases, N = 104		Controls, N = 104		
	n	%	n	%	p-value
Student	19	18.27	2	1.92	
Unemployed	41	39.43	67	64.42	
Others	0	0.00	1	0.96	
Economic status					0.979
High	16	15.38	15	14.42	
Medium	48	46.15	49	47.12	
Low	40	38.47	40	38.46	
Residence area					0.074
Rural	45	43.27	33	31.73	
Urban	59	56.73	71	68.27	
Smoking history					0.873
Non-smoker	82	78.85	87	83.65	
Smoker	22	21.15	17	16.35	
Previous history of OCD					**< 0.001**
Yes	50	48.08	0	0.00	
No	54	51.92	104	100.00	
Family history of OCD					**< 0.001**
Yes	36	34.62	6	5.77	
No	68	65.38	98	94.23	

Abbreviations: OCD, obsessive-compulsive disorder; BMI, body mass index. p-value < 0.05 indicates statistically significant (bold).

3.2 Comparison among serum levels of different markers

Biophysical characteristics, clinical features, and laboratory findings of the study participants are presented in Table 2. OCD patients demonstrated notably elevated BDNF levels of serum relative to their healthy counterparts. The mean serum BDNF concentration was 43.27 ± 38.28 ng/mL in the OCD group and 25.94 ± 22.56 ng/mL in the control group ($p < 0.001$). Similarly, serum IL-1β levels were significantly elevated in OCD patients, with a mean concentration of 10.73 ± 4.65 pg/mL compared with 5.60 ± 3.97 pg/mL among controls ($p < 0.001$). In contrast, no meaningful difference in serum ApoE levels was observed between the two groups, with mean values of 40.44 ± 22.31 mg/L in OCD patients and 39.89 ±

22.62 mg/L in healthy controls (p = 0.860). Boxplot graphs show the comparison of serum BDNF and IL-1β levels between the cases and controls (Fig. 1).

Table 2
Biophysical characteristics, clinical features, and laboratory findings of the study participants.

Parameters	**OCD patients (n = 104) Mean ± SD**	**Healthy controls (n = 104) Mean ± SD**	**p-value**
Age (in years)	28.51 ± 8.92	29.41 ± 10.22	0.498
BMI (kg/m^2)	23.29 ± 4.21	23.17 ± 3.38	0.815
Y-BOCS scores	21.16 ± 7.59	4.79 ± 2.18	**< 0.001**
Serum BDNF level (ng/mL)	43.27 ± 38.28	25.94 ± 22.56	**< 0.001**
Serum IL-1β level (pg/mL)	10.73 ± 4.65	5.60 ± 3.97	**< 0.001**
Serum ApoE level (mg/L)	40.44 ± 22.31	39.89 ± 22.62	0.860

Abbreviations: ApoE, apolipoprotein E; BDNF, brain-derived neurotrophic factor; BMI, body mass index; IL-1β, interleukin-1 beta; OCD, obsessive-compulsive disorder; SD, standard deviation; Y-BOCS, Yale–Brown obsessive–compulsive scale. p-value < 0.05 indicates statistically significant (bold).

3.3 Correlation among different study parameters

The correlation analysis among various study parameters is shown in Table 3. Among OCD patients, Y-BOCS score exhibited a significant positive correlation with serum BDNF level (r = 0.796, p = 0.026) and IL-1β level (r = 0.661, p = 0.004). In contrast, Y-BOCS score did not show a significant correlation with serum ApoE level among OCD patients (r = 0.054, p = 0.588). Among healthy counterparts, Y-BOCS score was not significantly correlated with BDNF (r = 0.158, p = 0.109), IL-1β (r = 0.024, p = 0.808), or ApoE (r = 0.086, p = 0.169). In OCD patients, serum BDNF level showed a notable positive correlation with serum IL-1β level (r = 0.456, p = 0.007). However, BDNF was not significantly correlated with ApoE among cases (r = 0.032, p = 0.747), and IL-1β was also not significantly correlated with ApoE (r = 0.061, p = 0.537). On the other hand, in healthy controls, no correlations were significant between BDNF and IL-1β (p = 0.452), BDNF and ApoE (p = 0.243), or IL-1β and ApoE (p = 0.417). Age and BMI were not significantly associated with Y-BOCS score or any of the measured serum biomarkers in either OCD patients or healthy controls. Similar nonsignificant correlations were observed among healthy controls for age and BMI with Y-BOCS score, BDNF, IL-1β, and ApoE.

Table 3
Correlation study among various research parameters among OCD patients.

