Evaluation of Serum Interleukin-3 Level in Obsessive-Compulsive Disorder: A Case-Control Study

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
BRAC University
May, 2026

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing 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 which 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 Serum Interleukin-3 Level in Obsessive-Compulsive Disorder: A Case-Control Study" submitted by Mahima Hoque (22146027) of Summer, 2025 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 7th May, 2026.

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Ethics Statement

Southeast University has provided the ethical approval. The ethical approval number is SEU/Pharm/CECR/024/2024.

Abstract

Obsessive compulsive disorder (OCD) is a mental health condition characterized by intrusive, unwanted thoughts and repetitive actions. The aim for this analysis is to determine relationship between OCD and IL-3. Interleukin-3; pleiotropic pro-inflammatory cytokine that plays a critical role in the production of many types of blood cells. The number of patients who participated in this study was 209 and the number of controls was 201. Participants with OCD were diagnosed by a qualified psychiatrist using the DSM-V criteria for OCD as opposed to healthy controls. The severity of OCD was measured using the Y-BOCS and cytokine level was measure by enzyme-linked immunosorbent assay (ELISA). Patients in this study had a mean cytokine concentration of (0.49 ± 0.01) pg/ml and the mean cytokine concentration of controls was (0.66 ± 0.02) pg/ml. IL-3 that might help with the early detection of patients and speeds up the process of gaining knowledge and making diagnosis of OCD. IL-3 can effectively differentiate between OCD patients and healthy individuals still more research is needed to for better diagnostic strategies treatment plans.

Keywords: *Obsessive Compulsive Disorder; Interleukin-3; Cytokine; Y-BOCS; Pro-inflammatory: Enzyme-Linked Immunosorbent Assay (ELISA)*

Dedication

Dedicated to my dearest parents, Sadik, Ebti, my four best friends and my thesis supervisor Dr. Md. Rabiul Islam.

Acknowledgement:

First and foremost, I am deeply grateful to Almighty Allah for His constant guidance, for always showing me the path, and for providing unwavering strength, which enabled me to overcome every challenge and successfully complete this research.

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List of Acronyms

OCD - Obsessive-Compulsive Disorder

IL-3 - Interleukin-3

DSM-5 - Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

ELISA - Enzyme-Linked Immunosorbent Assay

SSRIs - Selective Serotonin Reuptake Inhibitors

BMI - Body Mass Index

5 HT - 5-Hydroxytryptamine (commonly known as serotonin)

GABA - Gamma-Aminobutyric Acid

TSPO - Translocator Protein Positron Emission Tomography Scan

Y-BOCS - Yale-Brown Obsessive Compulsive Scale

GAD – General Anxiety Disorder

HPA – Hypothalamic-Pituitary-Adrenal (axis)

GM-CSF – Granulocyte-Macrophage Colony-Stimulating Factor

CSTC - Cortico-Striato-Thalamo-Cortical (circuit)

Chapter 1: Introduction

1. Introduction

1.1 Overview of Obsessive-Compulsive Disorder (OCD)

Obsessive-compulsive disorder (OCD) is a psychiatric disorder, which is usually related to the possession of obsessions or compulsions, which is most often linked to disturbances in certain neurotransmitter systems, particularly those of serotonin and dopamine (Marazziti et al., 2015). Obsessions come with repeated thoughts, imaginary pictures, emotions, and recurrent cravings that are not expected (Stein et al., 2019). Compulsions are a kind of thought process that people believe It is mandatory for them to do it repeatedly due to an obsession or strict restrictions, even if they know the action is not needed or is too much. The compulsions due to obsessive-compulsive disorder (OCD) cause marked distress, take too much time, or directly interact with the individual's usual daily schedule, professional functioning, or normal civic activities or connections (National Institute of Mental Health, 2023).

OCD has some symptoms, including compulsions, or repetitive behaviors, and obsessions, or recurring thoughts. The indications might take some time to appear. However, there were plenty of therapeutic treatments with the help of which patients overcame their illness and led better lives (National Institute of Mental Health, 2023). While most adults can identify when someone has both compulsions and obsessions, children may struggle to identify or discuss their obsessions. Behavioral-cognitive theories state that compulsions keep improving while having reactions with obsessions, which often increase pain or distress (Stein et al., 2019).

OCD patients often worry about getting dirty and feel the urge to clean and check everything all the time. Regardless of their demographic, 1-3% of people around the world experience OCD (Ujjwal et al., 2024). It has been having a long-term effect on employment and relationships at any age. By understanding neurological, genetic, and environmental factors, one can provide appropriate care.

Obsessions can be categorized into unwanted thoughts. Or instincts that cause suffering and are not merely exaggerated concerns regarding actual issues. Since, in case of people suffering grom OCD usually takes minimum an hour a day, it become hard to come up with the normal schedule.

Usually, OCD sufferers avoid challenging situations, which worsens their social ties and quality of life. There is a correlation between worse clinical outcomes and the duration of untreated OCD (Brock, Rizvi, & Hany, 2024). The indications might take some time to appear.

1.2 Etiology and Risk Factors of OCD

1.2.1 Etiology of OCD

The first possibility is that the issue with the circuits of the CSTC system is a potential cause. The CSTC systems are what allows us to comprehend our ability to understand a reward, how we physically react to something, and how our brains regulate themselves (Fornaro et al., 2009). Therefore, the connection between these three neurotransmitters makes a person's ability to comprehend what has happened to them in the past (the signs of a person having OCD or an individual who thinks about something they have done repeatedly) more negative if those systems are not functioning correctly (Fornaro et al., 2009). Neuroimaging of the structure and function of the human brain has shown us that the regions of the brain, which are responsible for making choices and how we react to those choices, are having problems. The brain regions of the brain are known as the orbitofrontal cortex and caudate nucleus, respectively; however, if one of these two regions is having problems, the symptoms of a person with obsessions and compulsions will be more negative (Fornaro et al., 2009).

Approximately 44% of individuals with OCD reported that they believed that the condition started after an incident, and 13.3% of those individuals reported that they believed it started after a stressful incident (Pinciotti & Fisher, 2022). Traumatic events, especially when an individual was a child, may result in more severe OCD, such as repeating behaviors and thoughts, such as those of contamination, symmetry, and collecting. Regardless of whether an individual has the stressful events or witnesses them, it is believed by most individuals with OCD that it is a catalyst for the condition. Individuals with OCD often perform compulsion behaviors to avoid more trauma or pain. Individuals with OCD have a tendency to check things too much when they are stressed, unsure, or have too much to do. Individuals check things for a reason, and that reason is that they are unsure about their memory or other brain functions. The psychological aspect, such as a sense of duty, has been found to influence behaviors such as obsessive checking, as revealed in research studies (Guo et al., 2025).

Genetics may also be the main factor playing a role in the improvement of OCD. Genetics alone cannot explain this phenomenon, but there are biological and environmental factors involved too. According to researches, almost fifty percent of those suffering from OCD inherited the disorder from their parents. It becomes even harder to determine if the person suffered from genetics when they experienced difficult situations while being kids (Brock et al., 2024). The significance of glutamate regulated by the SLC1A1 gene may be even greater than expected (Brock et al., 2024). The neurotransmitter called dopamine contributes to the pathogenesis of the illness and makes it difficult for patients to inhibit their repetitive behavior (Brock et al., 2024).

Most physicians believe that the reason of OCD; due to an imbalance in the brain circuit known as the CSTC (Brock et al., 2024). Most individuals suffering from OCD have signaling in their brains. It is quite common OCD patients suffer from other diseases such as Parkinson's disease, Sydenham chorea, or Tourette syndrome (Brock et al., 2024).

1.2.2 Neurotransmitter System

Serotonin:

Reports indicate that there is a connection between 5-HT function and violence, as both interpersonal hostilities, as well as criminal acts committed by persons with lower levels of CSF 5-HIAA are associated with violent suicide (Jalal et al. 2023). There have been speculations about the effect of the 5-HT system in the pathophysiology of OCD and its management with the use of SRIs; currently, studies are underway to establish the exact parts of the serotonergic system using PET scans (Jalal et al., 2023). Some of the SSRIs for OCD patients comprise five SSRIs, which include citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline, as well as one TCA, which is clomipramine. These agents work synergistically to inhibit the reuptake of 5-HT in the synapse, making more available to the receptor sites in the neurons (Jalal et al., 2023).

Dopamine:

Dopamine is basically a neurotransmitter, which is in the CNS, which influences emotions, thinking, perceptions, and rationality. It is believed that drugs acting upon the dopamine receptors can lead to symptoms associated with OCD. For instance, according to the findings of an experiment with selective D2/3 receptor antagonist quinpirole, the test subjects demonstrated

compulsive behavior through engaging in ritualistic activities (Jalal et al., 2023). It is seen by brain imaging that high levels of dopamine release in the right frontal cortex combined with injury lead to symptoms of OCD (Jalal et al., 2023). In contrast, reduced binding of the dopamine transporter was observed in the caudate and putamen portions of the basal ganglia among individuals having OCD (Jalal et al., 2023).

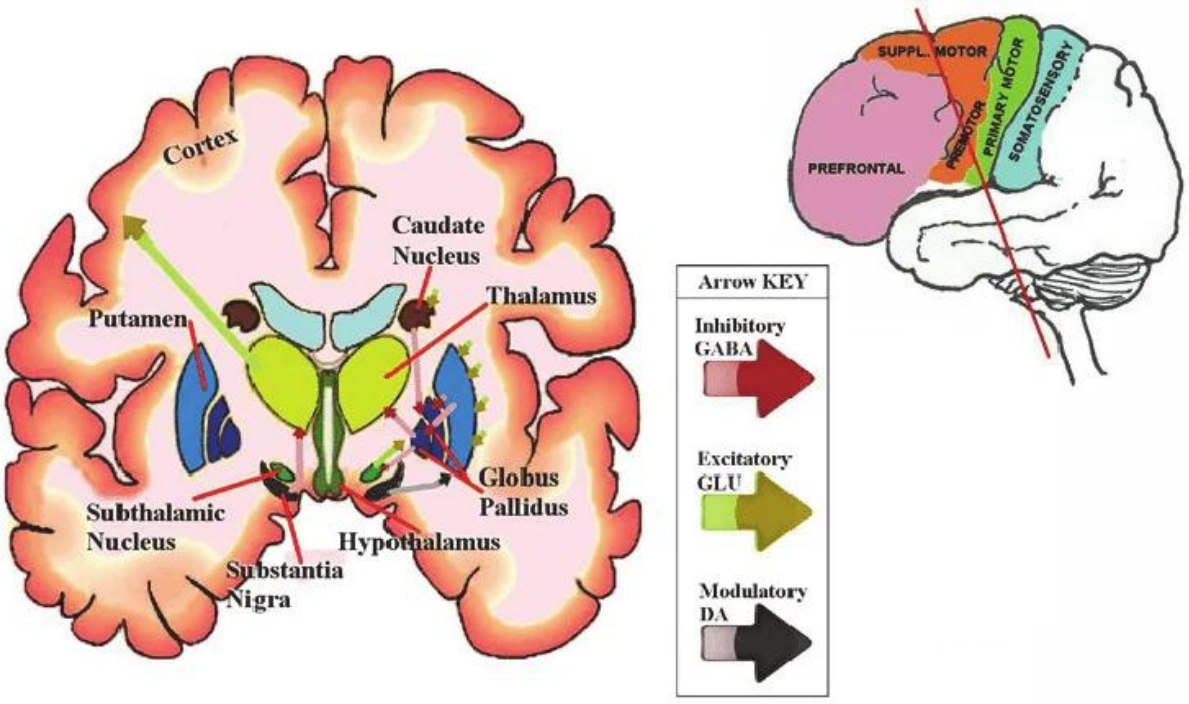

Figure 1: Caudate and Putamen Portions of Brain (Sandstrom et al., 2012)

Figure 1 guides to understand the brain part where binding of dopamine decreases in OCD patients in a more refined way and the picture is taken from the research paper of Sandstrom et al. (2012). It has been revealed that dopamine transporters in the striatum of treatment-naïve individuals with OCD are significantly reduced in contrast to the control group; therefore, the effectiveness of SSRIs or antipsychotics as dopamine receptor antagonists should be analyzed in relation to their effect on compulsions and habit formation (Jalal et al., 2023).

Glutamate:

The neurotransmitter known as glutamate is primarily classified as an excitatory neurotransmitter and is present in the CNS and enables the proper coordination of connection between different circuits. Some drugs that can increase or decrease glutamate activity have the potential to aid in

treating stroke and amyotrophic lateral sclerosis (ALS) as excessive stimulation of neurons through glutamate can result in the death of these neurons from toxicity resulting from over activation (Jalal et al., 2023). Research at Ruhr University, Germany has found significantly elevated levels of glutamate (Jalal et al, 2023) in individuals with OCD versus those without.

GABA

In addition, recent evidence suggests that the extremely elevated concentrations of glutamate along with low levels of GABA (GABA is considered an "inhibitory" or "anti-activation" neurotransmitter) may clarify the underlying mechanism of OCD; this was confirmed by MRS studies which also showed increased activation of glutamate transmission in the glomeruli of the CSTC circuit associated with OCD (Singh et al., 2023).

1.3 Causes of OCD

It was reported by about 44% of individuals with OCD that they perceived themselves to have developed their disorder following a specific trigger, while 13.3% believed they developed OCD following a stressful situation (Pinciotti & Fisher, 2022). Stressful experiences, particularly during childhood, can be related to the presence of more severe OCD features, which include repetitive behavior as well as the occurrence of themes such as contamination, symmetry, and hoarding. Individuals with OCD usually perform compulsions to avoid or cope with additional trauma or painful experiences. The hallmarks of OCD; an excessive amount of checking among other symptoms caused by stress, uncertainty, and excessive cognitive load. Checking occurs due to such reasons; however, they lead to a lack of confidence in one's recollection and other cognitive abilities. Research has shown that various psychological factors, such as obligation, are partially responsible for continuing compulsive checking habits (Guo et al., 2025). Some abnormal activity in part of the subcortical brain contributes to the development of OCD and includes those found in the cingulate cortex and caudate nucleus (Guo et al., 2025). Although OCD has various causes, some cases can be attributed to neurological causes such as the basal ganglia (Brock et al., 2024). Such reports provide some evidence of access to other regions of the brain, mostly globus pallidus or caudate as a potential cause of OCD (Brock et al., 2024). The findings from the studies of twins have helped in understanding the contribution of genetic and environmental causes of OCD. For example, in one of the twin studies' meta-analyses, the researchers found that the contribution of additive genetics was about 40%, while that of the non-shared environment contributed about 51%

in the case of obsessive-compulsive symptoms (Stein et al., 2019). Moreover, there is evidence available that suggests the involvement of gene-environment interaction in the etiology of OCD and the influence of very broad etiologic factors, such as negative emotionality, on the obsessive-compulsive symptoms (Stein et al., 2019).

Some of the influences for developing OCD can be attributed to epigenetics. Certain life events or trauma can also cause OCD, especially for those who are genetically susceptible to developing OCD. The potential to influence genetic expression (episomal change) and can create an opportunity for genetically transmitted depression to become active. Therefore, other factors in addition to epigenetic inheritance contribution to the development of OCD (Borrego-Ruiz and Borrego, 2025). Childhood trauma and stress in family dynamic are some of the leading psychological factors for developing OCD. Life stress can also be associated with the onset of OCD for those with a genetic predisposition to developing OCD. Whereby an individual's mind is flooded by thoughts on one thing, person, or idea in a pathological manner, such conditions are referred to as obsessions. Alternatively, compulsion, seen as an overwhelming urge to undertake some action, is described as irrational, foolish, or risky. Often, these symptoms are referred to as being ego-dystonic since the individuals cannot control them despite knowing that they are unreasonable or excessive (Lokhande et al., 2024). High susceptibility to contamination, pathological doubtfulness, the need for symmetry, intrusions, aggressive ideas, religious beliefs, and compulsions such as counting, arranging, cleaning, and verifying are examples of common phenomenological themes (Lokhande et al., 2024).

1.4 Subtypes and Comorbidity in OCD

1.4.1 OCD Subtypes

Various classifications of the disorder have been identified depending on the presentation of the symptoms. Some of the subtypes are contamination, hurting, hoarding, symmetry, obsessions, and certainty (Calamari et al., 2003). The contamination subtype includes individuals with contamination obsessions and hand washing compulsions (Calamari et al., 2003).

The individuals within the harming subgroup worry about the consequences of injuring themselves and others. More complicated theories have categorized the hoarding behaviors into their own cluster as well. "Symmetry" refers to those who are obsessed with symmetry and accuracy and

those compulsions associated with them. The obsessionals subtype is characterized by compulsive thoughts and obsessions with various ideas. Those who have certainty sub-types are individuals that require certainty and are perfectionists (Calamari et al., 2003).

In total, there are four groups of OCD symptoms, and all of them are characterized in accordance with the way how symptoms are manifested. Such subtypes as fears of contamination and cleanliness, thoughts about harming other people and excessive checking of things, need to organize items due to balance fears, and gathering useless stuff followed by its keeping are among those four subtypes of OCD.

1.4.2 Comorbid Psychiatric Conditions

It seems quite necessary to discuss common congenital variables, brain mechanisms, and treatment outcomes to illustrate the effect of depression, anxiety disorder, and OCD, since their manifestations cause similar neural processes.

First, it is crucial to mention that pathologies develop in a particular sequence of manifestation in patients suffering from plenty of diseases. Besides, such co-occurrence of syndromes is observed when patients are diagnosed impartially on DSM criteria (Goodwin, 2015).

1.5 Prevalence, Epidemiology and Impact

1.5.1 Epidemiology

Valleni-Basile et al. (1996) found out that the older an adolescent is, the more likely he or she will develop OCD. In another study, Zohar and Bruno (1997) discovered that the average score in the MOCI test of eighth-graders was significantly lower than that of sixth graders. But there were significantly more kids with extremely high MOCI scores (possibly having OCD) in the former. Also, in their study with children and adolescents ranging from 5 to 15 years old, Heyman et al. (2001) categorized OCD cases in age groups and revealed that the frequency of such cases increased exponentially based on age. This group also found out that OCD patients were significantly older than normal and psychiatric controls. As far as the adult population goes, it is believed that aging is linked to lower prevalence rates of obsessive-compulsive disorders (Degonda et al., 2003), as well as clinical cases of OCD (Fireman et al., 2001). According to Çilli et al. (2004), aging can influence females to develop OCD, since the 1-year prevalence of adult OCD in males decreased with increasing age, whereas it increased among females with age.

1.5.2 Impact on life

In most cases of obsessive-compulsive disorder, an individual tends to avoid confrontation with the situation at hand, hence affecting their relationships with people around them. Moreover, there is some evidence indicating the period an individual has been suffering from OCD before receiving medical attention based on clinical outcomes (Brock et al., 2024).

1.5.3 Prevalence in Bangladesh

A survey in Bangladesh found that 0.7% of adults over 18 had OCD in 2018-2019 (Hossain et al., 2024). According to the World Health (WHO), OCD is considered one of the most common mental health problems worldwide, and OCD is also one of the ten causes of disability globally. According to research on the spread of illness, the rate of OCD among Children and Adolescence in Bangladesh is 2%, and other studies have demonstrated similar prevalence rates for OCD among various cultures even though some differences exist in how people present with symptoms.

1.5.4 Global Incidence of OCD

Across the world, there are millions of people who have been suffering from OCD. The World Mental Health studies show that 3.0% of people in 10 different countries have OCD every year, and around about 4.1% of people have it at some point in their lives (Stein et al., 2025). Globally, OCD affects in between 1.5% and 3% of people, no matter how old they are (Hossain et al., 2024). Moreover, based on the WMH data, about 4.1% of the global population will suffer from OCD at least once throughout their life across the world (Stein et al., 2025).

