Evaluation of Interleukin-22 Levels in Obsessive-Compulsive Disorder Patients in Bangladesh

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons.)

School of Pharmacy

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May, 2026

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing my degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material that has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis titled “Evaluation of Interleukin-22 Levels in Obsessive-Compulsive Disorder Patients in Bangladesh” submitted by Tahsin Uddin Jisan (22346056) of Spring, 2026, has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.) on May 7, 2026.

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Ethics Statement

The study has been carried out in line with ethical considerations. Ethical permission was taken from the relevant institutional review board before starting the research study. The subjects were made aware of the objectives and methods that would be employed in conducting the study. Each of the participants had signed a detailed consent form before being involved in the study and blood collection. The confidentiality and anonymity of the participants were maintained throughout the research process.

Abstract

Obsessive-compulsive disorder (OCD) is a common neuropsychiatric disease with recurring obsessions and compulsions causing functional impairment. There is emerging literature indicating the association between immune dysregulation and cytokine profile in OCD. But there is no previous research about the Interleukin-22 (IL-22) amount present in the serum, which is pro-inflammatory as well as tissue-protective cytokine, in OCD patients. This case-control study was designed to investigate the serum level of IL-22 in OCD patients and its possible association with the disease. A total of 200 OCD patients and 176 controls with matched socio-demographic characteristics were enrolled in this study. OCD diagnosis was done using DSM-5 criteria, and Y-BOCS scale was utilized to find out the severity of the symptoms in patients. The serum level of IL-22 was estimated using ELISA method. It was found that the level of IL-22 in the serum of OCD patients (28.45 ± 0.54 pg/ml) was significantly lower when compared to healthy controls (32.22 ± 0.73 pg/ml), with $p<0.001$. However, considering the established knowledge concerning the involvement of IL-22 in the inflammation processes, it can be speculated that there is a certain problem in the regulatory mechanism of the immune response as well as tissue repair in patients. To the best of our knowledge, this appears to be the first study showing the IL-22 serum levels in patients with OCD in Bangladesh. Our findings indicate that the serum levels of IL-22 might be taken into account as a potential biomarker for OCD. Further research with larger sample sizes and broader cytokine panels is needed to confirm these findings and better understand the function and role of IL-22 in the disease progression in OCD.

Keywords:

Obsessive-compulsive disorder (OCD); Interleukin-22 (IL-22); Neuroinflammation; Cytokines; Immune dysregulation; Biomarkers.

Dedication

Dedicated to my wonderful parents, whose endless love, sacrifice, and unwavering support made this work possible.

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List of Acronyms

Acronym	Full Form
OCD	Obsessive-Compulsive Disorder
IL-22	Interleukin-22
IL-1β	Interleukin-1 beta
IL-6	Interleukin-6
IL-17	Interleukin-17
TNF-α	Tumor Necrosis Factor-alpha
CRP	C-reactive Protein
BBB	Blood-Brain Barrier
CNS	Central Nervous System
CSTC	Cortico-Striato-Thalamo-Cortical
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
Y-BOCS	Yale-Brown Obsessive Compulsive Scale
SSRIs	Selective Serotonin Reuptake Inhibitors
CBT	Cognitive Behavioral Therapy
ERP	Exposure and Response Prevention
TR-OCD	Treatment-Resistant Obsessive-Compulsive Disorder
MBCT	Mindfulness-Based Cognitive Therapy

ELISA	Enzyme-Linked Immunosorbent Assay
BMI	Body Mass Index
SPSS	Statistical Package for the Social Sciences
SEM	Standard Error of the Mean
NIMH	National Institute of Mental Health
OPD	Outpatient Department
IPD	Inpatient Department

Glossary

Term	Definition
Biomarker	A measurable biological indicator used to detect or monitor a disease or physiological condition.
Blood-Brain Barrier (BBB)	A selective semipermeable membrane that protects the brain by restricting the passage of substances from the bloodstream.
Body Mass Index (BMI)	A numerical value calculated from height and weight used to assess body fat and categorize individuals.
Central Nervous System (CNS)	The part of the nervous system consisting of the brain and spinal cord.
Cognitive Dysfunction	Impairment in mental processes such as memory, attention, or decision-making.
Cytokines	Small signaling proteins released by immune cells that regulate inflammation and immune responses.
ELISA	A laboratory technique used to measure the concentration of specific proteins, such as cytokines, in biological samples.
Glial Cells	Supportive cells in the CNS, including microglia and astrocytes, involved in immune defense and neuronal support.
Immune Dysregulation	Abnormal functioning of the immune system that can lead to excessive or insufficient immune responses.
Interleukin-22 (IL-22)	A cytokine involved in immune responses and inflammation, studied for its potential role in psychiatric disorders.
Neuroimmunology	The field of study that explores interactions between the nervous system and the immune system.
Neuroinflammation	Inflammatory response within the CNS, often involving activation of glial cells.

Term	Definition
Neurotransmitters	Chemical messengers that transmit signals between neurons in the brain.
Obsession	Recurrent, intrusive, and unwanted thoughts, urges, or images experienced in OCD.
Obsessive-Compulsive Disorder (OCD)	A mental disorder characterized by persistent obsessions and compulsions that interfere with daily life.
Peripheral Inflammation	Inflammatory processes occurring outside the central nervous system, often in the bloodstream or body tissues.
Serum	The liquid component of blood obtained after clotting, used for biochemical analysis.
Synaptic Activity	The process of signal transmission between neurons at synapses.
Yale-Brown Obsessive Compulsive Scale (Y-BOCS)	A standardized clinical tool used to assess the severity of OCD symptoms.
Vagus Nerve	A major nerve that connects the brain to various organs and plays a role in neuroimmune communication.

Chapter 1

Introduction

1.1 Obsessive-Compulsive Disorder (OCD)

1.1.1 Definition and Clinical Presentation

Obsessive-Compulsive Disorder (OCD) is a chronic disorder and severe mental health condition. It's defined by the experience of having unwanted and persistent thoughts known as obsessions. Even while wrestling with unwelcoming thoughts, people often find themselves pulled toward doing certain things over and over again. These are called compulsions. Unwanted ideas, impulses, or pictures keep coming back, causing clear unease, which experts call obsessions according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* guidelines. What counts isn't just physical routines but also hidden thinking patterns done to soothe inner pressure. Actions repeat not because they bring joy, but because stopping feels impossible under strict internal scripts (Stein et al., 2019). These symptoms are in conflict with self-image. This means they are experienced as alien and repulsive by the individual. They feel forced to perform them, even though they recognize their irrationality most of the time (Chowdhury et al., 2016). People with obsessions fight against their own thinking, which is the main distinction between obsession and delusion. On the other hand, a person suffering from a delusion genuinely thinks those ideas are essential and logical. For an official diagnosis of OCD in patients, obsessions and/or compulsions must cross a threshold of clinical significance. This happens when these behaviors substantially disrupt a person's everyday tasks and social interactions or take up more than an hour each day (Etkin et al., 2024). The condition feeds on a cycle of unwanted thoughts that make the person feel scared or in danger. Because of this, actions become automatic ways to handle fear. Although those acts bring short relief, they slowly teach the mind that repeating them matters, trapping thoughts in loops. Not everyone feels OCD the same way. A few find it barely noticeable, while others face it heavily. Although the level of insight varies, many patients gain an understanding of how illogical their attitudes and behaviors are. OCD often has a long history with periods of worsening and getting better. Moreover, it often goes along with other mental illnesses like anxiety disorders, depression, and tic disorders.

1.1.2 Global Epidemiology of OCD

OCD is a common mental health disorder that touches all socioeconomic groups, cultures, and ethnicities. According to the global epidemiology of OCD, it is a common form of psychopathology that has a significant impact on disability worldwide (Stein et al., 2019). Clinical studies have indicated that it was a rare disorder. However, a 1% to 3% lifetime incidence rate has been documented for a wide population using standardized criteria (such as DSM III) (Staley & Wand, 1995). According to current estimates, the lifetime prevalence of full-blown OCD is 2.5%, with a current prevalence of 1%. However, it has also been indicated that its subthreshold manifestation, which does not fulfill the requirements for an official diagnosis, occurs in as many as a third of the overall population (Torres et al., 2017). The disease is normally seen to start at late childhood or early adulthood with a bimodal onset pattern. Early onset OCD is normally seen as a neurodevelopmental subtype of the disorder. Males normally have an early onset of the disorder compared to females. However, the prevalence of the disorder is normally similar in both sexes (Girone et al., 2024). Despite the fact that there is a absence of cross-national data from middle and low-income countries, national surveys have identified OCD as a significant global problem. In addition to that, there has been more than 10,000 publications about OCD and related disorders globally since 2002 up to 2021 based on data from Scopus. (Grover & Gupta, 2022).

1.1.3 Prevalence and Social Context of OCD in Bangladesh

The prevalence and sociocultural context of OCD in Bangladesh has some unique problems as there is little information available on the prevalence of the disease, and mental illness is highly stigmatized. Children in Bangladesh were found to show a greater occurrence of OCD of 2% which is higher than before (Chowdhury et al., 2016). Little information exists on the epidemiology of OCD in Bangladesh, and no national survey of the country has ever been carried out. Community estimates show prevalence rates of 0.5-2.5% but this is restricted by methodological limitations such as low sample size, an absence of validated instrumentation to measure prevalence and possible underreporting of cases due to stigma. The clinical and sociodemographic characteristics of individuals with OCD have been documented in Bangladesh, and the cross-sectional studies have been carried out to illuminate their symptoms and severity (Algin, Sajib, and Arafat, 2020). An investigation in Dhaka, Bangladesh, revealed that OCD presented abnormally in patients in a cross-sectional study design (Hossain, Ferdush, and Rahman, 2020). A validated adaptation of the Dimensional Obsessive-Compulsive Scale

(DOCS) in Bangali is available, which can be utilized to accurately identify the severity of OCD (Algin, Nahar, Sajib, and Arafat, 2018).

Regardless of its apparent prevalence, the seeking of mental healthcare in Bangladesh is comparatively lower, in particular among females, due to a number of socio-cultural factors (Sheoti and Alam, 2025). Stigma regarding mental illnesses is universal in occurrence and constitutes an important hindrance in seeking help for their treatment, especially in both rural and urban parts of Bangladesh (Faruk et al., 2023). It may often be worsened by low mental health literacy and attributing symptoms to spiritual issues, for example, jinn possession. Some of the problems associated with the mental healthcare system in Bangladesh include low availability of qualified specialists (less than 0.1 psychiatrists for every 100,000 people), the lack of OCD public health policy, and no treatment guidelines within the country (Koly et al., 2024). Children and youths in Bangladesh have notable mental health problems with an estimated prevalence rate of mental illness of 12.6% in children aged between five and ten years old (Mullick & Goodman, 2005). Mental health service provision for children and youths in Bangladesh is quite scarce and poorly distributed as well (Khan & Mullick, 2024). Individuals with disabilities in Bangladesh also face significant barriers to mental health support, often prioritizing physical disability over mental health (Saba et al., 2024).

Comorbidity is an important feature of the OCD, greatly increasing the complexity, severity, and distress caused by the disorder (Torres et al., 2017). Research shows that OCD usually coexists alongside co-occurring psychiatric illnesses, such as mood and anxiety-related disorders, substance use disorders, somatic symptom disorders, impulse-control disorders, and tic disorders (Petribú, 2001). One of the most prevalent co-occurring disorders identified in pediatric OCD is Major Depressive Disorder (MDD) and the presence of this disorder can influence the manifestation of MDD (Strouphauer et al., 2024). One more personality disorder that is usually comorbid with OCD is Obsessive-Compulsive Personality Disorder (OCPD). According to certain studies, OCPD is the most prevalent personality disorder among OCD sufferers (Dondu & Sevincok, 2025). However, OCPD and OCD have to be differentiated due to the dissimilarity of their symptoms. Whereas OCPD is an ego-syntonic disorder (the person feels that his/her actions are right), OCD is an ego-dystonic disorder (obsessive and unwanted thoughts). Comorbidity generally increases disability and complicates treatment. In the case of comorbid major depressive or anxiety disorder, for example, OCD symptoms may be expressed differently (Viswanath et al., 2012).

Perinatal phase involves both pregnancy and postpartum periods, which increase the risk of developing or worsening OCD conditions. These kinds of OCD are commonly referred to as perinatal OCDs (pOCDs) (Norris et al., 2026). The highest levels of the global prevalence rate of pOCDs are recorded as 9.1% in the pregnancy period and 6.2% in the postpartum phase (Salari et al., 2024). It is important to note that pOCD should not be confused with postpartum psychosis because of the difference in reality recognition level. Etiology of OCD includes an intricate interaction of biological and non-biological factors, with familial aggregation being firmly established (Blanco-Vieira et al., 2023). Biologically, OCD is classified as hyperactivity of the CSTC circuitry, which is essential for decision-making and forming habits. Hyperactivity results in an ongoing "error signal" in the brain, which causes obsession and compulsions. Successful treatment modalities of OCD include Selective Serotonin Reuptake Inhibitors (SSRI) medication and ERP psychotherapy, which both affect such processes. SSRI increases serotonin concentration, thus resulting in neuroadaptation within the CSTC loop. ERP psychotherapy, on the other hand, seeks to develop a new inhibitory mechanism in order to negate any prediction of fear that connects obsessions to compulsions.

1.2 Pathophysiology of OCD

1.2.1 Neuroanatomical Abnormalities: Cortico-Striato-Thalamo-Cortical (CSTC) Circuit

Cortico-striato-thalamo-cortical (CSTC) circuit is commonly considered a key neuroanatomical basis of OCD. The circuit is connected to other parts of the brain, such as the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), striatum (caudate and putamen), and thalamus (Hu, 2024). This circuit is believed to be overactive in OCD patients and results in a long-standing error signal that is difficult to shut off by the brain. This is the internal alarm that makes the patient become obsessed and compulsive in a bid to solve a perceived threat that never actually goes away (D'Acquisto et al., 2023). The neuroimaging data have continually revealed hyperactivity in the OFC and caudate in patients with active OCD, which reduces after effective SSRI therapy (Kamble & Dandekar, 2023).

The CSTC circuit works by maintaining a balance between direct (Go) and indirect (No-Go) routes that have their origin in the striatum. The imbalance towards the direct pathway is proposed to be a reason in OCD, where the inhibitory output of the globus pallidus to the thalamus is insufficient to stop thalamocortical disinhibition and over-excitatory drive to the OFC and ACC. This forms a positive feedback loop that reverberates. The ACC is a key

mediator of conflict monitoring, and an increased activity of the ACC related to errors is a solid neurobiological observation of OCD. Other neuropsychiatric conditions such as Tourette syndrome (that commonly co-occurs with OCD) also involve dysregulation of these loops, suggesting that they share common neurobiological mechanisms (Kamble & Dandekar, 2023). In addition to the classical CSTC circuit, recent neuroimaging and rodent studies indicate that other neural regions and connectivity-level impairments may be involved in OCD, broadening the neuroanatomic knowledge of OCD (Jijimon et al., 2026). An example is the cerebellum, which is increasingly being acknowledged as a cause of OCD, and neuroimaging research has demonstrated that this brain region has structural and functional differences between OCD patients and healthy controls (Yang et al., 2025). The abnormalities of white matter, especially extensive decreases in white matter coherence across regions including the corpus callosum, anterior and posterior cingulate cortex, and prefrontal cortex have been also regularly found in OCD patients in diffusion tension imaging (DTI) (Masjoodi et al., 2024).

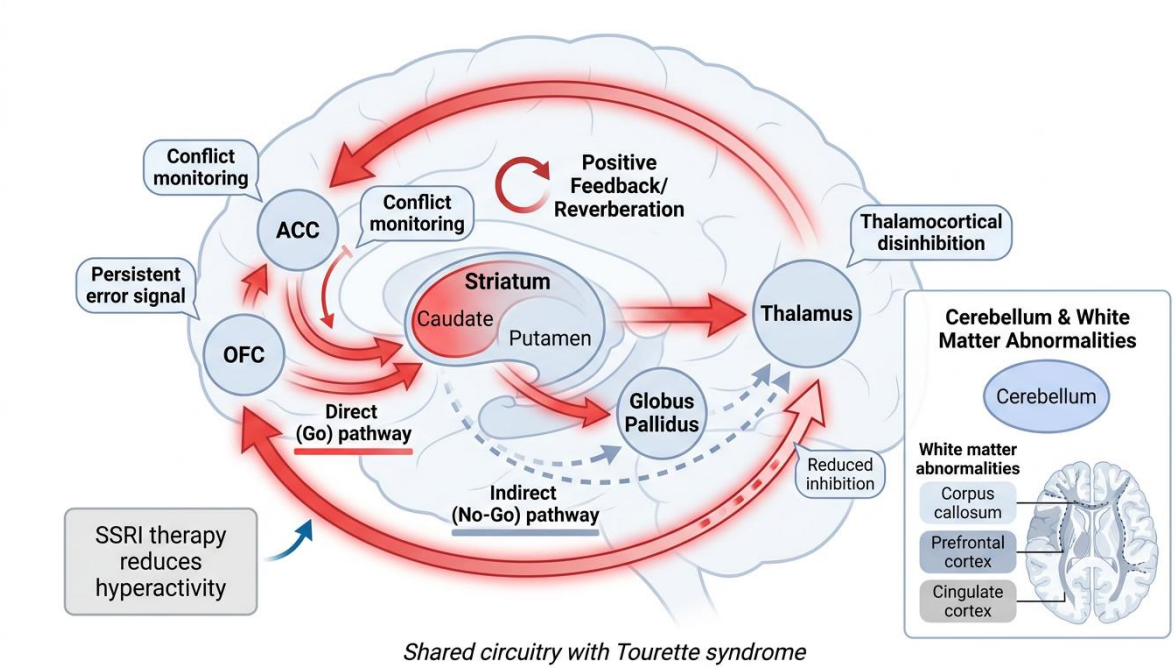


Figure 1: CSTC Circuit Dysfunction in OCD

1.2.2 Neurotransmitter Dysregulation: Serotonin, Dopamine, and Glutamate

The neurological understanding of OCD revolves around neurotransmitter abnormalities, specifically those involving serotonin, dopamine, and glutamate.

