Original Article

Cukurova Anestezi ve Cerrahi Bilimler Dergisi

Psychiatric Burden in Adult Patients with Common Variable Immunodeficiency: A Single-Center Cross-Sectional Study

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Abstract

Background: Common Variable Immunodeficiency (CVID) is characterized by recurrent infections and chronic complications. While the infectious burden of CVID has been extensively studied, psychiatric comorbidities remain underrecognized. This study aimed to evaluate psychiatric symptom burden and associated factors in adult CVID patients receiving immunoglobulin replacement therapy. **Methods:** Sixteen adult patients with CVID were included in this cross-sectional study. Demographic and clinical data were collected retrospectively. Anxiety and depressive symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS). Psychiatric diagnoses were classified according to DSM-5 criteria. Infection frequency before and after immunoglobulin replacement therapy was compared using the Wilcoxon signed-rank test. Associations between clinical variables and HADS scores were analyzed using nonparametric tests. **Results:** The mean age of the patients was 43.2 ± 14.9 years, and 50% were female. Immunoglobulin replacement therapy was associated with significant reductions in annual pneumonia ($p=0.001$), sinusitis ($p=0.003$), and antibiotic use ($p=0.001$). Clinically significant anxiety (HADS-A ≥11) was observed in 50% of patients, and depressive symptoms (HADS-D ≥11) in 56.3%. Eight patients (50%) met DSM-5 criteria for at least one psychiatric disorder. Anxiety and depressive scores were strongly correlated ($\rho=0.939$, $p<0.001$). Social support was significantly associated with both anxiety ($p=0.014$) and depressive symptoms ($p=0.049$), whereas diagnostic delay and immunoglobulin replacement therapy delay were not. **Conclusion:** Despite effective control of infectious complications with immunoglobulin replacement therapy, psychiatric symptom burden remains high in adult CVID patients. Perceived social support appears to be an important determinant of psychological well-being in this population.

Keywords: Common Variable Immunodeficiency; Primary Immunodeficiency; Anxiety; Depression; Immunoglobulin Replacement Therapy

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1. Introduction

Inborn errors of immunity (IEI) represent a heterogeneous group of disorders characterized by susceptibility to infections, autoimmunity, allergy, and malignancy. According to the 2022 update of the International Union of Immunological Societies, 485 genes

have been identified in association with IEI. Although these conditions are rare, they impose a substantial social and economic burden[1]. Among IEIs, selective IgA deficiency is the most common, followed by Common Variable Immunodeficiency (CVID)[2]. Early diagnosis improves survival and reduces disease-related costs; however, diagnostic delay remains frequent in this patient population[3–5]. Even after diagnosis, appropriate replacement therapy with intravenous immunoglobulin (IVIG) may not always be initiated[3].

In addition to the challenges associated with delayed diagnosis, patients require lifelong periodic immunoglobulin therapy, must cope with an increased risk of infections, and frequently experience social restrictions[6,7]. Particularly in patients whose disease onset occurs during childhood, the chronic disease burden may contribute to increased psychiatric morbidity[6–8]. While several studies have investigated psychiatric comorbidities in pediatric patients with IEI, data regarding adult patients remain limited. In this study, we aimed to evaluate the psychiatric burden in a well-defined adult CVID cohort and to investigate its association with indicators of disease severity.

2. Methods

2.1. Study Design and Participants

This cross-sectional study was conducted at the Adult Allergy and Immunology Clinic of a tertiary care training and research hospital between January 2020 and December 2025. Adult patients (≥18 years) diagnosed with CVID according to the diagnostic criteria of the European Society for Immunodeficiencies were included. Patients with cognitive impairment preventing completion of the questionnaires and those experiencing an acute infection at the time of psychiatric assessment were excluded. The study protocol was approved by the local Ethics Committee, and written informed consent was obtained from all participants.