1.6 Diagnosis of Obsessive-Compulsive Disorder

1.6.1 Diagnostic Criteria

As per DSM 5, an obsession or compulsion must capture considerable time for an individual to be suffering from OCD. A diagnostic interview that is semi-structured, is used for the analysis of a patient to be suffering from obsessive compulsive disorder (OCD) according to the criteria of DSM 5.

To make a diagnosis of OCD, a person must have a certain number of symptoms, which are outlined by the DSM 5, as well as how much impairment they might cause, which is done through a standardized diagnostic interview through the Y-BOCS-II, which determines how severe the

symptoms are (Rowa et al., 2025). The specifiers for OCD are insight specifiers and tic-related specifiers (Van Ameringen, Patterson, & Simpson, 2014). The DSM-5 has a diagnostic criterion for OCD as well as specifiers for OCD, which are used for determining how severe the symptoms are through a standardized measure of how severely they align with a diagnostic criterion for a diagnosis of obsessive-compulsive disorder (OCD), which is done through the Y-BOCS.

1.6.2 Diagnostic and Assessment Instruments

Y-BOCS and its dimensional version known as DY-BOCS proved to be the highest-performing measures available in interview format (Cervin, Perrin, Olsson, Claesdotter-Knutsson, & Lindvall, 2019). Structured diagnostic interviews including MINI-KID and Y-BOCS-derived scales are highly effective tools in research environments to measure the severity and burden of illness; monitor patients' treatment response and recovery; and increase the validity of the study (Cervin, Perrin, Olsson, Claesdotter-Knutsson, & Lindvall, 2019). Y-BOCS is an assessment tool that is commonly used by clinicians to assess the symptom intensity in OCD sufferers and involves two main categories of obsession and compulsion, each one measured between 0 and 4 (Hossain et al., 2024).

The assessment tool measures obsession through a number of features such as the amount of time involved in obsessive thoughts, how the obsession impacts the patient’s day-to-day functioning, the discomfort that the patient experiences, attempts to resist the obsessive thoughts, and the ability to control them (Hossain et al., 2024). Likewise, the measure assesses compulsion using variables such as the amount of time involved in repetitive behaviors, interference with the daily functioning of the patient, anxiety when the compulsion is resisted, resistance against the compulsion, and control. The Y-BOCS overall score is a way to assess the severity of OCD by 4 categories: 8-15 mild, 16-23 moderate, 24-31 severe, and 32-40 extremely severe (Hossain et al., 2024).

As to neuroinflammation detection tools, the main one is Translocator Protein (TSPO) imaging (Meyer, 2021). It is used because TSPO identifies microglial and astroglia activity, which stimulates inflammation in the brain. In TSPO PET scan-based research studies, it has been observed that binding occurs in those areas where the disease of OCD develops.

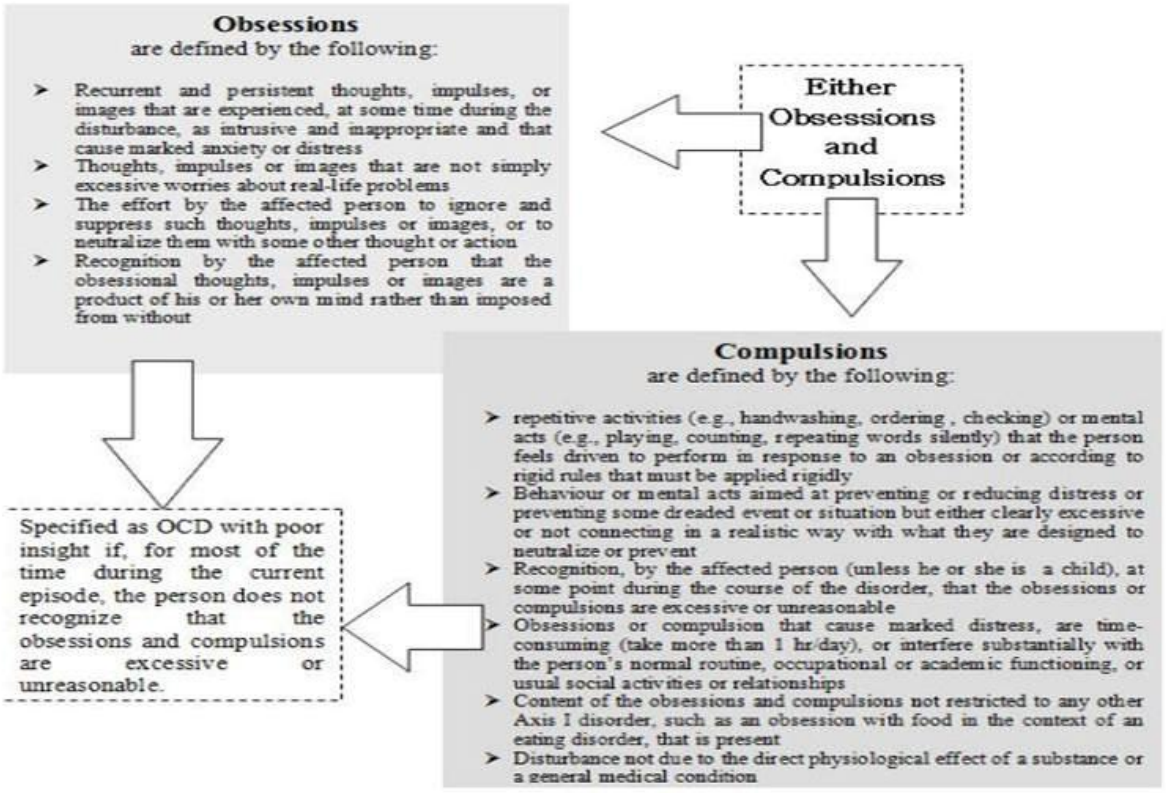

Figure 2: Diagnostic and Statistical Manual for OCD (Fornaro et al., 2009)

Figure 2 was taken from a study by Fornaro et al. (2009) for better visualization of diagnostic manual of OCD. With the help of TSPO PET scanning, it is possible to diagnose the condition of gliosis that triggers inflammation in OCD patients (Meyer, 2021). Researchers are working on several biomarkers like TNFα and PGE2 that could be used for detecting inflammation in OCD by considering the higher levels of TSPO expression (Meyer, 2021). This would be beneficial for the classification of individuals according to their illness. Hence, the technologies will be useful for detecting individuals suffering from OCD with inflammation, allowing for individual treatment for each patient.

1.6.3 Severity Assessment Tools

To find out severity of OCD, physicians take help of the Y-BOCS, a questionnaire developed in 1989 (Castro-Rodrigues et al., 2018). These 10 items are a sort of 5-point scale that explains the magnitude of compulsions (item 1), the disruption because of obsessions (item 2), the distress related to obsessions (item 3), the ability to withstand obsessions (item 4), the individual's ability to manage their obsessions (item 5), and objects that correspond to compulsions (items 6–10)

(Castro-Rodrigues et al., 2018). The therapeutic effects of medication have an impact on the Y-BOCS, and psychotherapy has much higher psychometric properties.

1.6.4 Diagnostic Distinction

Differentiation between OCD and other mental illness has always been crucial for both accurate diagnosis and developing a suitable course of treatment. An OCD diagnosis must include confirmation that the symptoms of other mental disorders are not able to adequately explain the presenting disruption or is not likely to. The most commonly encountered differential diagnoses and distinguishing features from OCD should be considered as an essential step in developing the diagnosis.

I) Compared to GAD, OCD includes the experience of irrational thought processes (obsession), followed by ritualistic behavior (compulsion) that is used to alleviate feelings of anxiety caused by the obsessive thoughts. GAD consists of worry based on real-life problems but does not include any form of compulsive behavior (Brock et al., 2024).

II) A specific phobia is characterized by a dread of a specific thing, person or situation and does not involve a ritualistic response to that fear (Brock et al., 2024).

III) Social Anxiety Disorder has the same general characteristics as specific phobias but involves interacting socially with others; instead of having avoidant or ritualistic behaviors they have fear of being embarrassed or humiliated.

IV) Major Depressive Disorder includes ruminating thoughts related to mood congruent content whereas obsessive thoughts in OCD do not relate directly to the person's mood.

V) Body Dysmorphic Disorder includes both obsessive thoughts and compulsive behaviors as they relate to appearance (Brock et al., 2024).

VI) Trichotillomania only includes the hair pulling behavior without any type of obsessive thinking, whereas the inability to get rid of belongings is a sign of hoarding disorder may have some relationship to OCD (Brock et al., 2024).

VII) Obsessive-Compulsive Disorders (OCD) refers to people with distressing thoughts and rituals while Obsessive-Compulsive Personality Disorder (OCPD) refers to individuals who are

perfectionists or who exhibit an obsessive need to control their environment but do not exhibit ritualistic behaviors.

1.7 Signs and Symptoms

1.7.1 Appraisal of Intrusive Thoughts in OCD

People suffering from OCD are thought to be spending at least one hour each day engaged in compulsions and exhibiting some level of distress or dysfunction in carrying out important activities of daily life (Frank et al., 2023). Lack of being able to function effectively or establish healthy relationships with other people is also among the criteria for OCD (Frank et al., 2023). The OCD disorder adversely affects one's physical and emotional well-being; however, the disorder can get worse with additional stress factors (Markarian et al.,2010). Compulsions related to the OCD consume much of one's time and affect daily routine. If left untreated, OCD typically develops into a chronic and progressive disorder resulting in long-term impairments in functioning (Perris et al., 2023).

Because this disease is considered ongoing and chronic, they can take a long time to develop and impact normal daily functioning and major responsibilities such as work and school responsibilities. The research literature has established that the duration of the illness will continue to be long without treatment and is related to individuals presenting in very poor condition and prognosis (Perris et al., 2023).

In addition, individual perceptions of symptoms may vary in different types of clinical care settings based on the type of provider involved and the personal checklists of symptoms created by the individual. Both the clinical care environments influence how people interpret and react to their symptoms of an illness and also affect the amount of stigma surrounding obsessive-compulsive disorder (OCD) and its different subtypes (e.g., violent). Patients with certain categories of OCD (e.g., violent subtype), will experience greater difficulty understanding their illness compared to a person suffering from a more accepted or conventional type of OCD and may, therefore, possess different degrees of insight into their illness (Perris et al., 2023).

1.7.2 Executive Dysfunction in OCD

Individuals who suffer from OCD regularly have trouble in transitioning from one task to another, thus having to compensate for this difficulty. Another area that has been researched is response

inhibition, as studies show that inhibition measured on Go or No-Go tasks typically yields poorer accuracy or longer response latencies (Tubío Fungueiriño et al., 2020). Changes in brain activity indicate whether the individual is attempting to adjust to a behavior even though it appears to be normal. Research has shown that executive function deficits associated with OCD can manifest as deficits in cognitive flexibility and set-shifting. This has been seen in research where participants without knowledge of their OCD make many more errors on WCST compared to participants who do know about their OCD (Manarte et al., 2021). Additionally, they will take much longer on the Trail Making Test, which suggests they will have a longer latency to switch tasks or learn new information (Manarte et al., 2021). Persons with OCD may have difficulty determining how to change their reaction patterns to create a more enjoyable life. Individuals with OCD typically struggle to stop or change their responses and behaviors because of their inherent tendency to frequently assess and evaluate their behaviors continually (Klawohn et al., 2014).

1.7.3 Imbalance between Habitual Learning and Goal-Directed Control

In individuals with OCD, behavior is governed by the interplay of two processes, whereby one selects acts depending on their present value while the other makes use of correlations between stimuli and responses and the performance of acts in relation to goals that no longer receive reinforcements (De Wit et al., 2012). The former is known as goal-directed system, while the latter is referred to as habit system, and people suffering from OCD might rely too heavily on habits rather than being guided by goal-directed processes (De Wit et al., 2012). The dual-system theory of instrumental behavior suggests that there are two different brain systems responsible for behavior (Jalal et al., 2023). Actions carried out purposefully and flexibly to achieve a particular goal are called goal-directed behaviors; for example, washing hands once upon using the bathroom as a means of hygiene. On the other hand, washing hands ten times upon using the bathroom would show a habitual pattern of behavior, which would be inflexible and mindless.

1.7.4 Impaired Self-Regulatory Processes

In general, patients suffering from OCD usually face challenges in controlling emotions, behaviors, and thoughts. This is due to the malfunctioning of executive functions of their brains.

It prevents them from abandoning undesirable actions, maintaining, and updating crucial information, as well as adapting quickly in the event of changes. In this respect, research suggests that numerous patients with OCD suffer from inhibitory deficits, cognitive flexibility, and impairments in working memory.

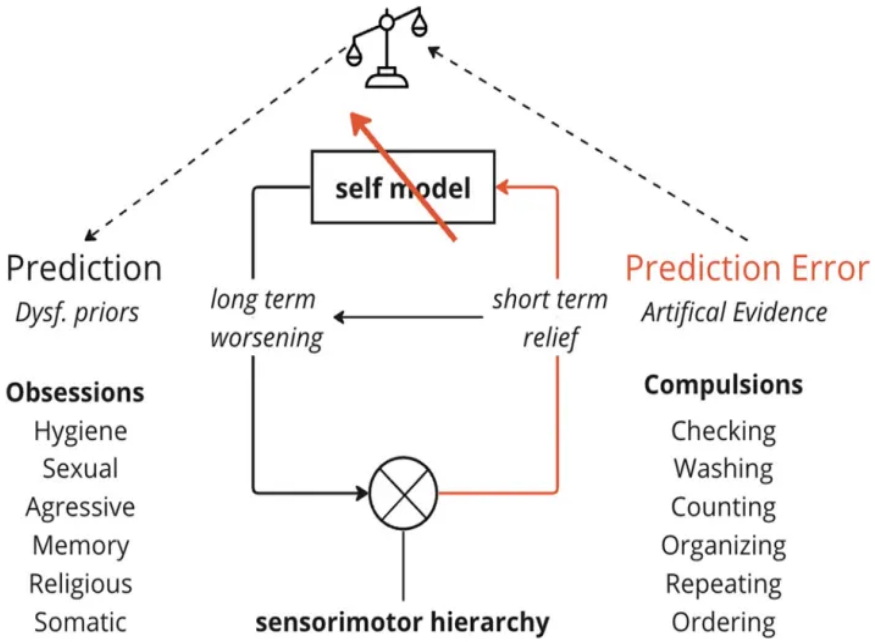

Figure 3: Impaired self-regulatory process (Schoeller, 2023)

Figure 3, is collected from a scientific paper of Schoeller (2023) which illustrates impaired self-regulatory process in an easier and better way. People with OCD have a difficult time stopping their harmful thoughts and actions (Robbins et al., 2019).

1.8 Pathophysiology of OCD

1.8.1 Cognitive Dysfunction

Research models of the cognitive-affective processes associated with OCD have also highlighted problems in mechanisms that may trigger heightened concern regarding harm (e.g., hypersensitivity to disgusting stimuli and overactive performance monitoring) or those that may prevent the control of responses to these concerns (e.g., problems with executive control processes, including impaired response inhibition and overactive stimulus-response associations) (Stein et al., 2019).

There are numerous indications that specific cognitive deficiencies are present in people suffering from OCD, such as impairment regarding the executive functions. OCD is associated with distinct symptoms, severity, onset, and co-morbidities, including tics disorder, depression, grooming disorders, and other conditions (Katerberg et al., 2010). Genetic epidemiology research has indicated that the beginning phase of OCD is genetically complex, and there are many environmental and hereditary factors that has influenced this condition (Katerberg et al., 2010).

1.8.2 Neurobiological Aspect in OCD

In this case, Shephard et al. (2021) showed how the CSTC model of habit learning could be used to demonstrate the role played by the amygdala in the development and management of fear for those with OCD because of challenges with regulation and inhibition. One of the main key issues that may lead to the manifestation of OCD is problems with the CSTC pathways. The CSTC pathways regulate reward recognition, motor responses, and functioning of the brain. It is believed that these pathways link together the serotonin, dopamine, and glutamate systems, leading to exacerbation of OCD features (Fornaro et al., 2009). Both structural and functional studies have shown problems within these pathways in certain brain areas, especially in the OFC and caudate nucleus, regulating decision-making and motor response control (Fornaro et al., 2009). Evidence shows that the problems within these brain areas may lead to worsening of rigid behaviors and thinking characteristic of OCD.

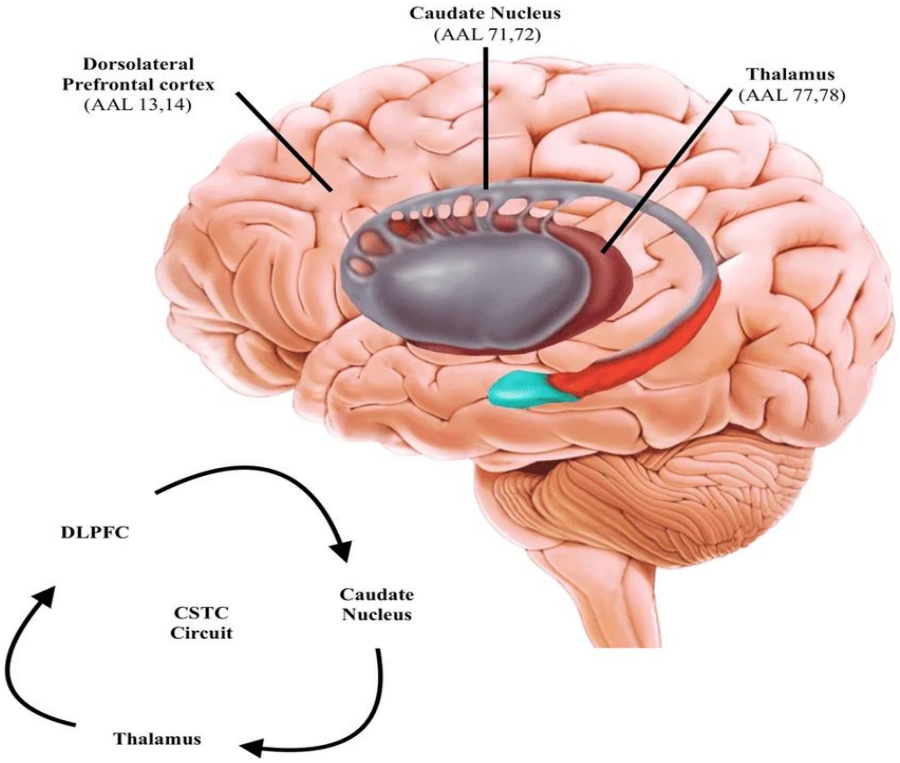

Figure 4: CSTC circuit (Chattun et al., 2020)

Chattun et al. (2020) highlighted a CSTC circuit diagram in his study which is used in figure 4 for better understanding and visualization of the circuit. Two of the key considerations regarding the orbitofrontal circuit as identified by Grant & Chamberlain (2020), include structural and functional impairments. In addition, these impairments involve three different parts of the brain within the orbitofrontal circuit. Two of these brain areas would significantly influence the regulation of compulsions for those diagnosed with OCD.

OCD has been classified as a disorder because of the inability of the brain to suppress repetitive task-like or compulsive behaviors, which leads to the obsessive habits. Furthermore, neuro-imaging studies have reported that individuals having OCD remarkably less volume of grey matter in the basal ganglia (putamen and globus pallidus) and that they also demonstrate a thinness of the cortex (Grant & Chamberlain, 2020).

1.8.3 Neurological Aspect in OCD

Neurological damage to certain brain regions results in obsessive-compulsive disorders. OCD might be a consequence of other brain regions' lesions, for instance, lesions found within the

frontal lobes, which suggests that the dysfunction Ing of front striatal regions might lead to OCD (Stein et al., 2019).

