Original Article

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The Impact of Immunoglobulin Replacement Therapy on Antibiotic Need in Adult Patients with Inborn Errors of Immunity

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Abstract

Aim: Patients with inborn errors of immunity (IEI) have a higher frequency of infections and long-term antibiotic usage. We aimed to assess the effects of immunoglobulin replacement therapy (IgRT) on infection rates, antibiotic usage, and treatment outcomes in patients with IEI.

Methods: We retrospectively analyzed demographic data, infection frequency, antibiotic prescriptions, and IgRT in 122 IEI patients between March 2014 and September 2023. Specific IEI diagnoses were made following the European Society for Immunodeficiencies criteria.

Results: The median age of patients was 29 years [interquartile range (IQR): 23-40], with 54.1% being male. The median age at diagnosis was 25 years (IQR: 13-36), with a diagnostic delay of 96 months (IQR: 24-180). IgRT was administered to 74.5% of patients, with a median treatment duration of 20 years (IQR: 10-33.5). Antibiotic use was higher in patients receiving IgRT (median: 27, IQR: 16-42) compared to those not on IgRT (median: 14, IQR: 8-22; $p<0.001$). Patients with bronchiectasis had lower baseline immunoglobulin G, $CD19^+$, and natural killer cell counts, with more frequent antibiotic use, though hospitalization rates were similar to those without bronchiectasis. Immunoglobulin replacement therapy use was higher in the bronchiectasis group (61.5%, $p<0.001$). No significant differences in antibiotic use or hospitalization rates were observed between intravenous and subcutaneous IgRT groups.

Conclusion: Patients with IEI face significant respiratory infections despite IgRT and prophylactic antibiotics. Bronchiectasis is a key risk factor for increased antibiotic use. Early diagnosis and personalized treatment are crucial in reducing infection burden and improving outcomes in this population.

Keywords: Bronchiectasis, immunoglobulin replacement therapy, inborn errors of immunity, prophylactic antibiotics, respiratory infection, primary immunodeficiency

Introduction

Inborn errors of immunity (IEI), previously referred to as primary immunodeficiencies, are a diverse group of over 450 genetically determined disorders characterized by defects in various immune system components (1). These defects can compromise the immune system's ability to respond appropriately to pathogens, increasing susceptibility to infections, autoimmune diseases, and malignancies.

Patients with IEI often experience recurrent, severe, or unusual infections, which can significantly impact their quality of life and may lead to life-threatening complications if not managed effectively (2). IEI lead to specific infection susceptibilities. For example, individuals with humoral immune deficiencies are more prone to infections by encapsulated bacteria due to a lack of antibody defense, though they can still combat intracellular infections. In contrast, those with combined immunodeficiency (CID) are highly susceptible to opportunistic pathogens, including viruses, mycobacteria, protozoa, and fungi, because of T-cell deficiencies. Patients with chronic granulomatous disease have impaired phagocyte function, making them particularly vulnerable to infections from mycobacteria,

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fungi, and certain bacteria like *Staphylococcus aureus* and *Escherichia coli*.

Respiratory infections are common and often the first sign of IEI, leading to significant hospitalizations and fatalities in affected individuals. Reducing the infection burden is crucial for improving life expectancy. Encapsulated bacteria are frequently the cause, though viral infections are also common (3,4). Preventive strategies typically include immunoglobulin replacement therapy (IgRT), facial masks, social distancing, and prophylactic antibiotics (5-7). The use of intravenous immunoglobulin (IVIG) in these patients has provided clear benefits by significantly reducing acute and chronic infections. Immunoglobulin replacement therapy should be initiated in all phenotypes of severe CID (8). However, despite these interventions, many IEI patients continue to experience respiratory infections, increasing their risk of developing bronchiectasis (9-11).

The study hypothesized that IgRT would impact the frequency of prescribed antibiotics, the rate of infections, and the hospitalization rates due to infections among patients with IEI. By examining a cohort of IEI patients, we seek to provide a comprehensive overview of current clinical practices and their outcomes.