Correlation parameters	*Cases*		*Controls*	
	r	*p-value*	*r*	*p-value*
Age and Y-BOCS score	0.005	0.963	0.049	0.619
Age and BDNF	0.047	0.645	-0.062	0.534
Age and IL-1β	-0.062	0.531	-0.008	0.936
Age and APOE	0.038	0.703	-0.136	0.168
BMI and Y-BOCS score	-0.134	0.176	0.018	0.859
BMI and BDNF	-0.019	0.849	0.056	0.569
BMI and IL-1β	0.059	0.554	0.078	0.428
BMI and APOE	0.086	0.383	0.131	0.184
Y-BOCS and BDNF	0.796	**0.026**	0.158	0.109
Y-BOCS and IL-1β	0.661	**0.004**	0.024	0.808
Y-BOCS and APOE	0.054	0.588	0.086	0.169
BDNF and IL-1β	0.456	**0.007**	0.024	0.452
BDNF and APOE	0.032	0.747	0.116	0.243
IL-1β and APOE	0.061	0.537	0.080	0.417

Abbreviations: APOE, apolipoprotein E; BDNF, brain-derived neurotrophic factor; BMI, body mass index; IL-1β, interleukin-1 beta; OCD, obsessive-compulsive disorder; r, Spearman's rank correlation coefficient; Y-BOCS, Yale–Brown obsessive–compulsive scale. p-value < 0.05 indicates statistically significant (bold).

3.4 Receiver operating characteristic curve analysis serum biomarkers

To explore the possible utility of BDNF, IL-1β, and ApoE as diagnostic indicators for OCD, receiver operating characteristic (ROC) curve analysis was performed for each biomarker, comparing their ability to discriminate OCD patients from healthy controls (Fig. 2). Serum BDNF demonstrated acceptable, though modest, discriminatory performance. The area under the curve was 0.760 (95% CI: 0.695–0.824), with a sensitivity of 64.4% and specificity of 73.1% at an optimal cut-off value of 26.42 ng/mL. Serum IL-1β, by contrast, exhibited considerably superior diagnostic performance. Its AUC of 0.880 (95% CI: 0.836–0.924) placed it firmly in the good-to-excellent discriminatory range, with a sensitivity of 81.7% and specificity of 80.8% at a cut-off of 6.04 pg/mL. Serum ApoE, consistent with the absence of a statistically significant between-group difference in mean levels, showed poor discriminatory ability and

did not demonstrate clinically useful diagnostic performance for differentiating OCD patients from healthy controls. Its ROC profile therefore did not support a meaningful diagnostic role for ApoE in this context.

4. Discussion

In the present study, BDNF levels in serum were significantly higher in Bangladeshi patients with obsessive-compulsive disorder than in healthy counterparts. In addition, BDNF levels demonstrated a meaningful positive association with Y-BOCS score among OCD patients, indicating that patients with greater obsessive-compulsive symptom severity tended to have higher circulating BDNF levels. No significant correlation between BDNF and Y-BOCS was observed among healthy controls. The present results indicate that elevated serum BDNF may be related not only to the presence of OCD but also to symptom burden in this Bangladeshi clinical population. The relationship between serum BDNF and OCD has been a subject of considerable investigation, yet the literature remains notably inconsistent. A 2022 meta-analysis by Hao et al., with nine studies, revealed that peripheral BDNF levels were significantly lower in OCD patients overall, particularly in drug-free samples [43]. Similarly, a broader network meta-analysis across psychiatric disorders reported decreased BDNF levels in several disorders, including OCD, compared with controls [44]. In population-based studies, lower BDNF levels in OCD were observed in Han Chinese, Indian, and Caucasian populations [45–47]. On the contrary, Akimoto et al. observed an elevated serum BDNF level in Japanese OCD patients (17.5 ± 7.3 ng/mL) while comparing it to healthy controls (12.7 ± 4.7 ng/mL). But they did not find any correlation between serum BDNF level and total Y-BOCS score, which was inconsistent with our findings. It must be noted that most of the patients (82%) from that study were under medication [35]. In another study, including pediatric patients (mean age 12.4 years), increased BDNF levels in OCD was also observed [48]. These studies, including ours, suggest that BDNF may not be a risk marker but rather a marker reflecting ongoing neuroplastic adaptation to symptom severity. OCD has long been conceptualized as a disorder involving CSTC circuit dysfunction. Recent reviews continue to support CSTC circuit dysregulation and glutamatergic dysfunction as central elements of OCD pathophysiology [49]. Therefore, increased serum BDNF in our patients may reflect an adaptive attempt to restore synaptic balance in response to ongoing circuit hyperactivity and maladaptive compulsive behavior. Also, in case of our study, the positive correlation between BDNF and Y-BOCS score strengthens this interpretation, because higher BDNF levels were found in patients with more severe symptoms. Rather than indicating a protective state alone, elevated BDNF may reflect greater neurobiological demand in patients with more intense obsessive-compulsive symptoms. Illness chronicity may further explain the elevated BDNF level. In the present study, nearly half of the OCD patients (48.08%) had a previous history of the disorder, suggesting that many had recurrent or persistent illness. Chronic OCD may involve repeated activation of symptom-related neural circuits and prolonged neurobiological adaptation. In our patients, elevated BDNF may therefore represent a marker of chronic adaptive neuroplasticity rather than an early vulnerability marker alone.