One area where the connection between OCD and neurology becomes even more prominent is when obsessive-compulsive behavior is triggered by an infection caused by bacteria belonging to the family Streptococcus. Much progress has been made in terms of diagnosis, investigation of autoimmune mechanisms, and therapeutic strategies for PANDAS. PANDAS is no longer the only diagnosis associated with OCD; OCD is now classified under a much broader pediatric acute onset neuropsychiatric syndrome hierarchy (Stein et al., 2019). This condition is diagnosed according to a child developing OCD-like symptoms following an episode of infection and physical trauma (Stein et al., 2019).

1.8.4 Neurodevelopmental Contributions

Physiological brain development increases at a rapid pace from childhood to teenage years. Numerous changes occur during this time including a reduction of unused synaptic connections and improved efficiency of communication between regions of the brain (myelination) (Spear, 2013). Although most of these changes occur due to the ongoing maturation of the brain, adolescents differ from one another in their degrees of development which may be related to their patterns of behavior in the future and their increased susceptibility to danger in this age group (Spear, 2013). The brain also has a great deal of plasticity during this period; therefore, both the limbic system and the prefrontal cortex (cognitive control system) will be very easily influenced by their developmental environment. As adolescents are at such a critical point in their development, it has been suggested by some researchers that adolescents may exhibit a greater response to changes in their environment during this period when the brain is going through so many changes because these changes could potentially be detrimental to the adolescent's developing brain circuits (Spear, 2013). Traumatic and adverse early experiences will have an impact on a teen’s growing brain, that may ultimately lead to abnormal brain development and mental illness (Lockhart, Sawa, & Niwa, 2018).

1.9 Management of Obsessive-Compulsive Disorder

1.9.1 Pharmacotherapy

The use of medications or drugs is a key aspect of treating OCD, and the first-line medications prescribed are the selective SSRIs. While clomipramine may be an effective alternative antipsychotic, comparative studies and network metanalyses fail to show this superiority. The first treatment to effectively treat obsessive-compulsive disorders was clomipramine, which has shown to be more efficacious when compared to SSRIs in several meta-analyses however, many of the early studies did not include treatment-resistant patients (Brock et al., 2024). The SSRIs have been used by researchers over many years as the foundation for development of the serotonergic system in OCD due to OCD's clinical response to SSRIs (Hossain et al., 2024). The role of the dopaminergic system in OCD was demonstrated during past decades, when researchers showed that dopamine D2 receptor antagonists added to SSRIs improved clinical response (Hossain et al., 2024).

When comparing efficacy directly between clomipramine and SSRIs, there is no significant difference in efficacy therefore, while SRIs are typically considered more efficacious when looking at long-term use due to safety and tolerability issues, both medications produce equivalent positive results when measuring immediate treatment effects (Brock et al., 2024). Clomipramine also has more potential side effects than do SSRIs, including side effects within the cardiovascular system.

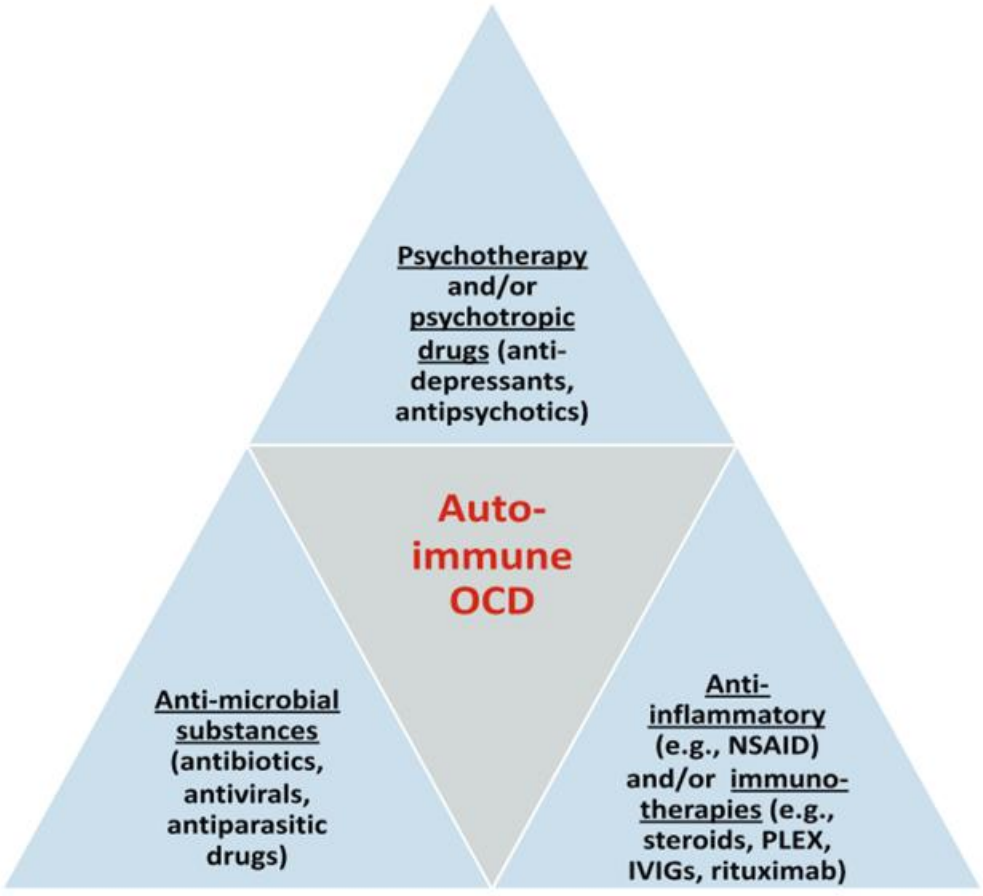

Figure 5: Key elements of OCD treatment (Endres et al., 2022)

Figure 5, the diagram was mainly published in a paper by Endres et al. (2022) and it is used for better understanding and visualization of key elements of OCD treatment. SSRIs continue to be the preferred pharmacological treatment alternative for those diagnosed with OCD. SSRIs either fail or cannot be tolerated; consequently, clomipramine is used sparingly (Janardhan Reddy et al., 2017).

1.9.2 Psychotherapy

Psychotherapy is an integral element while OCD is being treated, in which CBT, incorporating ERP, has been noted as the clinically supported psychological intervention that best helps in minimization of OCD (Tjelle et al., 2024). Many individuals recover with ERP, but it should be noted that not all patients fully recover in the process of regular psychological therapy. In addition,

it can be difficult to sustain this recovery long term. For this reason, new approaches that are stronger than traditional ERP have been introduced, (Tjelle et al., 2024).

It should be highlighted that concentrated ERP-based therapies, such as the Bergen 4-day therapy, have demonstrated effective results and high tolerability for patients suffering from OCD resistant to any other types of therapy (Tjelle et al., 2024). As a result, there can be a correlation between the improvement in symptoms over time and certain traits, such as insight in the ERP therapy itself. These changes will positively influence cost-effectiveness, increased efficiency in ERP treatment, peer effect, symptom normalization, and ERP homework compliance.

1.9.3 Lifestyle Modification and Supportive Interventions

Stress management interventions are usually effective and provide the most benefit to individuals with OCD (Brierley et al., 2022). Combining a lifestyle intervention strategy to these individuals should yield additional benefit when provided by a facilitator after starting treatment in first-line (Brierley et al., 2022). Numerous health issues are associated with OCD and may be a result of poor lifestyle behaviors (e.g., physical inactivity, high-fat intake, smoking and excessive alcohol consumption) (Holmberg et al., 2024). Dietary change and stress management strategies bring a balance in OCD patient's lifestyle.

1.9.4 Neuromodulation

There are few other evidence-based therapies for individuals who have not reacted to those treatments; therefore, more research is needed to establish alternatives for refractory patients suffering from obsessive-compulsive disorder.

i) There are numerous studies examining whether transcranial magnetic stimulation may be beneficial for the treatment of OCD (Brock et al., 2024). This includes individualized studies on various ways to use transcranial magnetic stimulation, including repetitive TMS and deep TMS (Brock et al., 2024). The results have been inconsistent.

ii) Dorsal anterior cingulotomy and anterior capsulotomy are considered the two primary methods of performing stereotactic ablation (Brock et al., 2024). Cingulotomy entails creating a lesion on the cingulum bundle area whereas capsulotomy involves producing a lesion on the anterior limb of the internal capsule area as both types of surgery aim to assist in regulating the excessive activity found within the CSTC circuitry that is associated with OCD (Brock et al., 2024)

iii) Deep brain stimulation (DBS) can be used as a treatment for severe OCD that is reversible with a success rate between 40% and 70% (Brock et al., 2024). DBS works by implanting an electrode that stimulates areas around it typically, DBS is implanted in the anterior limb of the internal capsule and may also be placed in the ventral striatum (Brock et al., 2024)

1.10 Biomarkers in Obsessive-Compulsive Disorder

1.10.1 Necessity for Biomarkers in OCD Research

A biomarker is any indicator of an increase, decrease, or likelihood of future occurrences, recurrences, or progression of medical events for a particular population (FDA-NIH Biomarker Working Group, 2016). It includes many kinds of molecular markers to help figure out whether a person has a given condition or disease (Garecia-Gutierrez et al., 2020). This biomarker may be used to distinguish disease subtypes. The rise of the stratified medicine era underlines that diagnostic molecular markers are useful not only for identifying disease in individuals but also for reclassifying it. This characteristic is important since several diseases have subgroups that respond differently to treatment or have different prognoses.

Biomarkers allow for the investigation into how OCD develops and progresses and how it can be treated. As reported by a study, biomarkers, including BDNF and DBH, could have a major impact on the treatment of OCD, considering their importance in neuronal survival, signaling, and neurotransmitter modulation (Sultania et al., 2024). Oxidative stress markers, such as MDA, can also reveal how much oxidative stress is involved in OCD, making them important not just in identifying OCD but also in monitoring how much worse this disorder can get (Sultania et al., 2024). We may potentially utilize genetic, neuroimaging, and brain characteristics as effective means of distinguishing between the various kinds of OCD (Proshina et al., 2025). Some of these biomarkers include differences in neurotransmitter systems, DNA characteristics, and brain activity.

1.10.2 Types of Biomarkers

A biomarker for diagnosis is a collection of biomarkers used to identify or validate a disease. (García-Gutiérrez and others, 2020) They are used in order to change how that disease is classified. This distinction is important because different diseases respond to treatment in different ways or

have different outcomes. So, diagnostic factors would help improve personalized medicine, which would make the treatment reaction work better.

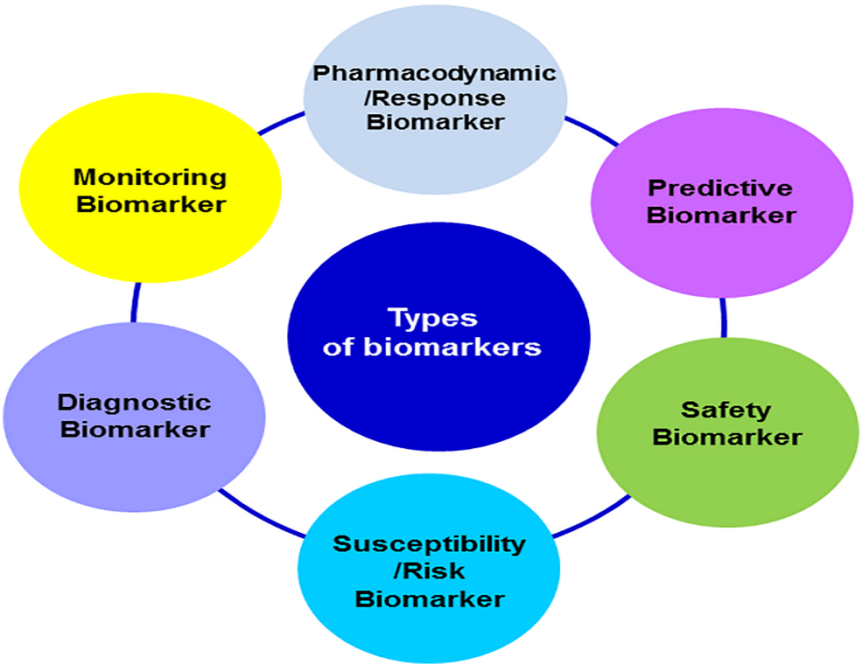

Figure 6: Variety of biomarkers (García-Gutiérrez et al., 2020)

Figure 6 was collected from published paper by author García-Gutiérrez et al. (2020) and we used it for clear and better illustration of varieties of existing biomarkers.

- Monitoring biomarker:

This group comprises biomarkers that are monitored over time to see how a disease is improving or worsening and how the body is responding to something, such as a drug or an external agent (García-Gutiérrez et al., 2020). Changes in the values of these biomarkers are believed to indicate that the state of the patient is worsening and that the drug reaction and other forms of clinical treatments are effective.

- Biomarker for pharmacodynamics or reaction:

In this situation, a pharmacodynamic marker changes due to some clinical events or interventions such as drug administration. For this reason, the type of biomarker is also named a tracking biomarker, since the test procedure is repeated several times. As for the primary function, the biomarker can provide physicians with vital data to determine whether the patient will be under

further therapy (García-Gutiérrez et al., 2020). Pharmacodynamic signs indicate the effectiveness of a medical procedure. Moreover, pharmacodynamic biomarkers are essential to the early phase detection of disease since they prove the existence of the relationship between drug-related physiological changes and its clinical effect on patients (García-Gutiérrez et al., 2020). Additionally, pharmacodynamic signs enable to design dose-response studies.

- Biomarker for forecasting:

In the current scenario, the indicator determines the group of patients who will undergo the surgery or divide them for the purpose. In particular, an indicator with good results proves that a new treatment method demonstrates higher efficacy compared to the control treatment group.

- Biomarker for Prediction:

There are many clinical events that individuals with a medical condition or disease may utilize a biomarker for to estimate their likelihood of experiencing the event. These events include the possibility of death, disease recurrence or growth, or a new illness. Prognostic factors are used to identify patients in clinical studies who are at higher risk of having an event or experiencing progression of their disease, and that allows researchers to group them into cohorts of higher-risk individual (García-Gutiérrez et al., 2020).

- Safety Marker:

During many research studies, it is vital to monitor the liver, kidneys, heart for the presence of any toxins to ensure that the treatment being investigated is safe. All safety biomarkers serve to identify or predict the presence of potential poisoning prior to signs of poisoning showing up on the NBSP and prior to the point in time that damage has occurred that cannot be repaired (García-Gutiérrez et al., 2020).

1.11 Cytokines: A Conceptual Overview

1.11.1 Definition and Classification of Cytokines

Cytokines are low-molecular glycoproteins produced by different types of cells in most organs and are essential for brain formation and proper brain functioning (Ludvigsson, 2022). Certain cell types produce cytokines, including lymphocytes and macrophages (Liu et al., 2021). Cytokines are very important as they provide signals necessary for the growth and development of the cells

of the immune system (Liu et al., 2021). Apart from their participation in the immune reaction, involving pro-inflammatory or anti-inflammatory processes or the immune cell recruitment at the location of tissue injury, cytokines can be harmful to the brain after an infection or an injury, and elevated concentrations of pro-inflammatory cytokines may impair memory, neural plasticity, and neurogenesis (Ludvigsson, 2022).

The immune system and CNS communicate through inflammatory cytokines and CNS and the cytokine levels can modulate inflammation within the brain that is fundamental for mental health conditions (Sarker et al., 2023). The cytokines can have a pro-inflammatory or anti-inflammatory potential and bring cells that are necessary to fight infection to the site of infection. A pro-inflammatory cytokine; however, can elicit an intense response from any nucleated cell due to the powerful nature of this molecule and may also be an immunosuppressing agent as well and is able to suppress inflammatory responses and contributes in preventing the development of the autoimmune diseases (Fabricius et al., 2022). For these reasons cytokines are typically categorized into functional categories including interleukins, interferons, tumor necrosis factors, chemokines, & colony-stimulating factors are some of the most frequent types of cytokines (Han & Liddelow, 2021).

1.11.2 Mechanisms of Cytokine Action

Cytokines are glycoproteins that are produced by various cells as a response to cell damage or infection. Cytokines regulate the immune system and brain functions. Neuroinflammation results from these cytokines, which affect the chemical composition of neurotransmitters that regulate serotonin, dopamine, and glutamate (Gonzalez & Bezzi, 2025)

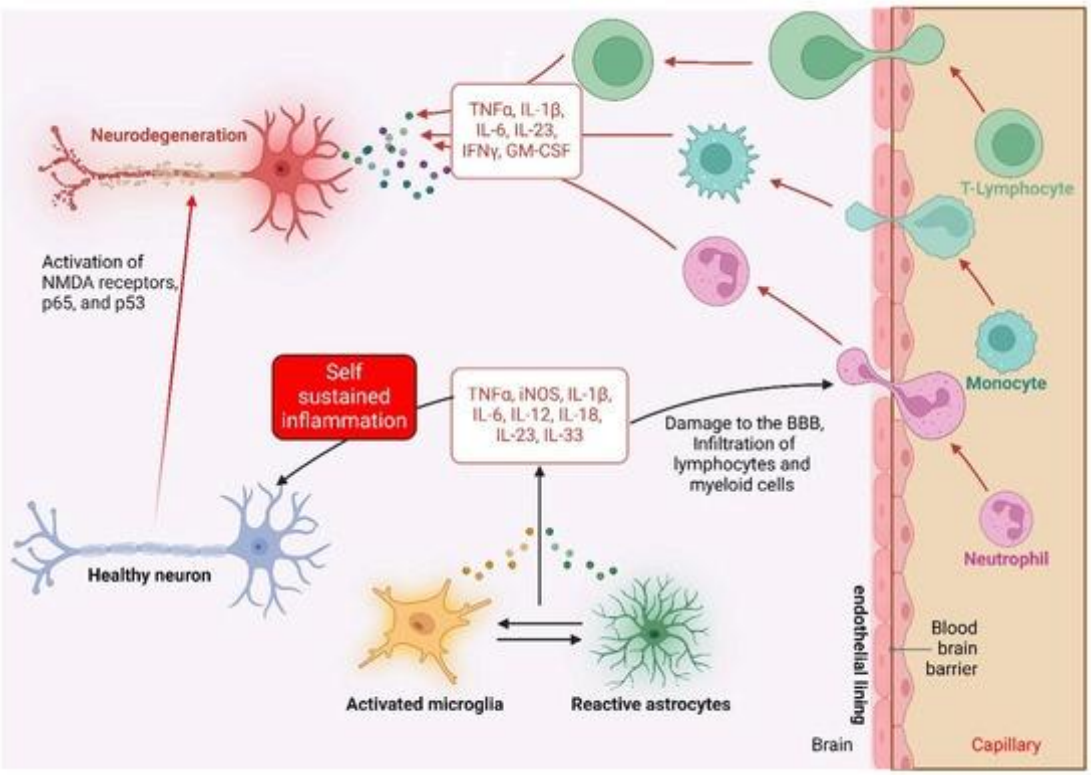

Figure 7: Cytokine pathways in neuroinflammation (Mallick et al., 2025)

Figure 7, sourced from a study owned by Mallick et al. (2025) for clear and proper visualization and understanding of how cytokine causes neuroinflammation. Cytokines are known to cause inflammation. They also work by stimulating the nerves that connect to the brain (Rao et al., 2015). Cytokines change how much of brain chemicals are available and they use a pathway called kynurenine to do this (Rao et al., 2015). When cytokines that promote inflammation are present, they activate an enzyme called indoleamine dioxygenase (IDO) and the activation of things in our body results in changes to how serotonin and glutamate work in the brain (Rao et al., 2015). These changes to serotonin and glutamate are strongly linked to the development of obsessive-compulsive disorder or OCD. Inflammation mediators, which are what cytokines are change brain chemical levels. This leads to serotonin and more glutamate being available. This imbalance of serotonin and glutamate is connected to the development of OCD. Inflammation plays a key role in OCD; cytokines affect brain chemicals and cause inflammation.

