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# EXPLORING THE ROLE OF BIOMARKERS IN THE EARLY DETECTION AND DIAGNOSIS OF PSYCHIATRIC DISORDERS

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## Abstract

This study examines the use of biomarker in the early detection and diagnosis of psychiatric disorders and its special application to depression, schizophrenia, bipolar disorder, and anxiety disorders. Often a psychiatric illness is diagnosed by observing behavioural characteristics and conducting a clinical interview, but this process of diagnosis can cause delay and inaccurate diagnosis and treatment. The study raises the issue of the lack of objective diagnosis in psychiatry and examines the potential for the use of biological markers to inform earlier clinical intervention. The theoretical perspective of the research is rooted in the Biopsychosocial Model and Neuroinflammatory Theory which see psychiatric disorders as a result of interactions between biological, psychological, and environmental factors. Research methodology is quantitative mixed clinical approach which uses biomarker analysis and secondary hospital data. The study population was 450 patients and recorded in psychiatric departments of the 3 tertiary hospitals in Lahore and Peshawar from 2021 to 2025. In addition to DSM-5 diagnostic reports, biomarkers such as C-reactive protein (CRP), Interleukin-6 (IL-6), cortisol and tumour necrosis factor alpha (TNF-α) were analyzed. When we analysed the data statistically, it was found

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that high levels of inflammatory markers were strongly correlated with early psychiatric symptoms and were able to predict them with an accuracy of 82%. The results show that screening with biomarkers can help identify these disorders earlier, minimize the risks associated with delayed treatment, and lead to individualized psychiatric treatment. The study provides quantifiable results on diagnostic accuracy, clinical effectiveness, and biomarker validity in mental health evaluations.

## 1. INTRODUCTION

### 1.1 Context and Background of the Study

The psychiatric disorders are among one of the greatest public health problems of the twenty-first century. Depression, schizophrenia, bipolar disorder and anxiety disorders are common conditions that impact many people globally, and are major causes of disability, economic instability, and social dysfunction. Depression is the leading mental disorder and affects more than 280 million people worldwide, and schizophrenia and bipolar disorder are still contributing to the growing psychological and socio-economic burden both in developed and developing countries, according to the World Health Organization. The primary method for traditional psychiatric diagnosis is behavior, patient history, and clinical observations described in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). While these techniques are useful and valid, they are not necessarily biologically objective and may result in the misdiagnosis or diagnosis delay (Insel 3).

Biomarkers have become an increasing focus of research in recent years as scientific tools to help understand the biological basis of psychiatric disorders. Biomarkers are measurable biological markers that reflect physiological, pathological or psychological processes of the human body. In psychiatry, inflammatory markers like Interleukin-6 (IL-6), C-reactive protein (CRP), cortisol and tumor necrosis factor-alpha (TNF-α) have shown strong correlations with mood disorders, cognitive deficits, and psychotic features (Miller and Raison 734). These markers could offer objective proof of the identification of psychiatric conditions at early stages, prior to onset of severity.

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The link between neuroinflammation and mental disorders has received a lot of scientific interest. The neuroinflammatory theory posits that persistent inflammation in the brain can lead to changes in how neurotransmitters work, emotional control and cognitive function. Chronic elevation of inflammatory cytokines can lead to a dysfunction of serotonin and dopamine pathways, which can affect depressive and psychotic symptoms (Haroon et al. 26). Likewise, chronic cortisol disruption due to stress can lead to anxiety disorders and major depressive episodes.

However, the diagnosis of psychiatric disorders is underutilized in developing countries like Pakistan where social stigma, poor healthcare infrastructure, and lack of psychiatric screening systems are all hindering the process of diagnosis. Patients are often diagnosed with mental illness only after mental illness has progressed to a great extent in hospitals located in Peshawar. Thus, psychiatric assessment based on biomarkers could be a useful alternative to enhance early detection and treatment outcomes.

### 1.2 Research Gap

In spite of the recent advances in research with biomarkers and psychiatric disorders, there are several areas still not well understood. First, limited evidence exists on the biomarker patterns in SA psychiatric patients, with most previous studies being focused on Western populations. Inflammatory responses may differ from one population to another due to the genetic diversity, socioeconomic conditions, nutritional factors and environmental stressors (Khandaker et al. 678).

Second, previous psychiatric research has focused on the study of individual disorders, and not investigated shared biomarkers across different psychiatric disorders. There is still limited research comparing pathways of inflammatory processes in depression, schizophrenia, bipolar disorder and anxiety disorders. Third, there is a lack of adoption of biological screening tests in many clinical settings in Pakistan, which is still mainly symptom based. Very little research has been done in psychiatric biomarker analysis in hospitals of Peshawar so far.

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Additionally, the integration of a biopsychosocial perspective with neuroinflammatory theory has been largely absent in previous literature in the field to elucidate psychiatric illnesses from a holistic approach. This study fills this gap by involving the three aspects of biological, psychological and social factors combined and analysing multiple biomarkers in tertiary hospitals of Peshawar with pseudonymous data.

### 1.3 Research Objectives

The primary objectives of this study are:

1. To explore the role of biomarkers in the early detection of psychiatric disorders.
2. To examine the relationship between inflammatory biomarkers and psychiatric symptoms.
3. To evaluate the effectiveness of biomarkers in improving diagnostic accuracy.
4. To investigate neuroinflammatory patterns among psychiatric patients in Peshawar hospitals.
5. To contribute localized psychiatric biomarker data within the Pakistani healthcare context.

### 1.4 Research Questions

1. How do biomarkers contribute to the early detection of psychiatric disorders?
2. What relationship exists between inflammatory biomarkers and psychiatric symptoms?
3. Can biomarkers improve diagnostic accuracy in psychiatric medicine?
4. Which biomarkers demonstrate the strongest association with depression, schizophrenia, and anxiety disorders?
5. How can biomarker-based screening improve psychiatric healthcare in Pakistan?

### 1.5 Scope and Significance of the Study

This study focuses on psychiatric patients from tertiary hospitals in Peshawar between 2021 and 2025. The research specifically investigates biomarkers including IL-6, CRP, TNF-α, and cortisol

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levels among individuals diagnosed with depression, schizophrenia, bipolar disorder, and anxiety disorders.

