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Immediate Hypersensitivity Reactions to Biologic Drugs in Children with Inflammatory Bowel Diseases

Sinem Polat Terece[a] Hacer Ilbilge Ertoy Karagol[a] Demet Teker Duztas[b] Gizem Koken[a] Hakan Ozturk[b] Dilek Yapar[c] Odul Egritas Gurkan[b] Sinan Sari[b] Buket Dalgic[b] Arzu Bakirtas[a]

[a]Department of Pediatric Allergy, Faculty of Medicine, Gazi University, Ankara, Turkey; [b]Department of Pediatric Gastroenterology, Faculty of Medicine, Gazi University, Ankara, Turkey; [c]Directorate of Muratpasa District Health, Antalya, Turkey

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Keywords
Biologics · Children · Hypersensitivity · Inflammatory bowel diseases

Abstract

Introduction: The increased use of biologic drugs (BDs) may lead to an increase in immediate hypersensitivity reactions (I-HSRs) in pediatric patients with inflammatory bowel disease (IBD). Our aim was to assess I-HSRs to BDs in pediatric IBD, examining frequency, clinical features, management, and associated risk factors. ***Methods:*** All children diagnosed with IBD at our institution between January 1, 2006, and August 1, 2023, and who developed I-HSRs related to any BD were included in the study. ***Results:*** In a study of 197 pediatric IBD patients, 61 used BD. Among these, 52.4% were male, with a median diagnosis age of 145 months (13–215). Out of a total of 1,679 administrations, 6 patients developed I-HSRs (5 with infliximab, 1 with adalimumab), resulting in a frequency of 9.8% per patient and 0.36% per administration. Of these, 66.7% were cases of Type 1 HSRs (skin test positivity $n = 1$), while the rest were infusion-related reactions (anti-drug antibody positivity $n = 4$), all of which were mild to moderate in severity. In the age and gender-adjusted logistic regression model, the presence of any comorbid allergic disease was significantly associated with the occurrence of I-HSR (aOR = 8.35; 95% CI = 1.24–56.38; $p = 0.029$). ***Conclusion:*** The frequency of I-HSRs to BDs in children with IBD is not rare but not severe in the long term. The presence of any comorbid allergic disease is a risk factor for the development of I-HSRs to BDs. © 2024 S. Karger AG, Basel

Introduction

Inflammatory bowel diseases (IBDs) are chronic inflammatory conditions affecting the gastrointestinal tract, characterized by remission and relapses [1]. The main subtypes of IBD are Crohn's disease (CD), ulcerative colitis (UC) and IBD unclassified (IBD-U) [1]. The treatment goals in pediatric IBD are to achieve and maintain remission, improve quality of life, and minimize the adverse effects (AE) of medications [2]. In children, it is crucial to achieve prompt disease control to prevent potential delays in development, growth, and pubertal maturation [2].

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karger@karger.com
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Correspondence to:
Hacer Ilbilge Ertoy Karagol, theilbilge@yahoo.com.au

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Biologic drug (BD) is a biotherapeutic protein product prepared by recombinant DNA technology [3]. These proteins are characterized by a high molecular weight and some are partially of non-human origin [4]. Biologic drugs have significantly changed the treatment approaches and disease progression of IBD in both adults and children [1]. Antitumor necrosis factor-alpha (anti-TNFa) agents, such as infliximab (IFX) and adalimumab (ADA), are utilized in pediatric IBD. Anti-integrin agents such as vedolizumab (VDZ) and anti-IL12/23 agents such as ustekinumab (UST) are commonly utilized as treatment options in pediatric patients with IBD [2].

As the use of BDs has increased, a corresponding rise in hypersensitivity reactions (HSRs) has been observed [5]. When examining HSRs with anti-TNF agents, which are frequently used in the treatment of IBD, the frequency is seen to range from 4.6 to 38.6%. In this study, we aimed to evaluate the frequency of immediate HSRs (I-HSRs) to all BDs in pediatric patients specifically with IBD, describe the clinical characteristics and management of these reactions, and identify risk factors related to the development of I-HSR.