Cytokines are crucial for controlling immunological responses to infections and injury to the brain and are primarily generated by CNS glial cells (Miller et al., 2013). When an individual is healthy,

the body produces small amounts of cytokines. However, if an individual's immune system becomes activated due to an infection or if neuroinflammation occurs, there is an increase in the level of cytokines produced (Miller et al., 2013). At high levels of pro-inflammatory cytokine activity during infection or injury, pro-inflammatory cytokines may become detrimental, leading to damage to memory, brain plasticity, and neurogenesis (Fabricius et al., 2022)

1.11.3 Key Characteristics of Cytokine Signaling

JAKs will facilitate communication of at least 60 types of cytokines, hormones and growth factors including hormones and growth factors that regulate the immune system like the interleukins (IL), the interferons IFN, the erythropoietin (EPO) and the thrombopoietin (TPO), or noting to many will affect the metabolism and development of living things, such as prolactin and GH (Hammarén et al., 2019). Cytokines will induce, by binding to the extracellular portions of their receptor chains, the ability to create a receptor oligomeric complex which activates the associated JAKs, eventually leading to an increase in catalytic activity (Hammarén et al., 2019).

All cell types that are part of the inflammatory process (beginning, continuing and ending inflammatory responses) are regulated positively and negatively through cytokine signaling interacting with a limited number of Jak-Stat pathways (O'Shea & Murray, 2008).

1.11.4 Association of OCD with Cytokines

Gray and Bloch looked at what happens with cytokines in people with OCD and found out that people with OCD have more of a thing called tumor necrosis factor-alpha or TNF-α for short in their blood (Alsheikh & Alsheikh, 2021). People with disorder who do not get treatment usually have more inflammatory markers in their blood than people with obsessive compulsive disorder who are getting treatment. This is something that has been observed in both children and adults with disorder. It seems like people with disorder have some issues with swelling in their body. OCD patients have more of these markers in their blood when they do not get treatment. Compulsive disorder seems to cause some swelling problems. People with disorder who get treatment for obsessive compulsive disorder have lower levels of these markers (Alsheikh & Alsheikh, 2021). This includes cytokines and interleukins which are all part of the immune system (Alsheikh & Alsheikh, 2021). OCD patients have been found to have abnormalities in the way their bodies produce these biomarkers. Inflammation in the body can have an impact, on OCD.

OCD behaviors are often a result of this inflammation. Researchers found out people with OCD can have levels of immune cells and cytokines which can cause neuroinflammation (Coelho et al., 2024).

1.12 Inflammation and Neuroinflammation in OCD

1.12.1 Peripheral and Central Inflammatory Findings

The possibilities in the future of medicine, relapses, and development of a particular community may be predicted from a molecular marker which is used as a prognostic (Fabricius et al., 2022). The predictive molecular marker is compared to some baseline data. The balance of GABA and glutamate, as well as the corticostriatal pathway, in individuals with OCD may be changed by the strains of microbes (Eghdami et al., 2025). Dysfunction of the HPA axis, which is observed in OCD patients, can affect brain-gut communication owing to the effect of cortisol and leakage in the gut and modification of microbiota.

Interleukin 3 is responsible for regulating the movement and activity of immune cells. It emphasizes the importance of IL-3 as a mediator in neuroinflammation in the CNS. The signaling process of IL-3 affects the activity of neuroglia and systemic immune cells, thus affecting the regulation of neuroinflammation in the CNS (Fontenelle et al., 2012).

1.12.2 Evidence of Central Neuroinflammation

Inflammation is a major factor in the investigation of the pathology of OCD, owing to the connection between the immune system and the brain through inflammation. TSPO stands for a protein that is present in the active microglia and astrocytes (Meyer, 2021). TSPO has been extensively employed as a vital means for examining inflammation in OCD. The findings of TSPO PET scan show a substantial level of gliosis specifically in the CSTC circuits of the brain that involve the brain and OCD (Meyer, 2021). High gliosis indicates that inflammation of the brain is a crucial factor in the behavior of the OCD patients.

1.13 Interleukin-3 (IL-3)

1.13.1 IL-3 as a Candidate Biomarker

IL-3 is mostly known as a hematopoietic growth factor made by activated T lymphocytes (Ullrich et al., 2023). IL-3 is a kind of cytokine that is included in the category of β common chain cytokines. IL-3 is mainly produced by neurons and some astrocytes of the CNS (Podolska et al.,

2024). IL-3 has features that make it like the rest of the cytokines of this type, namely to IL-5 and GM-CSF (Podolska et al., 2024). IL-3 receptors are characterized as heterodimers, consisting of an α-chain, known as IL-3 receptor (CD123), and the β-chain, known as common receptor of all cytokines of the family or CD131 (Podolska et al., 2024). The interleukin-3 makes use of the beta chain receptor subunit, which is common for IL-5 and GM-CSF receptors (Renner et al., 2016). One of the major receptors that the interleukin-3 uses is the IL-3 Receptor Alpha (IL-3Rα). The Interleukin-3 Receptor Alpha is not an individual cytokine receptor; instead, it is one of a number of receptors that work through the same process as JAK-STAT pathway (Renner et al., 2016). Besides T cells, which are the main source of interleukin-3, some other sources of IL-3 are B cells, basophils, neurons, and microglia. Among these target cell types are mast cells, basophils, monocytes, dendritic cells, B cells, T cells and endothelial cells (Renner et al., 2016).

IL-3, a pro-inflammatory cytokine which is basically inform neighboring cells about the infection or damaged tissues. Moreover, pro-inflammatory cytokines can be circulated within the body system to cause activation of immune cells and physiological changes such as fever and acute phase response (Liu et al., 2021). The functions of pro-inflammatory cytokines also includes immune functions that protect the host against bacterial invasion or any other microorganisms present in the environment and can also protect the host against invasion by their own microorganisms (Liu et al., 2021).

1.13.2 Structure of IL-3

The helices are stiff with the loops (especially the AB loops and CD loops) within that structure being subject to substantial motion. These motions contribute to the protein's functional activity (such as communication with and/or interaction with a receptor). The closeness of Helix A' to Helical Structure D and Loop Structure CD makes it clear just how stable each helical bundle is, considering the proximity it shares with another set of helical bundles. The presence of the specific α-chain is necessary for IL-3 recognition and interaction, whereas the β-chain serves the purpose of IL-3 signal transduction and helps in assembling the high-affinity heterodimer receptor (Podolska et al., 2024).

Helix A' contributes to this configuration and is important to the overall helical bundle structure (e.g., stability). The structural components include two pairs of long overhanging loops (AB &

CD) and a four-helix bundle. The CD loop is wrapped around both A' and D helices and essentially contributes to the structural integrity of the entire assembly (Feng, Klein, & McWherter, 1996).

The helices are relatively rigid, but the loops, particularly AB and CD, are very flexible relative to the overall assembly (Feng, Klein, & McWherter, 1996). These motions may facilitate the functional capabilities of IL-3, especially in the processes of transduction, as well as binary chemical interactions with IL-3 receptors.

1.13.3 Biological Functions of IL-3

IL-3 is a well-established factor used to support hematopoiesis for many years. Therefore, IL-3 is well known as a good stimulus for the growth and development of hematopoietic stem and progenitor cells (HSPCs) via keys to cellular differentiation in several pathways of blood cells including basophils, neutrophils, and other cells of the myeloid lineage (McAlpine et al., 2021). IL-3 will play an important role in emergency myelopoiesis when there is an urgent need for a large production of cells and with extramedullary myelopoiesis of the spleen for an urgent need for a large production of cells due to inflammatory states (McAlpine et al., 2021).

- Activation of Myeloid Cells:

IL-3 enhances the ability of immune cells to survive, grow, differentiate, polarize, and recruit to sites of inflammation in the process of the inflammation response; therefore, it will induce the production of IL-1 and chemokines (CCL2, CCL3, CCL7, and CCL12) that are typified by the macrophages' cytokine profiles by promoting the differentiation of monocytes to DCs. IL-3 enhances several functions within the macrophages, for example, phagocytosis, with nutrient acquisition during periods when IL-3 may help to modulate the activity of myeloid cells found within the CNS (central nervous system) (Lim et al., 2016). Finally, IL-3 promotes the survival, proliferation, differentiation, polarization, and immune cell recruitment to inflammatory areas (Lim et al., 2016). LPS-induced activation of TNF-α production in $CD14^+$ monocytes by IL-3 is enhanced by the addition of either IFNb or IL-4 to the activation of $CD14^+$ monocytes, which may result in the conversion of these cells to anti-inflammatory macrophages or dendritic cells (DCs) (Lim et al., 2016).

- Immune system regulation:

An important modulator for controlling the immune response is IL-3 and is involved with regulating the activity of both immune and non-immune cells. IL-3 signaling is a neuroprotective mechanism that protects neurons from degeneration (Lim et al., 2016).

1.13.4 IL-3 Receptor Biology and Signaling Pathways

Both the α chain (solely for cytokines) and β chain (functions for all receptors) comprise the IL-3 receptor, also known as the IL-3 receptor α chain (IL-3Rα / CD123) and βc (Liu et al. 2015). When CD123 heterodimerizes with βc, the IL-3 receptor becomes functional and has a high affinity for IL-3. While βc is essential for IL-3 receptor signaling, it is incapable of binding to cytokines alone. Also, because receptors for IL-3, IL-5, and GM-CSF require equipment such as βc, the above cytokines likely produce similar effects on the body (Liu et al. 2015). When the CD123 + βc receptor combination is bound by IL-3, signaling within the cell occurs primarily through the JAK/STAT, MAPK, and PI3K-AKT pathways (Liu et al., 2015). These pathways are also directly related to IL-3 in terms of how IL-3 assists in the production of hematopoietic cells and regulation of immunological responses (e.g., by stimulating and directing macrophages' response to infected sites, which may lead to decreased inflammation) (Acosta-Martinez & Cabail 2022).

1.13.5 Targets of IL-3 on the cellular level

Hematopoietic stem and progenitor cells (HSPCs):

IL-3 is of utmost importance when there is an inflammatory environment in which extramedullary hematopoiesis is generated in the spleen, which triggers hematopoiesis in the spleen and liver of mice (Podolska et al., 2024).

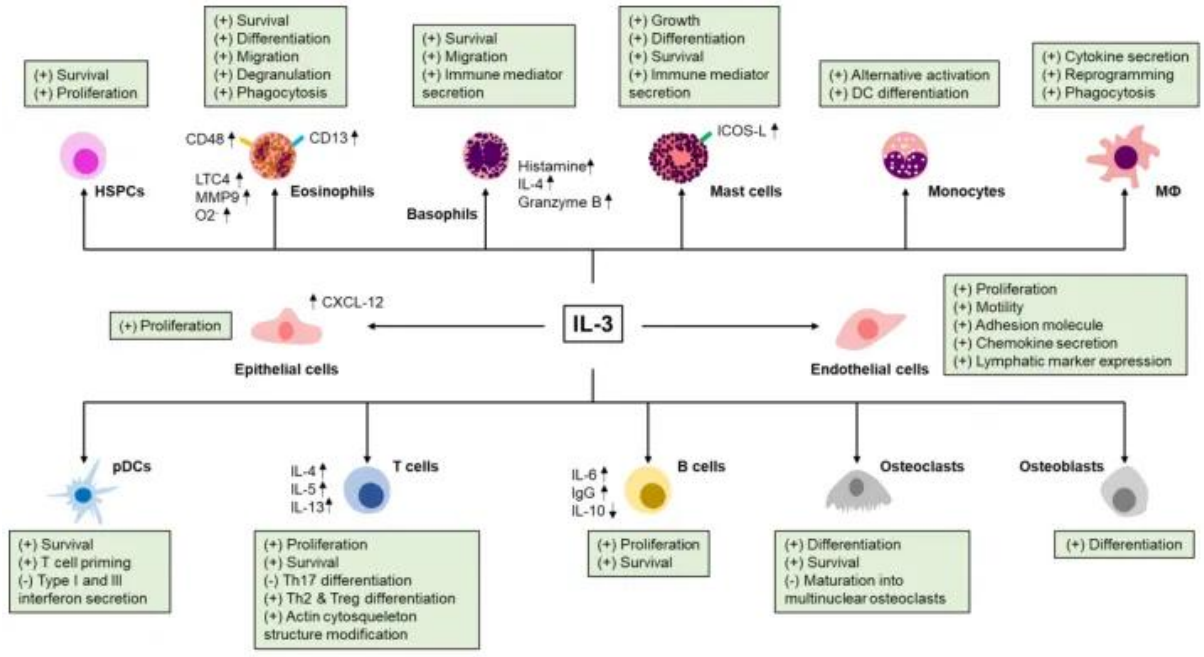

Figure 8: Effect of IL-3 on cells (Podolska et al., 2024)

Figure 8, the effects of IL-3 can be seen and it is extrapolated from the study by Podolska et al. (2024).

- Eosinophils:

Eosinophils are supported by IL-3 with respect to their differentiation, migration, chemotaxis, adhesion, and cytotoxicity versus helminths (worms), as well as their survival, basophils & Effector cells that contribute to allergic reactions also have their survival and activation regulated via IL-3 (Podolska et al., 2024).

- T and B cell:

T cell activation increases expression of the IL-3 receptor (CD123) on CD4+ and CD8+ T cells allowing production IL-3 to increase T cell survival and proliferation, allow growth of Th2 cells, and inhibit growth of Th17 cells by activating osteoblasts & osteoclasts contributing to bone homeostasis (Podolska et al., 2024).

1.14 Rationale and Objectives of the Present Study

IL-3 is present in the neurons and microglia and possesses neurotoxic as well as neuroprotective properties, regulating brain inflammation through microglia and astrocyte activation (Xiu et al., 2018). Peripheral IL-3 serves as a handy marker in immunology that is easy to evaluate in the blood or plasma. It enables research institutes to connect to the clinical features of mental disorders.

Rationale for studying IL-3 is due to the possibility of immune system alterations and autoimmune reactions in connection with OCD. IL-3 activity, can help understand the effect of OCD on immune system signaling. In case drug therapy influences immunity adversely and despite that it aggravates clinical signs of OCD, it can be seen.

To study the serum concentration of IL-3 in Bangladeshi patients diagnosed with OCD by ELISA method and determine the possible correlation between the serum level of IL-3 and manifestations of OCD. Purpose of research is to investigate IL-3's potential as a biomarker for inflammation in OCD and evaluate its ability to facilitate knowledge about OCD pathophysiology.

Chapter 2

Materials and Methods

2.1 Study Populations

A total of 420 people were involved in this case-control study. Participants in the case group were people with current symptoms of obsessional-compulsive disorder (OCD). A (N=209) patients, they were paired with control participants from the general population (N=201). Individuals constituted the sample for outpatients from the National Institute of Mental Health & Hospital. All patients were seen at ages 18 through to age 60 at the time of recruitment. A psychiatrist evaluated every individual participant. The psychiatrists made sure that a full psychiatric evaluation was carried out on each subject using the DSM-5 to establish if each patient had obsessive-compulsive disorder (OCD). Furthermore, the severity of OCD symptoms in all subjects was established using the UCLA-Brown Obsessive Compulsive Scale (Y-BOCS). All individuals with known psychiatric diagnoses or medical co-morbidity were excluded to limit the impact of confounding factors whenever possible.

2.1.1 Inclusion Criteria

1. The selected age range was 18 to 60 years
2. Both genders were applicable for enrolling in this research study.
3. Married and unmarried individuals were considered.
4. OCD patients were selected only if they had been evaluated by a certified psychiatrist.
5. Blood specimens and information were collected from volunteers who consented to this research.

2.1.2 Exclusion Criteria

1. Patients who were suffering from cognitive impairment or those who were unwilling to take part in the research.
2. Acute and severe medical conditions affecting the patient.
3. People suffering from liver or kidney failure even from the past and who have not taken any kind of medication, which may affect the level of IL-3.

4. Patients who suffer from intellectual disability and mental disorders will not be included in this study.
5. Individuals who have a history of severe physical conditions, infections, excessive weight, tardive dyskinesia brought on by neuroleptics, or alcohol and drug abuse.

2.1.3 Procedure of Data Collection

Three phases have been taken into consideration for OCD patient assessment. At first, a thorough assessment of the OCD patients was completed within the first phase of the study by the psychiatric specialist. Then, each of the patients were matched based on both the inclusion and exclusion criteria and selected the ideal patient; then socio-demographic data was collected. Finally, in the third phase, 5 ml of blood were taken from each participant's cephalic vein. The whole process of collecting blood samples from OCD patients is mentioned below:

1. Welcome.
2. After the verification of the diagnosis, the patient was enlightened with OCD regarding the objective of the study along with the issues relating to ethics.
3. A mandatory consent form was filled before the collection of data.
4. Data was obtained via in-person interviews at the psychiatry department.
5. It was verified whether each inclusion and exclusion criterion has been met or not.
6. Then data related to socio-demographic characteristics obtained via the use of a structured questionnaire which is attached in Appendix A.
7. A 5 ml blood specimen was drawn by an expert from each participant's cephalic vein.

For each patient, the procedure took about 30 minutes (approximately).

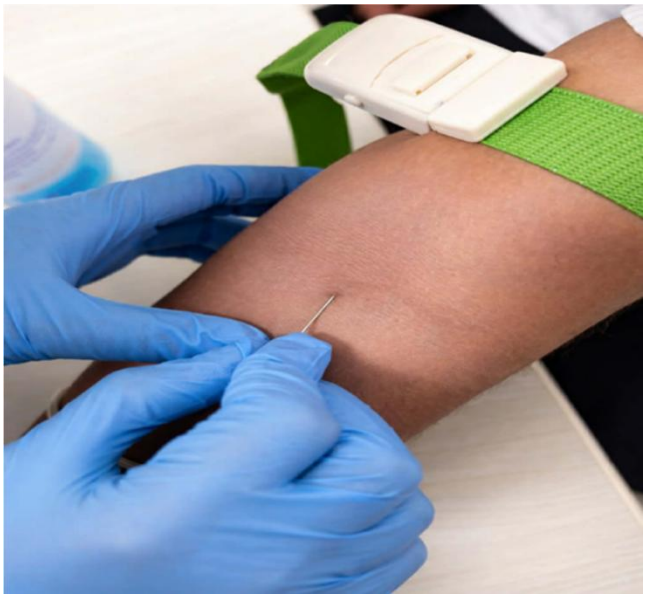

Figure 9: Blood sample collection from a participant

2.2 Kit Components

2.2.1 Materials Required for Blood Sample Collection

Materials used in blood sample collection from the participants are listed in the following table-

Table 1: Materials used in Blood Sample Collection

Materials	**Specifications**
Disposable syringe	6 mL
Band-Aid	
Tourniquet	
Butterfly needle	20G
Hexisol	250 mL
Sterile cotton	
Falcon Tube	15 mL
Eppendorf Tube	1.5 mL
Ice-Box	

Figure 10: Ice Box

Figure 11: Disposable Syringe

Figure 12: Butterfly needle

Figure 13: Band aid and Tourniquet

Figure 14: Hexisol and Cotton

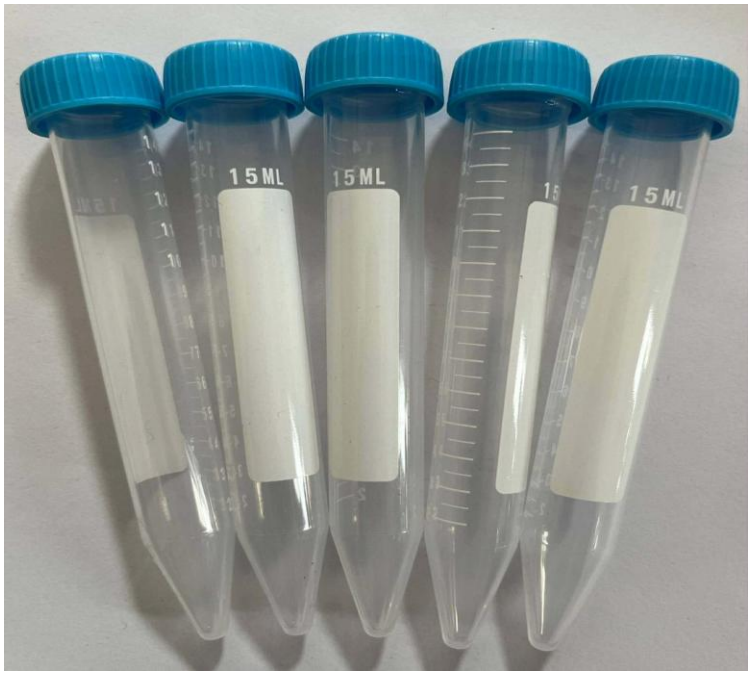

Figure 15: Falcon Tube

2.2.2 Separation of Serum and Storage

From the vein 5mL of blood was taken, from each OCD patient and healthy control. A tube with a stainless-steel needle to collect blood samples in a very clean room was used. The blood samples were then put into falcon tubes.