Methods

This retrospective observational cohort involved reviewing medical records of IEI patients who were under the care of the allergy immunology clinic at a tertiary hospital in Istanbul.

The inclusion criteria for this study were as follows: i) a confirmed diagnosis of IEI and ii) age over 18 years. Patients with secondary immunodeficiency were excluded from the study. Specific IEI diagnoses were made following the European Society for Immunodeficiencies criteria (12). The classification of patients with IEI was made based on the International Union of Immunological Societies (IUIS) and Middle East, North Africa, and Turkey (6,13).

Data Collection

Data were collected retrospectively from the medical records of the included patients between 2014 and 2023. The following variables were extracted: Demographic characteristics, including age, gender, and relevant family history; annual antibiotic prescriptions, including prophylactic and therapeutic use, were recorded. Over the study period, the number of hospitalizations for infection and without infection was documented. Comorbidities, such as autoimmune diseases, chronic lung disease, or malignancies, were gathered. A comprehensive list of medications, including those used for managing IEI, and details on IVIG and subcutaneous immunoglobulin (SCIG) therapies. Laboratory results, including complete blood counts, baseline immunoglobulin levels, and other relevant immunological parameters, such as lymphocyte subsets, were collected. Radiological findings, including Thorax computerized tomography performed during the study period, were reviewed to assess bronchiectasis or structural abnormalities related to immunodeficiency.

Ethical Considerations

The study was approved by the Ethics Committee of Marmara University, Faculty of Medicine (date: 10/7/22, approval no.: 1354). It was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients or their legal guardians, where applicable, for using their medical records for research purposes.

Statistical Analysis

All data was analyzed using the SPSS statistical software package version 22 (IBM Corp., USA) and GraphPad Prism 8 (GraphPad software California, USA). Median and interquartile range (IQR) values for continuous variables and the frequency and percentage for the categorical variables were calculated. Differences between ordinal data were evaluated with the Mann-Whitney U test and the Kruskal-Wallis test. Categorical variables were evaluated with the 2-tailed chi-square or Fisher's exact tests. A p-value of less than 0.05 was considered the significance level for differences.

Results

The study included 122 patients with IEI at a tertiary care hospital in Istanbul. The median age of all patients was 29 years (IQR: 23-40), and 54.1% (n=66) were male. The median age at diagnosis was 25 years (IQR: 13-36). The median diagnostic delay was 96 months (IQR: 24-180), and the median duration of IgRT was 20 years (IQR: 10-33.5). Table 1 summarizes the patients' demographic characteristics and laboratory results. Figure 1 displays the classification of diagnosis based on IUIS criteria.

A history of pneumonia was present in 84 patients (68.8%), sinusitis in 64 patients (52.4%), and otitis in 46 patients (37.7%). Immunoglobulin replacement therapy was administered to 91 patients (74.5%), and prophylactic antibiotic therapy was given to 54 patients (44.2%). A total of 64 (70.3%) patients received IVIG therapy, while 27 (29.6%) patients were on subcutaneous IgRT. The median frequency of outpatient prescribed antibiotics was 22 (IQR: 12-40). The median number of hospitalizations due to infections was 0 (IQR: 0-1). Figure 2 shows the treatment algorithm of all study groups.

The frequency of antibiotic use was higher in patients receiving IgRT, with a median of 27 (IQR: 16-42), compared to those not receiving IgRT [14 (IQR: 8-22), $p<0.001$]. There was no significant difference

between the two groups regarding hospitalization due to infections, non-infection-related hospitalizations, or total hospitalizations. $CD19^+$ and natural killer (NK) cell counts were significantly lower in the group receiving IgRT [median for $CD19^+$: 102 (IQR: 35.5-234) vs. 194 (IQR: 155-303), p=0.004; median for NK: 81 (IQR: 37.5-160) vs. 195 (IQR: 69.7-297), p=0.006]. Table 2 summarizes the demographic and laboratory characteristics of the groups receiving and not receiving IgRT. When comparing the IVIG and SCIG groups, there was no difference in hospitalizations due to infections, non-infection-related hospitalizations, or total hospitalizations. The frequency of antibiotic use did not differ significantly between the IVIG and SCIG groups [median: 24, (IQR: 13.2-42.7) vs. 33 (IQR: 21-42); p=0.12].