1.2.2.1 Serotonin

Serotonin plays a vital role in controlling mood and impulse control. Drugs that raise serotonin levels, including SSRIs, are the initial medications used in the treatment of OCD (Hu, 2024). The action of the SSRIs is to inhibit the reuptake of serotonin and raise its levels in the synaptic cleft. Thus, it causes adaptive modifications in the CSTC loops that contribute to suppressing hyperactivity. Nevertheless, OCD commonly needs more doses and extended periods of SSRIs treatment than other disorders, such as depression, implying a more profound and multifaceted serotonergic imbalance. It is believed that the therapeutic action of SSRIs is the desensitization of presynaptic 5-HT1A auto receptors and shifts in the expression and sensitivity of postsynaptic receptors in the CSTC loops (Kamble & Dandekar, 2023).

1.2.2.2 Dopamine

Dopamine is crucial in the processing of rewards, motivation, and learning of habits. It is dysregulated in OCD and especially in the development and maintenance of compulsions. Disturbances in the availability of dopamine receptors (particularly D2 receptors in striatum) and dysfunctional dopaminergic signaling of the CSTC circuits have been consistently identified in OCD (Mota et al., 2026). In patients whose OCD is difficult to treat with SSRIs or who also have comorbid tic disorders (many of which block dopamine D2 receptors), SSRIs may be augmented with low-dose atypical antipsychotics (Kamble and Dandekar, 2023). This implies the possibility of controlling the salience of obsessions and the temptation to engage in compulsions by modulating dopaminergic activity. The occurrence of hyperactivity of dorsal striatal dopamine transmission can lead to fronto-cortical hypoactivity and directly affect the anxiety and compulsive behaviors in rats, which suggests a causal relationship between the dopamine and CSTC circuit malfunction (Casado-Sainz et al., 2021).

1.2.2.3 Glutamate

According to the glutamate hypothesis of OCD, hyperactivity in the CSTC circuit due to the excitatory neurotransmitter glutamate is the source of the disorder (Restifo-Bernstein et al., 2026). A disturbance in the proportions between glutamate and gamma-aminobutyric acid (GABA) in the CSTC circuit is assumed to be directly linked with the development of OCD (Hou et al., 2025). Proton magnetic resonance spectroscopy (^{1}H MRS) imaging research efforts have explored glutamate levels in unmedicated OCD participants, with a meta-analysis showing that there is neurometabolic dysregulation in the CSTC circuits (Zhu et al., 2025). Too much glutamatergic signaling may result in maladaptive synaptic plasticity, in which the

learning mechanisms in the brain make the wrong decisions and have the pathological pathways reinforced and solidified, trapping the CSTC loops into non-welcoming, repetitive loops. This school of thought has stimulated the creation of new glutamatergic therapy of OCD. A case shows fast but short-lived relief from obsessive symptoms after one low-dose ketamine treatment, an agent blocking N-methyl-D-aspartate (NMDA) receptors - effects possibly tied to its stronger impact on inhibitory GABA nerve cells (Kamble & Dandekar, 2023). Glutamate and GABA balance, carefully managed by astrocytes, becomes disrupted when these brain support cells fail, contributing to OCD mechanisms; such breakdown might drive harmful overactivity in glutamate signaling (Gonzalez & Bezzi, 2025).

Neurotransmitter	Key Functions	Role in OCD	Citations
Serotonin	Regulates mood, impulse control, and emotional stability	Dysregulation leads to impaired control over intrusive thoughts and compulsive behaviors; requires higher SSRI doses, indicating complex serotonergic dysfunction	(Hu, 2024; Kamble & Dandekar, 2023)
Dopamine	Involved in reward processing, motivation, and habit learning	Altered D2 receptor activity and dopaminergic signaling contribute to compulsive behaviors and habit formation	(Mota et al., 2026; Casado-Sainz et al., 2021)
Glutamate	Main excitatory neurotransmitter; regulates synaptic plasticity and neural signaling	Excess glutamatergic activity causes CSTC circuit hyperactivity and maladaptive learning, reinforcing repetitive behaviors	(Restifo-Bernstein et al., 2026; Hou et al., 2025; Zhu et al., 2025; Gonzalez & Bezzi, 2025)

Table 1: Summary of Neurotransmitter Dysregulation in OCD

1.2.3 Genetic and Environmental Factors

OCD is a complex disorder that depends on environmental elements and genetic factors (Wilson et al., 2023). Genetic changes are essential to the pathophysiological course, as most of the situations are hereditary or family-related (Beheshti et al., 2023). Research has found

substantial genetic overlap between OCD and other disorders, such as Tourette Syndrome, indicating that there is shared polygenic risk that affects the formation of primary brain pathways, especially the CSTC circuit (Kamble & Dandekar, 2023). Epigenetic shifts, especially changes in how DNA is methylated, show up in OCD brains in regions like the anterior cingulate and orbitofrontal cortex, plus parts of the ventral striatum light up on scans. When kids face harsh environments like, home violence or mistreatment, it may leave lasting marks that shape mental health down the road. These early pressures don't act alone; they team up with inherited risks and quietly raise odds for problems such as OCD years later. Stress during growth stages sets a stage where genes and surroundings collide, nudging some toward clinical struggles. Though triggers differ, one pattern holds: body chemistry alters when experience shapes biology.

1.3 Neuroinflammatory Hypothesis of OCD

1.3.1 Immune System and Central Nervous System Crosstalk

There are an active, dynamic bi-way communication of the immune system and the central nervous system (CNS) that is important in the overall physiological homeostasis (Fan et al., 2024). The CNS has always been considered to be immunologically shielded i.e. it has never been in contact with the immune system. However, recent breakthroughs in the field of neuroimmunology have revealed that the CNS communicates with the immune system in a number of ways. Fan et al. (2024) also state that the communication between the immunological system and the CNS can be achieved via different pathways including a neural route, humoral route, and cellular route. In the neural route of communication, the process is carried out through the autonomic nervous system and the vagus nerve. In the humoral route of communication, the process is carried out through the immune molecules such as cytokines. These molecules can pass through the circumventricular organs of the brain because they are not fully covered with the blood-brain barrier. Moreover, the endothelial cells in the blood vessels of the brain can also participate in the process of communication.

Neuroinflammation, a vital part of this interaction, is defined by glial cell activation. Found within the spinal cord and brain, microglia, along with astrocytes, build a protective network across neural tissue. Following activation, such cells discharge various molecules tied to inflammation, altering how neurons communicate at synapses. These shifts often emerge quietly yet reshape local circuit behavior over time. Although neuroinflammation is considered a protective mechanism in the CNS, chronic activation can impair CNS functions (Farooqui,

2022). Additionally, the activation of peripheral immunity is another vital process that can influence CNS activity. After the activation of the innate immunity, various immune cells produce inflammatory cytokines, which are released into the bloodstream. These neurotransmitters and neuroendocrine functions may be affected by these inflammatory cytokines and eventually the behavior and cognition. Such mechanisms are being increasingly implicated in different psychiatric disorders, like OCD, and thus underscore the significance of the interaction between the CNS and the immune system (Fan et al., 2024).

Hypothesis/Model	**Description**	**Mechanism**	**Relevance to OCD**	**Citations**
Neural Pathway Hypothesis	Suggests direct communication between the immune system and CNS via neural circuits	Signals transmitted through the autonomic nervous system and vagus nerve	May influence brain activity and behavior through rapid signaling pathways	(Fan et al., 2024)
Humoral Pathway Hypothesis	Proposes that immune molecules mediate communication between peripheral immunity and the brain	Cytokines enter the brain via circumventricular organs or act through endothelial cells	Can alter neurotransmission and contribute to obsessive-compulsive symptoms	(Fan et al., 2024)
Neuroinflammation Hypothesis	Suggests that activation of immune cells within the CNS affects brain function	Activation of microglia and astrocytes leads to release of inflammatory mediators	Chronic neuroinflammation may disrupt neural circuits involved in OCD	(Farooqui, 2022)
Peripheral Immune Activation Hypothesis	Proposes that systemic immune	Peripheral cytokines affect	May contribute to behavioral and	(Fan et al., 2024)

Hypothesis/Model	Description	Mechanism	Relevance to OCD	Citations
	responses influence CNS activity	neurotransmitters and neuroendocrine systems	cognitive changes seen in OCD	

Table 2: Hypotheses of Immune System–CNS Crosstalk

1.3.2 Cytokines and Blood-Brain Barrier

Cytokines are small yet highly powerful signaling molecules which play a central role in regulating the immune response in the body. They are very crucial in maintaining homeostasis in the body. They mediate anti-inflammatory and pro-inflammatory actions. Studies conducted in recent years have shown that the disorder in the level of cytokines is intimately associated to the emergence of different forms of neuroinflammatory diseases, including psychiatric disorders, such as OCD. Changes in the levels of cytokines have also been identified to be the cause of abnormal brain functioning in humans. Blood-brain barrier (BBB) is a point of interface between the central nervous system (CNS) and peripheral circulation. The BBB is composed of specialized endothelial cells. These cells are linked via junctional proteins like claudin-5, occludin and zonula occludens. The structural components of the BBB ensure that no foreign particles and excess cytokines penetrate the CNS, thus maintaining homeostasis in the body (Greene et al., 2017).

Still, when systemic inflammation occurs, the blood-brain barrier can lose its tight control. That happens as inflammatory cytokines entering circulation alter how endothelial cells along the barrier operate. This would result in the increased permeability of the BBB. This would then enable the easy entry of the immune mediators of the peripheral immune system into the CNS. This would then expose the brain to the inflammatory mediators that may induce neuroinflammation. In various neuroinflammatory and neuropsychiatric conditions, such as OCD, the dysfunction of the BBB may be of critical importance. In this condition, the entry of the peripheral immune cells into the CNS through the disruption of the cytokine network may induce damage and the activation of the resident immune cells of the CNS, such as microglia. This would then induce a cycle of inflammation that may be responsible for the maintenance of the neuropsychiatric symptoms. Therefore, the interaction between cytokines and the BBB is now recognized as being of critical importance in the immunological aspects of OCD.

1.3.3 Evidence of Neuroinflammation in OCD

A considerable amount of evidence has pointed towards the function of neuroinflammation in the etiopathology of OCD. Various clinical and experimental research works have demonstrated changes in immune markers, especially pro-inflammatory cytokines, in persons with OCD. Pertinent cytokine levels of IL-1, TNF-α, IL-6, and IL-17 in the peripheral blood of OCD individuals have been clearly evidenced by numerous studies (Sarmin et al., 2024). These cytokines have been reported to be related to a number of biological processes, like inflammation and have been also implicated in the regulation of the functions of neurotransmitters and neuronal pathways. The involvement of these cytokines in OCD has further been demonstrated in various meta-analytical research works, which have demonstrated generalized changes in cytokine profiles in patients with OCD (Chen et al., 2024). IL-1β and IL-6 have especially been demonstrated to be involved in OCD, considering their strong pro-inflammatory properties and role in modulating various neurobiological functions associated with OCD (Sarmin et al., 2024). In addition, other cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-17 have also demonstrated significant associations with OCD in case-control research works (Sarker et al., 2023). Besides the cytokines, other indicators of inflammation have been observed in OCD patients. These are neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) that are often observed in patients with OCD. These ratios are regarded as indirect indicators of the activity of the immune system (Bulut et al., 2021). In addition, increased neutrophil gelatinase-associated lipocalin (NGAL) is also detected in patients with OCD (Raposo-Lima et al., 2021). In recent times, various global health issues such as the COVID-19 pandemic have also contributed to a better understanding of the relationship between inflammation and OCD. Some studies have indicated that increased inflammatory responses in patients with COVID-19 might trigger OCD symptoms (Nezgovorova et al., 2022). In addition, cytokine profiles have been detected in pediatric patients with OCD and related movement disorders (Fabricius et al., 2022).

1.4 Immunological Basis of Psychiatric Disorders

The activity of the immune system in mental health is a rapidly developing field of study, and an increasing number of studies are connecting immune dysregulation with a broad spectrum of psychiatric conditions (Evrensel and Tarhan, 2020).

1.4.1 Role of Immune System in Mental Health

The CNS and immune system are in tight relation and are constantly in contact with one another by complicated signaling mechanisms. The immune system and CNS have been found to not be two separate systems but closely interconnected and interrelated in a manner that they are essential to the overall physiological and psychological well-being of the human brain (Fan et al., 2024). The significance of the host defense mechanism in the overall health of the brain has been highlighted by diverse studies and observations in the last couple of years. We have seen that the immune system is highly related to the general well-being of the brain by the way of inflammatory responses. The evolution and progression of a number of neuropsychiatric conditions encompassig major depressive disorder and anxiety disorder have been linked to chronic low-grade inflammation. In the past few years, increased levels of inflammatory markers such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) have been observed in individuals with major depressive disorder and anxiety disorder. Such inflammatory reactions can send signals to the brain and cause central neuroinflammation, thus impacting the normal operation of the brain (Fan et al., 2024).

Among the outstanding effects of neuroinflammation is the stimulation of microglia, which plays the part of ensuring the immune functions in the CNS. The activation of microglia interferes with normal synaptic pruning. The distortion in synaptic pruning leads to an un-normal amount of elimination and inability to eliminate synaptic connections. The asymmetry of the pruning of the synapses is bound to disrupt the usual functions of the neural circuits. Moreover, neuroinflammation targets astrocytes, which play a critical part in ensuring a balance of neurotransmitters, particularly glutamate. This disruption of the normal activity of astrocytes will most likely lead to excitatory stress, which will further harm neural structures (Fan et al., 2024). These neural changes and their impact on neurons and astrocytes have profound impacts on neural circuits. As a result, deviant immune system and inflammatory mechanisms have been discovered in a number of psychiatric disorders. Such disorders are the bipolar disorder, the major depressive disorder, the schizophrenia, and the OCD. An understanding of the significance of immune processes in mental health offers a perspective on novel treatment of psychiatric diseases (Hughes and Ashwood, 2020).

1.4.2 Cytokine Imbalance in Psychiatric Disorders

One of the most significant aspects of dysfunction of the immune system during psychiatric disorders is the imbalance in cytokine networks, including the OCD. Cytokines are signaling molecules, which play a vital role in the normal operation of the immune system and mediate both inflammatory and anti-inflammatory responses (Hughes and Ashwood, 2020). In psychiatric disorders where pro-inflammatory cytokines are more predominant, including tumor necrosis factor-alpha (TNF-a), interleukin-1 (IL-1), and interleukin-6 (IL-6) these cytokines can have a marked impact on brain functions and behavior. Indicatively, higher concentration of these cytokines may cause sickness behavior, which is typified by loss of energy or reduced motivation, anhedonia, and withdrawal. Mechanistically, this is facilitated by downregulation of mesolimbic dopamine systems alongside hyperactivation of hypothalamic-pituitary-adrenal axis. Additionally, enhanced tryptophan metabolism via neurotoxic pathways ultimately affects neural plasticity and neurotransmitter homeostasis (Fan et al., 2024).

One of the examples which illustrate how the dysfuncturing of the immune system can affect cognition, emotion and behavior is the modulation of neurotransmission via cytokines. The process of inflammatory signaling has the potential to reasonably interfere with an essential neural circuitry that is implicated in psychiatric disorders. Emerging evidence has also pointed to the involvement of the gut-brain axis in psychiatric disorders, such as OCD. Systemic inflammation and cytokine imbalance have been linked to dysbiosis, or a lack of balance in the composition of gut microbiota. This interaction between the gut and the CNS has consequently indicated that there is an interrelation between the disturbances of the gut microbiota and immune modulation leading to a cytokine imbalance. The interconnection between gut microbiota and cytokines has thus pointed to an imbalance in cytokines not only being central to the immune system but also being modulated by peripheral immune modulation, thus incorporating various factors in psychiatric disorders (Fan et al., 2024). The disproportionate level of cytokines has therefore indicated a correlation between different elements in mental illnesses.

1.5 Biomarkers in Psychiatry and OCD

1.5.1 Definition and Importance of Biomarkers

Biomarkers are quantifiable signals of biological or disease-driven processes and can provide an objective window into complex conditions. In psychiatry, where conditions such as OCD

tend to be heterogeneous and clinically similar, biomarkers can assist in resolving diagnostic uncertainty and personalizing care (Evrensel & Tarhan, 2020). In the case of OCD, the development of reliable biomarkers is of significant interest in terms of differentiating between subtypes of the condition, predicting the response of the condition to treatment, and understanding the neurobiological and immunological substrates of the condition. They can include genetic factors, neuroimaging patterns, and biochemical factors such as cytokines and can provide a link between the molecular and clinical levels (Proshina et al., 2025).

1.5.2 Role of Peripheral Biomarkers

Peripheral biomarkers, particularly cytokines, have been of significant interest in psychiatric studies. This is because they can be easily measured and offer an opportunity to investigate the systemic immune system. In the case of OCD, the use of such biomarkers has been beneficial in detecting the presence of the disorder, measuring the level of symptoms demonstrated by the patients, and evaluating the response of the patients to the therapeutic interventions (D'Acquisto et al., 2023). Among those affected by the condition, scientific attention has turned toward certain immune signaling molecules - IL-17, IL-6, IL-1β, TNF-α. Because they interact with brain-immune pathways, their presence might help explain features seen in OCD (Coelho et al., 2024). Although various potential biomarkers such as hormonal factors, immunological factors, serological factors, and neuroimaging factors have been proposed in the case of OCD and other psychiatric conditions, no single marker has been universally accepted. This is attributed to the inherent heterogeneity of the disorder (Evrensel & Tarhan, 2020). However, studies carried out on the use of peripheral factors in OCD have shown the potential of such factors in the diagnosis and treatment of the disorder and in the understanding of the neurobiological factors involved in the disorder.