Interleukin 1β was also significantly elevated in OCD patients compared with healthy controls, and IL-1β showed a notable positive correlation with Y-BOCS score. These findings invigorate the role of

neuroinflammation in anxiety-related behavior and OCD [19]. Proinflammatory cytokine IL-1β can penetrate the CNS, activating microglia and astrocytes to initiate neuroinflammatory cascades that disrupt serotonergic and dopaminergic pathways through neurocircuit damage, leading to hyperexcitability, thereby exacerbating neuroinflammation in neurodegenerative and obsessive–compulsive-related disorders [23]. Our findings are highly consistent with recent evidence supporting immune-inflammatory involvement in OCD [36, 37, 50]. However, some studies have reported findings inconsistent with ours, demonstrating reduced serum IL-1β levels in patients with OCD [38, 51]. Additionally, a similar study had been conducted in Bangladesh prior to our investigation. Sarmin et al. also reported significantly higher serum IL-1β levels in OCD patients than healthy controls and found that IL-1β was positively correlated with Y-BOCS scores. That study also reported good discriminatory performance for IL-1β in ROC analysis, supporting its potential role as a blood-based marker of OCD-related inflammatory activation [20]. Our results reinforce this observation in a larger Bangladeshi sample, indicating that IL-1β elevation may be a reproducible finding in OCD patients from this population.

Among OCD patients in the present study, serum BDNF was significantly and positively correlated with serum IL-1β, a relationship that was absent among healthy controls. This might be best explained by the concept of a neuroimmune-neuroplastic response. IL-1β, as a pro-inflammatory cytokine, and BDNF, as a mediator of synaptic plasticity, neuronal survival, and circuit remodeling, are not biologically independent. Experimental and review evidence indicates that inflammatory pathways can directly influence BDNF signaling and that BDNF upregulation may itself represent part of the brain's adaptive response to inflammatory challenge or cellular stress [52]. In OCD, the correlated elevation of IL-1β and BDNF may reflect a shared neuroimmune mechanism rather than independent biological changes.

Serum ApoE levels did not differ significantly across the groups in our study, and ApoE was not significantly correlated with Y-BOCS score, BDNF, or IL-1β either. This suggests that circulating ApoE may not be directly related to OCD diagnosis or symptom severity in our sample. ApoE is mainly involved in lipid transport, cholesterol metabolism, neuronal repair, and neurodegenerative processes, rather than acute symptom expression [26]. Although serum ApoE levels have not been previously reported in OCD, altered ApoE levels have been documented in some related neuropsychiatric conditions. Serum ApoE has shown variability in schizophrenia and Parkinson’s disease, while plasma ApoE has been associated with suicidality in major depressive disorder and symptom severity in PTSD [53, 54]. The absence of a significant ApoE difference in our OCD sample may indicate that total serum ApoE is not a sensitive standalone biomarker for OCD.

In ROC curve analysis the accuracy of a biomarker assessed by the AUC was deciphered as follows: 0.90-1.00 = excellent, 0.80–0.90 = good, 0.70–0.80 = fair, 0.60–0.70 = poor, and < 0.60 = not useful [55]. In the present study, serum BDNF showed an AUC value of 0.760 (95% CI: 0.695–0.824; $p < 0.001$). At a cut-off value of 26.42 ng/mL, serum BDNF differentiated OCD patients from healthy controls with 64.4% sensitivity and 73.1% specificity. Serum IL-1β demonstrated stronger diagnostic potential, with an AUC of 0.880 (95% CI: 0.836–0.924; $p < 0.001$), indicating good discriminatory ability. At a cut-off value of

6.04 pg/mL, IL-1β showed 81.7% sensitivity and 80.8% specificity for identifying OCD patients. These results indicate that both serum BDNF and IL-1β may have potential utility as peripheral biomarkers for OCD, with IL-1β showing better diagnostic performance than BDNF in the Bangladeshi population in our study.