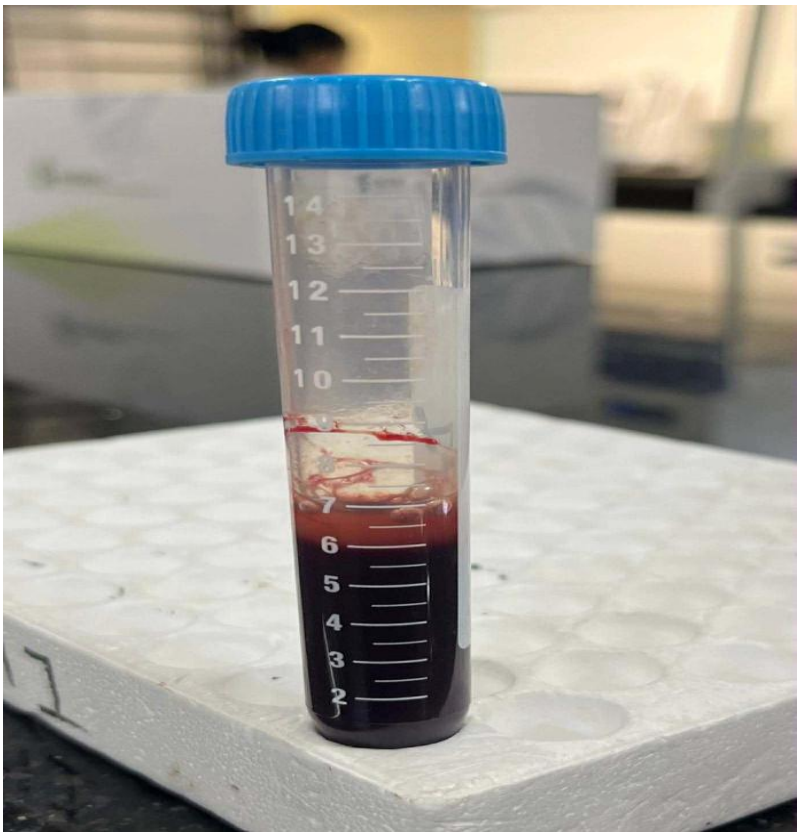

Figure 16: Before Serum Separation

The blood samples were allowed at room temperature to clot for thirty to sixty minutes. After that, placed them at room temperature for 15 minutes in the centrifuge at 3000 rpm for the separation of the liquid from the cellular component of the blood. The clotted sample was then spun down in the centrifuge to allow us to collect the liquid serum from the blood. Once we collected the serum, we stored it in microcentrifuge tubes at -80 °C in the dark until we need to use it for biological analysis of interleukin-3 (IL-3) and the levels of IL-3 in the blood. We performed the analysis of IL-3 using the Human IL-3 ELISA Kit. The manufacturer's protocol on how to perform the assay and how to make the reagents and standards for testing IL-3 in sample were followed.

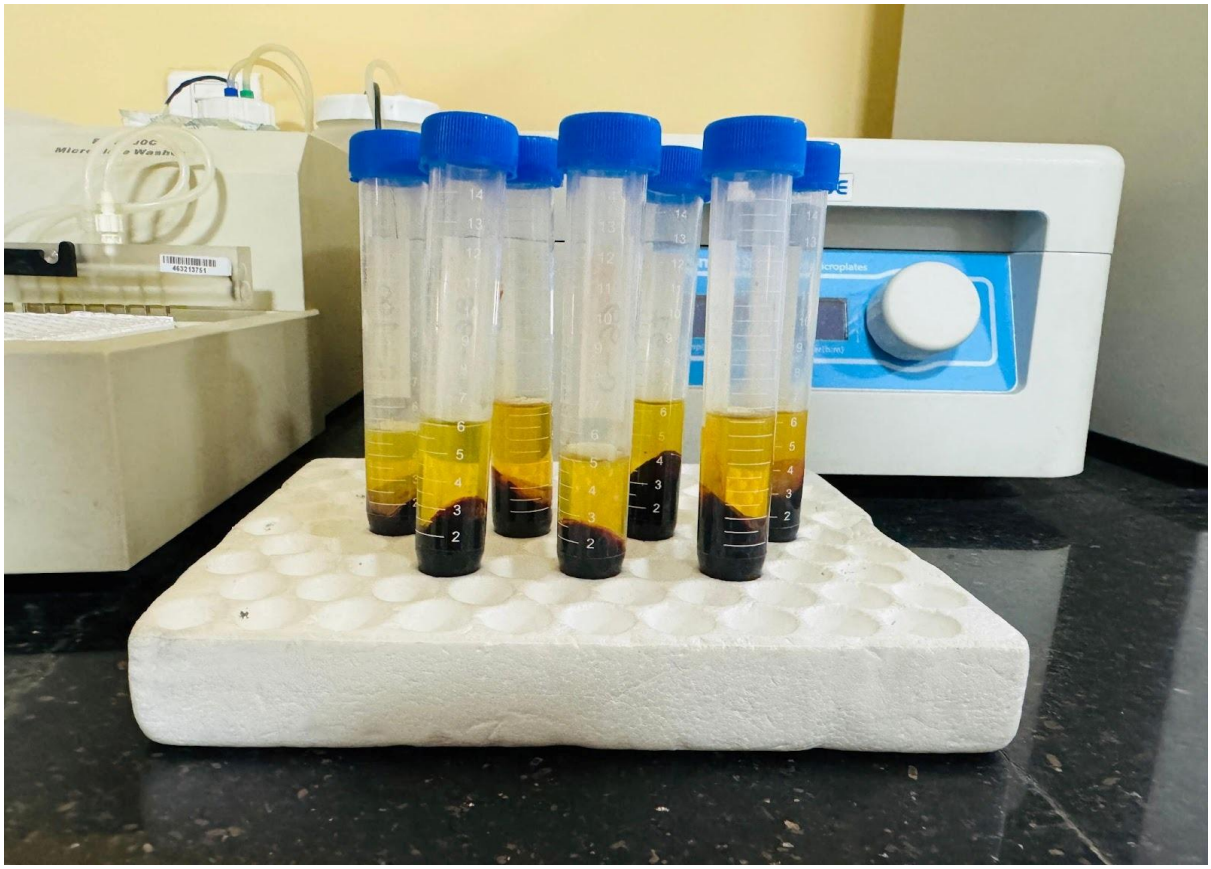

Figure 17: After Serum Separation

Figure 18: Refrigerator for sample storage

Figure 19: Centrifuge machine for serum separation

2.3 Materials and Reagents Used for Analysis of Serum IL-3

2.3.1 Reagents required for IL-3 Assay

For determination of serum concentration of IL-3 EZ-Set™ ELISA Kit (DIY Antibody Pairs) (Catalog number: EZ0402) was used.

Table 2: Materials used in analysis of serum IL-3

Apparatus/ Materials	**Specifications**
Micropipette tips	10µL-100µL
Micropipette tips	100 µL-1000 µL
Micropipette	10 µL-100 µL
Micropipette	100 µL-1000 µL
Volumetric flask	500 mL
Eppendorf tube	1500 µL
Multichannel micropipette	50 µL-300 µL
Microplate Reader	

Figure 20: Eppendorf tube

Figure 21: Multichannel micropipette (50 µL-300 µL)

Figure 22: Microplate Reader

2.3.2 Reagents used for Analysis of Serum IL-3

For determination of serum concentration of IL-3 Human IL-3 ELISA Kit EZ-Set™ (DIY Antibody Pairs) Catalog number: EZ0402 was used.

Table 3: Reagents used for analysis of serum IL-3

Description	Quantity/ Volume
Microplates	5
Plate Sealers	20
Lyophilized recombinant human IL-3 standard	10 ng/vial
Biotinylated Goat anti-human polyclonal antibody	500 µL/vial
Goat anti-human IL3 polyclonal antibody	500 µl/vial
Avidin-Biotin-Peroxidase Complex (ABC)	500 µL/vial
Reagent Diluent (10)	20 ml/vial
Stop Solution	10 ml/vial
Color Developing Reagent	10 ml/vial
PBS (20)	25 ml/vial
PBS-T (20)	25 ml/vial

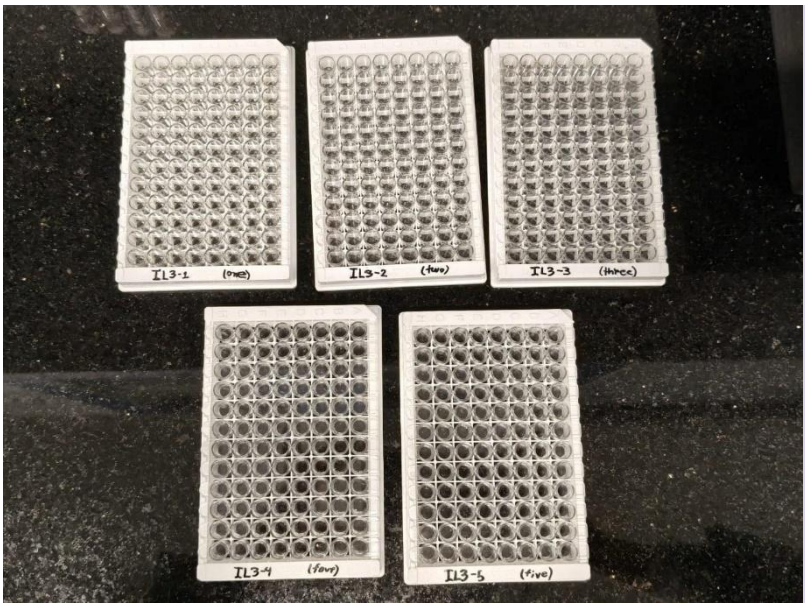

Figure 23: 96 Well Microplates

Figure 24: Reagent Diluent (10)

Figure 25: Stop Solution

Figure 26: PBS (20)

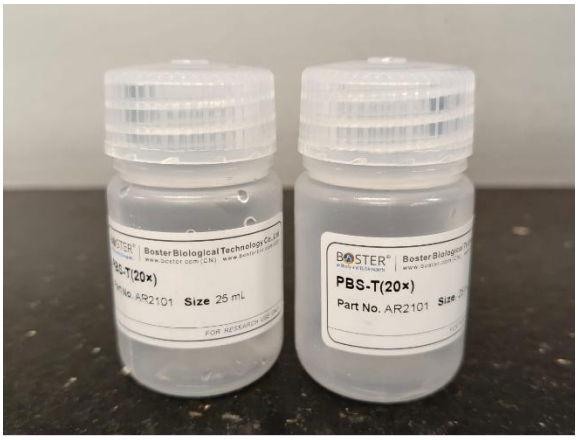

Figure 27: PBS-T (20)

Figure 28: Colour Developing Reagent (Tetramethylbenzidine)

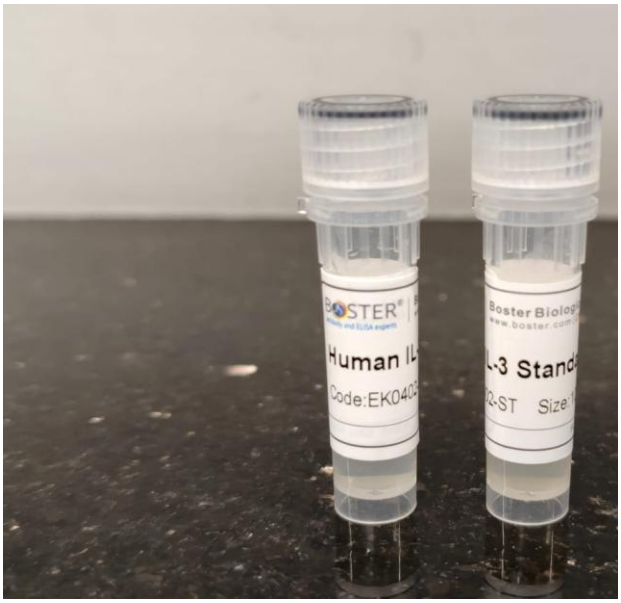

Figure 29: Lyophilized recombinant human IL-3 standard

Figure 30: Goat anti-human IL3 polyclonal antibody (Capture Antibody)

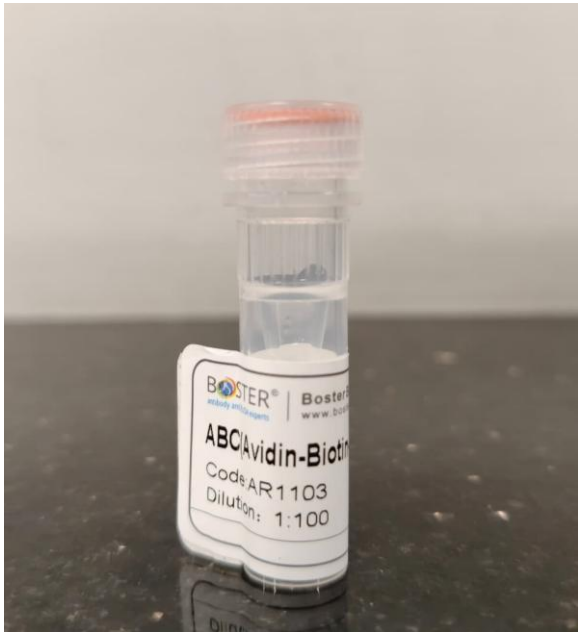

Figure 31: Avidin-Biotin-Peroxidase Complex (ABC)

2.4 Preparations Required for IL-3 Assay

2.4.1. Plate Preparation

1) Using Capture Antibody Diluent to dilute the control capture antibody to a 1:100 working concentration (e.g., for instance, if you were to use 1 µL of anti-Human IL3 Control capture antibody in 99 uL of Capture Antibody Diluent) then coat each well of a 96-well microtiter plate immediately with a 100 uL aliquot of the diluted Capture Antibody. Cover the plate and store it at 4 °C overnight.

2) After taking off the lid, any extra liquid from the wells into the proper waste container was transferred. Then flip the plate over on the bench, place it on top of a paper towel, and gently tap it, remove excess liquid from each well. Wells are to be kept damp (not completely dry) throughout the entire process.

3) To block the wells, add 200 µL Reagent Diluent to each well and store at 0–35 °C for 2 hours.

4) To wash the wells, removed the reagent diluent from each well by aspirating or by first pouring into an appropriate waste receptacle and then by washing with PBS. Each well needs to be filled with 300-350 µL of PBS using a squirt bottle, or a manifold dispenser, or by auto washing, and the liquid must be fully removed from each well. All liquid must be removed prior to proceeding to the next step. After the last wash, to remove residual PBS, aspirate or invert and gently blot the plate with clean paper towels.

2.4.2 Reconstitution of Human IL-3 Standard

For each experiment, one vial of IL-3 standard has 10 ng/mL in it. The vial was gently spun before being used. To obtain a stock concentration of 10 ng/ml, the standard was combined with 1 milliliter of reagent diluent. After 10 minutes, it is shaken gently before making the dilutions.

Serial dilution was performed to obtain the following Human IL-3 Standard: 1 to 8 tubes

1) Tube number 1: 1,000 pg/ml of IL-3 standard
2) Tube number 2: 500 pg/ml of IL3 standard
3) Tube number 3: 250 pg/ml of IL3 standard
4) number 4: 125 pg/ml of IL3 standard

5) Tube number 5: 62.5 pg/ml of IL3 standard
6) Tube number 6: 31.25 pg/ml of IL3 standard
7) Tube number 7: 15.625 pg/ml of IL3 standard

2.4.3 Preparation of Goat anti-human IL-3 polyclonal antibody working Solution (Capture Antibody)

1. Each vial contained 500 µl of goat-human IL-3 polyclonal antibody.
2. Mixed the goat-human IL-3 polyclonal antibody with Capture Antibody Diluent, 1 part to 100 parts.

2.4.4 Preparation of Biotinylated goat anti-human polyclonal antibody working solution (Detection Antibody)

The biotinylated goat anti-human IL-3 polyclonal antibody was diluted 1:100 with reagent diluent and mixed thoroughly. (i.e., Add 1 µl of Biotinylated goat anti-human IL3 polyclonal antibody to 99 µl of Reagent Diluent.)

2.4.5 Preparation of Avidin-Biotin-Peroxidase Complex (ABC) working solution

1. Each vial contained 500 µl of Avidin-Biotin-Peroxidase Complex (ABC).
2. The Avidin-Biotin-Peroxidase Complex (ABC) was diluted in a 1:100 ratio with the reagent diluent and mixed thoroughly.

2.4.6 Microplate Design for Assay Procedure of IL-3

Five 96 well microplates were used for analysis of serum IL-3. All the microplates had the same plate designs. The 5 plates were designed according to the following pattern.