1.5.3 Pro-inflammatory vs. Anti-inflammatory Cytokines

Neuroinflammation involves the interplay of the anti-inflammatory and the pro-inflammatory cytokines in the brain that must remain balanced in order to facilitate proper function of the brain. In OCD, there is a tendency towards the state of inflammation as seen by the increase in the expression of different cytokines including IL-17, IL-1β, TNF-α, and IL-6 (Sarmin et al., 2024). For instance, in unmedicated and comorbid-free OCD, it has been observed that the degree of IL-6 in the plasma is significantly high in OCD patients. However, the results may not always be consistent and may be attributed to various factors such as the absence of medication, the severity of the illness, and the presence of concurrent illnesses (Jose et al.,

2021). The elivated concentration of pro-inflammatory cytokines points to the engagement of the immune system in the disease mechanism of OCD. However, anti-inflammatory cytokines, like IL-10, occur at reduced levels, pointing to the absence of the normal inflammatory response. The difference in the levels of pro- and anti-inflammatory cytokines suggests the need for an investigation of the influence of the immune system in the pathophysiology of OCD and its possible use as a diagnostic tool for OCD (Maia et al., 2025).

1.5.4 Clinical Significance of Cytokine Biomarkers

The cytokine biomarkers have great potential for practical applications, specifically in the development of a more personalized approach to the management of OCD. It may be possible to identify different types of OCD, such as those with increased levels of immune responses, by the specific inflammatory profiles of the patients. This could be helpful in guiding the clinicians in the selection of the most suitable treatment approaches, including the administration of anti-inflammatory agents or those that are known to affect the immune responses (Nezgovorova et al., 2022). However, the results of the cytokine amount in OCD patients in the past studies have not been consistent, which could be due to differences in the design of the studies, the number of patients, and the approaches used in the investigations (Chen et al., 2024). Nevertheless, the current studies on cytokine levels in patients with OCD have great promise for the development of new approaches in the identification and the formation of innovative therapeutic approaches in the management of the illness (Bazarra Castro et al., 2024).

1.6 Interleukin-22 (IL-22)

IL-22 (interleukin-22) is a cytokine, which was identified as part of the cytokine family IFN-IL-10. IL-22 is linked with crucial physiological roles related to the host defense, tissue homeostasis, and tissue regeneration. Although the normal functions of the cytokine are significant, excess production and malfunction of the cytokine may lead to a number of diseases. This may involve autoimmune diseases, infectious diseases, heart diseases, allergic diseases and cancer. At the same time, the cytokine became the subject of study in connection with the nervous system; the cytokine can cause neuroinflammation and neuropsychiatric disorders, such as OCD (Seth & Dubey, 2023).

1.6.1 Biology and Cellular Sources of IL-22

IL-22 secretion is mainly by various classes of immune cells. These are the T helper type 17 cells, Th22 cells, gamma delta T cells and innate lymphoid cells type 3 that bear NKp46 markers on their surface. The importance of IL-22 as a cytokine, considering the involvement of innate and adaptive cells within the immune system, is crucial for cell communication within the immune system (Seth & Dubey, 2023).

1.6.2 IL-22 receptors and signaling pathways

IL-22 works with the IL-10R2 and IL-22R1chains that constitute the IL-22 receptor (Seth and Dubey, 2023). It is worth noting that these cellular targets are located in non-immune cells such as epithelial and stromal cells. After the binding of IL-22 to the binding site, the signaling cascades are triggered in the cell. The biggest IL-22 binding-initiated signaling cascade is the JAK-STAT one, especially, STAT3, which is activated (Chen et al., 2022). However, IL-22 signaling is also observed in the activation of MAPK and PI3K pathways due to IL-22 binding to the receptors. Hence, the role of IL-22 in the body is to maintain tissue barriers and repair.

1.6.3 Role in Systemic Inflammation and Autoimmunity

The IL-22 is implicated in systemic inflammation and auto-immune diseases. As a protective function, it helps in preserving the mucosal barrier, leading to tissue healing, which is observed in colitis. Conversely, in case there is a disturbance in IL-22, it can be responsible for causing illness. Indicatively, the IL-22 activates the effect of keratinocytes and synoviocytes leading to inflammation in psoriasis and rheumatoid arthritis (Chen et al., 2022). The above example shows that IL-22 effect differs in different conditions and is beneficial in some but detrimental in others.

1.6.4 Emerging Evidence in Neuropsychiatric Disorders

Appearing in recent analyses, IL-22 might contribute to neuropsychiatric conditions through its influence on communication between nervous and immune systems. While evidence remains tentative, work from Seth and Dubey's team in 2023 points toward an association with inflammatory processes in the brain. Immune cell activity inside nerve tissue seems to shift when this molecule is present. Instead of simply crossing passively, certain signals seem to encourage entry through altered barriers. One such change involves the interface guarding the brain from circulating factors. When activated, resident support cells respond in ways that amplify local chemical messaging. Consequently, inflammatory molecules rise in

concentration inside the nervous system. As part of this shift, more white blood cells accumulate where they normally remain scarce. IL-22 may be implicated in affecting the gut–brain axis, thereby linking peripheral immune effects to central nervous system effects. This is particularly relevant in relation to gut microbiota effects in psychiatric disorders. Some research has investigated IL-22 levels in pediatric patients with neurodevelopmental disorders, including autism spectrum disorder, as revealed by research conducted by Sallam et al. in 2024. These effects may be related to dysregulation of IL-22, thereby affecting immune response in the central nervous system. It is possible that IL-22 stimulates glial cell activity, which leads to improved pathways of inflammatory signals, possibly linked to central nervous system effects. Still, even with current data, evidence remains too weak to confirm any clear causal relationship involving IL-22 and OCD. Most research points merely to correlations - nothing definitive - suggesting deeper investigation is necessary before conclusions can be drawn. Changes might sit at the edges of immune function, involve brain inflammation, or emerge through immune-to-brain communication pathways.

1.7 Diagnosis and Assessment of OCD

1.7.1 DSM-5 Diagnostic Criteria

OCD can be diagnosed as per the provisions of the DSM-5 criteria. Occasionally, a clinician identifies OCD when persistent thoughts, repetitive behaviors, or some mix of the two take up substantial time - say, beyond an hour each day. These patterns might also cause notable emotional strain or interfere with relationships, work, or daily responsibilities. Sometimes, it's the disruption that signals something requires attention. Not always obvious, yet measurable through impact rather than appearance alone. Thoughts that intrude without warning (often disturbing, unwanted) define what people call obsessions; these clash with a person’s sense of self. Anxiety tends to follow closely behind such mental disruptions. Instead of accepting discomfort, someone might repeat certain routines: cleaning hands again, verifying locks multiple times, and arranging items precisely. These outward habits, along with inner rituals like silent prayers or fixed patterns of counting, make up compulsions. Their purpose? Lessening tension sparked by obsessive thinking or blocking feared outcomes believed to loom nearby. Such compulsions are normally associated with obsessions or are carried out based on a set of rules. These obsessions do not have any realistic links to the aversion of the dreaded occurrence. They do not occur as a result of substance use, medical condition, or any other psychiatric condition (Zdybel, Rdzanek, and Skrzypek, 2025).

1.7.2 Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is considered the "gold standard" of a clinical assessment that measures the intensity of the symptoms experienced by those with OCD (Fineberg, 2004). There are ten questions on the scale, five of which relate to obsessions, while the other five questions pertain to compulsions, ranging from zero to forty. A higher score on this scale indicates a higher severity of symptoms (Storch et al., 2015). Y-BOCS is a commonly used scale for measuring symptoms in both clinical and research settings. For a patient to be said to respond to a particular treatment, a reduction of more than 35% in Y-BOCS is required. Similarly, a patient must have low scores on Clinical Global Impression ratings and a Y-BOCS score of 12 or lower in order to be considered in remission (Ramakrishnan et al., 2024).

1.8 Treatment of OCD

1.8.1 Pharmacological Treatment

1.8.1.1 Selective Serotonin Reuptake Inhibitors (SSRIs)

One of the first-line treatment of OCD is the SSRI (Simpson, 2009). They work in a manner that they suppress the reabsorption of serotonin. The availability of serotonin is thus increased in the synaptic cleft. The CSTC circuits undergo adaptive alterations as a result of increased serotonin availability in the synaptic cleft, which reduces OCD symptoms (Nakao, Okada, & Kanba, 2014). Fluoxetine, fluvoxamine, citalopram, paroxetine, and sertraline are the SSRIs that are usually used to treat patients with OCD (Simpson, 2009). Higher doses of SSRIs are required to be used in the treatment of patients with OCD as compared with depression. The duration for which medication is required is for at least 10-12 weeks for an effective response. This is because OCD seems to need a more pronounced therapeutic effect and more pronounced neuroadaptive changes in the dysfunctional CSTC circuits. Commonly used SSRIs for treating OCD include fluoxetine (40-80 mg/day) and sertraline (150-200 mg/day), which have been proven to successfully reduce the severity of symptoms. However, of the patients with OCD, 40-60% individuals do not respond satisfactorily to SSRIs (Abudy, Juven-Wetzler, & Zohar, 2011).

1.8.1.2 Clomipramine and Other Agents

Clomipramine, a tricyclic antidepressant, has also been found to be highly effective in the treatment of patients with OCD and has the same efficacy as the SSRIs. However, it is usually considered a second-line treatment due to the unfavorable side-effect profile of the drug (Park, Jefferson, & Greist, 1997). Although it has a high efficacy in the inhibition of the reuptake of serotonin, it also has activity at a number of other receptors. This has resulted in a number of side effects, including anticholinergic side effects, sedation, and orthostatic hypotension, as well as the rare but dangerous side effect of cardiotoxicity (Pittenger, 2023). Intravenous administration of the drug has also been found to be effective in the treatment of patients with treatment-resistant OCD (Karameh & Khani, 2015).

Other antidepressants have also been found to be less effective in the treatment of patients with OCD or have not been studied well enough to determine their efficacy in the treatment of the disorder. Therefore, the SSRIs are the most effective pharmacological medications in the treatment of patients with OCD, with clomipramine used in patients who do not adequately respond to the SSRIs.

1.8.2 Psychotherapy

1.8.2.1 Cognitive Behavioral Therapy (CBT) and Exposure and Response Prevention (ERP)

Cognitive Behavioral Therapy (CBT) is considered to be the “gold standard” in treating OCD specially when it is integrated with Exposure and Response Prevention (ERP) (Seibell, Hamblin, & Hollander, 2015). Starting with small steps, CBT helps people notice thoughts that fuel their OCD. Rather than accepting these ideas, individuals learn to challenge them through guided practice. One key method within this approach involves facing fears without performing rituals - this is called ERP. Over time, repeated exposure reduces the power of obsessive urges. Instead of avoiding discomfort, patients build tolerance by staying present during anxiety spikes. This process reshapes how the mind reacts to intrusive thoughts. While not easy, many find relief grows gradually through consistent effort. In ERP, patients are exposed to situations they fear (exposure) and prevented from engaging in their compulsions (response prevention) (Jacoby et al., 2025). The idea behind ERP is to “reprogram” the brain by creating new “safety memories” to replace negative associations. In time, patients learn to recognize that their worst fears do not come true (Ong et al., 2024). ERP has also been observed to produce changes in

the brain, such as normalizing hyperactivity in CSTC circuits, making it both psychologically and physiologically effective.

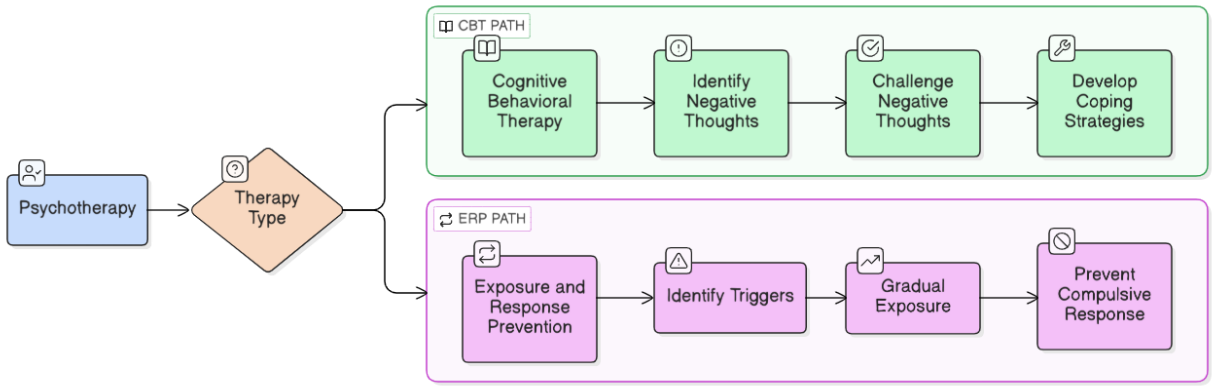


Figure 2: CBT and ERP pathways

1.8.3 Treatment-Resistant OCD (TR-OCD)

Many patients with OCD i.e., 40-60% fail to respond properly to the first treatments of SSRIs and/or CBT/ERP (Abudy, Juven-Wetzler, and Zohar, 2011). This is referred to as treatment-resistant OCD (TR-OCD) and normally diagnosed after consecutive two or more sufficient trials of SSRI and a complete course of ERP. Treatment of TR-OCD is often demanding and may require the use of multiple interventions. One such strategy is the augmentation of SSRIs with antipsychotics like risperidone and aripiprazole, which modulate the dopaminergic systems in the brain that are involved in compulsive behaviors and can be particularly effective in patients with comorbid tic disorders (Albert et al., 2019). Another technique is the involvement of clomipramine if it has not been previously tried. In severe cases of OCD, neuromodulation procedures like DBS can be considered (Dell'Osso et al., 2007). Mindfulness-based cognitive therapy (MBCT) is also being explored as a possible supplementary approach in the treatment of TR-OCD (De la Peña-Arteaga et al., 2024).

1.9 Rationale of the Study

OCD is a heterogeneous (and sometimes complicated) neuropsychiatric condition whose biological processes are not clearly understood. In spite of the fact that the current treatment methods of OCD such as the SSRI and CBT, have been proven effective in most patients, there are still a good number of patients who resist these therapies. This shows that the existing information on the pathophysiology underlying OCD is incomplete and that other biological aspects could be implicated. Recently, different studies have been used to indicate the significance of dysregulation of the immune system and neuroinflammation in psychiatric

diseases like OCD. As an example, the change of cytokine profiles is one of the potential drivers of OCD symptoms development and evolution. Among such cytokines, IL-22 is particularly interesting because it is a cytokine involved in the process of inflammation and immunoregulation. Although there is currently not much literature on the role of IL-22 in OCD, exploring this issue is of interest as it may offer greater insight into the underlying neuroimmune mechanisms of OCD and enrich the existing scientific literature on the issue.

1.10 Focus of the Study

The focus of the current research is to discuss the potential role that IL-22 plays in OCD pathophysiology, in specific, immune system dysfunction, and neuroinflammatory mechanisms. It will further explore the possibility of changes in the levels of IL-22 to be linked with the existence or severity of OCD. Moreover, it also tries to analyze the potential role of IL-22 as a potential peripheral correlate of neuroimmune inter-relations. In this regard, the purpose of the current research is to add to a deeper insight into the biological nature of OCD and the body of research in general on the potential role of immune system deviations.

Chapter 2

Materials and Research Methods

2.1 Study Framework and Population

This research was planned to be a prospective case-control study with 200 patients diagnosed with OCD, and 176 healthy control subjects. The population of the study was people who were recruited in the National Institute of Mental Health (NIMH) & Hospital, Dhaka, and the rest of the population of Dhaka city was the control group. The participants were all chosen according to stipulated inclusion and exclusion criteria. Cases and controls were attempted to be matched based on age, gender, and body mass index (BMI) in order to minimize the possibility of confounding variables. This similarity provided comparability of groups and enhanced reliability of findings.

2.1.1 Detection of OCD

According to the criteria provided by DSM-5 [American Psychiatric Association, 2013], a qualified psychiatrist recognized the patients with OCD. The theoretical level of the symptom severity of the patients was determined using the Y-BOCS that has high validity and reliability. It does not only determine the degree of symptom severity but also the kind of symptoms. Other than this a detailed clinical examination of all the patients was undertaken to make sure that there was no other psychiatric or neurological disorder leading to the symptoms of OCD.

2.1.2 Selection Criteria

The current case-control study had 200 patients having OCD and 176 healthy individuals of Bangladeshi descent. The OCD patients were recruited in the National Institute of Mental Health (NIMH) & Hospital, Dhaka. After a diagnosis, conducted by a professional psychiatrist, the patients took the form of structured questionnaires, as per the DSM-5 criteria. The current study only picked patients who met the proper criteria. The level of OCD symptoms was also determined using the Y-BOCS used to determine the severity of the symptoms. The healthy control individuals were selected in different areas of Dhaka city and were matched with the patients in terms of age, sex and the BMI. A psychiatrist also checked the controls and exposed them through structured questionnaires to make sure they had no previous history of psychiatric illness, drug abuse or neurological issues. Pre-designed questionnaires were used to gather socio-demographic and clinical data such as age, sex, height, weight, BMI, etc. The research

was conducted following the principles of the Declaration of Helsinki and the permission was granted by the corresponding review committee.

2.1.3 Criteria for Inclusion

All participants who joined this research study were Bangladeshi. In total, 200 patients diagnosed with OCD and 176 healthy individuals were selected, and both groups were matched based on age, gender, and BMI.

1. Patients who were clinically identified with OCD by a qualified psychiatrist according to DSM-5 criteria were included.
2. Individuals aged between 18 and 60 years were considered eligible for participation.
3. Patients with a Y-BOCS score indicating clinically significant OCD were included in the study.
4. Participants of both sexes (female and male) were recruited.
5. Patients from both inpatient (IPD) and outpatient (OPD) departments were considered.
6. Subjects who agreed to offer informed consent, blood specimens, and relevant information were enrolled.
7. Individuals with no history of alcohol or substance abuse were selected.
8. Both married and unmarried individuals were included in the study.

2.1.4 Criteria for Exclusion

As the levels of cytokines such as IL-22 can be affected by other physiological and pathological conditions, rigid exclusion criteria were used to reduce the number of confounding factors.