4.1 Strengths and Limitations of this Study

Despite employing comprehensive methodologies, limitations within the study could not be fully mitigated. First, the case–control design permits the assessment of associations but does not establish causal relationships. Therefore, these findings do not allow us to infer those alterations in serum BDNF, IL-1β, and ApoE levels contribute to the pathogenesis of OCD. Second, the study sample size is small, which makes our findings exploratory, not confirmatory. Results should be interpreted with caution. Third, potential confounding factors such as medication status, illness duration, comorbid depression or anxiety, dietary habits, sleep pattern, physical activity, recent infection, inflammatory conditions, lipid profile, and metabolic status were not fully controlled. Better-clarified results could be obtained through longitudinal studies involving larger and more homogeneous populations, repeated biomarker measurements, strict control of confounders, and simultaneous assessment of additional inflammatory, neurotrophic, genetic, and metabolic markers. Notwithstanding these limitations, the present study carries notable strengths, including the inclusion of both OCD patients and healthy controls under the same experimental conditions and the evaluation of multiple biologically relevant serum markers in an underrepresented Bangladeshi population.

5. Conclusion

Observations of this study suggest that Bangladeshi OCD patients had significantly higher serum BDNF and IL-1β levels than healthy controls, while serum ApoE levels showed no significant difference. This is the first time ApoE serum levels were quantified in an OCD cohort. BDNF and IL-1β were positively correlated with Y-BOCS scores, suggesting their association with OCD symptom severity. Their significant intercorrelation further indicates a possible neuroimmune–neuroplastic mechanism in OCD. ROC analysis showed that IL-1β had better discriminatory performance than BDNF. Overall, BDNF and IL-1β may serve as potential peripheral biomarkers of OCD, whereas serum ApoE appears to have limited diagnostic relevance.

Abbreviations

ApoE
apolipoprotein E
BMI
body mass index
CSTC
cortico-striato-thalamo-cortical

DSM-5
Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
ELISA
enzyme-linked immunosorbent assay
HCs
Healthy controls
IL-1β
interleukin-1 beta
OCD
obsessive-compulsive disorder
ROC
Receiver-operating characteristic
SD
standard deviation
SPSS
Statistical package for social sciences
VMH
ventromedial hypothalamus
Y-BOCS
Yale–Brown obsessive–compulsive scale

Declarations

Clinical trial number

Not applicable.

Funding

The author(s) didn't receive any specific funding for this research.

Ethics statements

The Research Ethics Committee of the University of Asia Pacific formally granted ethical clearance for this case-control study, under reference number UAP/REC/2025/102. In compliance with the Helsinki Declaration, the study was carried out.

Human ethics and consent to participate

All participants provided written informed consent prior to enrollment. Informed consent for the publication is not applicable to this study."

References

1. Ruth Ross, R. Ross, Blair H. Simpson, B. H. Simpson, Brian A. Fallon, and B. A. Fallon (2000) What Is Obsessive-Compulsive Disorder?. J. Psychiatr. Pract. 6(2):109–110
2. American Psychiatric Association and None American Psychiatric Association, “Diagnostic and Statistical Manual of Mental Disorders”.
3. Leckman JF, Grice DE, Boardman J, Zhang H, Vitale A, Bondi C, Alsobrook J, Peterson BS, Cohen DJ, Rasmussen SA, Goodman WK, McDougle CJ, Pauls DL (1997) Symptoms of obsessive-compulsive disorder. Am J Psychiatry 154(7):911–917
4. Garg R, Kaur R, and Raj R (2023) Quality of life among patients with obsessive compulsive disorder: Impact of stigma, severity of illness, insight, and beliefs. Ind. Psychiatry J 32(1):130–130
5. Mahjani B, K. Bey, Boberg J, and Burton CL (2021) Genetics of obsessive-compulsive disorder. Psychol. Med 51(13):2247–2259
6. Monzani B, Rijsdijk F, Harris J, Mataix-Cols D (2014) The structure of genetic and environmental risk factors for dimensional representations of DSM-5 obsessive-compulsive spectrum disorders. JAMA Psychiatry 71(2):182–189
7. Pauls DL (2010) The genetics of obsessive-compulsive disorder: a review. Dialogues Clin. Neurosci 12(2):149–163
8. Swedo SE (1994) Pathophysiology of OCD. Neuropsychopharmacology 11(4): 262–262
9. Levy F (2011) Cortico-Striatal-Thalamic-Cortical (CSTC) Circuits, Tourette’s Disorder, and OCD. Adhd Rep 19(2):8
10. Autry AE, Monteggia LM (2012) Brain-derived neurotrophic factor and neuropsychiatric disorders. Pharmacol Rev 64(2):238–258
11. Notaras M, van den Buuse M (2020) Neurobiology of BDNF in fear memory, sensitivity to stress, and stress-related disorders. Mol Psychiatry 25(10):2251–2274
12. Jo YH (2012) Endogenous BDNF regulates inhibitory synaptic transmission in the ventromedial nucleus of the hypothalamus. J Neurophysiol 107(1):42–49
13. Luo Y, Chen X, Wei C, Zhang H, Zhang L, Han L, Sun K, Li B, Wen S (2022) BDNF alleviates microglial inhibition and stereotypic behaviors in a mouse model of obsessive-compulsive disorder. Front Mol Neurosci 15:926572
14. Li P, Huang J, Wu H, Fu C, Wang M, Yuan J (2021) Intermediation of perceived stress between early trauma and BDNF metabolism in obsessive-compulsive disorder. J Affect Disord 286:212–219
15. Endres D, Pollak TA, Bechter K, Denzel D, Pitsch K, Nickel K, Runge K, Pankratz B, Klatzmann D, Tamouza R, Mallet L, Leboyer M, Prüss H, Voderholzer U, Cunningham JL, ECNP Network Immuno-NeuroPsychiatry, Domschke K, Tebartz van Elst L, Schiele MA (2022) Immunological causes of obsessive-compulsive disorder: is it time for the concept of an autoimmune OCD subtype? Transl Psychiatry 12:5