	1	2	3	4	5	6	7	8	9	10	11	12
A	Std-1	Std-2	Std-3	Std-4	Std-5	Std-6	Std-7	Blank	P-01	P-02	P-03	P-04
B	P-05	P-06	P -07	P-08	P-09	P-10	P-11	P- 12	P-13	P-14	P-15	P-16
C	P-17	P-18	P-19	P-20	P-21	P-22	P-23	P- 24	P-25	P-26	P-27	P-28
D	P-29	P-30	P-31	P-32	P-33	P-34	P-35	P- 36	P-37	P-38	P-39	P-40
E	P-41	P-42	P-43	P-44	C-01	C-02	C-03	C- 04	C-05	C-06	C-07	C-08
F	C-09	C-10	C-11	C-12	C-13	C-14	C-15	C- 16	C-17	C-18	C-19	C-20
G	C-21	C-22	C-23	C-24	C-25	C-26	C-27	C- 28	C-29	C-30	C-31	C-32
H	C-33	C-34	C-35	C-36	C-37	C-38	C-39	C- 40	C-41	C-42	C-43	C-44

Figure 32: Microplate design for Plate-1

	1	2	3	4	5	6	7	8	9	10	11	12
A	Std-1	Std-2	Std-3	Std-4	Std-5	Std-6	Std-7	Blank	P-45	P-46	P-47	P-48
B	P-49	P-50	P-51	P-52	P-53	P-54	P-55	P-56	P-57	P-58	P-59	P-60
C	P-61	P-62	P-63	P-64	P-65	P-66	P-67	P-68	P-69	P-70	P-71	P-72
D	P-73	P-74	P-75	P-76	P-77	P-78	P-79	P-80	P-81	P-82	P-83	P-84
E	P-85	P-86	P-87	P-88	C-45	C-46	C-47	C-48	C-49	C-50	C-51	C-52
F	C-53	C-54	C-55	C-56	C-57	C-58	C-59	C-60	C-61	C-62	C-63	C-64
G	C-65	C-66	C-67	C-68	C-69	C-70	C-71	C-72	C-73	C-74	C-75	C-76
H	C-77	C-78	C-79	C-80	C-81	C-82	C-83	C-84	C-85	C-86	C-87	C-88

Figure 33: Microplate design for Plate-2

	1	2	3	4	5	6	7	8	9	10	11	12
A	Std-1	Std-2	Std-3	Std-4	Std-5	Std-6	Std-7	Blank	P-89	P-90	P-91	P-92
B	P-93	P-94	P-95	P-96	P-97	P-98	P-99	P-100	P-101	P-101	P-102	P-103
C	P-104	P-105	P-106	P-107	P-108	P-109	P-110	P-111	P-112	P-113	P-114	P-115
D	P-116	P-117	P-118	P-119	P-120	P-121	P-122	P-123	P-124	P-125	P-126	P-127
E	P-128	P-129	P-130	P-131	C-89	C-90	C-91	C-92	C-93	C-94	C-95	C-96
F	C-97	C-98	C-99	C-100	C-101	C-102	C-103	C-104	C-105	C-106	C-107	C-108
G	C-109	C-110	C-111	C-112	C-113	C-114	C-115	C-116	C-117	C-118	C-119	C-120
H	C-121	C-122	C-123	C-124	C-125	C-126	C-127	C-128	C-129	C-130	C-131	C-132

Figure 34: Microplate design for Plate-3

	1	2	3	4	5	6	7	8	9	10	11	12
A	Std-1	Std-2	Std-3	Std-4	Std-5	Std-6	Std-7	Blank	P-132	P-133	P-134	P-135
B	P-136	P-137	P-138	P-139	P-140	P-141	P-142	P-143	P-144	P-145	P-146	P-147
C	P-148	P-149	P-150	P-151	P-152	P-153	P-154	P-155	P-156	P-157	P-158	P-159
D	P-160	P-161	P-162	P-163	P-164	P-165	P-166	P-167	P-168	P-169	P-170	P-171
E	P-172	P-173	P-174	P-175	C-133	C-134	C-135	C-136	C-137	C-138	C-139	C-140
F	C-141	C-142	C-143	C-144	C-145	C-146	C-147	C-148	C-149	C-150	C-151	C-152
G	C-153	C-154	C-155	C-156	C-157	C-158	C-159	C-160	C-161	C-162	C-163	C-164
H	C-165	C-166	C-167	C-168	C-169	C-170	C-171	C-172	C-173	C-174	C-175	C-176

Figure 35: Microplate design for Plate-4

	1	2	3	4	5	6	7	8	9	10	11	12
A	Std-1	Std-2	Std-3	Std-4	Std-5	Std-6	Std-7	Blank	P-176	P-177	P-178	P-179
B	P-180	P-181	P-182	P-183	P-184	P-185	P-186	P-187	P-188	P-189	P-190	P-191
C	P-192	P-193	P-194	P-195	P-196	P-197	P-198	P-199	P-200	P-201	P-202	P-203
D	P-204	P-205	P-206	P-207	P-208	P-209	P	P	P	P	P	P
E	P	P	P	P	C-177	C-178	C-179	C-180	C-181	C-182	C-183	C-184
F	C-185	C-186	C-187	C-188	C-189	C-190	C-191	C-192	C-193	C-194	C-195	C-196
G	C-197	C-198	C-199	C-200	C-201	C	C	C	C	C	C	C
H	C	C	C	C	C	C	C	C	C	C	C	C

Figure 36: Microplate design for Plate-5

1. **2.4.7** After adding 100 µl of the diluted capture antibody to each well, the plate was covered with foil. The dish was covered and left to incubate for the entire night.
2. The liquid was disposed of by flipping the microplate onto a worktop, placing a paper towel beneath it, and gently tapping off any extra liquid. The wells were not completely dried out.
3. To block the plates, 200 µl of Reagent Diluent was poured to each well. The plates were then left at room temperature for two hours.
4. Each well's contents were disposed of and cleaned with PBS following the incubation. The wells must be cleaned three times with 300 µl PBS. For accurate test results, the liquid from the well was effectively evacuated.
5. Following the final wash, PBS was extracted from each well by either inverting the plate and blotting against a fresh paper towel or aspirating the liquid out.

Assay procedure of IL-3

I. The materials and reagents were synthesized in accordance with the earlier data.

II. The excess microplate strips were taken out of the plate frame. Each well received 100 µl of the standard, sample, or control. The ingredients were incubated at room temperature for 120 minutes using the supplied plate sealer.

III. The top was taken off and the liquid in the wells was disposed of. After that, the dish was placed upside down on a paper towel on the work surface, and the liquid was gently blotted with a tap.

IV. Each well received 100 µl of the 1x biotinylated goat anti-human IL-3 polyclonal antibody solution. After applying a sealant, the plate was left to sit at room temperature for ninety minutes.

V. Three PBS washes were performed on the plate. The liquid was dumped in the proper garbage container within the wells. To get rid of any extra liquid, the plate was placed upside down on a paper towel on the tabletop and gently tapped. At never time were the wells allowed to dry completely.

VI. After adding 300 µl of PBS to each test well, wash them once more. They need to be left to sit for 60 seconds in between washes for a crisper backdrop. Two additional times, the procedures were carried out.

VII. After discarding the wash buffers, the plate was placed upside down on a paper towel on the work table and gently tapped to blot the liquid.

VIII. Each well received 100 µl of the 1x Avidin-Biotin-Peroxidase complex, which was then incubated for 40 minutes at room temperature.

IX. Five PBS-T washes were performed on the plate, with 300 µl of PBS-T per well and a 60-second interval between washes. The plates were blotted and the liquid was dumped after five washes.

XI. After adding 100µl of stop solution to each well, several of the wells' colors changed to yellow.

XII. Using a microplate reader, the reaction's absorbance at 450 nm was measured 30 minutes after the stop solution was added.

Figure 37: Plates before addition of color developing reagent

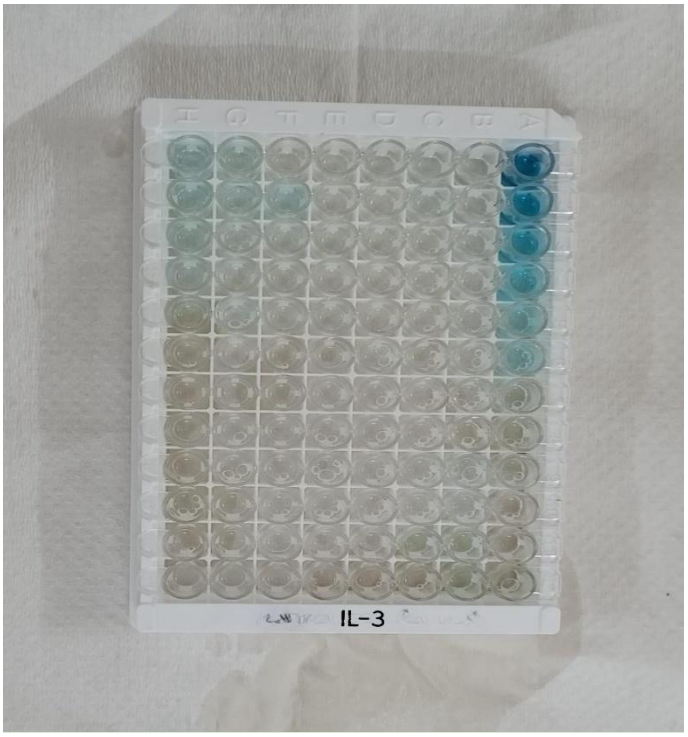

Figure 38: After addition of color developing reagents and incubation

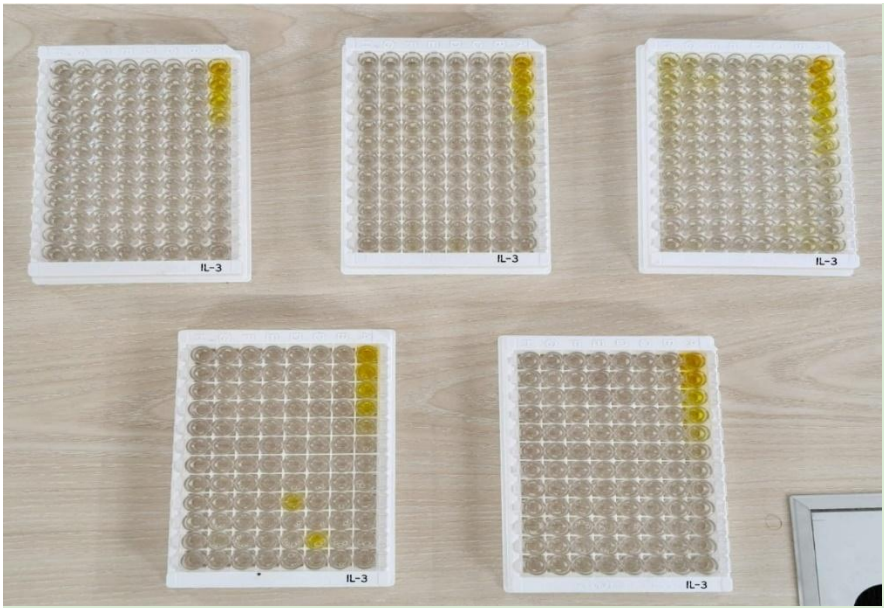

Figure 39: After addition of Stop Solution

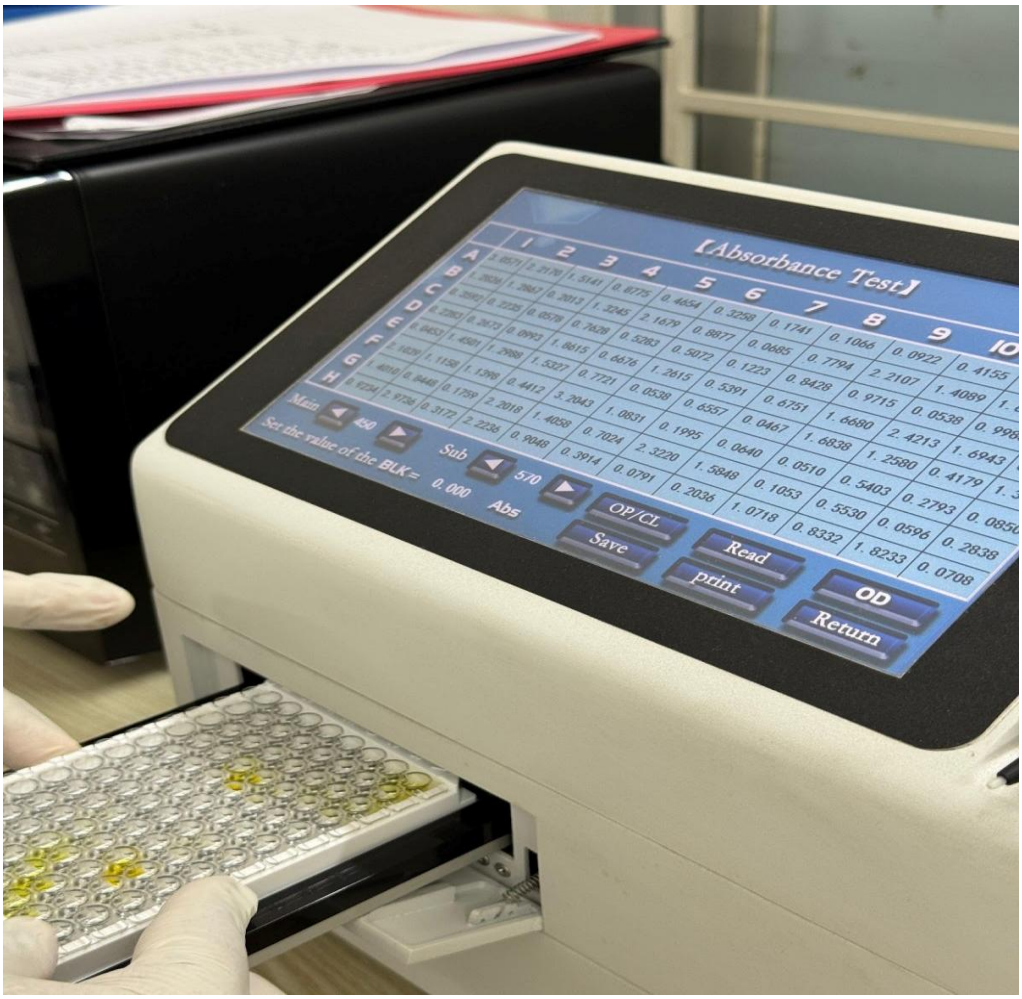

Figure 40: Measurement of Absorbance using Microplate Reader

2.5 Statistical Analysis

We analyzed data from our study using SPSS as well as MS Excel and conducted both a Pearson Chi-Square Test and an Independent T-Test in order to ascertain the amount of IL-3 present in each person's blood who suffer from OCD. The presentation of results was done using box plot charts. Standard errors of the means were used in the presentation of results. P-values of ≤ 0.05 were used in establishing statistical significance. Any value that was below 0.05 was significant statistically for the analysis.

3. Result

3.1 Socio-demographic Details of the Study Population

209 patients and 201 healthy volunteers participated in this study. Marital status, education, occupation, economic impression, residence, smoking history, BMI, age range, gender, family history; factors were assessed.

Table 4: Socio-demographic profile of the study population

Characteristics	Patient (Mean ± SEM or n (%))	Control (Mean ± SEM or n (%))	p value
Age in years	28.12 ± .632	29.11 ± .613	0.399
18 − 24	93 (44.50%)	81 (40.30%)	
25 − 39	90 (43.06%)	94 (46.77%)	
40 − 45	14 (6.70%)	14 (6.97%)	
46 − 60	12 (5.74%)	12 (5.97%)	
Sex			0.465

Male	127 (60.77%)	115 (57.21%)	
Female	82 (39.23%)	86 (42.79%)	
Marital status			0.096
Married	91 (43.54%)	104 (51.74%)	
Unmarried	118 (56.46%)	97 (48.26%)	
BMI (kg/m^2)	23.45 ± 0.27	22.88 ± .244	0.010
Below 18.5 (CED)	20 (9.57%)	17 (8.46%)	
18.5–25.0 (normal)	119 (56.94%)	142 (70.65%)	
Above 25.0 (obese)	70 (33.49%)	42 (20.90%)	

Education level			< 0.001
Illiterate	9 (4.31%)	3 (1.49%)	
Primary level	29 (13.88%)	4 (1.99%)	
Secondary level	91 (43.54%)	73 (36.32%)	
Graduate and above	80 (38.28%)	121 (60.20%)	
Occupation			< 0.001
Business	3 (1.44%)	6 (2.99%)	
Service	69 (33.01%)	59 (29.35%)	
Unemployed	82 (39.23%)	61 (30.35%)	

Student	3 (1.44%)	58 (28.86%)	
Others	52 (24.88%)	17 (8.46%)	
Economic status			0.279
High	26 (12.44%)	36 (17.91%)	
Medium	117 (55.98%)	102 (50.75%)	
Low	66 (31.58%)	63 (31.34%)	
Smoking history			0..062
Nonsmoker	164 (78.47%)	172 (85.57%)	
Smoker	45 (21.53%)	29 (14.43%)	

Residence area			< 0.001
Rural	80 (38.28%)	39 (19.40%)	
Urban	129 (61.72%)	162 (80.60%)	

In Table 4, sociodemographic data for patient and control shows that both (patients & controls) groups are comparable on numerous variables. Mean ± standard error (SEM) and percentages are used for the values. For the patient group and healthy individual age, the mean was respectively (28.12 ± .632) and (29.11 ± .613), with no statistical significance. Additionally, in term of BMI for patients and healthy individuals the values of mean is (23.45 ± 0.27) and (22.88 ± .244); which has statistically insignificant. The percentage of patients who are married (43.54%) was not statistically different from the percentage of married controls (51.74%) (p=0.118), likewise, (56.46%) of the patients, and (48.26%) of controls were unmarried. A very small proportion of both patients and controls were unemployed; so, there was also a statistically significant difference in both occupations (p< 0.001). There were significant differences in pre-existing smoking history as well as in place of residence (p), with only 38.28% of patients residing in a rural setting compared to (19.40%) of controls; while (61.72%) of patients were in urban areas compared to (80.60%) of controls. Similarly, with respect to individuals with a prior smoking history, the percentage of patients being (21.53%) and that of controls is 14.43%. Participants were divided into three BMI categories based on their BMI values; CED (<18.5); normal (18.5 - 25.0); overweight (>25). The distribution was statistically similar (p=0.118) between patients and controls, as (33.49%) of patients & (20.90%) of controls were classified as overweight. Relatively, (56.94%) of patients & (70.65%) of controls were classified as normal; as being classified as CED the percentage for patients is (9.57%) and that of controls is ((8.46%). The total amount of patients

that were 18-24 years of age was (44.50%), and the percentage for controls was 40.30%. The total number of patients aged 25 to 39 contained (43.06%), and (46.77%) for controls. The overall count of patients and controls that were 40-45 years consist of (6.70%) and (6.97%). In between 46-60 years of age the percentage for patients was (5.74%) and that of controls was (5.97%).

3.2 Clinical Features and Laboratory Findings

Table 5: Clinical Features and Laboratory Findings of the study population

Parameters	Patients (n=209) (mean ± SEM)	Healthy controls (n=201) (mean ± SEM)	p value
Age (years)	28.12 ± 0.63	29.11 ± 0.61	0.264
BMI	23.45 ± 0.28	22.88 ± 0.24	0.122
Y-BOCS score	21.62 ± 0.52	4.33 ± 0.14	< 0.001
Serum IL-3 (pg/ml)	0.48± 0.01	0.663 ± 0.02	< 0.001

We found the patients (n=209) and the controls (n=201) in the variable analysis shows mean ± SEM and p-values for both the patients and the controls, based on the parameters age, BMI, Y-BOCS score, Serum IL-3 (pg/ml). The patients and controls mean ages were (28.12 ± 0.63) and (29.11 ± 0.61), having no statistical difference (p-value = 0.264). For BMI value, the mean for patients stands (23.45 ± 0.28) and for healthy controls it is (22.88 ± 0.2), with the p-value of 0.122.

As for Y-BOCS scores, in the case of patients mean score is 21.62 ± 0.52, in contrast to healthy volunteers, mean score is (4.33 ± 0.14); the difference was statistically significant ($p<0.001$). In addition, the concentration of IL-3 (p-value < 0.001) in the serum samples in patients and healthy controls is (0.49 ± 0.01) pg/ml and (0.66 ± 0.02) pg/ml respectively. Thus, it can be stated that the disease severity among patients was significantly higher compared to that in the control group members.