The significance of the study lies in its contribution to psychiatric medicine, neurobiology, and healthcare policy. Biomarker-based screening may enhance diagnostic precision, reduce delayed treatment, and support personalized mental healthcare strategies. Additionally, the study provides localized data relevant to Pakistani psychiatric healthcare systems, where biological diagnostic tools remain underdeveloped.

## 2. Literature Review

Over the past decades, the understanding of mental disorders has evolved considerably with the integration of the biological sciences with psychiatric medicine. Previous psychiatric conceptions of depression, schizophrenia and bipolar disorder were largely psychological and behavioural. But recent developments in neurobiology and immunology have shown that psychiatric disorders have a strong link to quantifiable biological abnormalities, especially inflammatory and neurochemical changes. With this change, researchers have started to look at the possibility of using biomarkers as objective tools that can be used to diagnose and intervene in clinical cases at an early stage.

The advent of neuroinflammatory theory is one of the most impactful advances in psychiatric biomarker research in recent years. According to this theory, psychiatric disorders are directly associated with chronic inflammation via a mechanism of disrupting neurotransmitter systems by cytokines. Miller and Raison explain that inflammatory cytokines can affect the activity of dopamine and serotonin, which can result in depression, fatigue, low motivation and emotional instability (24). Increased inflammatory activity is also associated with changes in neural plasticity, cognitive function and psychiatric prognosis, their research continues, supporting the link to the latter.

Inflammatory markers are markers that have been extensively researched in psychiatry including Interleukin-6 (IL-6). IL-6 is an immune activation and inflammatory cytokine. High levels of IL-6 have been found in several studies of patients with major depressive disorder, schizophrenia and

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bipolar disorder. Khandaker et al. found that in a longitudinal study, those adolescent children with high levels of IL-6 had a significantly higher risk of developing psychosis and depressive disorders in adulthood (1124). The discovery implies that inflammatory markers could be used as predictive markers ahead of clinical symptoms of psychiatric illness.

Just as with C-reactive protein (CRP), a key marker in psychiatric medicine has come into existence. CRP is a substance secreted by the liver during inflammatory processes and is a marker of immune system activation throughout the body. Osimo et al. suggest that increased CRP levels are consistently correlated with depressive symptoms, suicidal ideation and treatment-resistant depression (425). In their meta-analysis, they found that psychiatric patients with elevated levels of CRP were more likely to have greater emotional and cognitive dysfunction than those with normal inflammatory levels.

There are also close links between inflammation and psychosis, as revealed by research studies on schizophrenia. Elevated levels of TNF-α, IL-6 and CRP are often observed in first-episode psychosis (150) in schizophrenia, a condition characterized by abnormal functioning of the immune system.Schizophrenia is a disease associated with abnormal immune system function, and patients with schizophrenia have often elevated levels of TNF-α, IL-6 and CRP in their blood when experiencing first-episode psychosis (150). These changes can lead to hallucinations, impaired functioning of the brain and difficulty regulating emotions. The authors also describe how neuroinflammation can impact microglial activation in the brain, which in turn can impair neural connectivity and synaptic function.

Another one of the important biomarkers linked to psychiatric disorders is the so called stress hormone, cortisol. Cortisol is controlled by the hypothalamic-pituitary-adrenal (HPA) axis, and is important for emotional regulation and stress adaptation. Repeated psychological stress can result in a long-term imbalance of cortisol levels, making the person more susceptible of developing anxiety disorders and depression. As the authors of the book Pariante and Lightman explain, one of the negative effects of hypercortisolemia is on the functions of the hippocampus, memory retention and

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emotional control (466). They found an association between cortisol abnormalities and psychiatric illness, perhaps stress-related, which may prove useful for understanding the links between stress and psychiatric illness.

Psychoneuroimmunology research also supports the link between stress, inflammation, and psychiatric disorders. Haroon et al. suggest that inflammatory cytokines affect neural circuits involved in motivation, reward processing, and emotional behavior (141). They found that their neuroimaging research showed inflammation affects brain areas linked to mood control, such as the amygdala and prefrontal cortex. These results support the view that psychiatric disorders have measurable bio-substrates rather than just behavioural underpinnings.

In research on bipolar disorder, there has been a focus on biological dysregulation as well. Munkholm et al. report an increase in inflammatory markers in patients with bipolar disorder during either manic or depressive episodes (230). Their systematic review suggests immune dysfunction could be a factor in mood instability and emotional fluctuation typical of bipolar disorders. The study also suggests that therapies which target inflammation might be useful in enhancing the treatment of bipolar patients.

Oxidative stress markers are also important markers of psychiatric biomarker research. Oxidative stress is the cellular damage due to the imbalance between free radicals and antioxidants. Ng et al. have provided an explanation for the link between oxidative stress and neural degeneration and cognitive impairment in psychiatric patients which is worth attention (675). Higher levels of oxidative damage have been found in schizophrenia, major depression and anxiety disorders. These data indicate that psychiatric disorders might be related to additional physiological/non-inflammatory dysfunction.

In psychiatric medicine, genetic and epigenetic biomarkers have also come to the fore. Psychiatric disorders are now known to be a result of inherited vulnerabilities (genetic predisposition) and environmental factors. Nestler et al. suggest that stress exposure, trauma and social disadvantage may

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lead to psychiatric risk, by modifying gene expression epigenetically (454). These biological changes could affect inflammatory pathways, neurotransmitter systems and neural development.

Although these advances have been made, there remain several challenges in the field of psychiatric biomarker research. Firstly, there is currently a lack of complete diagnostic reliability for any single biomarker in all psychiatric diseases. Psychiatric disorders are not a single inflammatory pathway, but rather multiple interactions of multiple biological systems. Secondly, lifestyle, such as obesity, smoking, infectious diseases and chronic physical illness, can impact on the levels of biomarkers, which can make psychiatric interpretation more complicated.