16. Mataix-Cols D, Frans E, Pérez-Vigil A, Kuja-Halkola R, Gromark C, Isomura K, Fernández de la Cruz L, Serlachius E, Leckman JF, Crowley JJ, Rück C, Almqvist C, Lichtenstein P, Larsson H (2018) A total-population multigenerational family clustering study of autoimmune diseases in obsessive-compulsive disorder and Tourette's/chronic tic disorders. Mol Psychiatry 23(7):1652–1658
17. Wang LY, Chen SF, Chiang JH, Hsu CY, Shen YC (2019) Systemic autoimmune diseases are associated with an increased risk of obsessive-compulsive disorder: a nationwide population-based cohort study. Soc Psychiatry Psychiatr Epidemiol 54(4):507–516
18. Attwells S, Setiawan E, Wilson AA, Rusjan PM, Mizrahi R, Miler L, Xu C, Richter MA, Kahn A, Kish SJ, Houle S, Ravindran L, Meyer JH (2017) Inflammation in the neurocircuitry of obsessive-compulsive disorder. JAMA Psychiatry 74(8):833–840
19. Furtado M, Katzman MA (2015) Neuroinflammatory pathways in anxiety, posttraumatic stress, and obsessive compulsive disorders. Psychiatry Res 229(1–2):37–48
20. Sarmin N, Roknuzzaman ASM, Sarker R, Rashid MO, Hasan A, Qusar MMAS, Kabir ER, Islam MR, Mahmud ZA (2024) Exploring the role of interleukin-1β and interleukin-6 in the pathophysiology of obsessive-compulsive disorder. PLoS ONE 19(6):e0306125
21. Mendiola AS, Cardona AE (2018) The IL-1β phenomena in neuroinflammatory diseases. J Neural Transm 125(5):781–795
22. Miller AH, Haroon E, Raison CL, Felger JC (2013) Cytokine targets in the brain: impact on neurotransmitters and neurocircuits. Depress Anxiety 30(4):297–306
23. Hirschtritt ME, Bloch MH, Mathews CA (2017) Obsessive-compulsive disorder: advances in diagnosis and treatment. JAMA 317(13):1358–1367
24. Garcia-Delgar B, Morer A, Luber MJ, Coffey BJ (2016) Obsessive-compulsive disorder, tics, and autoinflammatory diseases: beyond PANDAS. J Child Adolesc Psychopharmacol 26(9):847–850
25. Jiang Y, Cai Y, Teng T, Wang X, Yin B, Li X, Yu Y, Liu X, Wang J, Wu H, He Y, Zhu ZJ, Zhou X (2024) Dysregulations of amino acid metabolism and lipid metabolism in urine of children and adolescents with major depressive disorder: a case-control study. Psychopharmacology 241(8):1691–1703
26. Zorkina Y, Ushakova V, Ochneva A, Tsurina A, Abramova O, Savenkova V, Goncharova A, Alekseenko I, Morozova I, Riabinina D, Kostyuk G, Morozova A (2024) Lipids in psychiatric disorders: functional and potential diagnostic role as blood biomarkers. Metabolites 14(2):80
27. Incontro S, Musella ML, Sammari M, Di Scala C, Fantini J, Debanne D (2025) Lipids shape brain function through ion channel and receptor modulations: physiological mechanisms and clinical perspectives. Physiol Rev 105(1):137–207
28. Sun Y, Wei K, Liao X, Wang J, Gao L, Pang B (2025) Lipid metabolism in microglia: emerging mechanisms and therapeutic opportunities for neurodegenerative diseases. Int J Mol Med 56(3):1–19
29. Liao F, Yoon H, Kim J (2017) Apolipoprotein E metabolism and functions in brain and its role in Alzheimer's disease. Curr Opin Lipidol 28(1):60–67