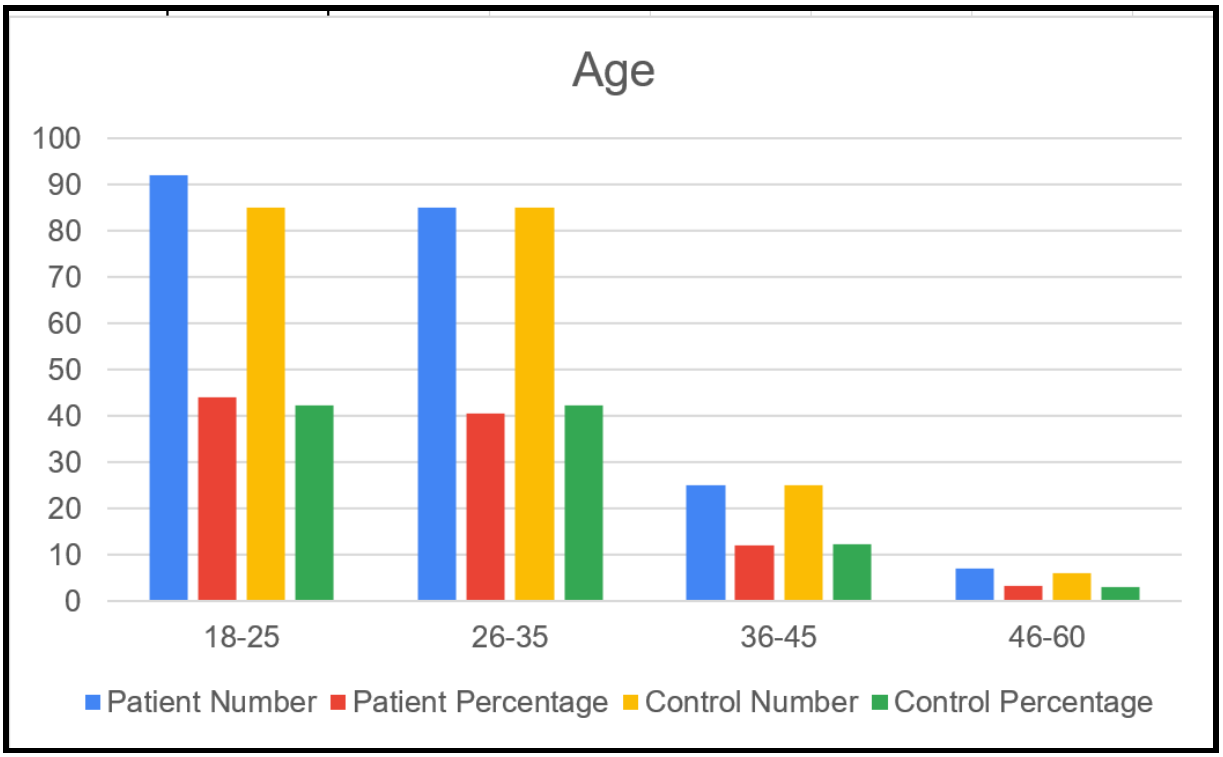

Figure 41: Age Distribution of Healthy Controls and Patients

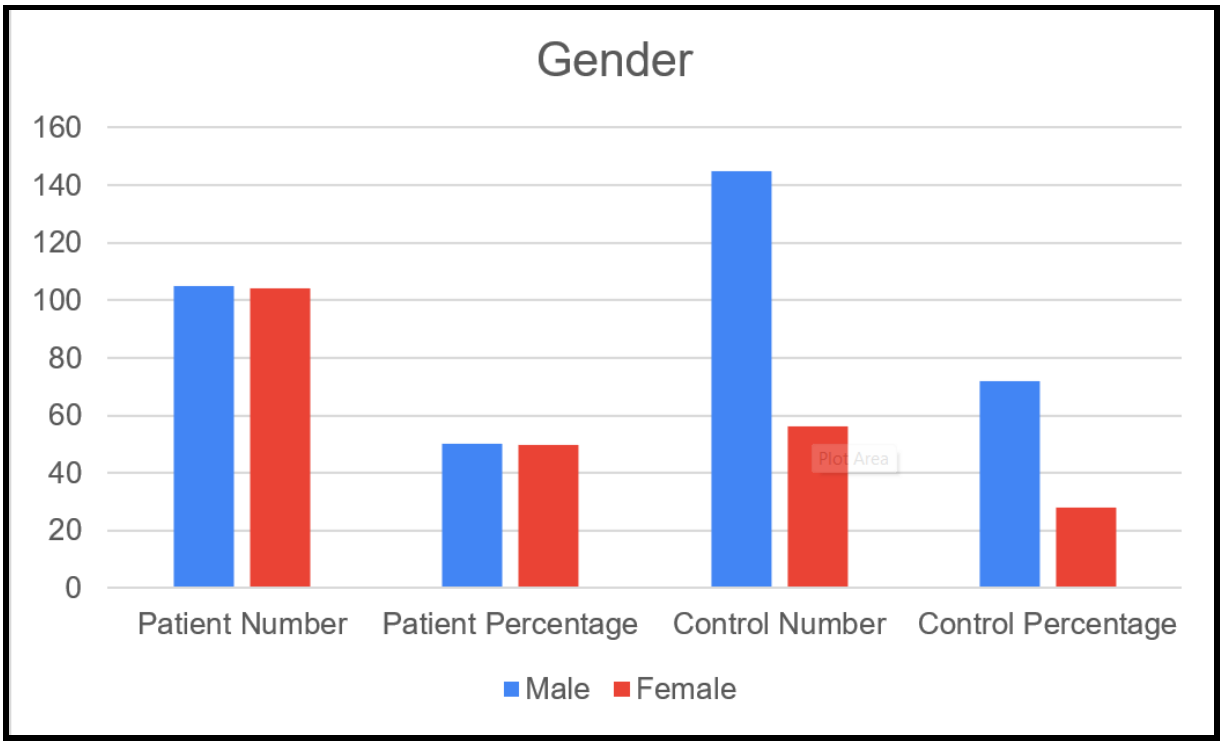

Figure 42: Distribution of Study Population according to Gender

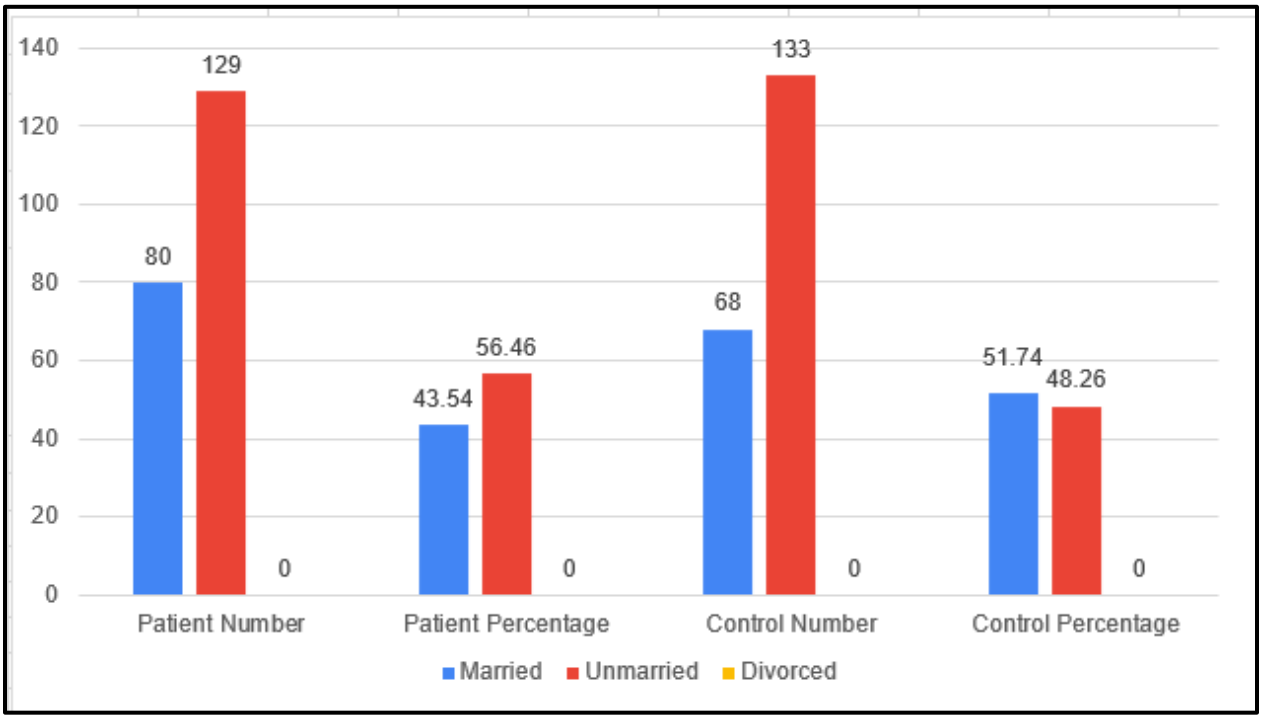

Figure 43: Comparison of Patient's and Healthy Controls of Marital Status

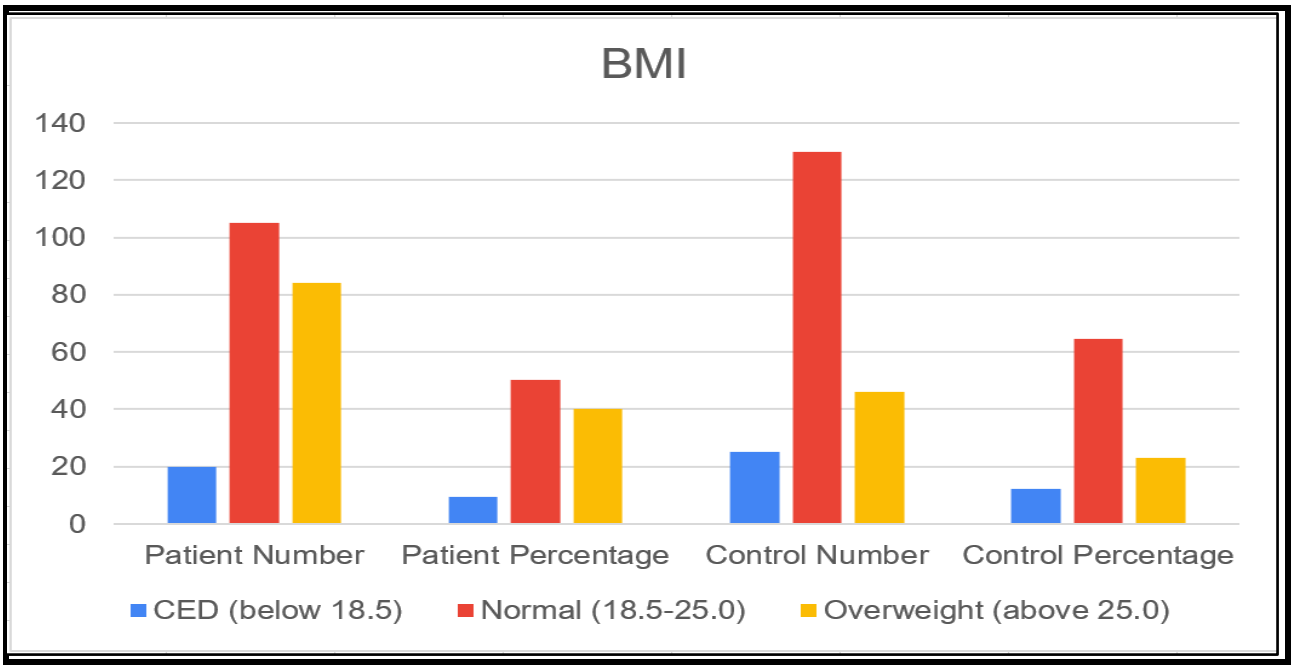

Figure 44: Distribution of BMI between Patients and Healthy Controls

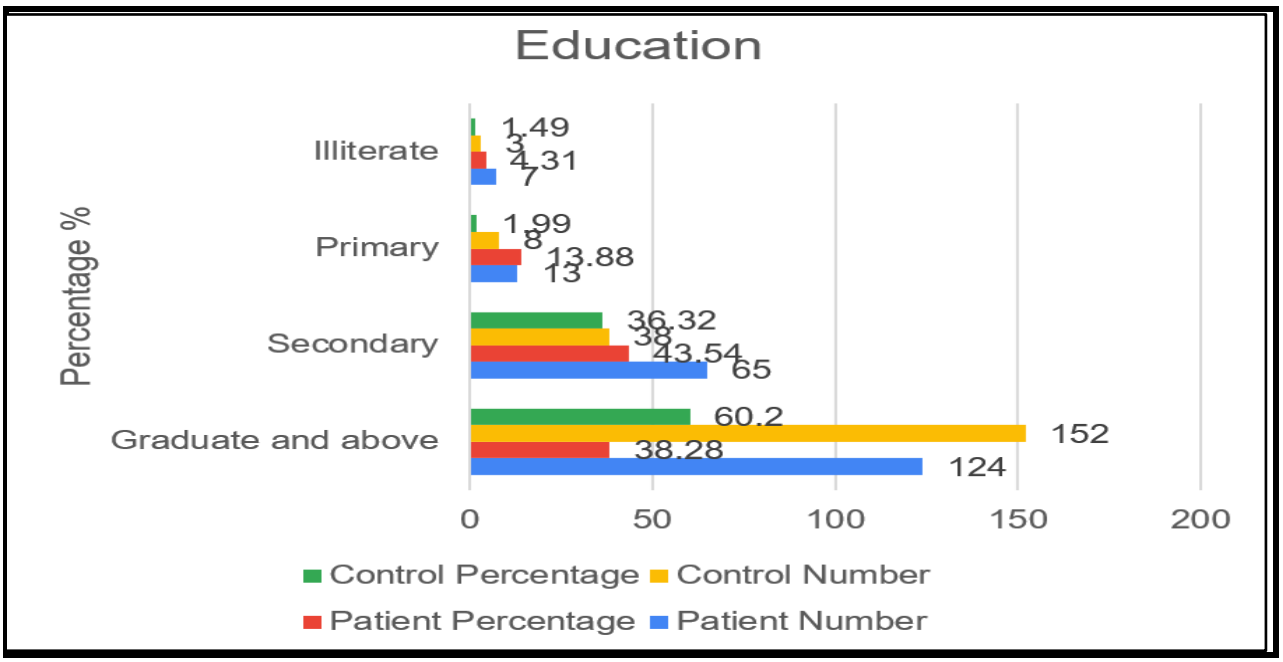

Figure 45: Comparison of education level between Patients and Healthy Controls

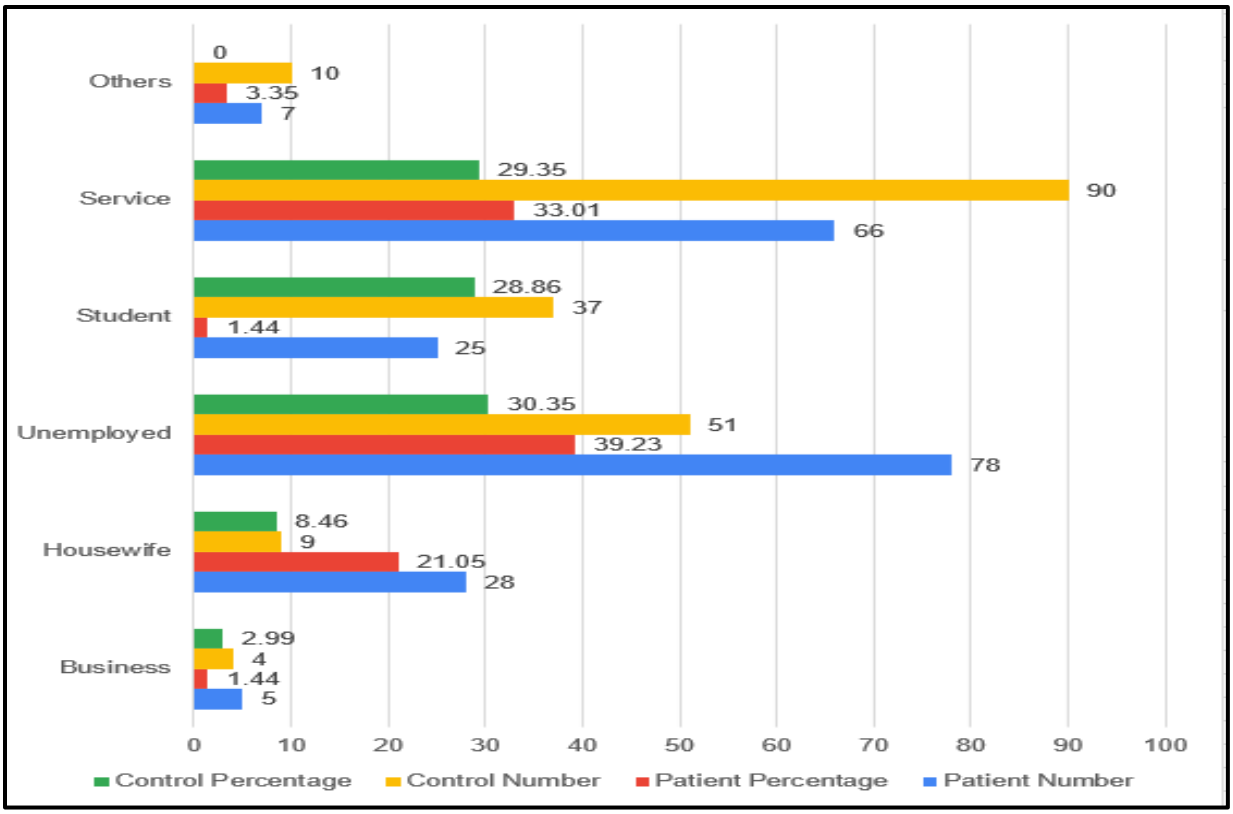

Figure 46: Distribution according to occupation between Patients and Controls

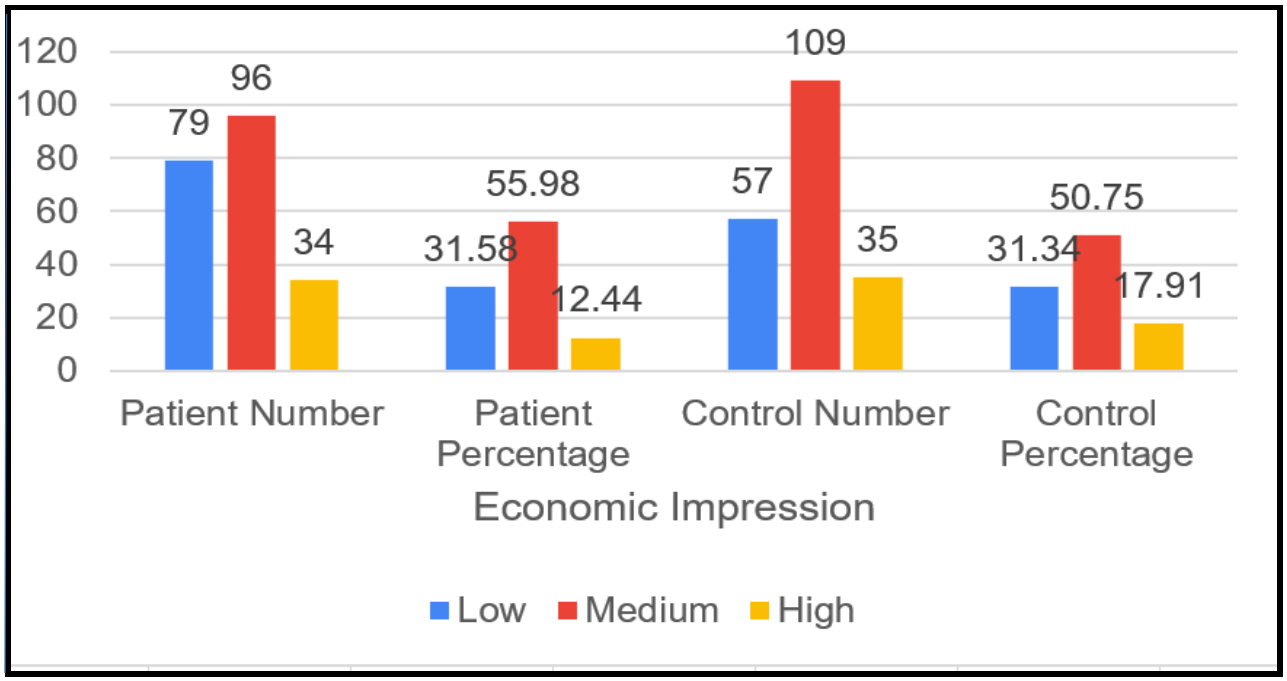

Figure 47: Distribution of Economic Status between Patients and Controls

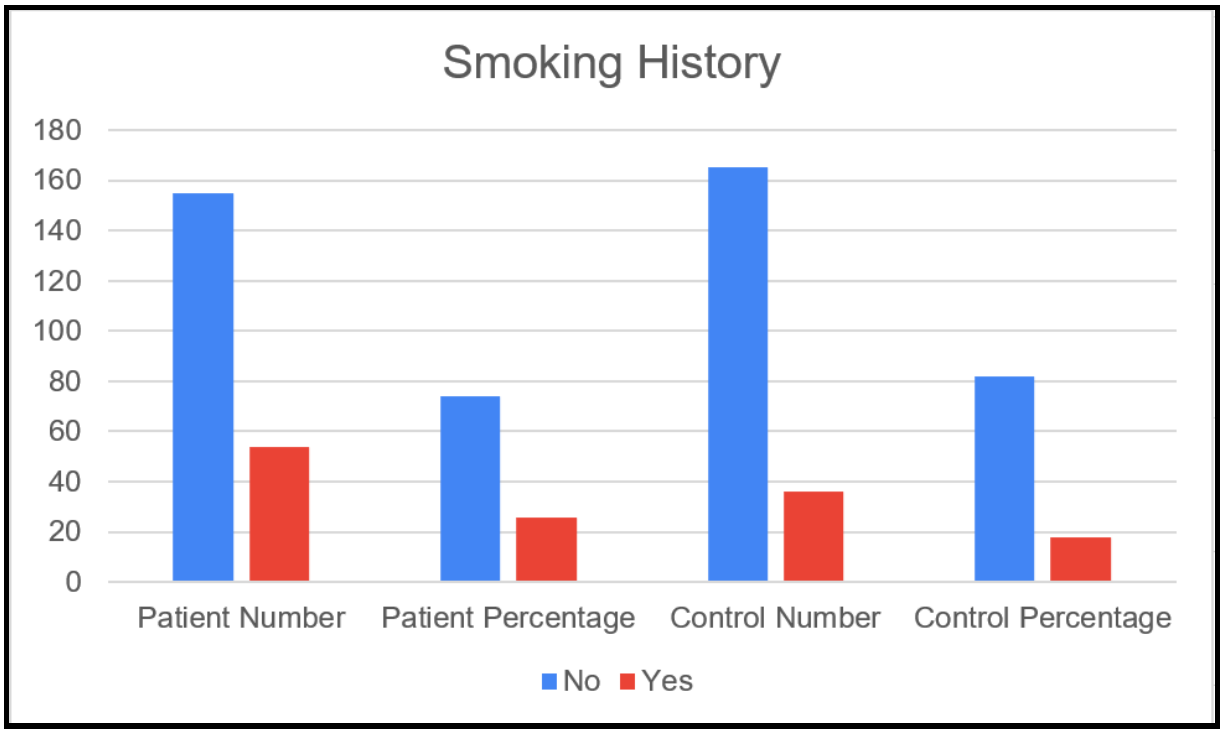

Figure 48: Distribution of smoking habit among study population

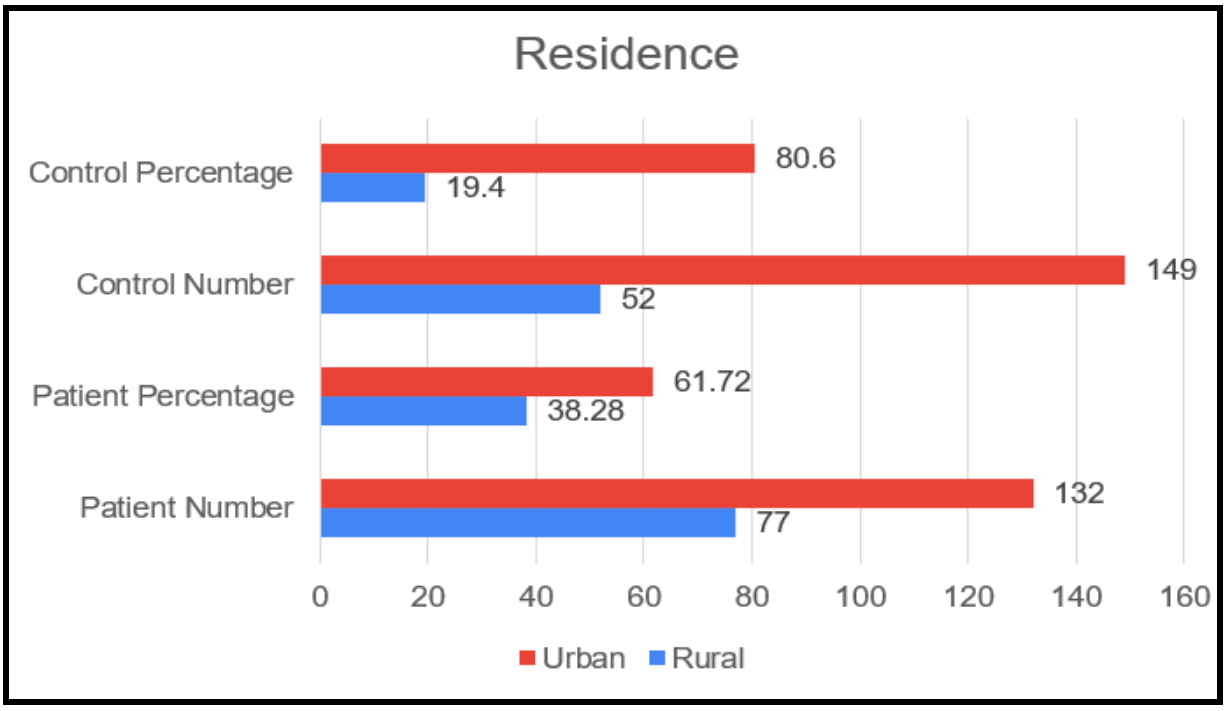

Figure 49: Comparison of Patients and Healthy Controls Residential Area

3.3 Absorbance of Interleukin-3

Table 6: Concentration and Absorbance of IL-3

Standard	Standard Concentration (pg/mL)	Standard Absorbance
1	1000	0.11165
2	500	0.08693
3	250	0.03919
4	125	0.0421
5	63	0.03276

6	31	0.02261
7	16	0.02055

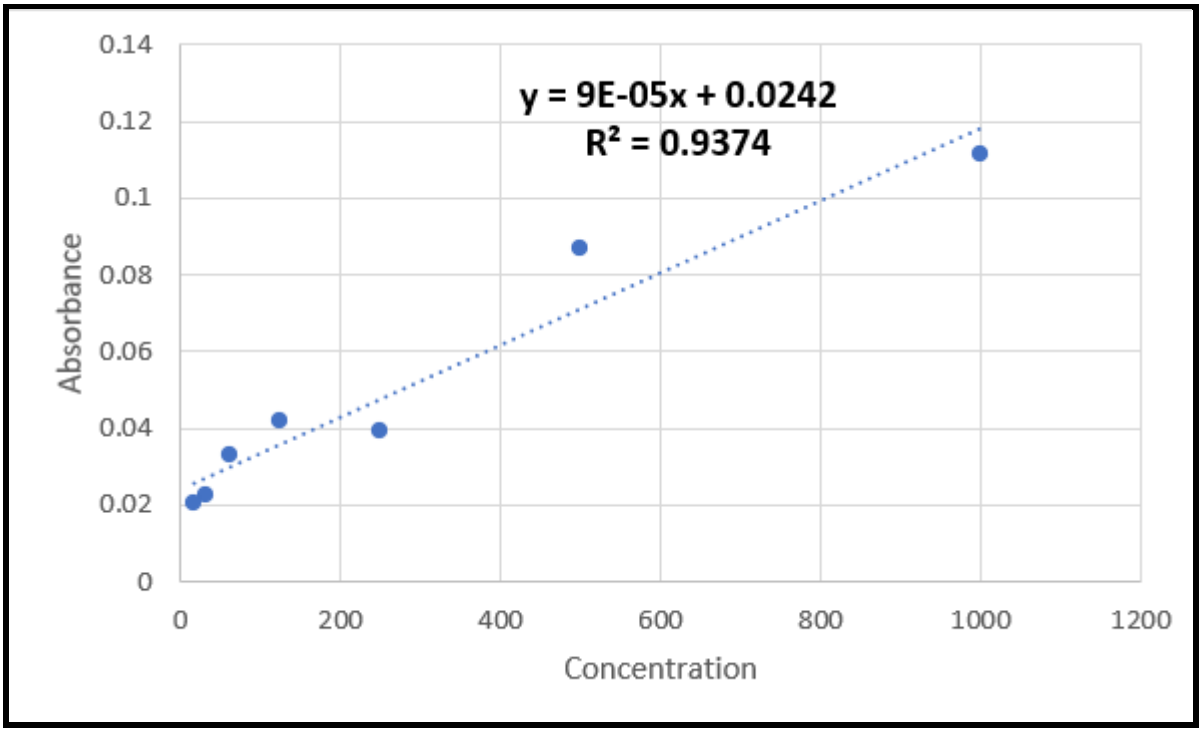

Figure 50: Standard Curve of IL-3

3.4 Severity of the Disease and Cytokine Concentration

Table 7: Severity of disease and IL-3 Concentration

Status	Number	Conc IL-3 (pg/ml)
Mild	52	0.490
Moderate	66	0.496
Severe	91	0.480
Non-existent (Control)	201	0.663

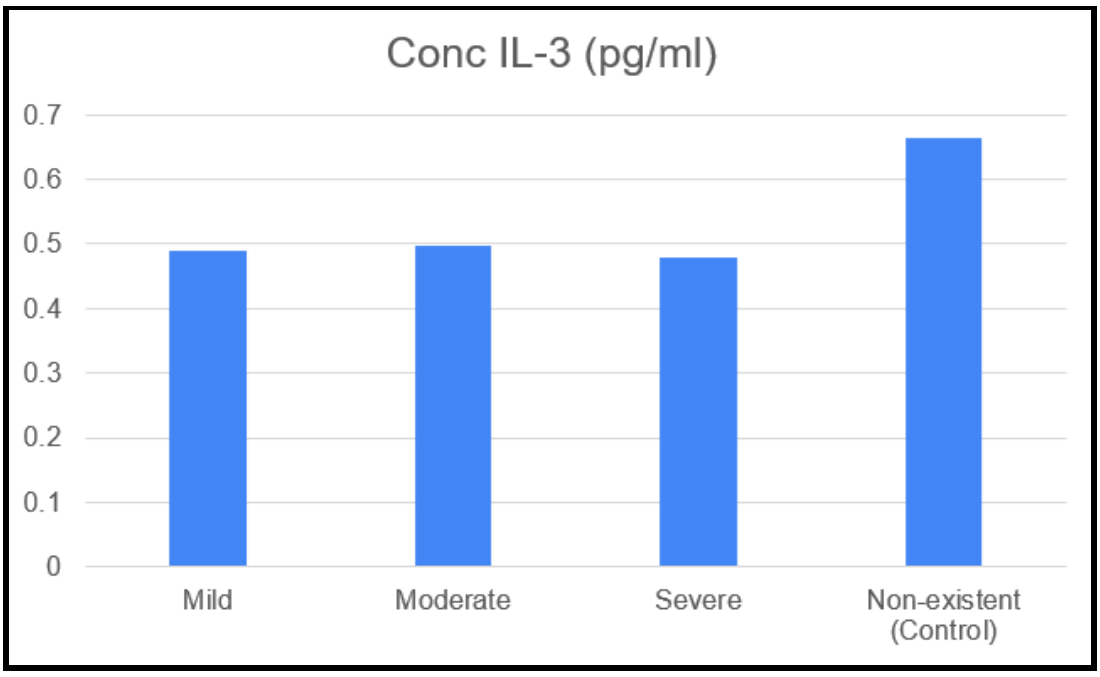

Figure 51: Severity of disease with IL-3

The present table illustrates the correlation between the level of symptom severity and serum IL-3 levels. IL-3 serum concentrations (n=52) averaged 0.490 pg/ml, (n=66) averaged 0.496 pg/ml, and (n=91) averaged 0.480 pg/ml. By contrast, normal controls (n=201) had IL-3 serum concentration (n=0.663 pg/ml).

Chapter 4

Discussion

In this case-control study, the IL-3 level in patients (0.48± 0.01 pg/ml) whereas HCS had higher amount of IL-3 level (0.663 ± 0.02 pg/ml) was found. Additionally, the result was also statistically significant; p value was less than 0.001. There was no statistically significant difference in age and BMI level of patients and controls.

OCD is such a severe disease where there is presence of obsessions and compulsions and it is clinically evaluated through DSM-5 criteria (Gerentes et al., 2019). IL-3 was referred to as a multi-CSF because of its previously described ability to support all forms of myelopoiesis, such as: the formation of granulocytes, monocytes, macrophages; as well as eosinophils, basophils and mast cells from which all are derived from precursor cells in the bone marrow (Dougan et al., 2019). An investigation performed on MDD patients showed that changes in levels of anti-inflammatory cytokines (IL-4) correlate with changes in levels of pro-inflammatory cytokines too (Sarmin et al., 2024). In our study, IL-3 has been decreased therefore it might be that because of the reduction of anti-Inflammatory cytokine levels, pro-Inflammatory cytokine levels might have been also decreased to bring back into homeostatic balance. In another study by Akter et al. (2023) highlighted that abnormal level of IL-3 is found within mood disorder patients. We found levels of IL-3 in the blood (1,024.73 ± 29.84) pg/mL but the p value was not significant in a study by Akter et al., (2023), whereas in our study the serum IL-3 levels, in patients and healthy controls were (0.49 ± 0.01) pg/mL and (0.66 ± 0.02) pg/mL and the result was statistically significant. Fu et al. (2016) also showed that L-3 level has been significantly reduced in drug-naives in comparison to healthy controls. In this current study, both patients who consumes medicine and just freshly diagnosed patients have taken into consideration which might be a probable reason for the alteration in IL-3 level in serum. Another study found, Lipocalin-2 has been decreased which is a pro-inflammatory cytokine, but inflammatory activities has been increased and due to absence or less amount of Lipocalin-2 inflammation gets increased (Akter et al., 2023). This study might be a potential guideline for assessing OCD and for further reseach. Eary risk assessment would be more convenient and easier for OCD early diagnosis. This will add more insight about cytokine IL-3 and OCD.

IL-3 is a growth factor that gets secreted by activated T-cells (Feng et al., 2022). So, if the hematopoietic immune support mechanism is not balanced in our body, then imbalance is also seen in IL-3 level. So, due to this reason, in our study, it might be a probable cause for the lower level of IL-3, IL-3 also makes impact on immune regulation. When immune regulation in the body is not up to the mark, then the IL-3 level might be found imbalance. IL-3 is expressed by neuron and astrocyte and if any type of homeostasis imbalance happens in the body, then IL-3 level is also impaired. Moreover, IL-3 level might be found less in those who intakes anti-inflammatory drug, which takes the amount of inflammation. IL-3 is expressed by T-cells found in a study by Podolska et al., (2024), so if T-cells reduces then IL-3 level might also get reduced. Stress triggers the release of pro-inflammatory cytokine which is mentioned in a study by Beurel (2024), so it also could be reason that IL-3 level might get decreased. Those who have much chronic nutritional deficiency, it effects of their immune response and cytokine activity also gets reduced (Rossio, 1999). So, it could be one of the main reasons of IL-3 level being reduced. The gut microbiota influences the host immune response and causes an imbalance in cytokine levels if the microbiome is imbalanced (Liu et al., 2021). Some proteins reduce IL-3 by negatively regulating it, such as, E3 ubiquitin ligase MARCH3 explained by Feng et al., (2022) in his research which might be the reason of IL-3 being reduced. When T cells are activated by antigens, they mostly produce IL-3 which helps connect the system and the blood cell production system, it is also linked to immune-related diseases (Akter et al., 2023). This means IL-3 levels also affects how our body deals with infections and diseases. Presence of any other disease or infection might alter the levels of IL-3.