1. Patients who had very high or very low BMI (16 kg/m^2 or 40 kg/m^2) were excluded.
2. OCD patients with mild characteristics or subclinical cases, as they appear based on low Y-BOCS scores, were excluded.
3. The patients who had any type of serious acute or chronic physical illness were not incorporated.
4. Individuals with major medical issues such as cardiovascular diseases, kidney or liver diseases, seizures, uncontrolled hypertension, or endocrine (such as thyroid malfunction) were excluded.
5. Consumers using drugs with controlled hypertension who were neither known to have compromised immune nor psychiatric state were not rejected.
6. Pregnant women and individuals with other significant comorbidities (psychiatric or neurological) were excluded.

7. Those with moderate and severe cognitive impairments, communication problems, or individuals not willing to take part were excluded.
8. The patients who had undergone medication within the past few hours that was known to impact the level of Cytokine or/and immune function were not included in the study.

2.1.5 DSM-5 Criteria

Expected common criteria in OCD diagnosis include those contained in the DSM-5. According to DSM-5, OCD is defined by the existence of obsessions, compulsions, or both; the obsessions, compulsions, or both must be time-consuming and cause a considerable amount of emotional distress or impairment in day-to-day functioning.

Obsessions can be characterized by:

1. Repeated and compulsive recurring thoughts, urges, or imagined scenarios, which are considered unwelcome and disruptive, and lead to intense anxiety or distress.
2. The person trying to disregard, repress, or neutralize the thoughts in other ways (compulsions).

Compulsions are characterized by:

1. Repeat behavior (e.g., hand cleaning) or mind activity (e.g., counting, praying) that one is compelled to engage in due to an obsession or following strict rules.
2. These actions are geared to alleviatory or avoidance of a feared event; but they are not linked in any realistic way to the feared event or are obviously excessive.

Additionally:

i. Obsessions or compulsions take a significant amount of time (taking more than one hour/day). The manifestations show clinically significant distress or inability in social, occupational, or other areas of functioning of importance. The issue is not due to the physiological effect of a substance or some other medical condition.
ii. The clinical signs cannot be attributed to some other mental condition.

2.1.6 Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

A common, well-known, and reliable measure of the range of OCD is the Y-BOCS. It is a reliable and systematic approach to assessing both the obsessions and also compulsion. A Y-BOCS scale is attached in the Appendix C.

1. Y-BOCS has 10 items in total with 2 subscales:
    i. 5 items for obsessions (1-5)
    ii. 5 items for compulsions (6-10)
2. Each item is assessed on a scale from 0 to 4, which results in a total ranging from 0 to 40.
3. Higher total scores indicate greater severity of OCD symptoms.
4. The scale assesses key dimensions, including:
    i. Time spent on obsessions and compulsions
    ii. Interference with daily activities
    iii. Level of distress
    iv. Resistance against symptoms
    v. Degree of control over thoughts and behaviors
5. Based on the total score, level of OCD is typically categorized as:
    i. 0–7: Subclinical (below the threshold for clinical OCD)
    ii. 8–15 = Mild level OCD
    iii. 16–23 = Moderate level OCD
    iv. 24–31 = Severe level OCD
    v. 32–40 = Extreme level OCD
6. In this study, the Y-BOCS was administered after clinical diagnosis to quantify symptom severity in OCD patients.
7. The use of Y-BOCS ensured a standardized, reliable, and consistent assessment of OCD severity across all participants.

2.1.7 Ethical Consideration

This study was undertaken according to the code of ethics presented in the Helsinki Declaration. There will certainly be a few ethical perspectives there since this was a study of human beings. We took great caution when it came to this investigation's ethical considerations. It was made sure that each patient was convinced before taking a blood sample. Moreover,

every individual signed a written consent form. They had also acquired ethics permission of the Research Ethical Committee, Southeast University, Dhaka.

The following ethical principles were upheld:

1. The patients, as well as the healthy controls, were aware of the objectives and intent of the study.
2. An information gathering sheet containing details about the present study, in Bangali was developed to the advantage of all participants.
3. The participants were only required to provide their consent before blood drawing was done and this was not done by any outside factor.
4. Written informed consent of the participants was done, when they freely gave consent to give samples of blood.
5. All the important precautions were followed regarding the safety of the personal information of the participant.
6. No adverse effects of our research on further medical care of the patient.
7. We gave an answer to all questions the participants needed and they are also advised to contact the researcher with any other questions.

Prior to supplying a sample or information, study participants were properly informed of the following information:

- Outlines the aims of the study.
- Further elucidation on the kind of study.
- Rationale of the method and time taken to undertake the study.
- The study was done solely on research interests and there was not going to be any monetary beneficiary to any person with regards to this study.
- They were provided with proper explanations as to their right to participate or not.

2.1.8 Consent Form

Each participant was clearly informed about the aim, objectives, and procedures of the work before including them. Proper written consent was obtained from all volunteers before adding them in the study.

1. Participants were provided with detailed information regarding the purpose of the study, sample collection procedures, and confidentiality of their data.

2. Participation was entirely voluntary, and individuals had the right to walk away from the study at any stage with no consequences.
3. For patients whose ability to provide independent consent was considered impaired, written consent was obtained from their primary caregiver or legal guardian.
4. Confidentiality and anonymity of all personal and clinical information were strictly maintained throughout the study.

The consent form template is included in Appendix A.

2.1.9 Questionnaire Form Applied in the Data Collection Process

A standardized written questionnaire/survey form was utilized to gather the socio-demographic information from both OCD patients as well the Healthy Controls (HCs), which is given in Appendix B.

2.1.10 Ethical Approval

The ethical approval for this study was granted by the Committee for Ethical Compliance in Research of Southeast University, Dhaka, Bangladesh. (CECR Reference No.: SEU/Pharm/CECR/024/2024

2.2 Collection of Blood Sample

After obtaining informed consent, each participant completed the required questionnaire. Their height and weight were then measured, followed by the collection of approximately 5 mL of venous blood by a trained phlebotomist from the cephalic vein.

2.2.1 Requirements of Materials for Collection of Blood Sample

SL.	Required Materials	Volume
1	Syringe (Disposable)	10 ml
2	Hexisol	100 ml
3	Test Tube	10 ml
4	Eppendorf Tubes	1.5 ml
5	Falcon Tubes	15 ml

6	Ice Box	4.75 ml
7	Sterile Cotton	q.s.
8	Band-aid	q.s.
9	Tourniquet	q.s.

Table 3: Materials List for the Blood Sample Collection Process

Figure 3: Falcon Tubes, Ice box, Refrigerator

2.2.2 Collection of Blood from Patients

From individuals who are OCD patients, a total of 200 blood samples (5 mL each) were taken from the National Institute of Mental Health (NIMH) & Hospital, Dhaka. The criteria of inclusion and exclusion were predetermined and patients were included based on these criterion after a trained psychiatrist had evaluated them. Appropriate consent was sought, and pertinent clinical and demographic data were gathered about each patient. This involved sex, age, weight, height, BMI, degree of OCD symptoms (measured by Y-BOCS), length of illness, medical treatment history and family history of psychiatric disorders.

2.2.3 Collection of Blood from Healthy Controls

176 blood samples (5 mL each) were taken out of healthy persons who were chosen in various regions of Dhaka city. The control group and the patient group was compared and matched in terms of age, gender and BMI to ascertain comparability. All the participants were acknowledged regarding the aims and methods of the study before the collection of the blood samples. Only informed consent was obtained to collect blood samples. Short medical history

was also provided in order to make sure that the chosen people did not have any psychiatric or other significant medical history.

2.2.4 Separation of Serum from Blood Sample and Storage

A sterile syringe was used to collect the venous blood of the participants, about 5 mL of blood, in the cephalic vein. The blood samples were moved into the right collection tubes and left to clot in room temperature of about one hour. After the formation of clots, 15 minutes centrifugation at 3000 rpm was carried out to separate the serum and blood cells. The transparent supernatant (serum) was gently placed and put in clean Eppendorf tubes. The serum samples were subsequently frozen at -80 o C awaiting further analysis to determine cytokines, such as IL-22.

Figure 4: Blood Samples

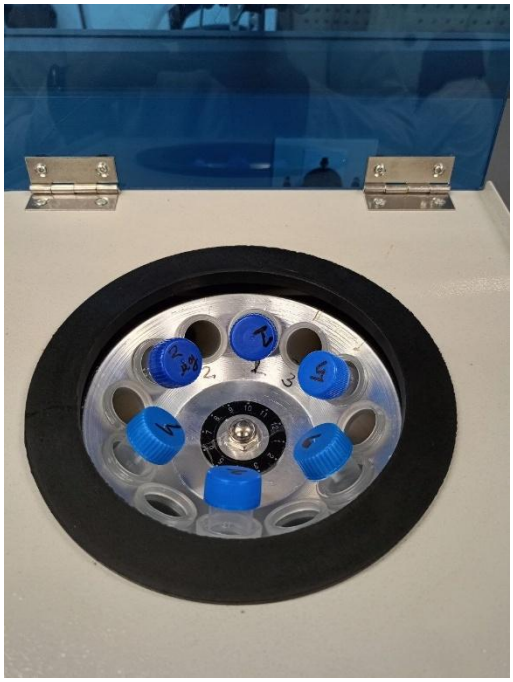


Figure 5: Serum Separation Using Centrifugation Machine

2.3 Blood Sample Analysis

The concentration of IL-22 in the patients' serum was determined using specific ELISA kits (Booster Bio, USA).

2.3.1 Required Materials for the Serum IL-22 Analysis

To measure Human IL-22, an ELISA kit was used. Human IL-22 Pre-coated ELISA kit consists of the following components:

SL	Description	Volume
1	ELISA microplates 96-welled (Precoated with IL-22)	5 plates/kit
2	Human IL-22 Standard	10ng
3	Polyclonal antibody (Biotinylated goat anti-human IL-22) (100x)	500µl
4	Polyclonal antibody (Rabbit anti-human IL-22) (100x)	500µl
5	Avidin Biotin Peroxidase Complex (100x)	500µl
6	Avidin Biotin Peroxidase Diluent	12ml
7	Capture Antibody Diluent [PBS]	12ml
8	Reagent Diluent [1% BSA in PBS]	30ml
9	Color Developing Reagent (TMB)	10ml
10	Stop Solution	50ml
11	Wash Buffer [PBS and PBS-T]	q.s.
12	Plate Sealers	q.s.

Table 4: Required Materials for the Analysis of Serum IL-22

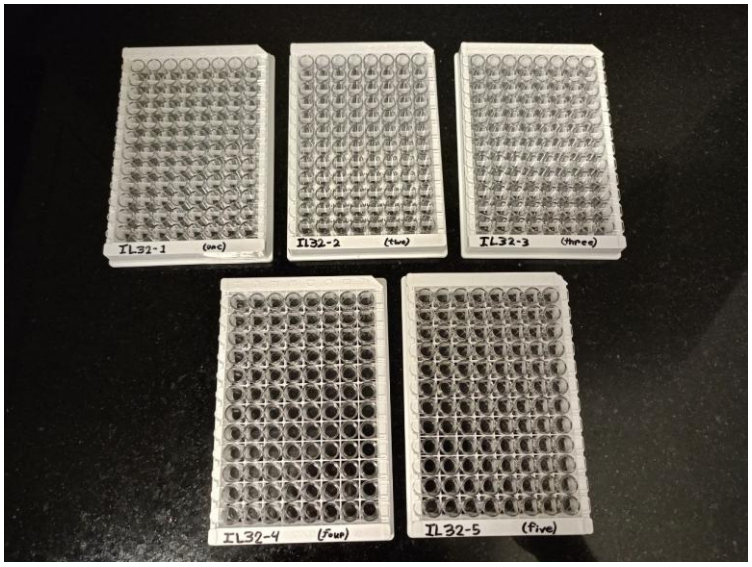
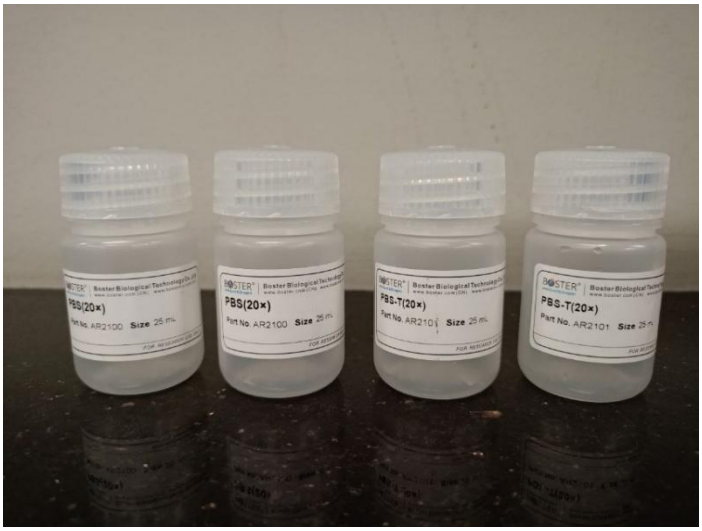


Figure 6: 96 Well Microplates



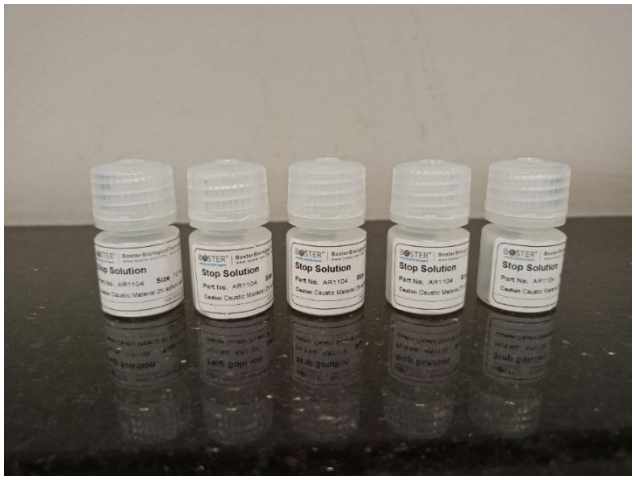


Figure 7: Wash Buffer, Substrate Solution, Stop Solution

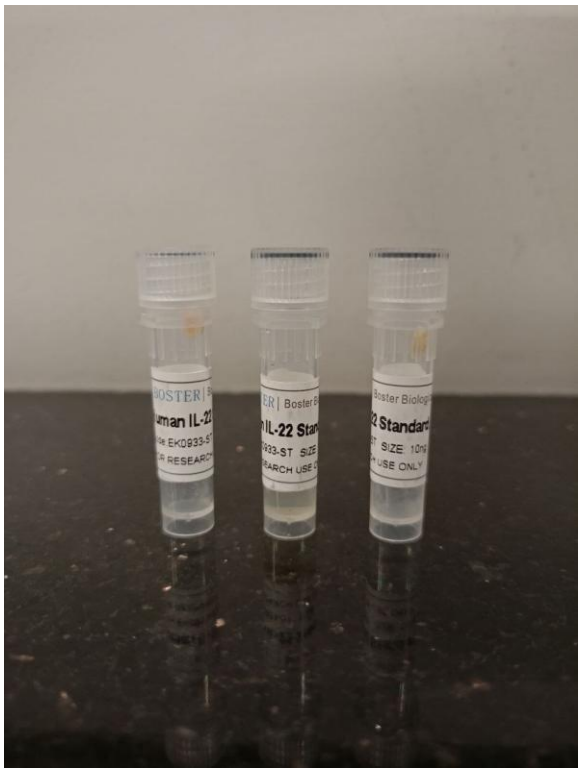


Figure 8: Human IL-22 Standards

Figure 9: Avidin-Biotin-Peroxidase Diluent, Capture Antibody

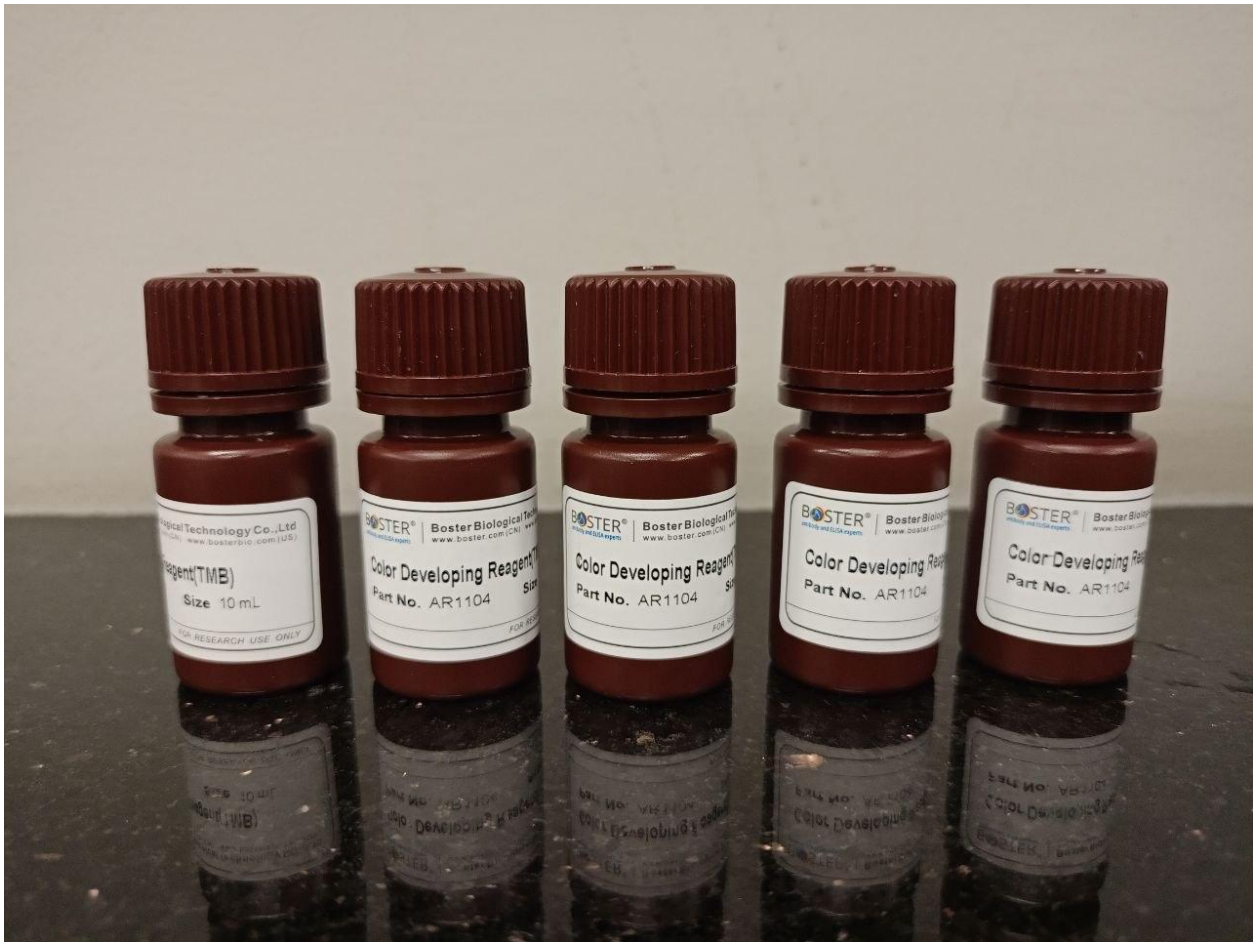


Figure 10: Color Developing Reagent

2.3.2 Reagent Preparation for IL-22

All reagents were brought to room temperature before use. The dilutions required for the research work were prepared and used immediately.