The age of hospital admission for patients with bronchiectasis was significantly lower than those without bronchiectasis [median years: 18 (IQR: 7-32.5) vs. 27 (IQR: 18.7-38.2), p=0.004]. The presence of bronchiectasis was statistically significant regarding the frequency of antibiotic use. The median frequency of antibiotic use was 33.5 (IQR: 21-57.2) in the bronchiectasis group, compared to 15.5 (IQR: 9-24) in the non-bronchiectasis group (p<0.001). There was no significant difference in

Table 1. Demographic features of all study populations (n=122)	
Gender; male (%)	66 (54.09)
Current age, year (median, IQR)	29 (23-40)
Age at diagnosis (median year, IQR)	25 (13-36)
Age at admission to immunology (median year, IQR)	24 (10-37)
Symptoms onset-age (median year, IQR)	9.5 (3-25)
Diagnostic delay (median months, IQR)	96 (24-180)
Treatment	**n (%)**
IgRT -Intravenous route -Subcutaneous route No IgRT -Prophylactic antibiotic	91 (74.5) 64 (70.3) 27 (29.7) 31 (25.4) 54 (44.2)
Number of prescribed antibiotics (median, IQR)	22 (12-40)
Hospitalization, n, IQR -Infection-related -Non-infection related -Total	 0 (0-1) 0 (0-0.25) 0 (0-1)
Lung screening	**n (%)**
-Bronchiectasis, n (%) -Number of affected lobes, mean±SD	60 (49.1) 1.47±1.67
Types of bronchiectasis	
-Tubular -Cystic	36 (60) 24 (40)
Complete blood count	**Median (IQR)**
Leucocytes ($x10^3$/mL) Lymphocytes ($x10^3$/mL) Hemoglobin ($x10^3$/mL) Granulocytes ($x10^3$/mL) Eosinophils ($x10^3$/mL) Monocytes ($x10^3$/mL) Platelets ($x10^3$/mL)	6550 (5200-8625) 1800 (1200-2600) 13.2 (11.5-14.5) 3970 (2900-5225) 30 (10-72.5) 500 (400-700) 242 (180-299)
Serum immunoglobulins	**Median (IQR)**
IgG (baseline) (mg/dL) IgG (trough) (mg/dL) IgA (baseline) (mg/dL) IgM (baseline) (mg/dL) IgE (baseline)	486 (277-1007) 989 (837-1331) 18 (5-80) 40 (13-130) 1 (0.2-14)
Lymphocyte subsets (absolute count)	**Median (IQR)**
$CD3^+$ $CD4^+$ $CD8^+$ $CD19^+$ NK	1324 (862-1915) 642 (413-906) 599 (409-867) 141 (51-266) 91 (41-189)

Values are presented as median [IQR], and categorical variables are presented as n (%). Differences between groups were evaluated using chi-square or Fisher's exact test, as appropriate.
IQR: Interquartile range, NK: Natural killer, IgRT: Immunoglobulin replacement therapy, SD: Standard deviation, Ig: Immunoglobulin

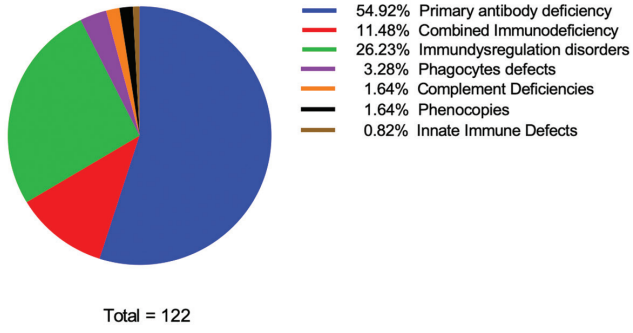

Figure 1. Classification of diagnoses according to IUIS criteria
IUIS: International Union of Immunological Societies