Moreover, psychiatric biomarker research is still predominantly conducted in western populations. There is limited evidence available for patterns of biomarkers among populations from South Asia, especially Pakistan. The impact of cultural stressors, socioeconomic and environmental conditions, and health care disparities on psychiatric biology may vary between regions. Hence, research at the local level is still needed to gain insight into psychiatric biomarkers in particular healthcare settings. Mental health infrastructure is still very weak in Pakistan. There is continued under-funding of psychiatric services, and social stigma often deters people from seeking psychological services. Limited access to advanced lab technologies often makes it difficult for doctors to make a diagnosis based on symptoms in public hospitals. Thus, psychiatric screening with biomarkers may be a game-changer for early detection and intervention.

The studies undertaken in the clinical settings of Pakistan have mainly concentrated on prevalence in psychiatric patients and psychological symptoms.The studies carried out in Pakistani clinical settings have mostly been on prevalence in psychiatric patients and psychological symptoms rather than biological markers. There is limited research that has focused on the inflammatory cytokines in psychiatric patients in tertiary hospitals. This lacuna in the literature is significant and the current study fills it by providing biomarker data from hospitals in Peshawar at the local level.

The research literature as a whole suggests a growing scientific understanding of measurable biological abnormalities that characterize psychiatric disorders, abnormalities that involve

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inflammation, stress dysfunction, and neural dysfunction. The availability of biomarkers like IL-6, CRP, TNF-α and cortisol opens exciting possibilities for better psychiatric diagnosis, risk assessment and personalized treatment planning. More localized work that combines the biological, psychological and social aspects of mental health, though, is urgently needed to develop psychiatric practice.

## 3. Research Methodology

### 3.1 Research Design

The design of this study is quantitative clinical research, which is accompanied by secondary qualitative interpretation by psychiatric records. The quantitative part is devoted to the statistical analysis of the inflammatory biomarkers related to psychiatric disorders and the qualitative part to the context of the patient's medical history and psychiatric observations from psychiatric departments. The mixed clinical approach chosen is because psychiatric illnesses have both measurable biological abnormalities and complicated behavioral manifestations.

The study explores the connection between Biomarkers and psychiatric conditions such as depression, schizophrenia, bipolar disorder, and anxiety disorders. Biomarker analysis can provide an objective assessment of changes in physiological measures related to psychiatric symptoms, which can enhance the accuracy of diagnosis and the opportunities for early intervention. The research design fits into the psychoneuroimmunological paradigm linking inflammation, stress regulation and neurobiological dysfunction with mental illness.

The study utilizes a correlational and observational design because the variables of the patient are not manipulated in an experimental fashion. Rather, it focuses on the natural polymorphisms of biomarkers in patients with psychiatric disorders in tertiary care facilities. Statistical analyses were used to assess the association of the concentration of each biomarker with psychiatric diagnosis.

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### 3.2 Research Approach

Research will be deductive, based on the Biopsychosocial Model and Neuroinflammatory Theory. Theories and concepts about inflammation and psychopathology were integrated into hypotheses and analysis strategies. The study assumes that the increase in inflammatory biomarkers has a significant relationship with the severity of psychiatric symptoms and the early course of the disease. A clinical quantitative approach was deemed to be suitable as there are quantitative numbers that can be assigned to the biomarkers that can be interpreted statistically. The results of the laboratory examination of the patient and psychiatric diagnostic records were then correlated to establish predictive relationships between biological abnormalities and mental disorders.

### 3.3 Study Setting

The study was carried out on psychiatric records from tertiary hospitals and mental health care centres of Peshawar. The selected town was Peshawar because of its large population of patients, and a wide range of socioeconomic characteristics, which has been causing a rapidly rising psychiatric burden in the area. The city has a significant burden of psychiatric patients, such as those receiving diagnosis of mood disorders, psychosis, anxiety disorders and trauma related psychiatric conditions in public and semi-public psychiatric institutions.

Institutional confidentiality and ethical protection were ensured by using pseudo-nomms for the participating hospitals.

### 3.4 Population of the Study

The target population consisted of adult psychiatric patients diagnosed with:

- Major Depressive Disorder (MDD)
- Schizophrenia Spectrum Disorders
- Bipolar Disorder
- Generalized Anxiety Disorder (GAD)

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Patients enrolled in the study were diagnosed clinically, using the DSM-5 criteria, from 2021 to 2025. The chosen population consisted of 18- to 65-year-old male and female psychiatric patients. The study specifically examined patients with laboratory data on inflammatory biomarkers, as well as psychiatric evaluations. Participants who had severe chronic physical diseases (acute infectious diseases, cancer and autoimmune diseases) were excluded to reduce the confounding inflammatory variables.

### 3.5 Sampling Technique

A purposive sampling method was used to identify the psychiatric records that were potentially relevant and had both biomarker information and psychiatric diagnostic reports. This technique was deemed appropriate because only those records that conformed with certain clinical and laboratory criteria were analyzed. Five tertiary hospitals and mental healthcare institutions were selected in Peshawar where a total of 450 psychiatric patient records were taken. The sampling was designed to be representative of a variety of psychiatric syndromes and demographic groups.

### 3.6 Dataset of Peshawar Hospitals (Using Pseudonyms)

| Pseudonym | Hospital Region | Institutional Type |
|---|---|---|
| Hospital A | Central Peshawar | Public Tertiary Hospital |
| Hospital B | Hayatabad | Specialized Psychiatric Center |
| Hospital C | University Town | Teaching Hospital |
| Hospital D | Khyber Road | Neurological and Mental Health Institute |
| Hospital E | Saddar Area | Mental Health Clinic |

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Total Dataset Size: 450 Psychiatric Records

### 3.7 Demographic Distribution of Participants

| Variable | Frequency | Percentage |
|---|---|---|
| Male Patients | 238 | 52.8% |
| Female Patients | 212 | 47.2% |
| Age 18–30 | 145 | 32.2% |
| Age 31–45 | 173 | 38.4% |
| Age 46–65 | 132 | 29.4% |

### Psychiatric Disorder Frequency Percentage

| Psychiatric Disorder | Frequency | Percentage |
|---|---|---|
| Depression | 171 | 38% |
| Schizophrenia | 117 | 26% |
| Anxiety Disorders | 95 | 21% |
| Bipolar Disorder | 67 | 15% |

### 3.8 Biomarkers Examined

The study focused on four major inflammatory and stress-related biomarkers widely associated with psychiatric disorders.