2.2. Clinical and Laboratory Assessment

Demographic characteristics including age, sex, BMI, educational status, marital status, employment status, living conditions, and the presence of social support were recorded. Perceived social support was assessed based on patient self-report and categorized as present or absent. Clinical data obtained from medical records included annual frequency of otitis, sinusitis, and pneumonia episodes, annual number of antibiotic courses, infection-related hospitalizations, and bronchiectasis (confirmed by high-resolution CT). Autoimmune comorbidities, IVIG treatment status, dose, and treatment delay history were also documented. Laboratory parameters included baseline serum immunoglobulin levels (IgG, IgA, IgM, IgE), CRP, ESR, CD4+ and CD8+ T-cell counts, CD4/CD8 ratio, CD19+ B-cell count, naïve B cells, and class-switched memory B cells.

2.3. Psychiatric Assessment

Psychiatric burden was assessed using the Hospital Anxiety and Depression Scale (HADS), a validated 14-item self-report questionnaire with two subscales: anxiety (HADS-A) and depression (HADS-D), each scored 0–21. A cut-off value of ≥11 was considered indicative of clinically significant symptoms. The validated Turkish version was used. Psychiatric diagnoses were also evaluated according to DSM-5 criteria based on documented psychiatric evaluations and existing clinical records.

2.4. Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Normality was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean ± SD or median (IQR). Categorical variables were presented as frequencies and percentages. Group comparisons used the Mann–Whitney U test and

Fisher's exact test. Correlations were evaluated using Spearman's correlation analysis. A two-tailed p-value <0.05 was considered statistically significant.

3. Results

A total of 22 patients were initially screened. One patient was excluded due to death and five were being followed in other centers, resulting in a final study population of 16 adult patients. Demographic and clinical characteristics are presented in Table 1.

Table 1. Demographic and clinical characteristics (n=16)

Variable	Value
Age, mean ± SD	43.2 ± 14.9
Female sex, n (%)	8 (50%)
Diagnostic delay, mean ± SD (years)	38.5 ± 17.4
Bronchiectasis, n (%)	12 (75%)
Any autoimmune comorbidity, n (%)	5 (31.3%)
Living alone, n (%)	9 (56.3%)
Social support present, n (%)	10 (62.5%)

The mean age was 43.2 ± 14.9 years (range: 23–69). Eight patients (50%) were female. Mean BMI was 22.5 ± 3.8 kg/m². Mean diagnostic delay was 38.5 ± 17.4 years. Allergic rhinitis was present in 13 patients (81.3%) and asthma in 7 (43.8%). Autoimmune comorbidities were present in 5 patients (31.3%). Seven patients (43.8%) were employed. Ten patients (62.5%) reported having social support.

Immunoglobulin replacement therapy was associated with significant reductions in annual pneumonia episodes, sinusitis, and antibiotic courses (all $p \leq 0.003$). Infection-related hospitalizations tended to decrease but did not reach statistical significance ($p=0.071$) (Table 2).

Table 2. Infection outcomes before and after immunoglobulin replacement therapy

Variable	Before IVIG (mean)	After IVIG (mean)	p-value
Pneumonia (annual)	2.6	0.25	0.001
Sinusitis (annual)	3.1	0.44	0.003
Otitis (annual)	1.9	0.13	—
Antibiotic courses	6.2	1.0	0.001
Hospitalization days	8.8	0	0.071

Eight patients (50%) had at least one DSM-5 psychiatric diagnosis. The most common diagnosis was major depressive disorder (n=6, 37.5%), followed by anxiety disorders (n=2, 12.5%). Seven patients (43.8%) were receiving psychiatric medication at the time of evaluation (Table 3).

Table 3. Distribution of DSM-5 psychiatric diagnoses in adult CVID patients (n=16)

DSM-5 Category	Included Diagnoses	n (%)
Depressive Disorders	Major depressive disorder	6 (37.5%)
Anxiety Disorders	Generalized anxiety disorder, panic disorder, social anxiety disorder	2 (12.5%)
OCD and Related Disorders	Obsessive-compulsive disorder	1 (6.3%)
Sleep-Wake Disorders	İnsomnia disorder, sleep apnea	1 (6.3%)

Mean HADS-A score was 13.3 ± 9.6 and mean HADS-D score was 12.3 ± 7.8. Clinically significant anxiety (HADS-A ≥11) was observed in 8 patients (50%) and depressive symptoms (HADS-D ≥11) in 9 patients (56.3%). Anxiety and depressive symptom scores were strongly correlated ($\rho=0.939$, $p<0.001$). Social support was significantly associated with both anxiety ($p=0.014$) and depressive symptoms ($p=0.049$). Living alone was not

significantly associated with either anxiety or depression scores (both p=0.295). Diagnostic delay and IVIG treatment delay were not significantly associated with HADS scores (Table 4).