2.3.2.1 Plate Design

5 microplates were designed for the analysis of IL-22 levels in OCD patients.

	1	2	3	4	5	6	7	8	9	10	11	12
A	Std1	Std2	Std3	Std4	Std5	Std6	Std7	B	P	P	P	P
B	P	P	P	P	P	P	P	P	P	P	P	P
C	P	P	P	P	P	P	P	P	P	P	P	P
D	P	P	P	P	P	P	P	P	P	P	P	P
E	P	P	P	P	C	C	C	C	C	C	C	C
F	C	C	C	C	C	C	C	C	C	C	C	C
G	C	C	C	C	C	C	C	C	C	C	C	C
H	C	C	C	C	C	C	C	C	C	C	C	C

Figure 11: Design of the ELISA Plate

2.3.2.2 Preparation of Plates

1. A 1 in 100 dilution of the Capture Antibody in its Diluent was performed to achieve the desired strength (1 µl anti-Human IL-22 Capture Antibody into 99 µl its Diluent). Each well of a microplate received 100 µl of the diluted Capture Antibody and was promptly coated. Plates were sealed and left for incubation overnight at 4°C.
2. Sealing was removed, and the fluid in each well was removed and disposed of in a dedicated dispense bucket. The plate was flipped over a paper towel in an upside down position on the bench surface and carefully patted to remove any liquid if left. The wells were maintained in a moist condition throughout the entire process.
3. Blocking was performed by dispensing 200 µl of Reagent Diluent into each well, followed by a 2 hour incubation period at room temperature.
4. The contents of each well were aspirated and subsequently rinsed with PBS, with the washing step repeated twice to complete three wash cycles. Each well was rinsed by dispensing 300–350µl of PBS using a multichannel pipette and waste bucket. Thorough elimination of fluid at every stage was maintained to achieve the best possible results. Following the final wash cycle, PBS (if left) was removed either with pipettes or by overturning the plate and keeping it firmly pressed against a clean absorbent paper towels.

2.3.2.3 Reconstitution of Human IL22 Standard

1. Standards were freshly prepared within 2 hours of the experiment. A single vial holding 10 ng of lyophilized human IL-22 standard was gently spun, then reconstituted to a stock solution having a concentration of 10 ng/ml using Reagent Diluent (1ml), and allowed to equilibrate with gentle agitation before serial dilutions were performed.

2.3.2.4 Dilution of Human IL22 Standard

2. Tubes were numbered from Tube #1– #8. Final strenghts were: Tube # = 1,000 pg/ml; Tube #2 = 500 pg/ml; Tube #3 = 250 pg/ml; Tube #4 = 125 pg/ml; Tube #5 = 62.5 pg/ml; Tube #6 = 31.2 pg/ml; Tube #7 = 15.6 pg/ml; and Tube #8 = 0.0 pg/ml (blank).

- The Standard 1 in Tube #1 was made by combining the 100 µl of the reconstituted stock solution (10 ng/ml) with Reagent Diluent (900µl) of to get a final volume of 1,000 µl. This was followed by even mixing.
- Then, Tubes #2–7 each received 300 µl of Reagent Diluent.
- Standard 2 was obtained by adding 300 µl of standard 1 into tube #2, making a final volume of 600 µl, and followed by proper mixing.
- To generate standard 3, 300 µl of standard 2 from tube #2 was added to tube #3 to obtain a final volume of 600 µl. The solution was mixed thoroughly.
- The serial dilution was continued in the same manner for tubes #4–7.
- Tube #8 was the blank throughout the analyses.

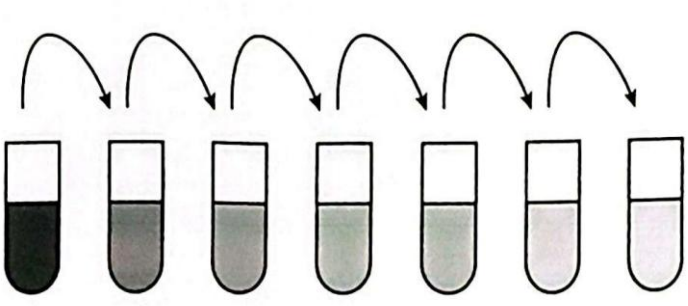


Figure 12: Serial Dilution of Standards

2.3.2.5 Polyclonal Antibody (Rabbit Anti-Human IL22) Solution Preparation

1. 500 µl of Rabbit anti-human IL-22 polyclonal antibody was in every vial.
2. To prepare the diluted solution, the antibody was prepared at a 1 in 100 dilution in Capture Antibody Diluent and thoroughly mixed (specifically, 1µl of the antibody was combined with Capture Antibody Diluent of 99 µl).

2.3.2.6 Polyclonal Antibody (Biotinylated Goat Anti-Human IL22) Solution Preparation

1. 500 µl of Biotinylated goat anti-human IL-22 polyclonal antibody was in every vial.
2. The polyclonal antibody was prepared at a 1 in 100 dilution in Reagent Diluent and thoroughly mixed; specifically, 1 µl of the antibody was combined with Reagent Diluent of 99 µl.

2.3.2.7 Avidin Biotin Peroxidase Complex (ABC) Solution Preparation

1. 500 µl of Avidin Biotin Peroxidase Complex (ABC) was in every vial
2. The ABC complex was diluted at a 1 in 100 with Reagent Diluent and mixed evenly (i.e., 1 µl of ABC was added to Reagent Diluent 99 µl).

2.4 Laboratory Assay Protocol

The reagent solutions and other materials were brought to the room temperature (18–25°C) before commencing the research, as outlined in the preparation section.

1. All reagent solutions and standards were made as directed.
2. Extra microplate strips were removed from the plate and then sealed and stored in the main packaging it came with.
3. In each well, 100 µl of the standard, samples, or control was added carefully. It was recommended that at least two replicates of each standard, sample, or control.
4. The plate was covered with the plate sealer and kept in an incubator for 2 hours at room temperature (or 1.5 hours at 37°C).
5. The cover was taken off and the liquid in the wells was removed into an appropriate waste receptacle. The plate was inverted on the benchtop onto a paper towel and tapped to gently blot any remaining liquid. It was ensured that the wells were not allowed to completely dry at any time.

6. 100 µl of the previously prepared 1x Biotinylated goat anti-human IL22 polyclonal antibody was added to each well.
7. The plate was sealed and left to incubate for 1.5 hours at room temperature (or 1 hour at 37°C).
8. The plate was subjected to three rounds of PBS washing.
   a) The liquid in the wells was discarded into an appropriate waste receptacle. The plate was then inverted onto a paper towel and tapped to remove residual liquid. It was ensured that the wells were not allowed to dry completely.
   b) 300 µl of PBS was added to each well. For cleaner background, the plate was incubated for 60 seconds between washes.
   c) Steps (a) and (b) were repeated two additional times.
   d) After the final wash, the buffer was discarded, and the plate was inverted and blotted against clean paper towels to remove remaining liquid.
9. 100 µl of the prepared 1x ABC Complex was added to each well and incubated at room temperature for 40 minutes (or ½ hours at 37°C).
10. The plate was washed 5 times with the solution PBS-T:
    a) The liquid was discarded, and the plate was inverted and blotted as described previously.
    b) 300 µl of PBS-T was added to each well, followed by a 1 minute incubation for improved clarity.
    c) Steps (a) and (b) were repeated four more times.
    d) After the final wash, the buffer was discarded, and residual liquid was removed by inversion and blotting.
11. 90 µl of Color Developing Reagent was added to each well and incubated in the dark for 30 minutes at room temperature (or 25–30 minutes at 37°C). The optimal incubation time was determined empirically, with blue coloration observed in the top standard wells while lower standards remained clear.
12. 100 µl of Stop Solution was added to each well, resulting in an immediate color change to yellow.
13. Within 30 minutes of stopping the reaction, the optical density (O.D.) absorbance was measured using a microplate reader at 450 nm.

Figure 13: Incubator, Microplate Reader

2.5 Statistical Analysis

Using the SPSS software, version 23.0 (IBM Corp., Armonk, NY), all statistical analyses were performed. The data obtained were thoroughly scrutinized, cleaned, and validated to avoid any mistakes. The descriptive statistics of socio-demographic and clinical characteristics of OCD patients and control subjects were done to get an overview of the two sets of participants. Descriptive statistics of continuous variables were reported as Mean ± SEM. For comparisons among different groups, Independent Samples t-tests were employed to analyze continuous variables. The correlation between Y-BOCS scores and serum IL-22 level was determined using Pearson's correlation. Results are shown in tabular form and graphical form wherever applicable. Significance level was taken as < 0.05 ($p < 0.05$).

Chapter 3

Results and Discussion

3.1 Results

A picture of the microplates after completion of the analysis is attached below (Figure 14).

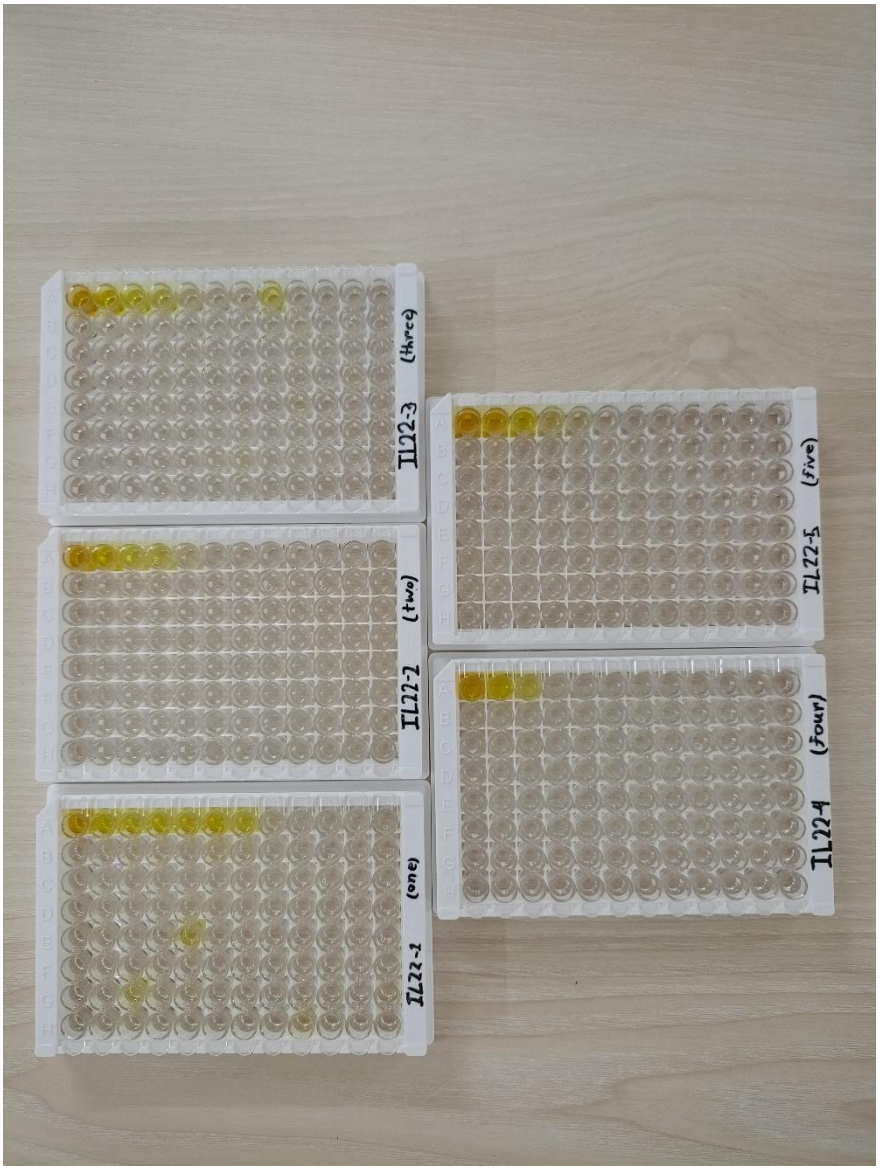


Figure 14: Microplates after Analysis is Performed

3.1.1 Socio-demographic Data

The table-5 gives a detailed analysis of the socio-demographic data of the enrolled population with respect to a number of characteristics. There are 200 patients and 176 controls involved in the study and the respective sample sizes are indicate as "n" as each group. The table has

also presented the percentage (%) of the number of participants in each category of the patients and controls.

Concerning the marital status, most of the patients were found to be unmarried (52.00%), with less percentage married (48.00%). However, the scenario was opposite in controls. Comparatively, 46.59% were not married and 53.41% married of those who were among the controls. The p-value is 0.295 and this means that there is no statistically significant difference between the two groups about marital status.

In the case of education level, the distribution was as follows among the patients, 5.00% were illiterate, 9.00% had primary level of education, 40.00% had secondary level of education, 46.00% had graduation or above level of education. The proportion of controls who are illiterate was 0% and who have primary, secondary and the proportion of graduates and above were 10.23%, 36.93%, and 52.84%, respectively. The p-value of this comparison is 0.018, which shows that there is no statistically significant difference between the education level of the patient and the control group.

The patients had the following occupations: 2.50% were engaged in business, 18.50% were housewives, 13.00% were students, 29.00% were service-holders, 33.00% were unemployed, and 4.00% were involved in other kinds of jobs. The controls were 5.68% occupied with business, 18.18% were housewives, 16.48% were students, 28.41% were service-holders, 28.98% unemployed and 2.27% had other jobs. The p-value on this comparison is 0.493, implying that there is no statistically significant difference in occupation between these two groups.

When it comes to economic impression, the patients' economic statuses were grouped as follows: 11.00% economic impression was high, 59.00% economic impression was medium and 30.00% economic impression was low. The controls consisted of 17.04% high economic impression participants, 51.14% medium economic impression and 31.82% low economic impression. This comparison has a p-value of 0.164 which indicates no statistically significant difference with occupation between the groups.

Regarding area of residence, 30.00% of the patients resided in the rural areas, and 70.00% in the urban areas. Of the controls, 30.11% resided in the rural location, and 69.89% were residing in the urban location. The p-value of this comparison is 0.981, which is not statistically significant that there is a difference in the area of residence of the patient and control groups.

Based on the smoking history, the majority of the patients (82.50%) had never smoked, whereas 17.50% were smokers. Contrastingly, of the controls, 82.39% were not smokers, and 17.62% were smokers. The p-value of this comparison is lower than 0.977, reflecting the absence of a statistically meaningful difference in smoking history between both groups.

Finally, as far as religion is concerned, most patients (94.00%), as well as controls (96.02%), were identified as Muslims (Islam). Remaining 5.50% and 0.50% of the patients were Hindu and Buddhist respectively. For the controls, 3.98% were Hindus and there were no Buddhists (0.00%). This comparison has a p-value of 0.501, which indicates that with religious affiliation between the two groups, there is no statistically significant difference.

Comparison among different parameters is represented in figure 15-21.