Methods

Patients

All pediatric patients who were diagnosed with IBD between January 1, 2006, and August 1, 2023, were reviewed. The inclusion criteria were being aged 0–18 at diagnosis, using at least one BD for IBD, and attending regular follow-up visits. Patients who did not meet these criteria were non-compliant with the treatment or received immunosuppressive or BDs therapy for indications other than IBD, as well as those with types 2, 3, and 4 HSRs related to BDs, were excluded from the study. Characteristics (gender, age at the diagnosis, type of IBD, duration of follow-up, comorbid allergic [included in atopic dermatitis, food allergy, asthma, allergic rhinitis, and drug allergy], non-allergic chronic diseases, family history of allergic diseases and IBD, presence of extraintestinal manifestations) and treatment status of patients were obtained from medical charts. The study was approved by the Ethics Committee of the Gazi University (Approval No. 2022-942). Informed consent was obtained from parents of patients with specific HSRs testing.

Definitions

Diagnosis of IBD

The diagnosis of IBD was established in accordance with the guidelines, and subtypes were classified as CD, UC, and IBD-U [6].

Biological Drug Administration

IFX, chimeric with 75% human and 25% murine components, was administered intravenously. In the initial dose, a graded challenge protocol was used, followed by subsequent doses using the standard protocol. An accelerated protocol was not employed [7]. ADA, being fully human, is administered subcutaneously (SC) every 2 weeks. In the case of an inadequate response, a switch to weekly administration is considered. VDZ (humanized) was also administered intravenously infusion and UST (fully human) was also administered intravenously infusion for the first dose and subsequent doses given SC [5]. Intravenous BDs were administered in the clinic setting under physician observation. Subcutaneous BDs were initially administered with clinical training at our clinic until patients or their caregivers felt confident to self-administer at home. For those who preferred not to administer SC at home, the injections continued in the clinic. No premedication was applied before the use of any BD.

Immediate Hypersensitivity Reactions

All patients receiving BD treatment were monitored at our pediatric gastroenterology clinic. During their follow-up, if there was suspicion of HSR related to any BD, patients were evaluated by pediatric allergists (H.I.E.K. and A.B.).

We classified reactions occurring within the first 1–6 h after the administration or infusion of BD as I-HSR [4] and graded their severity according to modified Brown criteria as mild, moderate, or severe [8].

The I-HSRs were classified into 4 subgroups [4, 5, 9]:

1. Type 1 HSR (IgE/non-IgE) was defined as the sudden onset of one or more symptoms or findings such as cutaneous (flushing, pruritus, urticaria, angioedema), respiratory (dyspnea, chest tightness, wheezing, cough, oxygen desaturation), throat (itchy, tickle, lump in throat, tightness, swelling, hoarse voice, difficulty swallowing, stridor), cardiovascular (chest pain, tachycardia, bradycardia, hypotension, hypertension, presyncope/syncope), gastrointestinal (nausea, vomiting, diarrhea, abdominal pain), and loss of consciousness, within minutes to a few hours.
2. Cytokine release syndrome (CRS) was defined as quickly developing within minutes to a few hours following exposure and including specific symptoms (headache, low blood pressure, pain of the chest and back, fever, myalgia, arthralgia, and rigors) and nonspecific symptoms (rash, fatigue, dyspnea, throat tightness, dizziness/hypotension, vomiting, diarrhea).

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3. Mixed reactions refer to cases that exhibit overlapping features of both type 1 reactions and CRS.
4. Infusion-related reactions (IRRs) are characterized by the presence of pruritus, flushing, dyspnea, chest discomfort, myalgia, nausea, and headache which usually occurs during the first administration, and premedication with steroids/antihistamines along with a slower infusion rate may prevent the reaction. These reactions are generally self-limiting upon subsequent exposures. The difference between IRRs and CRSs is the self-limiting nature of IRR on repeat exposure and the response to premedication.