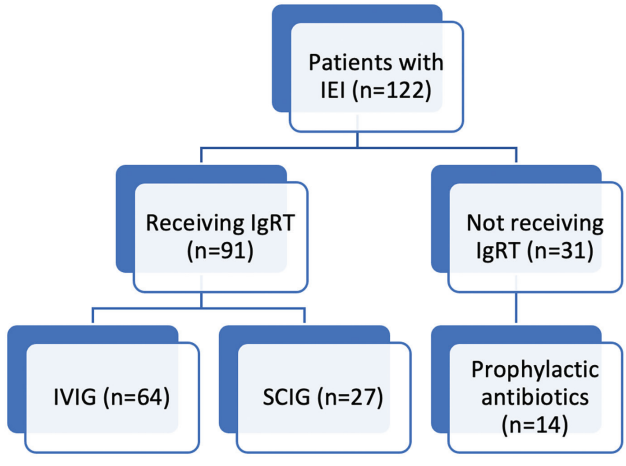

Figure 2. Treatment algorithm for patients with inborn errors of immunity
IEI: Inborn errors of immunity, IgRT: Immunoglobulin replacement therapy, IVIG: Intravenous immunoglobulin, SCIG: Subcutaneous immunoglobulin

the frequency of hospitalizations due to infections, non-infection-related hospitalizations, or total hospitalizations between those with and without bronchiectasis. Baseline immunoglobulin G (IgG) levels were significantly lower in patients with bronchiectasis compared to those without [median: 440 (IQR: 145-788) vs. 604 (IQR: 347-1090), p=0.03]. $CD19^+$ and NK cell counts were also significantly lower in the bronchiectasis group compared to the non-bronchiectasis group [median $CD19^+$: 102 (IQR: 33-218) vs. 168 (IQR: 63.7-294), p=0.04; median NK: 72.5 (IQR: 34.3-159) vs. 119.5 (IQR:58-235), p=0.02]. The rate of IgRT was higher in the bronchiectasis group (56 patients, 61.5%; p<0.001). Table 3 summarizes the demographic and laboratory characteristics of patients with and without bronchiectasis.

When comparing patients on prophylactic antibiotics to those not receiving them, the frequency of antibiotic use was notably higher among those on prophylactic therapy [median: 33.5 (IQR: 21-46) vs median: 14 (IQR: 8-29), p<0.001]. However, the two groups observed no significant differences in other clinical parameters.

Over a 9-year follow-up of 122 patients, a total of 3,606 infection episodes were documented, resulting in an antibiotic treatment rate of 3.28 infections per patient-year.

In the past five years, 12 (9.8%) patients experienced 18 infection episodes requiring hospitalization while on IgRT. Among these, 12 episodes were due to pneumonia, and 2 were caused by pyelonephritis. Additionally, 4 patients received outpatient treatment for pneumonia. None of the patients had low IgG trough levels.