Characteristics	**Patients (n=200)** n	**%**	**Controls (n=176)** n	**%**	**p-value**
Marital status					0.295
Married	96	48.00	94	53.41	
Unmarried	104	52.00	82	46.59	
Education level					0.018
Illiterate	10	5.00	0	0.00	
Primary	18	9.00	18	10.23	
Secondary	80	40.00	65	36.93	
Graduate and above	92	46.00	93	52.84	
Occupation					0.493
Business	5	2.50	10	5.68	
Housewife	37	18.50	32	18.18	

Characteristics	Patients (n=200) n	%	Controls (n=176) n	%	p-value
Service holder	58	29.00	50	28.41	
Unemployed	66	33.00	51	28.98	
Others	8	4.00	4	2.27	
Economic impression					0.164
High	22	11.00	30	17.04	
Medium	118	59.00	90	51.14	
Low	60	30.00	56	31.82	
Area of residence					0.981
Rural	60	30.00	53	30.11	
Urban	140	70.00	123	69.89	
Smoking history					0.977
Non-smoker	165	82.50	145	82.39	
Smoker	35	17.50	31	17.62	
Religion					0.501
Islam	188	94.00	169	96.02	
Hindu	11	5.50	7	3.98	
Buddhist	1	0.50	0	0.00	

Table 5: Socio-demographic Profiles of the Enrolled Population

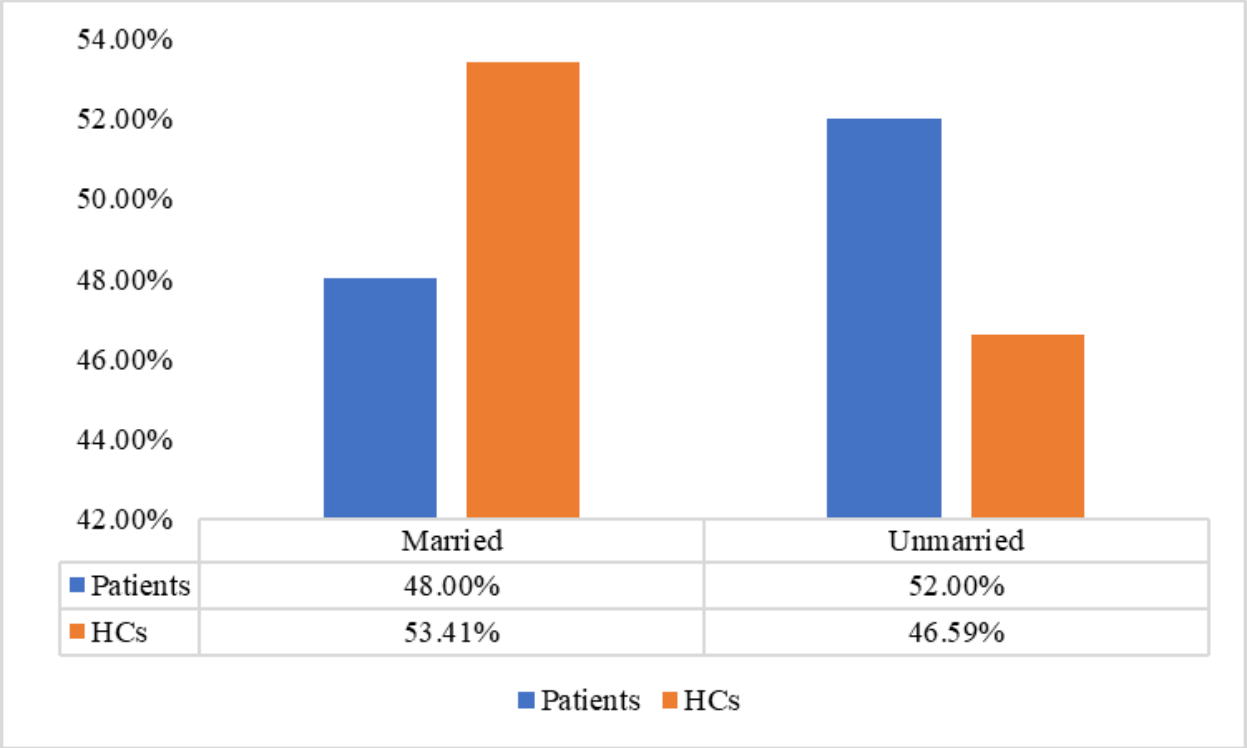


Figure 15: Distribution of Marital Status across Patients and Control Groups

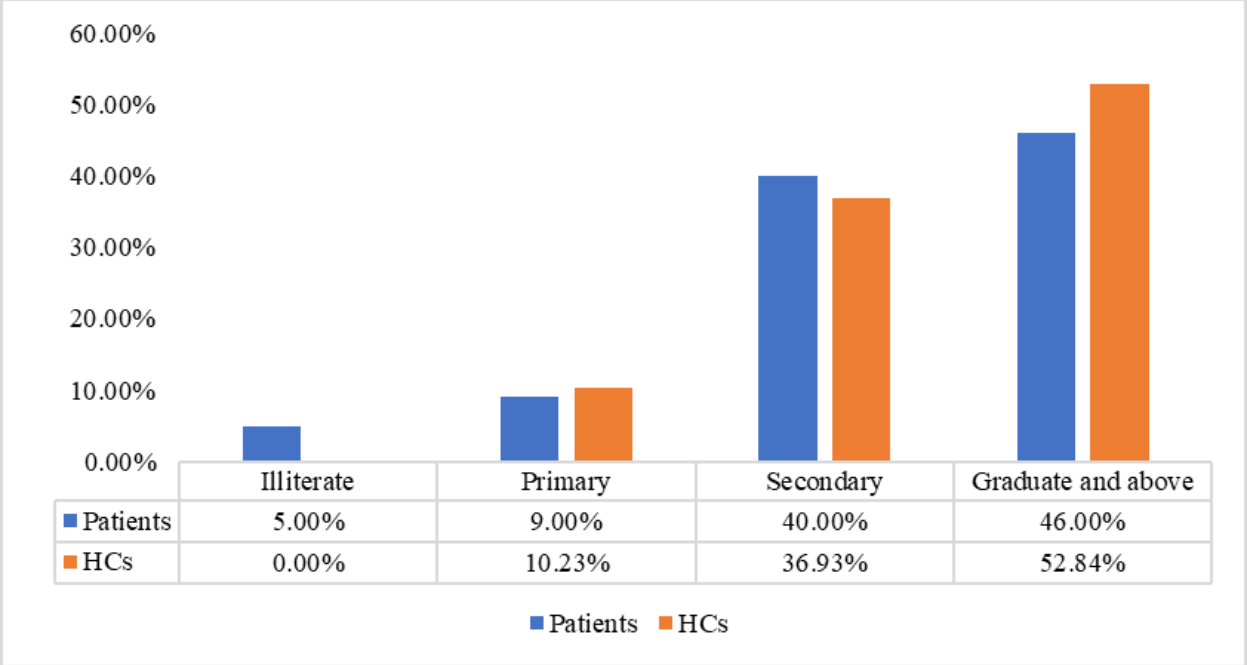


Figure 16: Distribution of Education Level across Patients and Control Groups

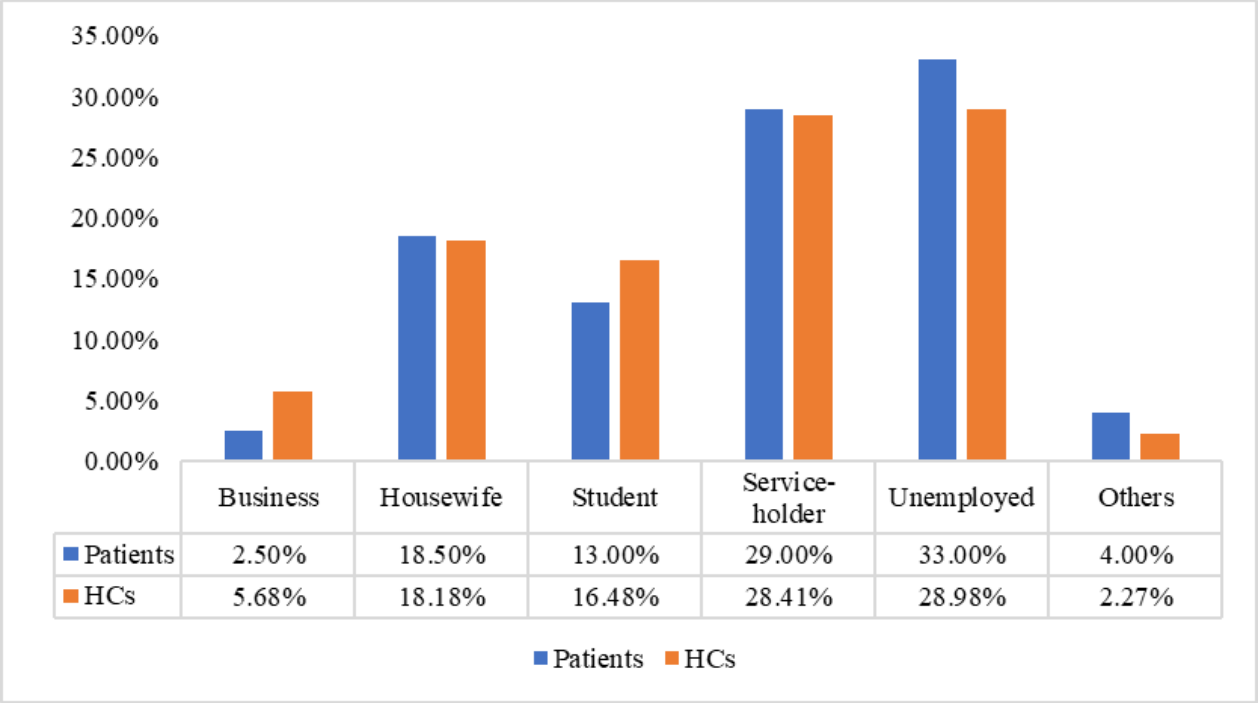


Figure 17: Distribution of Occupation across Patients and Control Groups

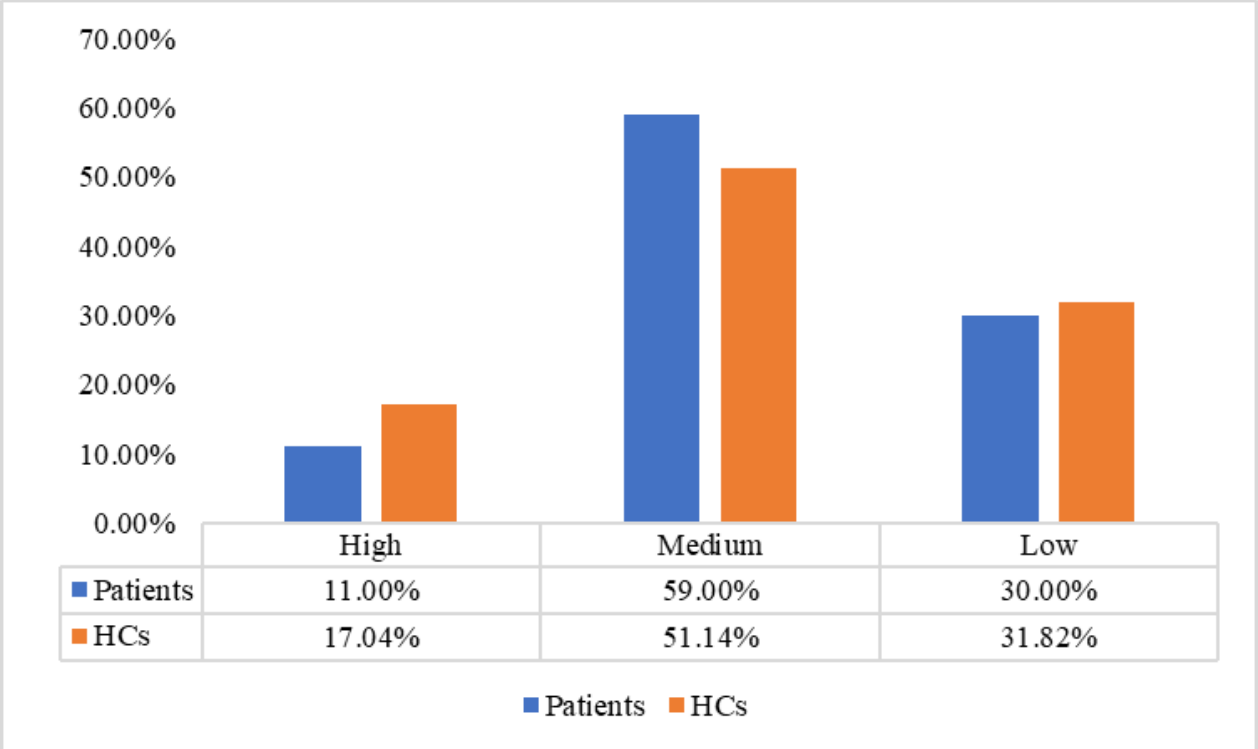


Figure 18: Distribution of Financial Status across Patients and Control Groups

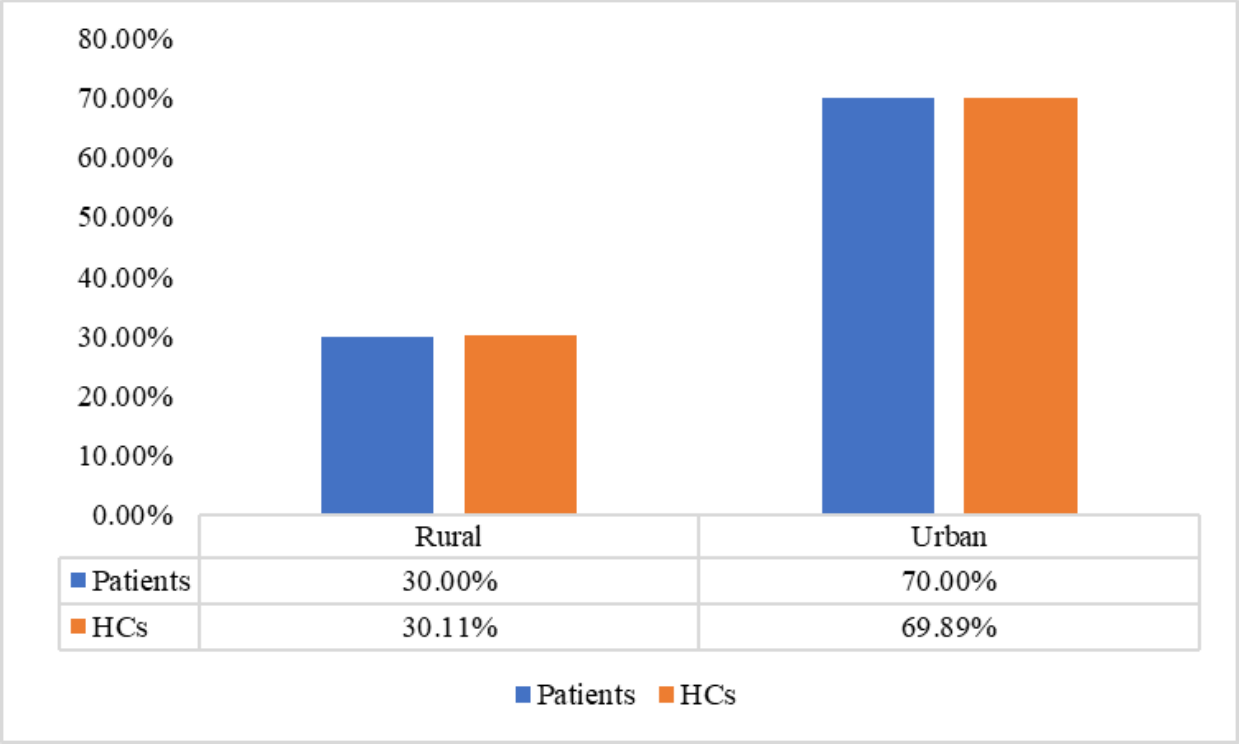


Figure 19: Distribution of Residence Area across Patients and Control Groups

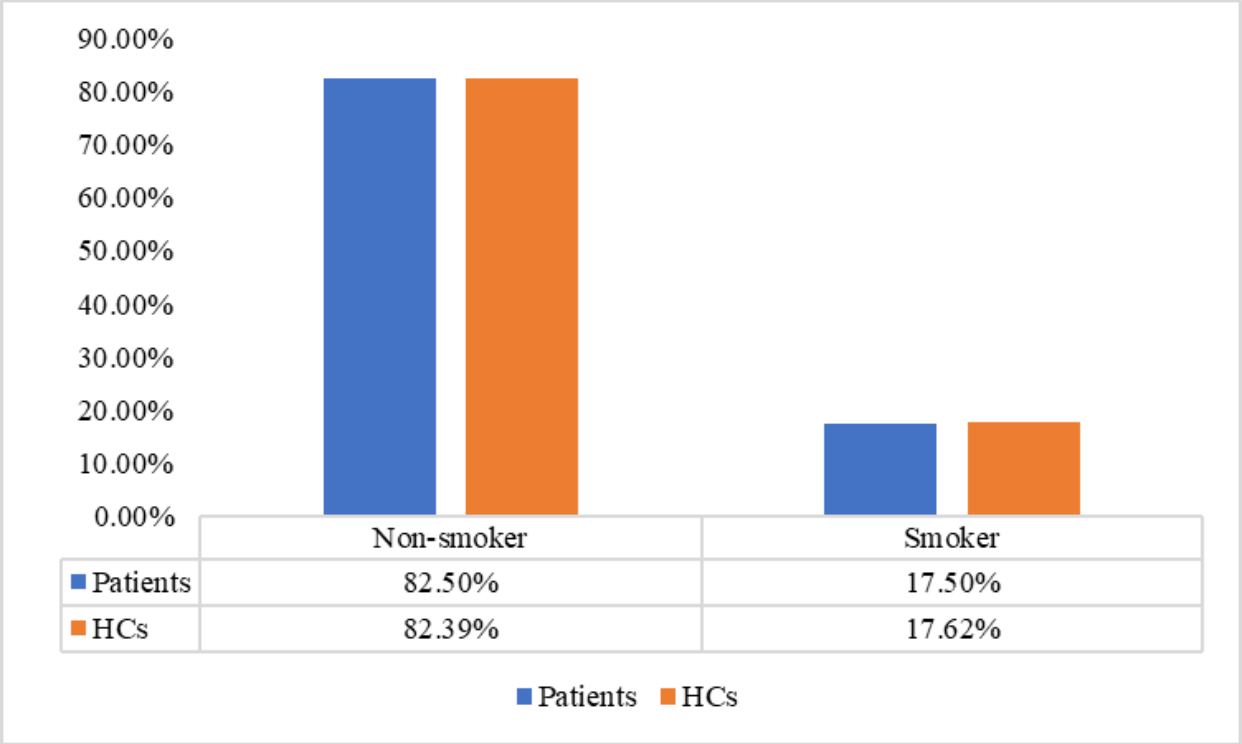


Figure 20: Distribution of Smoking History across Patients and Control Groups

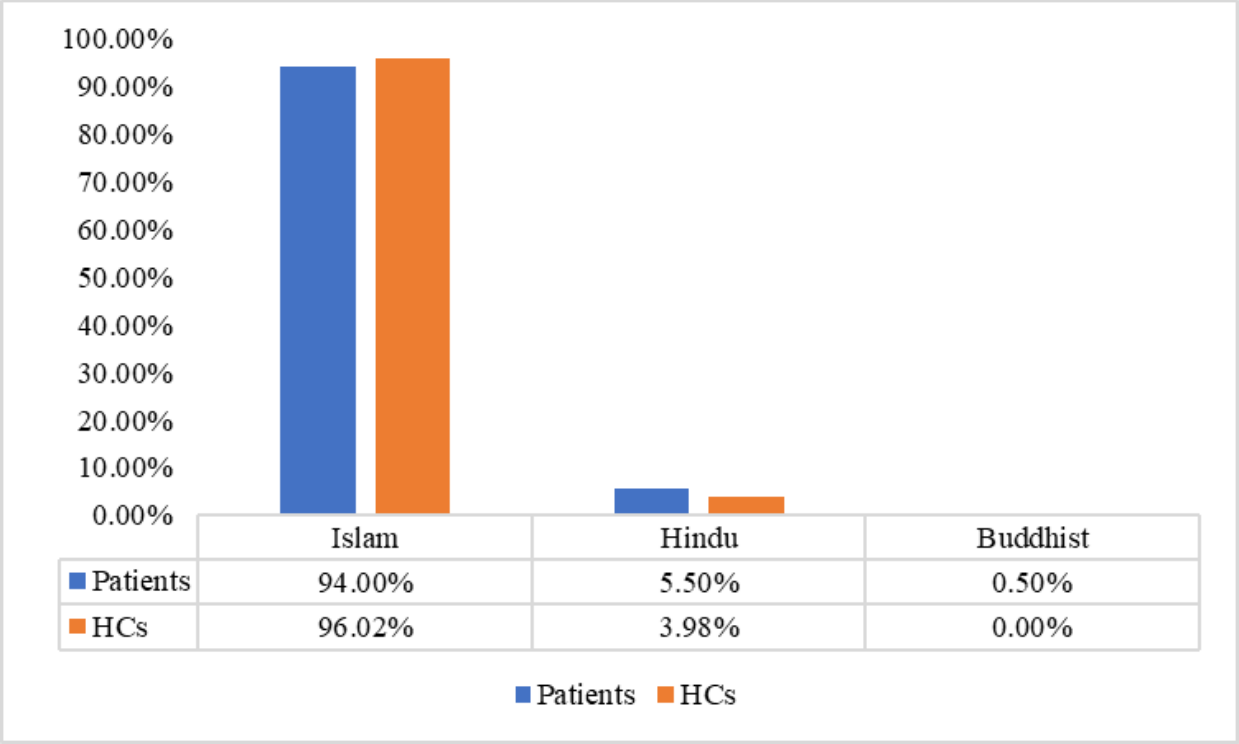


Figure 21: Distribution of Religion across Patients and Control Groups

3.1.2 Biophysical Attributes

Table 6 illustrates the biophysical attributes of the study population.