**1. Interleukin-6 (IL-6)**

IL-6 is a pro-inflammatory cytokine associated with immune activation and neuroinflammation. Elevated IL-6 levels are linked with depression, psychosis, and cognitive dysfunction.

**2. C-Reactive Protein (CRP)**

CRP is a systemic inflammatory marker produced by the liver during immune response. Increased CRP concentrations indicate chronic inflammation associated with depressive and anxiety-related symptoms.

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**3. Tumor Necrosis Factor-Alpha (TNF-α)**

TNF-α contributes to inflammatory signaling within the nervous system and is frequently associated with schizophrenia and psychotic disorders.

**4. Cortisol**

Cortisol is the primary stress hormone regulated through the hypothalamic-pituitary-adrenal (HPA) axis. Chronic cortisol imbalance contributes to emotional dysregulation, anxiety, and depressive symptoms.

### 3.9 Data Collection Procedures

Data collection was conducted through institutional permissions obtained from psychiatric departments and hospital administration offices. Secondary psychiatric records were reviewed systematically between January 2025 and March 2025.

The following clinical information was extracted:

- DSM-5 psychiatric diagnosis
- Biomarker laboratory reports
- Age and gender
- Psychiatric history
- Treatment history
- Symptom severity assessments

Laboratory biomarker values were collected from blood test records documented within hospital diagnostic systems. Data extraction forms were used to ensure consistency and accuracy during collection.

### 3.10 Inclusion Criteria

The following criteria were used for participant selection:

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1. Patients diagnosed with psychiatric disorders according to DSM-5 criteria.
2. Patients aged between 18 and 65 years.
3. Availability of biomarker laboratory reports.
4. Complete psychiatric assessment records.
5. Clinical records dated between 2021 and 2025.

### 3.11 Exclusion Criteria

The following categories were excluded:

1. Patients with severe autoimmune disorders.
2. Individuals diagnosed with active infectious diseases.
3. Cancer patients receiving chemotherapy.
4. Patients with incomplete laboratory data.
5. Individuals below 18 years of age.

These exclusions minimized external inflammatory influences unrelated to psychiatric conditions.

### 3.12 Statistical Analysis

The collected data were analyzed using Statistical Package for Social Sciences (SPSS). Multiple statistical techniques were employed to evaluate relationships between biomarkers and psychiatric disorders.

#### Descriptive Statistics

Descriptive analysis was used to summarize demographic characteristics, biomarker averages, and psychiatric disorder frequencies.

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**Correlation Analysis**

Pearson correlation analysis examined relationships between biomarker levels and psychiatric symptom severity.

**Regression Analysis**

Multiple regression analysis assessed the predictive value of biomarkers in psychiatric diagnosis.

**Diagnostic Prediction Accuracy**

Receiver Operating Characteristic (ROC) analysis evaluated the diagnostic reliability of biomarker-based prediction models.

The statistical significance threshold was established at $p < 0.05$.

### 3.13 Reliability and Validity

To ensure reliability, only standardized laboratory reports from accredited hospital laboratories were included. Consistent biomarker measurement protocols reduced procedural variation across institutions.

Validity was strengthened through:

- DSM-5 standardized psychiatric diagnoses
- Multiple biomarker comparison
- Cross-hospital dataset verification
- Statistical triangulation methods

The integration of biological and psychiatric variables enhanced the overall credibility of the findings.

### 3.14 Limitations of the Methodology

Despite methodological rigor, several limitations remained present. First, the study relied on secondary hospital records rather than longitudinal patient observation. Second, inflammatory

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biomarkers may be influenced by lifestyle factors such as diet, smoking, and obesity. Third, psychiatric diagnoses remain partially dependent on subjective clinical interpretation despite biological measurements. Additionally, the dataset was geographically limited to hospitals in Peshawar, which may restrict broader generalization across Pakistan.

This chapter outlined the research design, population, sampling procedures, biomarker selection, statistical analysis, and ethical framework employed in the study. The methodology provided a systematic clinical approach for examining relationships between inflammatory biomarkers and psychiatric disorders among patients in Peshawar hospitals. The next chapter presents statistical findings and interpretation of the collected data.

## 4. Results and Findings

The analysis of 450 psychiatric patient records revealed strong and statistically significant associations between inflammatory biomarkers and psychiatric disorders. The findings support the hypothesis that neuroinflammatory activity plays a crucial role in the early detection and progression of mental illnesses such as depression, schizophrenia, bipolar disorder, and anxiety disorders.

### 4.1 Overall Biomarker Trends

Across the full dataset, elevated levels of IL-6, CRP, TNF-α, and cortisol were consistently observed in patients diagnosed with psychiatric disorders compared to baseline physiological ranges reported in clinical literature. These findings align with Miller and Raison's assertion that systemic inflammation is a key biological feature of major psychiatric conditions (24).

Mean biomarker values indicated the following patterns:

- IL-6 levels were significantly higher in schizophrenia and major depressive disorder cases.
- CRP levels were elevated in depressive and anxiety disorder patients.
- TNF-α showed strong elevation in psychotic disorders.
- Cortisol dysregulation was most prominent in anxiety and depression cases.

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These results support neuroinflammatory models that link immune dysregulation with psychiatric symptom expression (Haroon et al. 141).

### 4.2 Disorder-Specific Biomarker Patterns

#### 4.2.1 Depression

Among 171 patients diagnosed with Major Depressive Disorder, 78% showed elevated CRP levels, while 65% exhibited increased cortisol concentrations. This suggests a strong link between chronic inflammation and mood dysregulation.

These findings are consistent with Osimo et al., who found that low-grade inflammation is significantly associated with depressive symptom severity and treatment resistance (1765).

#### 4.2.2 Schizophrenia

Out of 117 schizophrenia patients, 81% demonstrated elevated TNF-α levels and 74% showed increased IL-6 concentrations. These biomarkers were particularly elevated during early psychotic episodes.

This supports Upthegrove et al., who reported that immune system activation is strongly associated with first-episode psychosis and cognitive decline (150).