Table 2. Clinical and immunological features of patients based on the IgRT

	With IgRT, n=91	**Without IgRT, n=31**	**p-value**
Gender, male (%)	48 (52.7)	19 (61.2)	0.67
Current age (years, median, IQR)	29 (23-42)	28 (23-38)	0.59
Age at admission (years, median, IQR)	20 (7-37)	25 (21-37)	0.18
Age at symptom onset (years, median, IQR)	7 (3-24)	12 (7-29)	0.08
Age at diagnosis (years, median, IQR)	24 (11-36)	25 (22-36)	0.1
Age at IgRT (years, median, IQR)	20 (10-34.5)	23 (10-30)	0.8
Treatment n, (%) **Prophylactic antibiotic**	40 (74)	14 (26)	1
Number of prescribed antibiotics (median, IQR)	27 (16-42)	14 (8-22)	<0.001
Hospitalization, n, IQR			
Infection-related Non-infection related Total	0 (0-1) 0 (0-1) 0 (0-2)	0 (0-0) 0 (0-0) 0 (0-1)	0.09 0.7 0.15
Complete blood count			
Leucocytes ($x10^3$/mL) Lymphocytes ($x10^3$/mL) Hemoglobin ($x10^3$/mL) Granulocytes ($x10^3$/mL) Eosinophils ($x10^3$/mL) Monocytes ($x10^3$/mL) Platelets ($x10^3$/mL)	6500 (5000-8600) 1700 (1000-2700) 13 (10.8-14) 3800 (2720-5300) 23 (60-70) 500 (400-700) 234 (164-295)	6700 (5900-8700) 2000 (1500-2400) 13.9 (12-15.2) 4200 (3200-5100) 20 (50-93) 500 (400-600) 254 (214-309)	0.4 0.28 0.008 0.4 0.01 0.84 0.17
Serum immunoglobulins, median (IQR)			
IgG (baseline) (mg/dL) IgG (trough) (mg/dL) IgA (baseline) (mg/dL) IgM (baseline) (mg/dL) IgE (baseline) (mg/dL)	395 (219-635) 989 (847-1371) 10 (4-45) 25 (10-80.5) 0.5 (0.2-5.2)	981 (484-1176) 1000 (615-1322) 39 (5-253) 92 (26-174) 6.5 (0.4-70)	<0.001 0.4 0.01 0.002 0.01
Lymphocyte subsets (absolute count, median, IQR)			
$CD3^+$ $CD4^+$ $CD8^+$ $CD19^+$ NK	1287 (800-1946) 619 (355-900) 599 (413-914) 102 (35-234) 81 (37-160)	1458 (997-1897) 683 (479-913) 592 (401-802) 194 (155-303) 195 (69-297)	0.6 0.5 0.6 0.004 0.006

Comparisons between groups were performed using the Mann-Whitney U test for non-normally distributed data. Differences between groups were evaluated using chi-square or Fisher's exact test, as appropriate.
IQR: Interquartile range, NK: Natural killer, IgRT: Immunoglobulin replacement therapy, Ig: Immunoglobulin

Table 3. Clinical and immunological features of patients based on the presence of bronchiectasis			
	With bronchiectasis	**Without bronchiectasis**	**p-value**
Gender, male (%)	36 (60)	30 (48.3)	0.2
Current age (years, median, IQR)	28.5 (22.2-40.7)	29 (23-40)	0.88
Age at admission (years, median, IQR)	18 (7-32.5)	27 (18.7-38.2)	0.004
Age at symptom onset (years, median, IQR)	6 (2.2-17.7)	15.5 (7-29)	<0.001
Age at diagnosis (years, median, IQR)	21 (9-32)	27.5 (19-38)	0.01
Age at IgRT (years, median, IQR)	20 (8-33)	27.5 (17-36)	0.06
Treatment n, (%) IgRT -Intravenous route -Subcutaneous route No IgRT -Prophylactic antibiotic	 56 (61.5) 34 (60.7) 22 (39.2) 4 (6.6) 30 (50)	 35 (38.4) 30 (85.7) 5 (14.2) 27 (43.5) 24 (38.7)	 <0.001 0.2
Number of prescribed antibiotics (median, IQR)	33.5 (21-57.2)	15.5 (9-24)	<0.001
Hospitalization, n, (IQR) Infection-related Non-infection related Total	 0 (0-1) 0 (0-1) 0 (0-2)	 0 (0-0) 0 (0-0) 0 (0-1)	 0.6 0.6 0.3
Complete blood count			
Leucocytes (x10^3/mL) Lymphocytes (x10^3/mL) Hemoglobin (x10^3/mL) Granulocytes (x10^3/mL) Eosinophils (x10^3/mL) Monocytes (x10^3/mL) Platelets (x10^3/mL)	6435 (5125-8975) 1950 (1025-2600) 12.8 (10.6-14.4) 3870 (2785-5475) 22 (4-70) 500 (400-700) 224 (152-305)	6650 (5350-8425) 1700 (1300-2550) 13.3 (11.8-14.7) 4050 (2975-4950) 42 (16-90) 500 (400-600) 251 (210-299)	0.8 0.9 0.1 0.8 0.03 1 0.2
Serum immunoglobulins, median (IQR)			
IgG (baseline) (mg/dL) IgG (trough) (mg/dL) IgA (baseline) (mg/dL) IgM (baseline) (mg/dL) IgE (baseline) (mg/dL)	440 (145-788) 982 (840-1305) 5.5 (4-43) 25 (10-124) 0.2 (0.2-4.2)	604 (347-1090) 1026 (803-1429) 27 (7-124) 47 (18-132) 2.9 (0.2-27)	0.03 0.8 0.01 0.2 0.01
Lymphocyte subsets (absolute count, median, IQR)			
$CD3^+$ $CD4^+$ $CD8^+$ $CD19^+$ NK	1354 (847-2111) 589 (333-906) 647(440-972) 102 (33-218) 72 (34-159)	1299 (918-1897) 713 (490-903) 560 (387-801) 168 (64-294) 119 (58-235)	0.6 0.2 0.09 0.04 0.02
Comparisons between groups were performed using the Mann-Whitney U test for non-normally distributed data. IQR: Interquartile range, NK: Natural killer, IgRT: Immunoglobulin replacement therapy, Ig: Immunoglobulin			