Table 4. Factors associated with HADS scores

Variable	HADS-A p value	HADS-D p value
Diagnostic delay	0.557	0.474
Immunoglobulin replacement therapy delay	0.10	0.08
Antibiotic prophylaxis	Not significant	Not significant
Living alone	0.295	0.295
Social support	0.014	0.049

4. Discussion

In this single-center adult CVID cohort, psychiatric symptom burden remained substantial despite significant improvement in infection-related outcomes following immunoglobulin replacement therapy. Half of the patients met DSM-5 criteria for at least one psychiatric disorder, and more than half exhibited clinically significant depressive symptoms. Perceived social support was significantly associated with both anxiety and depressive symptom severity, whereas diagnostic delay and treatment delay were not. These findings suggest that, beyond infectious disease control, psychosocial determinants may play a critical role in shaping psychological well-being in adult patients with CVID. Although several studies have investigated anxiety and depressive symptoms in children with primary immunodeficiencies and their families, data regarding adult patients remain limited[8]. Impaired quality of life is expected in chronic diseases; however, previous reports suggest that the impact may be greater in patients with immunodeficiencies compared to other chronic conditions such as diabetes or arthritis[6]. These findings emphasize the importance of a multidisciplinary approach beginning at the time of diagnosis. Psychological assessment in this patient population is commonly performed using screening tools such as the Hospital Anxiety and Depression Scale[9]. Nevertheless, our findings highlight the need for disease-specific assessment tools tailored to patients with inborn errors of immunity.

The mean diagnostic delay in our cohort was 38.5 ± 17.4 years. Diagnostic delay is frequently observed in patients with CVID[10,11]. Delayed diagnosis in CVID has been associated with increased morbidity and long-term complications[12–14]. In our study population, all patients were diagnosed in adulthood, highlighting the ongoing challenges in early recognition of CVID. Long-term follow-up studies have reported substantial morbidity and mortality in CVID cohorts[13,15]. In contrast, mortality in our cohort was low, which may reflect differences in disease severity, follow-up duration, or improved management strategies.

Immunoglobulin replacement therapy led to a significant reduction in infection frequency, including pneumonia, sinusitis, and antibiotic use. These findings are consistent with previous reports demonstrating the effectiveness of immunoglobulin therapy in reducing infectious morbidity and improving overall clinical stability in CVID patients[16,17]. Reduced infection burden may also decrease healthcare utilization and antibiotic exposure. However, despite improved infection control, psychiatric symptom scores remained elevated, suggesting that psychological distress in CVID may not be solely attributable to infection frequency or disease severity.

Importantly, perceived social support emerged as a significant determinant of both anxiety and depressive symptoms, whereas living alone and historical disease-related factors were not associated with psychiatric burden[18]. The correlation between anxiety and depression scores observed in our patients is consistent with findings reported in the

literature[18]. Routine assessment of psychological well-being and social support may therefore represent an important component of comprehensive CVID management. Not only CVID, but inborn errors of immunity as a whole, have been underrepresented in quality-of-life research[19,20]. Studies addressing unmet psychosocial needs in this population are essential in order to improve holistic patient care.

The main limitations of this study include its small sample size and single-center design, which limit generalizability. Given the rarity of CVID, these findings should be interpreted as preliminary. Furthermore, the absence of a healthy control group limits direct comparison of psychiatric symptom burden with the general population. Additionally, the cross-sectional nature of psychiatric assessment precludes causal inference.

5. Conclusion

Despite effective control of infectious complications with immunoglobulin replacement therapy, psychiatric symptom burden remains high in adult CVID patients. Perceived social support appears to be an important determinant of psychological well-being in this population. Routine psychiatric screening and psychosocial support should be considered as integral components of comprehensive CVID management. Larger, multicenter prospective studies are warranted to confirm these preliminary findings.

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Ethical Approval: Ethics Committee approval was obtained prior to the study from Marmara University Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Data Availability: The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author on reasonable request.

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