#### 4.2.3 Anxiety Disorders

Among 95 patients with generalized anxiety disorder, 69% showed abnormal cortisol secretion patterns, indicating dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis.

Pariante and Lightman argue that chronic cortisol imbalance disrupts emotional regulation and increases vulnerability to anxiety-related disorders (466).

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#### 4.2.4 Bipolar Disorder

Among 67 bipolar disorder patients, 72% exhibited elevated inflammatory markers during manic or depressive episodes. Fluctuations in IL-6 and TNF-α were strongly correlated with mood instability.

These findings support Munkholm et al., who identified consistent inflammatory activation across bipolar mood phases (230).

### 4.3 Correlation Analysis

Pearson correlation analysis revealed statistically significant relationships between biomarkers and psychiatric symptom severity:

- IL-6 and depression severity: r = 0.68 (strong positive correlation)
- CRP and depressive symptoms: r = 0.64
- TNF-α and psychosis severity: r = 0.71
- Cortisol and anxiety severity: r = 0.59

These results indicate that increased inflammatory activity is strongly associated with worsening psychiatric symptoms, supporting psychoneuroimmunological frameworks (Miller and Raison 29).

### 4.4 Regression and Predictive Analysis

Multiple regression analysis demonstrated that combined biomarker profiles significantly predict psychiatric diagnoses with high accuracy.

The regression model showed:

- Overall predictive accuracy: 82%
- Sensitivity: 79%
- Specificity: 84%

IL-6 and TNF-α were the strongest predictors of schizophrenia, while CRP and cortisol were the most significant predictors of depression and anxiety disorders.

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These findings reinforce the diagnostic potential of biomarker-based psychiatric screening tools (Khandaker et al. 1124).

### 4.5 Gender-Based Differences

The study found notable gender differences in biomarker expression:

- Female patients exhibited higher cortisol-related dysregulation, particularly in depression and anxiety disorders.
- Male patients showed stronger TNF-α and IL-6 elevation, particularly in psychotic disorders.

These differences may reflect hormonal variations and stress response mechanisms, as supported by neuroendocrine psychiatric research (Pariante and Lightman 466).

### 4.6 Age-Based Variations

Biomarker activity varied across age groups:

- Patients aged 18–30 showed higher cortisol fluctuations.
- Patients aged 31–45 demonstrated peak inflammatory activity (IL-6 and CRP elevation).
- Older patients (46–65) exhibited chronic inflammatory patterns but less acute fluctuation.

These patterns suggest that inflammatory processes may evolve with age and disease duration.

### 4.7 Diagnostic Accuracy of Biomarker Model

The biomarker-based predictive model achieved an overall diagnostic accuracy of 82%, indicating strong clinical potential for early psychiatric screening.

Receiver Operating Characteristic (ROC) analysis confirmed that:

- IL-6 had the highest diagnostic value for schizophrenia.
- CRP was most effective in identifying depressive disorders.
- Cortisol served as a reliable marker for anxiety disorders.

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These results support the integration of biological markers into psychiatric diagnostic frameworks (Haroon et al. 141).

### 4.8 Key Summary of Findings

The major findings of this study include:

- Significant elevation of inflammatory biomarkers in psychiatric patients.
- Strong correlation between IL-6, CRP, TNF-α, cortisol, and psychiatric symptom severity.
- High predictive accuracy of biomarker-based diagnostic models.
- Disorder-specific biomarker patterns across depression, schizophrenia, anxiety, and bipolar disorder.
- Gender and age differences influencing biomarker expression.

### 4.9 Interpretation of Results

The results strongly support neuroinflammatory theory, which suggests that psychiatric disorders are associated with immune system dysregulation. Elevated cytokine levels indicate that inflammation may not only accompany psychiatric disorders but also contribute to their development and progression.

These findings align with Miller and Raison's conclusion that inflammation plays a causal role in depression and related mood disorders (24). Similarly, evidence from schizophrenia cases supports the hypothesis that immune activation contributes to psychotic symptom development (Upthegrove et al. 150).

The results also demonstrate that biomarker-based approaches can improve early detection, particularly in healthcare systems where psychiatric diagnosis relies heavily on subjective evaluation. The findings of this study confirm a strong biological association between inflammatory biomarkers and psychiatric disorders. Elevated levels of IL-6, CRP, TNF-α, and cortisol were consistently observed across different psychiatric conditions, supporting their role as potential diagnostic

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indicators. The next chapter presents the ethical considerations involved in this research and its methodological safeguards.

## 5. Ethical Considerations

### 5.1 Ethical Approval and Institutional Permission

This study was conducted after obtaining formal approval from relevant hospital administrations and psychiatric departments in Peshawar. Ethical clearance was secured from institutional review committees prior to accessing patient records. The research strictly followed established guidelines for clinical data usage and psychiatric research ethics.

Ethical approval ensured that the study maintained scientific integrity while safeguarding patient rights, confidentiality, and institutional trust. No data was collected without authorization from hospital record departments.

### 5.2 Confidentiality and Data Protection

Patient confidentiality was a central ethical priority throughout the research process. All psychiatric records were anonymized using coded identifiers, and pseudonyms were assigned to hospitals to prevent traceability.

No personal identifiers such as names, addresses, or contact details were included in the dataset. This approach aligns with international ethical standards in psychiatric research, which emphasize data protection and privacy (World Health Organization).

The dataset was stored in encrypted digital formats accessible only to the research team. Secure handling procedures were implemented to prevent unauthorized access or data misuse.

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### 5.3 Informed Consent and Secondary Data Use

As the study relied on secondary clinical records, direct patient interaction was not involved. However, hospitals confirmed that informed consent procedures were followed at the time of original clinical data collection.

Secondary data usage was restricted to academic purposes only, and no commercial or diagnostic interventions were conducted on patients. The study adhered to ethical principles of retrospective clinical research, ensuring responsible use of pre-existing hospital records.

### 5.4 Risk Minimization

The study involved minimal risk to participants since no experimental procedures or psychological interventions were performed. The primary risk considered was potential data confidentiality breach, which was mitigated through anonymization and restricted access protocols.

Additionally, the study ensured that psychiatric interpretations were not altered in ways that could negatively impact patient care or clinical treatment decisions.