Diagnostic Allergy Workup

Patients who experienced I-HSRs with BDs underwent skin testing 4 weeks after the reaction occurred. Patients were checked to ensure they had not taken antihistamines, steroids, or immunosuppressive agents before the skin test, and that they did not have dermographism. If skin prick tests with undiluted forms of the BDs produced negative results, subsequent intradermal tests were conducted using dilutions of 1/100 and 1/10, respectively. The results of the tests were accepted as positive if the wheal area was >3 mm greater than the negative control (0.9% saline). Histamine (10 mg/mL) was used as positive control.

In patients with suspected I-HSR, anti-drug antibodies were collected if available. Solid-phase enzyme-linked immunosorbent assay (ELISA) qualitative method was used to determine non-isotype antibodies to BDs in serum samples.

Statistical Analysis

The data were analyzed using SPSS 22.0. Descriptive statistics were provided as numbers, percentages, mean ± standard deviation, and median (minimum; maximum). Normal distributions for continuous variables were assessed with visual (histograms and probability graphics) and analytic methods (Shapiro-Wilk's test). Measurements of variables determined not to follow a normal distribution will be evaluated between independent binary groups using the Mann-Whitney U test. The frequency differences between groups for categorical variables will be compared using χ^2 tests. Variables that were significant in univariate analyses ($p < 0.05$) were included in the logistic regression analysis to examine their association with the occurrence of I-HSR. Logistic regression analysis and multivariate analyses were performed to identify risk factors for the development of I-HSR with BDs. The statistical significance level of the study was accepted as $p < 0.05$.

Results

Patients Characteristics

Over a study period, 197 (54.8% UC, 44.2% CD, 1% IBD-U) pediatric patients diagnosed with IBD were examined (shown in Fig. 1). Among these patients, it was determined that 61 (31%) had used any BD at any time during the treatment of the disease. The demographic data of patients using BDs are detailed in Table 1. Thirteen of these patients were found to have 16 different comorbid allergic diseases. These were as follows: other drug allergies ($n = 5$), asthma ($n = 4$), food allergy ($n = 3$), allergic rhinitis ($n = 2$), and atopic dermatitis ($n = 2$).

Four different BD were administered a total of 1,679 times in 61 patients (shown in Fig. 2). It was observed that 14 (23%) of them received two different types of BD, and one (1.6%) of them received three different types of BD during the treatment. I-HSRs developed in 6 patients. The frequency of I-HSR was determined 9.8% per patient and 0.36% per administration.

Characteristics of I-HSR

Four of 6 patients developed type 1 HSR, while two developed IRR. The 2 patients who developed IRR had received their first infliximab infusions without any issues. A reaction occurred during the second infusion, which was found to be administered more quickly than the infusion protocol recommended. No reactions occurred in patients from the third infusion onward, which was given at the protocol-specified rate. Mixed reactions and CRS were not detected. All reactions were mild or moderate; no severe reaction was observed.

The skin tests were examined in 5 patients, and 1 of them had positive results. In 5 patients in whom anti-drug antibodies could be evaluated, 4 (80%) were found to be positive. Detailed information about these patients is provided in Table 2.

Management of I-HSR

Patient 1 successfully received infliximab 17 times through an 11-step rapid drug desensitization (RDD) protocol starting at one hundred-thousandth of the cumulative dose was implemented [10]. Patients 2 and 3, who developed IRRs, received subsequent administrations smoothly with appropriate infusion duration. However, in these 3 patients, due to an inadequate treatment response observed during follow-up, IFX was switched to ADA. Patients 4 and 5, who did not accept RDD with the culprit BD, were initiated on UST treatment. Unfortunately, in the case of patient 6, the patient died due to complications associated with IBD before any treatment modification could be made.