30. Yeh FL, Wang Y, Tom I, Gonzalez LC, Sheng M (2016) TREM2 binds to apolipoproteins, including APOE and CLU/APOJ, and thereby facilitates uptake of amyloid-beta by microglia. Neuron 91(2):328–340
31. Dondu A, Caliskan M, Orenay-Boyacioglu S (2024) Link between obsessive-compulsive disorder and ApoE gene polymorphisms. Neuropsychiatr Dis Treat 20:159–166
32. Dos Santos IM, Ciulla L, Braga D, Ceresér KM, Gama CS, Kapczinski F, Ferrão YA (2011) Symptom dimensional approach and BDNF in unmedicated obsessive-compulsive patients: an exploratory study. CNS Spectr 16(9):179–189
33. Mina S, Dhiman R, Singal P, Gangopadhyay S, Verma P, Kathuria S (2023) A study of serum brain-derived neurotrophic factor level in individuals with obsessive compulsive disorder and their first-degree relatives as compared to the healthy population. Indian J Psychiatry 65(9):922–927
34. Maina G, Rosso G, Zanardini R, Bogetto F, Gennarelli M, Bocchio-Chiavetto L (2010) Serum levels of brain-derived neurotrophic factor in drug-naive obsessive-compulsive patients: a case-control study. J Affect Disord 122(1–2):174–178
35. Akimoto T, Sutoh C, Kuno M, Matsuzawa D, Niitsu T, Iyo M, Shimizu E (2021) Serum levels of brain-derived neurotrophic factor in patients with obsessive-compulsive disorder in a Japanese population. Open J Psychiatry 11(1):20–28
36. Brambilla F, Perna G, Bellodi L, Arancio C, Bertani A, Perini G, Carraro C, Gava F (1997) Plasma interleukin-1β and tumor necrosis factor concentrations in obsessive-compulsive disorders. Biol Psychiatry 42(11):976–981
37. Rodríguez N, Morer A, González-Navarro EA, Serra-Pages C, Boloc D, Torres T, García-Cerro S, Mas S, Gassó P, Lázaro L (2017) Inflammatory dysregulation of monocytes in pediatric patients with obsessive-compulsive disorder. J Neuroinflammation 14(1):261
38. Maes M, Meltzer HY, Bosmans E (2008) Psychoimmune investigation in obsessive-compulsive disorder: assays of plasma transferrin, IL-2 and IL-6 receptor, and IL-1β and IL-6 concentrations. Neuropsychobiology 30(2–3):57–60.
39. Averill LA, Abdallah CG, Levey DF, Han S, Harpaz-Rotem I, Kranzler HR, Southwick SM, Krystal JH, Gelernter J, Pietrzak RH (2019) Apolipoprotein E gene polymorphism, posttraumatic stress disorder, and cognitive function in older U.S. veterans: results from the National Health and Resilience in Veterans Study. Depress Anxiety 36(9):834–845
40. Zhu SG, Chen ZL, Xiao K, Wang ZW, Lu WB, Liu RP, Huang SS, Zhu JH, Zhang X, Wang JY (2024) Association analyses of apolipoprotein E genotypes and cognitive performance in patients with Parkinson's disease. Eur J Med Res 29:327
41. Arbanas G (2015) Diagnostic and statistical manual of mental disorders (DSM-5). Alcohol Psychiatry Res 51(1):61–64
42. Hartsock JT, Koran LM (2018) Yale-Brown Obsessive Compulsive Scale (YBOCS). StatPearls Publishing