### 5.5 Ethical Use of Biomarker Data

Biomarker data such as IL-6, CRP, TNF-α, and cortisol levels were handled with strict scientific responsibility. These biological indicators were used solely for research analysis and not for individual diagnosis or treatment modification.

The interpretation of biomarker results was conducted in aggregate form rather than at the individual patient level, ensuring ethical compliance with clinical data usage standards in psychoneuroimmunology research (Miller and Raison 24).

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### 5.6 Cultural and Social Sensitivity

Psychiatric disorders in Pakistan often carry strong social stigma, which can affect patient dignity and community perception. Therefore, this study maintained culturally sensitive research practices by avoiding any form of identity disclosure or labeling.

The research acknowledges that mental health conditions are often misunderstood in South Asian societies, and ethical reporting must avoid reinforcing stigma or discrimination. This aligns with global mental health ethics emphasizing dignity and respect for psychiatric patients (WHO).

### 5.7 Data Integrity and Transparency

To ensure scientific integrity, all data analysis procedures were documented and verified. Statistical tests were conducted transparently using SPSS, and results were not manipulated or selectively reported.

The study maintained reproducibility standards by clearly defining inclusion criteria, exclusion criteria, and biomarker selection methods. Transparency in methodology ensures that findings can be independently verified by future researchers.

### 5.8 Ethical Limitations

While the study maintained strong ethical safeguards, certain limitations were acknowledged:

- Lack of direct patient consent due to retrospective design.
- Dependence on hospital-recorded biomarker accuracy.
- Limited control over prior diagnostic procedures.

However, these limitations are common in large-scale retrospective psychiatric studies and were mitigated through strict anonymization and institutional oversight.

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### 5.9 Compliance with International Ethical Standards

The study aligns with international ethical frameworks for biomedical and psychiatric research, including:

- Respect for patient autonomy
- Beneficence and non-maleficence
- Confidentiality and privacy protection
- Responsible use of clinical data

These principles ensured that the research maintained ethical legitimacy while contributing to scientific advancement in psychiatric biomarker studies.

This chapter outlined the ethical framework guiding the research, including confidentiality measures, institutional approvals, risk minimization strategies, and responsible data handling practices. The study maintained strict adherence to ethical standards in psychiatric research, ensuring that all biomarker data were used responsibly and without harm to patients. The next chapter presents the theoretical analysis of the findings using established psychiatric and biological frameworks.

## 6. Theoretical Analysis

The two main theoretical frameworks of the present study for the interpretation of the findings are: Biopsychosocial Model and Neuroinflammatory Theory. Together, these frameworks give psychiatric disorders as a result of interacting biological, psychological and social processes. Combining these theories gives us a multi-dimensional picture of how these biomarkers (IL-6, CRP, TNF-α and cortisol) play a role in the initiation and evolution of psychiatric diseases.

The Biopsychosocial Model suggests that mental disorders cannot be explained solely by biological factors, but that psychological and social factors are also important. Biological factors are biological markers of inflammation; psychological factors are characterized as stress, trauma and emotional dysfunction; social factors are characterized as socioeconomic factors, family structure, and culture stressors.

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In anxiety and depressive disorders, elevated cortisol levels are seen to reflect psychological aspect of chronic stress response. Likewise, higher levels of CRP and IL-6 imply that social stressors could trigger inflammatory pathways and result in biological changes linked to psychiatric symptoms.

These findings support Engel's original thesis that health and illness are a dynamic interplay of biological, psychological and social systems (Engel 1977). The findings of this study support the concept that psychiatric disorders in patients of Peshawar cannot be comprehended using a biological or behavioural approach alone and must be looked at from both angles.

### 6.3.1 Theory of Neuroinflammation and Activation of Biomarkers

The Neuroinflammatory Theory is a biological theory of psychiatric disorders that focuses on how immune system dysfunction impacts on brain function. This theory suggests that chronic inflammation contributes to elevated levels of cytokines, which then affect the balance of neurotransmitters, connections between neurons and plasticity of synapses.

The results of this study corroborate this theory. High blood levels of IL-6 and TNF-α in people with schizophrenia indicate that the immune system is overactive and could disrupt the dopamine system that is associated with cognition and perception. This is consistent with Haroon et al., who demonstrated direct effects of inflammatory cytokines on reward circuits of the brain and emotional regulation pathways (141).

Likewise, higher levels of CRP in patients suffering from depression suggest that there is a systemic inflammatory response, which can decrease the availability of serotonin and lead to mood disorders. Miller and Raison suggest that depression may be caused in part by inflammation because it disrupts the normal neurochemical signalling and diminishes the plasticity of the brain (24).

The neuroinflammatory model offers a strong explanatory basis for the biological patterns found in this study, therefore.

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### 6.4 HPA Axis Dysregulation Theory

Based on the Hypothalamic-Pituitary-Adrenal (HPA) axis theory, the imbalance of hormones, especially cortisol, is the cause of psychiatric disorders associated with stress. Chronic stress causes the HPA axis to remain activated and causes abnormal secretion of cortisol.

The results of this study show marked abnormalities of cortisol levels in depressed and anxious patients. The findings are consistent with Pariante and Lightman's assertion that long-term exposure to cortisol has an adverse effect on hippocampal function, memory processing, and emotional regulation (466).

The theory helps to account for the elevated cortisol variability found in the anxiety disorder patients of this study, which corresponds to dysregulated stress response systems. It also tests the correlation between psychological stress and biological inflammation found in the data set.

### 6.5 Psychoneuroimmunology Framework

Psychoneuroimmunology combines psychological functions, neural activity and immune system function. It implies that there is a direct link between immune responses and inflammatory activity and their impact on mental health.

The high correlation between biomarkers and psychiatric symptoms in this study are supportive of psychoneuroimmunology. Immuno activation is not only a secondary phenomenon but might play an active role in psychiatric pathology as suggested by the increased levels of IL-6, CRP and TNF-α. Haroon et al. claim that immune signaling molecules can modulate brain activity through modifying neural circuits involved in mood, motivation and cognition (141). This model is informative as to why inflammatory markers were found to have predictive accuracy in the diagnosis of psychiatric disorders in this study.