Discussion

Based on our findings among IEI patients, the frequency of prescribed antibiotics was higher in the IgRT group compared to the non-IgRT group. Additionally, the frequency of antibiotic use was higher in patients with bronchiectasis than those without bronchiectasis. Within the IgRT group, no significant differences were observed regarding hospitalization rates and antibiotic usage frequency between patients receiving IVIG and those receiving SCIG.

One of the key observations from our study is the substantial diagnostic delay, with a median of 8 years from the onset of symptoms to diagnosis. This delay is concerning, as earlier diagnosis and intervention could potentially mitigate some of the severe complications associated with IEI, such as recurrent infections and the development of bronchiectasis. In a study conducted with common variable immune deficiency (CVID) cases, patients with bronchiectasis had significantly lower trough IgG levels and efficacy and required a longer time to achieve target IgG levels than those without bronchiectasis. This delay was significantly associated with an increased frequency of infections. The presence of bronchiectasis was significantly associated with a prolonged time to reach target IgG levels. These long-term differences between

patients with and without bronchiectasis have important clinical implications (14). According to our findings, patients with bronchiectasis required more frequent antibiotic use despite maintaining adequate trough IgG levels. This result aligns with the existing literature.

The median age at diagnosis (25 years) suggests that many patients endure years of unmanaged symptoms before receiving appropriate care. This underscores the need for increased awareness and early screening, particularly in high-risk populations.

One of the mainstays of treatment for many IEI patients is IgRT. This therapy helps to restore some of the immune functions by supplying patients with the necessary antibodies to fight infections and modulate immune responses (5,15-17). Immunoglobulin replacement therapy has been shown to reduce the frequency and severity of infections in patients with antibody deficiencies and other forms of IEI (18).

Respiratory infections emerged as a predominant issue, with a high prevalence of pneumonia, sinusitis, and otitis among the patients. The fact that 68.8% of patients had a history of pneumonia indicates the vulnerability of IEI patients to severe respiratory infections, which is consistent with previous studies. Despite the widespread use of IgRT and prophylactic antibiotics, many patients continue to experience frequent infections, suggesting that current preventive strategies may not be entirely adequate for all individuals. This persistent risk of infections emphasizes the importance of personalized treatment approaches, which may include more aggressive prophylactic measures or adjustments in IgRT dosing.

Despite adequate IgRT, recurrent respiratory tract infections remain the most common clinical manifestation of CVID (19), often leading to the development of progressive bronchiectasis (9,10,20). While these infections were traditionally attributed mainly to encapsulated bacteria, recent studies also suggest a significant role for viral infections (4,21,22). Although respiratory tract infections are prevalent and severely impact the quality of life in primary antibody deficiency syndromes, the specific nature of the symptoms during these episodes is not well understood (23). Patients frequently receive antibiotics to manage respiratory infections, both as "rescue" treatments for acute episodes and as prophylactic measures to reduce infection frequency (24). However, the specific symptomatic triggers for initiating antibiotics and the clinical outcomes of these interventions remain unclear.