Characteristics	**Patients (n=200) n**	**%**	**Controls (n=176) n**	**%**	**p-value**
Age in years					0.161
18-25	102	51.00	73	41.48	
26-35	54	27.00	64	36.36	
36-45	32	16.00	25	14.20	
46-60	12	6.00	14	7.96	
Sex					0.841
Male	115	57.50	103	58.52	

Characteristics	Patients (n=200) n	%	Controls (n=176) n	%	p-value
Female	85	42.50	73	41.48	
BMI (kg/m^2)					<0.001
Below 18.5 (CED)	28	14.00	0	0.00	
18.5-25.0 (Normal)	130	65.00	120	68.18	
Above 25.0 (Obese)	42	21.00	56	31.82	

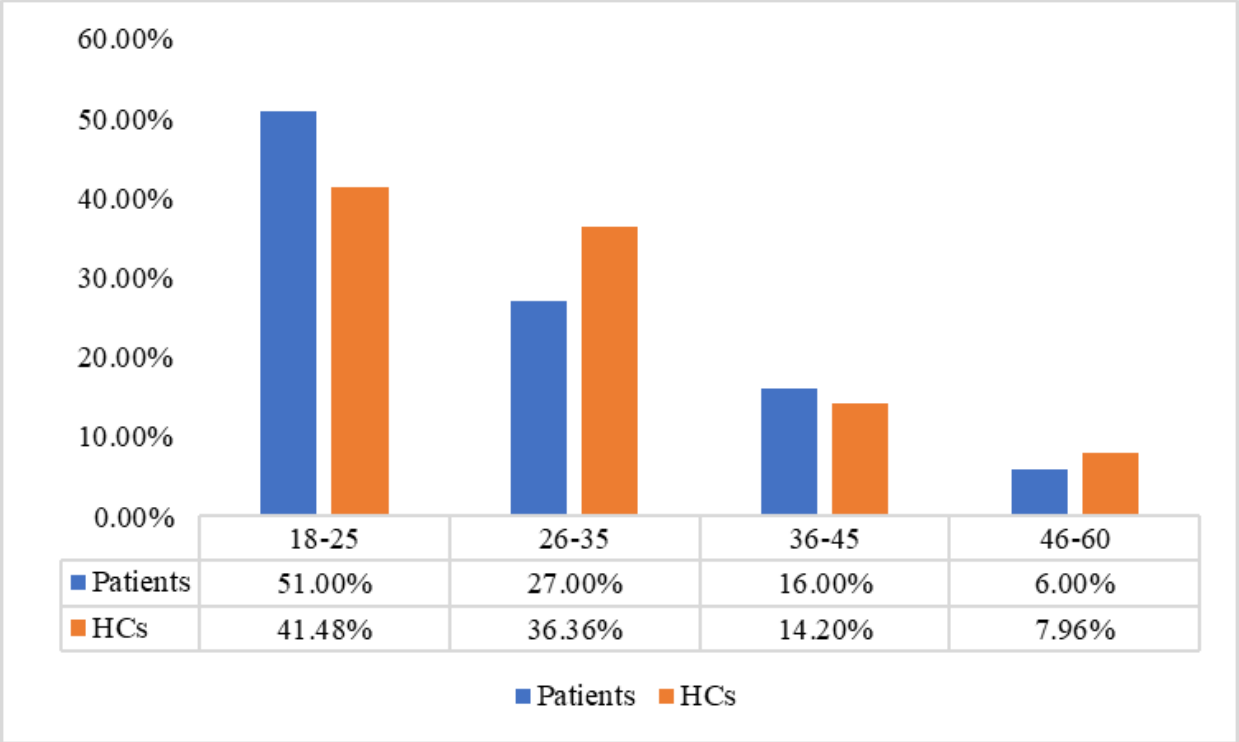
Table 6: Biophysical Attributes of the Enrolled Population

The table 6 represents the biophysical characteristics of the study population. This table compares patients (n = 200) and controls (n = 176) in different categories. Before selecting OCD patients and healthy controls (HCS) for the study purpose, age range was strictly monitored and maintained. The age distribution is as follows in the group of patients: 51.00% of individuals were between 18-25 years old, 27.00% were between 26-35 years old, 16.00% were between 36-45 years old, and 6.00% were between 46-60 years old. In the control group, 41.48% were between 18-25 years old, 36.36% were between 26-35 years old, 14.20% were between 36-45 years old, and 7.96% were between 46-60 years old. The p-value for the age distribution is 0.161, reflecting the absence of a statistically meaningful difference between both groups.

Sex-wise, 57.50% were males, and 42.50% females in patient group. Regarding the control group, 58.52% were males and 41.48% females. The P-value for sex distribution between the two groups is 0.841, meaning that there is no significant difference between the two populations.

The BMI distribution was analyzed using three BMI groups as those falling below 18.5 (CED), 18.5-25.0 (normal), and greater than 25.0 (obese). Among patients, 14.00% fall below 18.5 (CED), 65.00% were within the normal range, and 21.00% were categorized as obese. In the control group, none fell below 18.5 (CED), 68.18% fall within the normal range (18.5-25.0), and 31.82% were classified as obese.

However, the p-value for BMI is <0.001, indicating there might be a significant difference between the two groups. Although a statistically significant association was observed, the mean BMI (Patients 22.19 ± 0.34; Controls 23.47 ± 0.11) of the study population remained within the normal range (<25 kg/m²), suggesting that the difference may not be clinically meaningful. Therefore, the reported p-value is presented as it is, but should be interpreted with caution in terms of clinical relevance. It is not a necessity that the statistically significant correlation between BMI and OCD indicates a causal relation since the association can be affected by various other factors, including different lifestyle behaviors, eating habits, exercise routines, or drug reactions, for instance. Consequently, one needs to interpret the results of the study with caution and conduct additional research. Since one cell has 0 (Control, CED), Chi-square assumptions may be slightly violated. Other tests, such as a Fisher's Exact Test, would be more accurate to check the significance.



	18-25	26-35	36-45	46-60
Patients	51.00%	27.00%	16.00%	6.00%
HCs	41.48%	36.36%	14.20%	7.96%

Figure 22: Distribution of Age across Patients and Control Groups

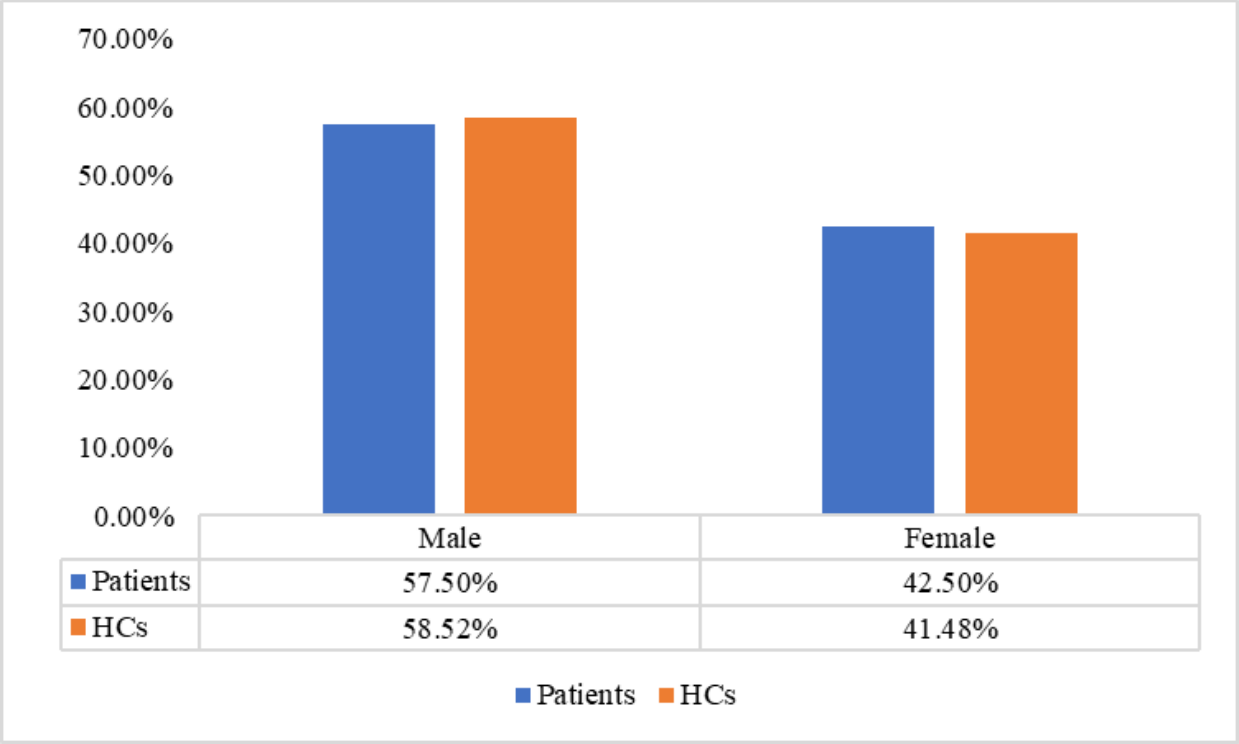


Figure 23: Distribution of Sex across Patients and Control Groups

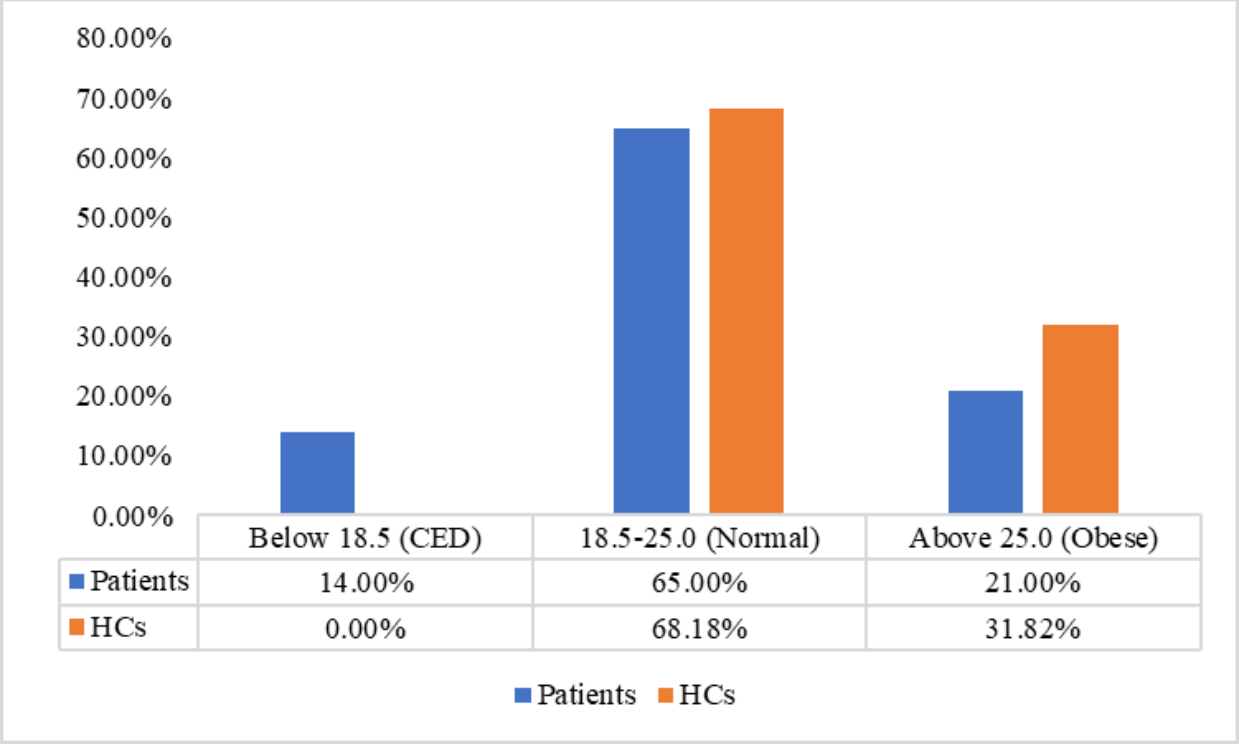


Figure 24: Distribution of BMI across Patients and Control Groups

3.1.3 Preparation of Standard Curve

We followed the guidelines of the ELISA Manufacturer Company (Booster Bio, USA) for the preparation of the standard curve in order to obtain an accurate result. Absorbance of the

standard curve for the determination of serum level of IL-22 was read at 450 nm wavelength. When a graph is plotted, concentration is taken on the x-axis and absorbance on the y-axis, and a straight line is obtained.

The concentration of the solutions as well as the absorbance is given in table 7.

Concentration of Standard Sol^n ($^{pg}/_{ml}$)	**Absorbance**
1000	2.5024
500	1.4194
250	0.4534
125	0.3223
63	0.1032
31	0.0604
16	0.0587

Table 7: Absorbance and Concentration Value of IL-22 Standard

As depicted in Figure 25, a curve was generated by plotting concentration along the x-axis and absorbance along the y-axis. The graph gives us a straight line with R^2=0.9888

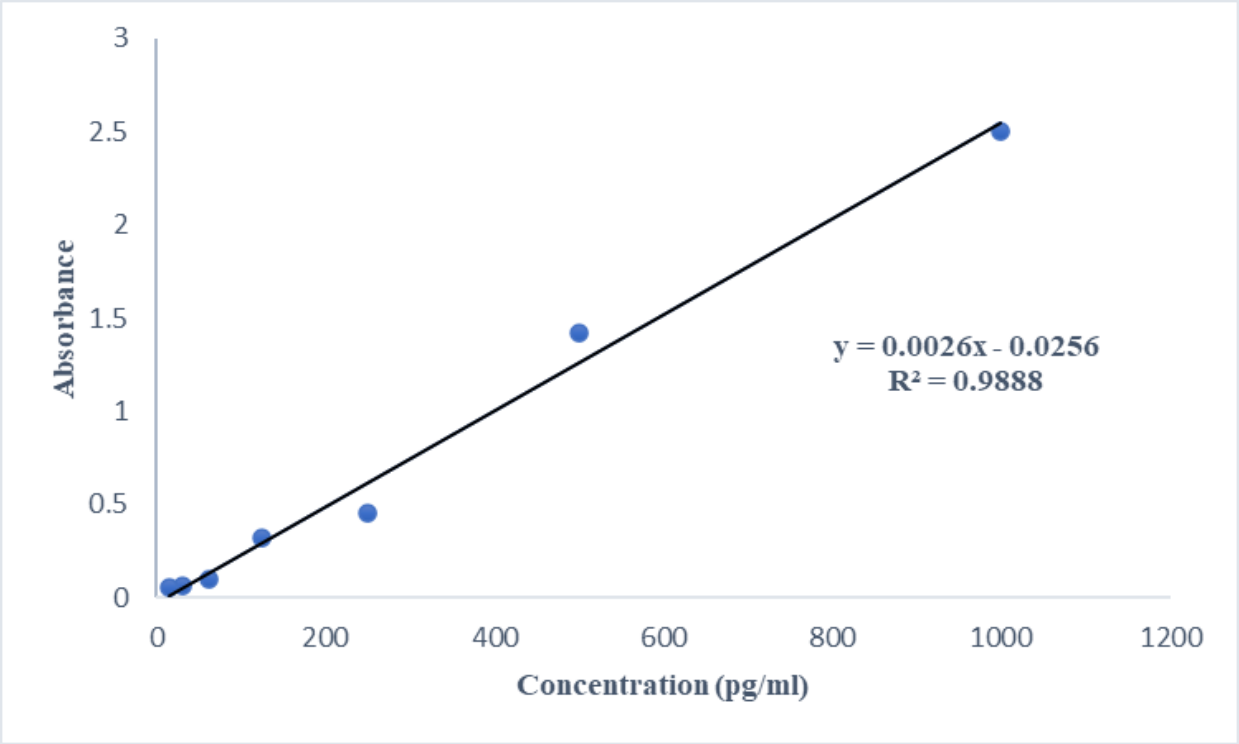


Figure 25: IL-22 Standard Curve

The IL-22 standard curve yielded a straight line and a linear regression, given as:

$$\mathbf{y = 0.0026x - 0.0256}$$

From the above-mentioned equation, the concentration of IL-22 was obtained by putting the absorbance value.

$$\textbf{Concentration} = \frac{\boldsymbol{Absorbance\ (y) - 0.0256}}{\mathbf{0.0026}}$$

3.1.4 Clinical Profile and Analytical Findings

The table 8 shows the clinical data and analytical findings of the study population, with various parameters measured and compared between two groups: Patients and Controls. The first parameter, Age in years, shows no significant difference between the two groups ($p = 0.161$). Among the Patients group ($N = 200$), the mean age was 28.66 ± 0.65 years, whereas among the Controls group ($N = 176$), the mean age was 29.97 ± 0.67 years. However, for the second parameter, BMI (kg/m^2), there was significant difference observed between the Patients and Controls ($p < 0.001$). But the Patients group had a mean BMI of 22.19 ± 0.34, while the Controls group had a mean BMI of 23.47 ± 0.11. Although the result is statistically significant, the average BMI of the participants falls within the normal range (<25 kg/m^2), so it may not have much clinical importance. Therefore, the p-value is reported as it is, but should be

interpreted with some caution. The Patients group had a considerably higher mean Y-BOCS score of 22.74 ± 0.52, while the Controls group had a mean score of 3.44 ± 0.15. Moving on to the laboratory findings, the serum IL-22 levels did show a significant difference between the Patients and Controls ($p < 0.001$). Among the Patients group, the mean serum IL-22 level was 28.45 ± 0.54 pg/ml, whereas among the Controls group, the mean level was 32.22 ± 0.73 pg/ml.