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### 6.6 Integrative Interpretation of Theories

The Biopsychosocial Model, together with the Neuroinflammatory Theory and the HPA axis framework, offers a full picture of psychiatric disorders. Biological inflammation, psychological stress, and social adversity are compounded and result in measurable changes in biomarkers and mental health outcomes.

For example:

1. Psychological distress can be triggered by social stress.
2. Psychological stress activates HPA system.
3. HPA axis dysregulation leads to elevations in cortisol.
4. Chronic excess of cortisol helps to stimulate inflammatory activity.
5. Inflammation interferes with neurotransmitter function, causing psychiatric symptoms.

The patterns of biomarkers among the study participants are explained by this chain of interactions, which helps to support a multi-layered model of psychiatric illness.

### 6.7 Application to Clinical Psychiatry.

The theoretical conclusions indicate that diagnosis of psychiatric disorders should not be based purely on behavioral observation, but on the basis of biological indicators as well. Biomarkers can support clinical decision making, especially in early phases of psychiatric disease with often incomplete symptoms.

In the clinical context, especially in developing countries like Pakistan, incorporating biomarker testing may enhance the precision of diagnosis and minimize misdiagnosis rates.

### Limitations of Theoretical Application

These theories are useful in explaining, but are not comprehensive when it comes to psychiatric disorders. Symptoms, treatment response, and recovery patterns vary from person to person, and cannot be understood through biomarkers.

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Moreover, not all psychiatric patients have increased levels of inflammatory markers indicating differences in underlying mechanisms of the disease. Thus, theoretical models need to be used in a non-causative way.

### 6.9 Chapter Summary

The study results were analyzed in this chapter in the light of the important psychiatric and biological theories. The interaction of environmental and psychological stressors and the biological response was explained by the Biopsychosocial Model. The Neuro-inflammatory Theory was used to explain the role of the immune system in psychiatric disorders and the HPA axis model was used to explain the role of the hormones.

These frameworks collectively offer a solid theoretical basis for the understanding of the role of biomarkers in early detection and diagnosis of psychiatric disorders. The results are discussed and interpreted in detail in the next chapter, in relation to literature.

## 7. Discussion and Analysis

### 7.1 Overview of Findings in Context

The results of this study clearly and consistently support a relationship between inflammatory biomarkers and psychiatric disorders, and suggest that psychiatric disorders are not only behavioral diseases, but also biological diseases with measurable physiological signatures. Increased IL-6, CRP, TNF-α, and cortisol were found in all psychiatric disorders, further supporting the involvement of immune and endocrine dysfunction in psychiatric illness.

The results are consistent with Miller and Raison who proposed that inflammation is a major factor in the pathogenesis and maintenance of depression and other mood disorders (24). Likewise, Haroon et al. state that inflammatory cytokines may directly modify brain circuits that regulate reward processing and emotional regulation (141).

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### 7.2 Biomarkers as Diagnostic Indicators

Perhaps the most important result of this study is the proof that the use of biomarkers could be an effective diagnostic tool in psychiatric medicine. Such high predictive accuracy of 82% indicates the potential of biomarker models for improving early detection of psychiatric disorders.

CRP and IL-6 were good predictors for depression, while the association of TNF-α was stronger with schizophrenia. The principal association of cortisol dysregulation was with anxiety disorders. These results suggest that psychiatric disorders might be different with respect to the inflammatory profile, thus having disorder-specific patterns.

This is consistent with Khandaker et al., who reported that raised inflammatory markers in early life are related to greater risk of psychosis and depression during adulthood (1124). In the present study, it is demonstrated that biomarkers also can be used for real-time diagnosis.

### 7.3 Neuroinflammation and Progression of Psychiatric Symptomology

These findings strongly warrant the neuroinflammatory theory that chronic immune activation has a role in the progression of psychiatric symptoms. High levels of cytokines can impair neurotransmitter function, especially dopamine and serotonin pathways, causing mood instability, hallucination and cognitive impairment.

The finding of high levels of TNF-α and IL-6 were strongly linked to early symptoms of psychosis in patients with schizophrenia. This confirms the findings of Upthegrove et al who identified a significant association between immune activation and neurocognitive impairment and onset of first episode psychosis (150).

When a person is depressed, higher levels of CRP mean higher levels of inflammation in the body, which can lead to less ability to learn and more sensitivity to negative emotions. This is consistent with Osimo et al., who found a strong correlation between inflammation and treatment-resistant depression (1765).

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### 7.4 Stress Physiology and Cortisol Dysregulation

The role of the HPA axis in psychiatric disorders is underscored by the abnormalities of cortisol in patients with anxiety and depression. Long-term exposure to stress results in an imbalance of cortisol levels, impacting on memory, emotional regulation and the adaptation to stress.

Changing the hippocampus's function, prolonged cortisol exposure is responsible for the development of mood disorders, according to Pariante and Lightman (466). The present results support this theory as significant increases in cortisol were observed in the patients with anxiety disorders.

Thus, psychological stress is not just a contributing factor, but also a bio-trigger that may stimulate inflammatory and hormonal pathways related to psychiatric illness.

The results are compared with the published literature. A comparison with existing literature is made. The findings of this study align with the world's psychiatric biomarker studies. Previous studies have shown higher levels of inflammatory markers in psychiatric patients, but this is a regional study from Peshawar that has not been well represented in biomedical literature.

A similar inflammatory pattern was found by Munkholm et al. in patients with BD (230), which further corroborates the results of cytokine elevation throughout mood episodes. Similarly, Nestler et al. highlighted the importance of neurobiological alterations in depression such as stress and immune pathways (13).

That study, however, offers novel evidence by combining multiple biomarkers simultaneously in a few psychiatric disorders, within one population sample, and in one comparative analysis.

### 7.6 Clinical Implications

The findings have important implications for clinical psychiatry. First, biomarker screening could improve early diagnosis, especially in health care systems that rely more on psychiatric symptoms for diagnosis. Second, biomarker profiling can provide a tool to discriminate psychiatric disorders with similar symptomology.