Longitudinal studies examining IL-3 over extended periods of time will help determine how IL-3 levels fluctuate relative to OCD symptomatology and treatments. Information from such work will help define IL-3's role in influencing OCD through the use of the neuroimmune impact of IL-3 in the neuroimmune process and in specific regions of the brain (e.g., caudate nucleus and orbitofrontal cortex). These findings may help guide future studies investigating immune-based new therapies aimed at OCD, which would entail either increasing IL-3 levels or targeting other pathways associated with IL-3 for use in patients with treatment-resistant OCD. In addition, by comparing levels of IL-3 across disorders of the nervous system, we may better identify the specificity of IL-3 for OCD. Finally, examining the level of IL-3 according to different subtypes of OCD will allow the identification the specific types of IL-3 to be used to develop an effective treatment for OCD.

The study found that people with OCD have lower levels of IL-3, than people who are healthy. This means that OCD might be changing how the immune system of the body works. OCD might not just be about what's going on in the brain. It might also have to do with how the system becomes inflamed. IL-3 aids in cell regulation. Il-3 levels could be a sign of a specific type of OCD related to the immune system. This could help find a way to diagnose OCD. It could be used to help assess risk monitor disease and develop treatment plans. The test for IL-3 is important for research on biomarkers and it could help improve our understanding of OCD. This could lead to treatments for OCD. Further study is required for better and deeper understanding for better treatment plans and patient compliance.

This case-control study contains no co-morbidity related to other diseases and we have also been able to maintain a level of diversity within the participant population. This will provide insightful information about unregulated inflammation processes associated with the disorder, which will also help to understand more about the assessment of OCD that may develop over time. This information will also help in our understanding of the pathophysiology of OCD, and allow us to develop personalized target therapies, as well as, increase the accuracy of the diagnoses for healing purposes.

This research has some limitations because the dietary habits, physical activity, and sleep patterns among participants was not covered. Additionally, there are many other parameters which would be beneficial in terms of assessing in greater detail. The study comprised such participants in our study who were both medicated and unmedicated.so did not distinguish or separate between these two groups. This study should be considered an initial evaluation. More research needs to be done involving both anti and pro inflammatory cytokine across greater samples.

Conclusion

This study represented OCD patients has lower level of IL-3 than in healthy controls. This could reflect an abnormal response of the body to attacks from the immune system. The changes may also provide new information regarding the biological basis for OCD and assist in determining if a person has a greater likelihood of developing OCD. It can be useful in identifying OCD before it shows up in patients, and consequently therapies will be developed that could be personalized according to each individual patient. Cytokine can be used as a risk indicator and early detection might be very useful in managing the disease in a more effective way. More consistent research works would assist in doing a better assessment of these results and could provide more information regarding the importance of these markers in OCD.

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Appendix A

Patient 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 _____

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):

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

15% Overall Similarity

The combined total of all matches, including overlapping sources, for each database.

Filtered from the Report

- Bibliography
- Quoted Text

Match Groups

152 Not Cited or Quoted 10%
Matches with neither in-text citation nor quotation marks

83 Missing Quotations 5%
Matches that are still very similar to source material

0 Missing Citation 0%
Matches that have quotation marks, but no in-text citation

0 Cited and Quoted 0%
Matches with in-text citation present, but no quotation marks

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9% Internet sources
7% Publications
11% Submitted works (Student Papers)

Integrity Flags

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A flag is not necessarily an indicator of a problem. However, we'd recommend you focus your attention there for further review.