43. Hao LS, Du Y, Chen L, Jiao YG, Cheng Y (2022) Brain-derived neurotrophic factor as a biomarker for obsessive-compulsive disorder: a meta-analysis. J Psychiatr Res 151:676–682
44. Zou Y, Zhang Y, Tu M, Ye Y, Li M, Ran R, Zou Z (2024) Brain-derived neurotrophic factor levels across psychiatric disorders: a systemic review and network meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 131:110954
45. Wang Y, Mathews CA, Li Y, Lin Z, Xiao Z (2011) Brain-derived neurotrophic factor (BDNF) plasma levels in drug-naïve OCD patients are lower than those in healthy people, but are not lower than those in drug-treated OCD patients. J Affect Disord 133(1–2):305–310
46. Maina G, Rosso G, Zanardini R, Bogetto F, Gennarelli M, Bocchio-Chiavetto L (2010) Serum levels of brain-derived neurotrophic factor in drug-naïve obsessive-compulsive patients: a case-control study. J Affect Disord 122(1–2):174–178
47. Mina S, Dhiman R, Singal P, Gangopadhyay S, Verma P, Kathuria S (2023) A study of serum brain-derived neurotrophic factor level in individuals with obsessive compulsive disorder and their first-degree relatives as compared to the healthy population. Indian J Psychiatry 65(9):922–927
48. Şimşek Ş, Gençoğlan S, Yüksel T, Kaplan İ, Alaca R (2016) Cortisol and brain-derived neurotrophic factor levels prior to treatment in children with obsessive-compulsive disorder. J Clin Psychiatry 77(7):e855–e859
49. Jijimon F, Mehak SF, Mohammed Z, Praharaj SK, Gangadharan G (2026) Rewiring the OCD brain: insights beyond cortico-striatal networks. Neurobiol Dis 218:107216
50. Karagüzel EÖ, Arslan FC, Uysal EK, Demir S, Aykut DS, Tat M, Karahan SC (2019) Blood levels of interleukin-1 beta, interleukin-6 and tumor necrosis factor-alpha and cognitive functions in patients with obsessive compulsive disorder. Compr Psychiatry 89:61–66
51. Gray SM, Bloch MH (2012) Systematic review of proinflammatory cytokines in obsessive-compulsive disorder. Curr Psychiatry Rep 14(3):220–228
52. Tong L, Balazs R, Soiampornkul R, Thangnipon W, Cotman CW (2008) Interleukin-1β impairs brain derived neurotrophic factor-induced signal transduction. Neurobiol Aging 29(9):1380–1393
53. Gupta AK, Rani K, Swarnkar S, Kumar GK, Khan MI, Pokhriyal R, Kumar DR, Goyal V, Tripathi M, Gupta R, Chadda RK, Vanamail P, Hariprasad G (2018) Evaluation of serum apolipoprotein E as a potential biomarker for pharmacological therapeutic efficacy monitoring in dopamine dictated disease spectrum of schizophrenia and Parkinson's disease: a preliminary study. J Cent Nerv Syst Dis 10:1179573518803585
54. Lei X, Fang X, Ren J, Teng X, Guo C, Wu Z, Yu L, Wang D, Chen Y, Zhou Y, Wu Y, Zhang Y, Zhang C (2024) Plasma Apo-E mediated corticospinal tract abnormalities and suicidality in patients with major depressive disorder. Eur Arch Psychiatry Clin Neurosci 274(5):1167–1175
55. Won GH, Kim JW, Choi TY, Lee YS, Min KJ, Seol KH (2018) Theta-phase gamma-amplitude coupling as a neurophysiological marker in neuroleptic-naïve schizophrenia. Psychiatry Res 260:406–411