In a study involving 278 participants, despite receiving adequate IgRT, 6.9% continued to experience severe or very severe infections. Additionally, a substantial proportion of participants (84.9%) reported that infections imposed significant limitations on their daily lives. Notably, 18.3% of the participants who were dissatisfied with their treatment demonstrated a higher disease burden, characterized by more frequent non-routine healthcare visits, increased antibiotic use, and more days missed from school, work, or other responsibilities (25). In this study, the severe infection rate among patients with IgRT was 9.8%, similar to other studies. Our data also show that patients receiving IgRT had a higher frequency of antibiotic use than those not on IgRT. This finding could reflect a more severe clinical phenotype in the IgRT group, necessitating increased antibiotic prophylaxis to prevent infections. Interestingly, while IgRT was associated with lower $CD19^+$ and NK cell counts, it did not significantly impact hospitalization rates for infections or other causes. This suggests that while IgRT effectively reduces the severity of infections, it may not completely eliminate the need for hospital care, especially in patients with more severe immune deficiencies.

Despite these interventions, a significant number of IEI patients continue to experience respiratory infections, which heightens the risk of developing bronchiectasis (11). In a cohort study, patients with CVID observed over an average follow-up period of 11 years, 34.2% had chronic lung disease at the time of diagnosis, and this percentage increased to 46.3% during the follow-up, even with the administration of IgRT (26). Bronchiectasis, a common complication in IEI patients, was associated with more frequent antibiotic use and lower baseline IgG, $CD19^+$, and NK cell counts (5). These findings are in line with the understanding that bronchiectasis often results from chronic and recurrent infections, which may further impair immune function. The lower IgG levels in patients with bronchiectasis underscore the need for careful monitoring and potential adjustments in IgRT to ensure adequate immune protection.

The study also highlights the significant impact of bronchiectasis on the clinical course of IEI. Patients with bronchiectasis had an earlier age of hospital admission and a higher rate of IgRT use, indicating a more severe disease trajectory. This underscores the importance of early detection and management of bronchiectasis in IEI patients, as it can profoundly affect their quality of life and long-term prognosis.

Prophylactic antibiotic therapy is often employed to prevent bacterial infections, which are a common complication in these patients due to their impaired immune systems (20). In our study, patients on prophylactic antibiotics have more frequent antibiotic use despite receiving IgRT.

Study Limitations

Our study has several limitations. First, due to its retrospective design, we were unable to obtain detailed information about the patient's presenting symptoms.

Second, some of the antibiotics prescribed to these patients may have been unnecessary, as they could have been given during viral infections. However, the frequency of antibiotic prescriptions in these patients indicates frequent hospital visits. Despite these limitations, this study provides valuable insights into the impact of IgRT on infection frequency, antibiotic use, and hospitalization rates in severe IEI patients, offering a comprehensive view of clinical practices and outcomes.

Conclusion

Our study reinforces the critical role of early diagnosis, personalized treatment strategies, and vigilant monitoring in managing IEI patients. The high prevalence of respiratory infections and the development of bronchiectasis among these patients indicate the need for ongoing research to optimize preventive and therapeutic interventions. Future studies should focus on identifying biomarkers to predict which patients are at the highest risk for complications like bronchiectasis and tailoring treatment protocols accordingly to improve outcomes. This study provides valuable insights into the clinical efficacy of IgRT profiles in patients with IEI. The findings highlight the significant challenges these patients face, particularly in terms of diagnostic delays, infection-related complications, and the long-term management of their condition. This research will contribute to a better understanding of the challenges in managing these complex conditions and may offer insights into optimizing treatment strategies to improve patient outcomes.

Footnote

Ethics Committee Approval: The study was approved by the Ethics Committee of Marmara University, Faculty of Medicine (date: 10/7/22, approval no.: 1354). It was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from the patients participating in the study.

Financial Disclosure: The author declare that this study has received no financial support.

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