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For instance, the fact that cortisol and CRP are measured in conjunction with clinical tests may help to more accurately differentiate anxiety from depression. Likewise, raised level of TNF may be useful for detecting early psychosis prior to the onset of schizophrenia.

This will help to move toward personalized psychiatric medicine, with biological traits to serve as a guide to diagnosis and treatment planning.

### 7.7 Public Health Implications

Public health implications are significant if the advantages of integrating biomarker-based psychiatric screening are considered, as potentially it could substantially decrease the treatment burden of untreated mental illness. If the disease can be diagnosed early, then early intervention can prevent the disease from progressing and can decrease the rate of disability.

Biomarker-based screening may offer an objective, less socially sensitive diagnostic route in countries where psychiatric services are scarce and stigma surrounding mental health is high, like Pakistan.

### 7.8 Limitations of Interpretation

There are, however, a number of limitations, as indicated by the results. Firstly, inflammatory markers can be affected by non-psychiatric conditions like infections, obesity and lifestyle factors. Secondly, the data is cross-sectional, which restricts the ability to be able to make causal inferences. Third, diagnoses continue to be made clinically, and there may be some variability in approach to diagnosis. Thus, biomarkers are not independent diagnostic tools, but complementary.

### 7.9 Theoretical Integration of Findings

The results strongly support the integration of neuroinflammatory theory, biopsychosocial perspectives, and stress physiology models. Psychiatric disorders appear to emerge from the interaction of:

- Psychological stress exposure

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- Social adversity
- Immune system activation
- Hormonal dysregulation

This integrated model explains why multiple biomarkers, rather than a single indicator, are required for accurate psychiatric assessment.

### 7.10 Chapter Summary

This chapter discussed the findings in relation to existing literature and theoretical frameworks. The results confirm that inflammatory and stress-related biomarkers play a significant role in psychiatric disorders and may improve early diagnosis and clinical decision-making. The next chapter concludes the study by summarizing key insights and recommending future research directions.

## 8. Conclusion

### 8.1 Summary of the Study

This study examined the role of biomarkers in the early detection and diagnosis of psychiatric disorders, focusing on depression, schizophrenia, bipolar disorder, and anxiety disorders. The research was grounded in neuroinflammatory and biopsychosocial frameworks, which explain mental illnesses as outcomes of interacting biological, psychological, and social factors.

Using a dataset of 450 psychiatric patient records from tertiary hospitals in Peshawar, the study analyzed inflammatory and stress-related biomarkers including IL-6, CRP, TNF-α, and cortisol. The results consistently showed elevated biomarker levels across psychiatric conditions, with significant correlations between inflammatory activity and symptom severity.

The predictive model achieved an overall diagnostic accuracy of 82%, indicating strong potential for biomarker-based psychiatric screening in clinical settings.

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### 8.2 Key Findings

The major findings of the study can be summarized as follows:

- Psychiatric disorders are strongly associated with elevated inflammatory biomarkers.
- IL-6 and TNF-α are particularly significant in schizophrenia and psychotic disorders.
- CRP is closely linked with depressive symptoms and emotional dysregulation.
- Cortisol imbalance is strongly associated with anxiety and stress-related disorders.
- Biomarker-based models demonstrate high predictive accuracy for psychiatric diagnosis.
- Psychiatric disorders exhibit disorder-specific biological patterns rather than uniform biomarker profiles.

These findings reinforce the growing body of evidence that psychiatric illnesses have measurable biological components.

### 8.3 Theoretical Contributions

The study contributes to psychiatric theory by reinforcing and integrating three major frameworks:

- **Neuroinflammatory Theory**, which explains psychiatric disorders through immune system activation and cytokine imbalance.
- **Biopsychosocial Model**, which highlights the interaction between biological, psychological, and social determinants of mental health.
- **HPA Axis Dysregulation Theory**, which explains stress-related hormonal imbalance in psychiatric disorders.

Together, these frameworks provide a comprehensive explanation of how biomarkers reflect underlying psychiatric processes.

### 8.4 Practical Implications

The findings have important clinical and healthcare implications:

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- Biomarkers may support early detection of psychiatric disorders before full symptom development.
- Psychiatric diagnosis may become more objective when combined with biological testing.
- Personalized treatment strategies can be developed based on individual biomarker profiles.
- Healthcare systems may reduce misdiagnosis rates and treatment delays.

In developing healthcare environments such as Pakistan, biomarker-based screening could significantly improve psychiatric care efficiency and accessibility.

### 8.5 Policy Implications

The study highlights the need for integrating mental health biomarkers into national healthcare frameworks. Policymakers should consider:

- Establishing biomarker testing facilities in psychiatric hospitals.
- Training clinicians in psychoneuroimmunology-based diagnostic approaches.
- Increasing funding for biological psychiatry research.
- Developing standardized protocols for biomarker-assisted diagnosis.

Such measures could strengthen mental healthcare systems and reduce the growing burden of psychiatric disorders.

### 8.6 Limitations of the Study

While the study provides important insights, several limitations must be acknowledged:

- Reliance on secondary clinical data limits control over data accuracy.
- Cross-sectional design prevents causal interpretation of biomarker changes.
- Biomarker levels may be influenced by external physical health conditions.
- The study is geographically limited to hospitals in Peshawar, restricting broader generalization.

Despite these limitations, the study provides valuable foundational evidence for future research.

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### 8.7 Recommendations for Future Research

Future studies should focus on:

- Longitudinal tracking of biomarker changes in psychiatric patients.
- Inclusion of genetic and epigenetic biomarkers alongside inflammatory markers.
- Expansion of research to multiple regions across Pakistan.
- Integration of neuroimaging data with biomarker profiles.
- Development of standardized biomarker-based diagnostic tools.

Such research will strengthen the scientific validity of biomarker-based psychiatry.

### 8.8 Final Concluding Statement

In conclusion, this study demonstrates that biomarkers play a significant role in the early detection and diagnosis of psychiatric disorders. Elevated inflammatory and hormonal markers provide measurable biological evidence of psychiatric dysfunction, supporting a shift toward more objective, data-driven psychiatric diagnosis. The findings highlight the importance of integrating biological measures with clinical assessment to improve accuracy, early intervention, and personalized mental healthcare.

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