Figures

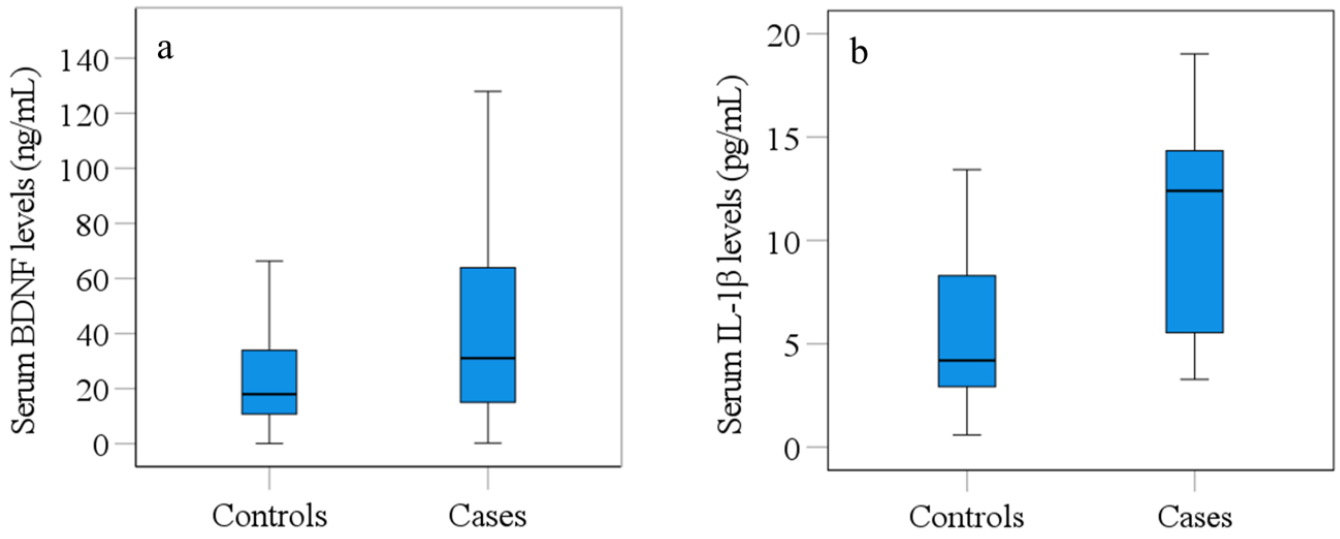


Figure 1

Comparison of serum BDNF and IL-1β levels between the cases and controls. Boxplot graphs show the median, maximum and minimum value range.

Abbreviations: BDNF, brain-derived neurotrophic factor; IL-1β, interleukin-1 beta.

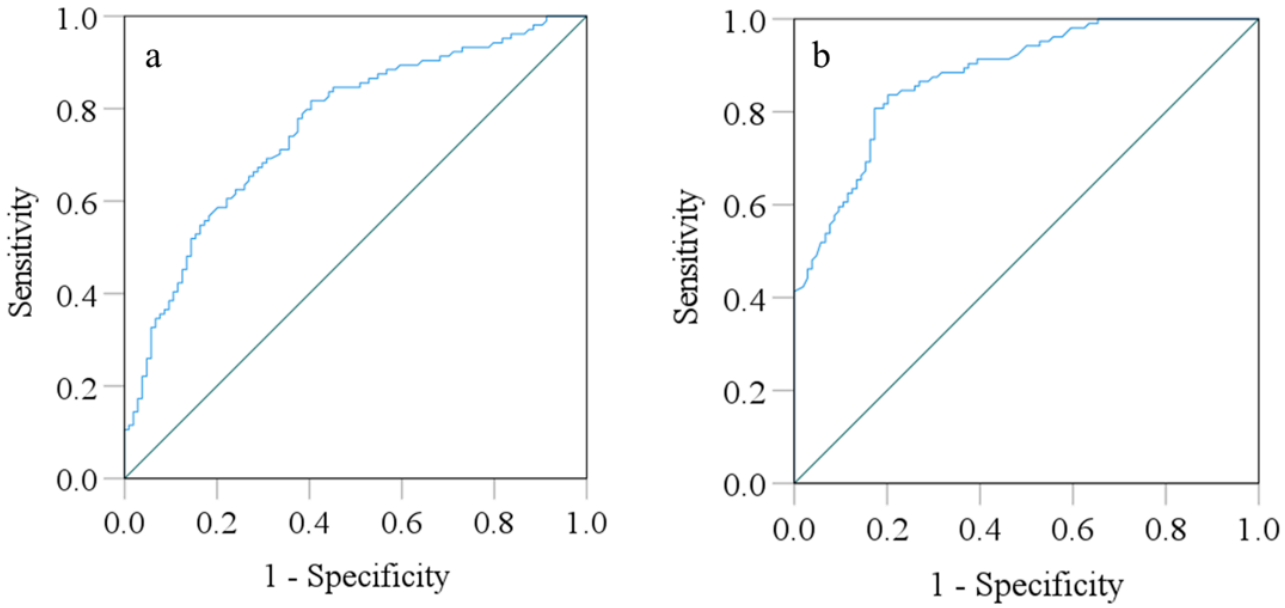


Figure 2

Receiver operating characteristic (ROC) curve analysis of serum BDNF (a) and IL-1β (b) levels study participants ($p<0.001$). For serum BDNF, ROC curve reveals area under the curve (AUC), sensitivity, and

specificity as 0.760 (95% CI: 0.695-0.824), 64.4%, and 73.1% at cut-off value 26.42 ng/ml. For serum IL-1β, ROC curve reveals area under the curve (AUC), sensitivity, and specificity as 0.880 (95% CI: 0.836-0.924), 81.7%, and 80.8% at cut-off value 6.04 pg/ml.