Parameters	Groups	N	Mean ± SEM	p-value
Age				0.161
	Patients	200	28.66 ± 0.65	
	Controls	176	29.97 ± 0.67	
BMI (kg/m^2)				<0.001
	Patients	200	22.19 ± 0.34	
	Controls	176	23.47 ± 0.11	
Y-BOCS Score				<0.001
	Patients	200	22.74 ± 0.52	
	Controls	176	3.44 ± 0.15	
Serum IL-22 levels (pg/ml)				<0.001
	Patients	200	28.45 ± 0.54	
	Controls	176	32.22 ± 0.73	

Table 8: Patient Profile and Analytical Findings of the Enrolled Population

3.2 Discussion

In this case control study, there was a statistically significant decrease in the serum level of IL-22 in OCD patients (28.45 ± 0.54 pg/ml) as compared to the healthy control (32.22 ± 0.73 pg/ml) with a p-value of <0.001. While IL-22 is normally regarded as an pro-inflammatory

cytokine, the reduced serum levels seen in our OCD patients seem contrary to expectations based on the known association between inflammation and OCD pathology. Yet there are several reasons why such an unexpected observation may occur from a closer examination of the functions of cytokines in neuropsychiatric disorders.

The broader scope of immune dysregulation in OCD has also been shown by a series of scientific evidences. According to a meta-analysis of 12 different studies, there is an observed decrease in plasma levels of IL-1β among patients with OCD, possibly mediated by age, the use of medication, and comorbid depression on other types of cytokines (Gray & Bloch, 2012). This tells us that not all types of cytokines that are pro-inflammatory increase in concentration in patients with OCD, and some may even decrease. The complexity of the immune system in OCD implies that our results concerning decreased levels of IL-22 fit into this paradigm.

The reason for the reduced expression of IL-22 observed in this study could be attributed to the phenomenon known as immune exhaustion or regulatory inhibition. In cases of long-term inflammation, the body's immune system tends to go into regulation mode to avoid extensive damage to the tissues. The IL-22 cytokine is crucial for protecting the body against pathogens by regulating tissue repair and epithelial barrier function. It is inhibited by several factors, including TGF-β and IL-27, as a form of feedback regulation (Wei et al., 2020). It is therefore plausible that in OCD patients with chronically activated immune pathways, IL-22 production may be actively suppressed as part of this regulatory response.

An interesting cause could be related to the Th-17 axis. Both IL-17 and IL-22 are secreted concomitantly by Th-17 cells, and their concentration levels may correlate with each other. Nevertheless, some studies have suggested that there can be a dissociation between IL-17 and IL-22 in certain conditions. Intriguingly, according to a case control study conducted using ELISA, patients with OCD showed higher concentration levels of serum IL-17 than normal individuals, implying that IL-17 may be implicated in the physiopathology of OCD (Sarker et al., 2023). In addition to the increase in the concentration level of IL-17, the decrease in the level of IL-22 concentration in our study raises an interesting speculation of the presence of a possible imbalance of Th17 cells favoring the production of IL-17 but inhibiting IL-22. This kind of dissociation between Th17-related cytokines has been observed in other inflammatory conditions and warrants further investigation in OCD.

Gut-brain axis involvement might also be implicated here. IL-22 is critical for the maintenance of gut barrier integrity and highly correlated with the gut immune system and the microbial

composition of the gut, the production of which is highly dependent on the microbiome status (Li et al., 2014). The correlation between gut dysbiosis and neuropsychiatric diseases is becoming increasingly clear. Elevated cytokine concentration in the peripheral blood will affect the brain via several mechanisms, and cytokines have the ability to enhance the function of the serotonergic reuptake pump, decreasing serotonin concentrations in the synaptic cleft – this is very relevant to OCD, where the disruption of the serotonergic neurotransmission system is a major factor (Kearns, 2024). If IL-22 levels are reduced, gut barrier function may be compromised, potentially allowing microbiome-derived inflammatory signals to reach the brain and influence OCD-related neurotransmitter systems.

It would be prudent to take into consideration the double-edged role that this cytokine plays. This is because this cytokine, IL-22, while it produces protective functions such as wound healing and regeneration of tissues, it also triggers inflammation in case of overexpression (Zhao et al., 2023). It is possible that in OCD, the reduced IL-22 levels reflect a failure of this protective, tissue-repairing function rather than a reduction in inflammation by itself. The body may be less able to regulate or repair damage associated with chronic neuroinflammatory stress, leading to worsening of the underlying disease process.

In addition, the difference between the current findings and those that would have been predicted by a simple pro-inflammatory paradigm highlights an important general principle in OCD immunology; the disruption of immunological responses seen in OCD includes not only neuroinflammation but also changes in monoamine neurotransmission and glutamate signaling, and the interaction between these systems remains unknown (Najjar et al., 2013). In summary, our data support the hypothesis that IL-22, which belongs to the IL-10 family of cytokines, which serve as regulators of the immune system as well as protective factors for epithelial barriers, could be part of a dysfunctional compensatory process in OCD patients.

To our knowledge, this is the first study to report serum IL-22 levels in OCD patients. Given the novelty of the finding, replication in larger and more diverse populations is essential. In addition, future research would need to look into the association between serum IL-22 concentration and OCD symptoms scores as well as other Th17-axis cytokines in the same cohort of patients.

3.2.1 Limitations of the Present Study

Despite yielding novel results regarding serum IL-22 concentration in patients with OCD, this research is not free of any limitations. First, the sample size is appropriate but could have been

increased to obtain more substantial conclusions about the relationship between OCD and serum IL-22. For instance, researchers could compare the serum concentrations of the examined cytokine in patients with various types or degrees of OCD. Second, this research paid no attention to the impact of medication on the immune system of the studied individuals. Most patients who suffer from OCD are administered SSRIs, known for their anti-inflammatory action. Therefore, low IL-22 concentration can be explained by pharmacotherapy rather than being a characteristic feature of this condition. Lastly, this research employed a cross-sectional approach, meaning that the serum samples were collected only once. So it was impossible to determine whether the low serum level of IL-22 leads to OCD or vice versa. Finally, some confounders such as diet, exercise, smoking habits, and associated diseases might have affected the amounts of IL-22 in patients and controls.

3.2.2 Practical Implications

In spite of their preliminary nature, the results of the current research might have several implications for our understanding and potential management of OCD. First, being the first study on serum IL-22 levels in OCD patients, it helps open a new perspective for the detection of OCD-related biomarkers. As OCD is currently diagnosed only using clinical interviews, this study suggests that the future research should pay special attention to the investigation of serum IL-22 concentration, or other cytokine markers in OCD patients, in order to find an objective method of OCD diagnosis. Second, the alterations of IL-22 levels also indicate that the regulation of the immune system should be considered among the potential options for the treatment of OCD. Since research indicates that the body's defense system plays a part in the manifestation of OCD symptoms, the administration of additional treatments such as anti-inflammatory therapy along with traditional serotonin reuptake inhibitors will allow for better patient outcomes. Finally, the association between increased serum IL-22 and the dysfunction of the gut-brain axis indicates that interventions directed at improving the state of the gut barrier should also be considered within the context of the OCD treatment.

Chapter 4

Conclusion

As far as we are aware, this study is the first case-control study conducted on the levels of IL-22 in serum samples of OCD patients among the Bangladeshi population. In order to maintain proper uniformity between cases and controls, the healthy subjects were also matched in regards to their socio-demographic and biophysical characteristics. The main result obtained from this study was the presence of significantly lower level of IL-22 in OCD patients as compared to the healthy individuals. This finding shows that IL-22 might participate in the pathogenesis of the disease but the exact mechanism has not yet been determined. Such abnormality in IL-22 indicates the likelihood of using this factor as a potential blood-based biomarker for the disease. Nevertheless, more researches should be done in order to investigate causality between IL-22 level and the disease's pathology, which in turn would lead to the possibility of discussing normalization of the mentioned factor via specific therapy. If reliable and objective biological markers will be found in the future, it may become helpful for more precise diagnostics of the illness and innovation of novel therapeutic techniques which will address the abnormalities in the immune system.

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Appendix

Appendix A

✓ English Version of Volunteer Consent Form

Consent Form

1. Have you fully understood the nature, purpose, and methodology of this research work?	**Yes / No**
2. Have you been informed that blood will be collected by nurses in this research?	**Yes / No**
3. Is your understanding regarding the outcome and potential benefits of this research clear?	**Yes / No**
4. Have you been able to independently make the decision to participate, cooperate, or refrain from this research work?	**Yes / No**
5. Are your fundamental human rights being violated as a result of participating in the research work?	**Yes / No**
6. Are you fully aware that the confidentiality of your information will be maintained?	**Yes / No**
7. Are you adequately informed that you will not be given any remuneration or travel allowance for participating in the research work?	**Yes / No**

Authorization Letter

Having gained a full understanding of the purpose, methodology, and utility of this research work, I express my consent to its ethical principles. I have not been influenced by any individual or group to participate in this research work, nor have my fundamental human rights been violated. Therefore, subject to proper review, I am voluntarily signing this authorization letter.

Name: _____ **Signature:** _____

✓ **Bengali Version of Volunteer Consent Form**

সম্মতিপত্র

১.	এই গবেষণা কর্মের ধরণ, উদ্দেশ্য এবং পদ্ধতি সম্পর্কে কি পুরো জানতে পেরেছেন?	:	হ্যাঁ / না
২.	এই গবেষণায় নার্সদের মাধ্যমে রক্ত সংগ্রহ করা হবে, এ বিষয়ে কি অবহিত হয়েছেন?	:	হ্যাঁ / না
৩.	এই গবেষণার ফলাফল এবং সম্ভাব্য কল্যাণের বিষয়ে আপনার ধারনাটি স্পষ্ট হয়েছে কি?	:	হ্যাঁ / না
৪.	এই গবেষণা কর্মে অংশগ্রহণ, সহযোগিতাদান, অথবা বিরত থাকার সিদ্ধান্ত আপনি কি স্বাধীনভাবে গ্রহণ করতে পেরেছেন?	:	হ্যাঁ / না
৫.	গবেষণা কর্মে অংশগ্রহণের ফলে আপনার মৌলিক মানবাধিকার কি ক্ষুণ্ন হচ্ছে?	:	হ্যাঁ / না
৬.	আপনি কি পরিপূর্ণ ভাবে জ্ঞাত যে, আপনার তথ্যাবলির গোপনীয়তা বজায় রাখা যাবে?	:	হ্যাঁ / না
৭.	গবেষণা কর্মে অংশগ্রহণের জন্য আপনাকে কোন পারশ্রমিক অথবা ভ্রমণভাতা দেয়া হবে না, এ বিষয়ে কি যথেষ্ট অবহিত আছেন?	:	হ্যাঁ / না

অনুমতি পত্র

এই গবেষণা কর্মের উদ্দেশ্য, পদ্ধতি ও উপযোগিতা সম্পর্কে পূর্ণ ধারণা পেয়ে, এর নীতিগত বৈশিষ্ট্য সমূহের প্রতি আমার সম্মতি প্রকাশ করছি। গবেষণা কর্মে অংশগ্রহণের জন্য আমি কোন ব্যাক্তি বা গোষ্ঠী দ্বারা প্রভাবান্বিত হইনি অথবা আমার মৌলিক মানবাধিকার ক্ষুণ্ন হয়নি। অতএব, যথাযথ পর্যালোচনা সাপেক্ষে আমি স্ব-প্রণোদিত হয়ে এই অনুমতি পত্রে স্বাক্ষর করছি।

নাম: স্বাক্ষর

_____ _____

Appendix B

Questionnaires Form

Study of BDNF, IL-1 Beta, and ApoE in Obsessive-Compulsive Disorder Patients among Bangladeshi Population

1. Identification

1.1 ID Code:

1.2 Name

1.3 Father's/Husband's Name:

1.4 Sex

Male		Female	

1.5 Marital Status

1.6 Date of Birth(dd/mm/yy)

1.7 Age(Yr)

1.8 Phone No

1.9 Permanent Address

1.10 Religion

1.11 Nationality

2. Personal History

2.1	Area of residence	Rural	Urban	S-Urban	Others

1	Where have you spent your Childhood(1-15y)?				
2	Where have you spent at least 3/4th more of your lifetime?				

2.2	**Education Level**		**2.3**	**Occupation**		
	Illiterate			Professional/Managerial/Business/		
	Can read only			Clerical		
	Can write a letter			Technical		
	SSC or equivalent			Skilled Worker		
	HSC or equivqlent			Unemployed/Pensioner		
	Graduate or Higher			Housewife		
	Others			Others		

2.4	**Impression about Social Class**		**2.4**	**Family Expenses/Month**
	Rich			
	Upper Middle			
	Lower Middle			
	Poor			
	Destitute			

2.6	Smoking Habit		2.7a	Current Smoker	
	Never			Sticks/Day	
	Ex-smoker>6months		2.7b	Ex-smoker	
	Current smoker			Sticks/Day	

3. Previous History of Psychiatric Disorder Y N

4. Family History of Psychiatric Disorder: Y N

5. Case: New Old

6. Biological Characteristics:

6.1 Height(cm):

6.2 Weight(kg):

6.3 Pulse/min:

6.4 Temperature:

6.5 BP(sys/dias):

Appendix C

YALE-BROWN OBSESSIVE COMPULSIVE SCALE (Y-BOCS)

Questions 1 to 5 for obsessive thoughts

1. How much of your time is occupied by obsessive thoughts?
   0 = None
   1 = Less than 1 hr/day
   2 = 1 to 3 hrs/day
   3 = Greater than 3 and up to 8 hrs/day
   4 = Greater than 8 hrs/day
2. How much do your obsessive thoughts interfere with your work, school, social or other important role functioning?
   0 = None
   1 = Slight interference, but overall performance not impaired
   2 = Definite interference, but still manageable
   3 = Substantial interference
   4 = Incapacitating
3. How much distress do your obsessive thoughts cause you?
   0 = None
   1 = Not too disturbing
   2 = Disturbing, but still manageable
   3 = Very disturbing
   4 = Near constant and disabling distress
4. How much of an effort do you make to resist the obsessive thoughts?
   0 = Try to resist all the time
   1 = Try to resist most of the time
   2 = Make some effort to resist
   3 = Yield to all obsessions without attempting to control them
   4 = Completely and willingly yield to all obsessions
5. How much control do you have over your obsessive thoughts?
   0 = Try to resist all the time
   1 = Try to resist most of the time
   2 = Make some effort to resist
   3 = Yield to all obsessions without attempting to control them
   4 = Completely and willingly yield to all obsessions

Questions 6 to 10 for compulsive behaviors

6. How much time do you spend performing compulsive behaviors?
   0 = None
   1 = Less than 1 hr/day
   2 = 1 to 3 hrs/day
   3 = Greater than 3 and up to 8 hrs/day
   4 = Greater than 8 hrs/day
7. How much do your compulsive behaviors interfere with your work, school, social or other important role functioning?
   0 = None
   1 = Slight interference, but overall performance not impaired
   2 = Definite interference, but still manageable
   3 = Substantial interference
   4 = Incapacitating
8. How would you feel if prevented from performing your compulsion?
   0 = None
   1 = Only slightly anxious if compulsions prevented
   2 = Anxiety would mount, but remain manageable if compulsions were prevented
   3 = Prominent and very disturbing
   4 = Incapacitating anxiety
9. How much of an effort do you make to resist the compulsions?
   0 = Try to resist all the time
   1 = Try to resist most of the time
   2 = Make some effort to resist
   3 = Yield to all obsessions without attempting to control them
   4 = Completely and willingly yield to all obsessions
10. How strong is the drive to perform the compulsive behavior?
   0 = Complete control
   1 = pressure to perform the behavior
   2 = Make some effort to resist
   3 = Very strong drive to perform behavior
   4 = Drive to perform behavior experienced as completely involuntary

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