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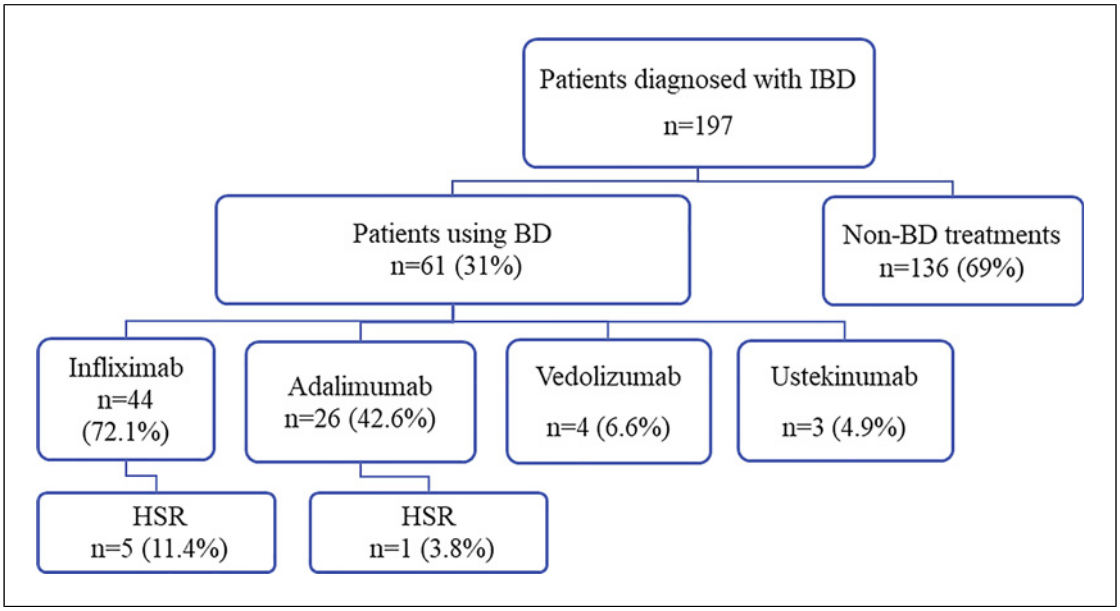


Fig. 1. Study population.

Table 1. Characteristics of patients using BD (*n* = 61)

Age at the diagnosis, months, median (min–max)	145 (13–215)
Male, *n* (%)	32 (52.4)
Subtype of IBD, *n* (%)	
CD	38 (62.3)
UC	21 (34.4)
IBD-U	2 (3.3)
Duration of follow-up, month, median (min–max)	44 (2–210)
Extraintestinal manifestations, *n* (%)	15 (24.6)
Comorbid chronic diseases, *n* (%)	
Allergic	13 (21.3)
Non-allergic	28 (45.9)
History of a previous drug allergy, *n* (%)	5 (8.2)
Family history of allergic diseases, *n* (%)	7 (11.5)
Family history of IBD, *n* (%)	4 (6.6)

CD, Crohn's disease; UC, ulcerative colitis; IBD-U, IBD-unclassified; IBD, inflammatory bowel diseases.

Risk Factors for I-HSR

Patients with or without I-HSRs were compared in terms of gender, age at diagnosis, type of IBD, duration of follow-up, presence of any comorbid allergic disease and its type, drug allergies, comorbid non-allergic chronic diseases, presence of extraintestinal manifestations, duration until the initiation of a BD, and prior use of different BDs. A statistically significant difference was observed between individuals with a comorbid allergic disease, at 33.3% (3 out of 9), and the non-allergic disease group, which had a reaction rate of 5.8% (3 out of 52), with a p value of 0.037, while no significant difference was observed between the groups in terms of other parameters ($p > 0.05$). In the age and gender-adjusted logistic regression model, the presence of any allergic disease was significantly associated with the occurrence of I-HSR (adjusted odds ratio [aOR] = 8.35; 95% CI = 1.24–56.38; $p = 0.029$).

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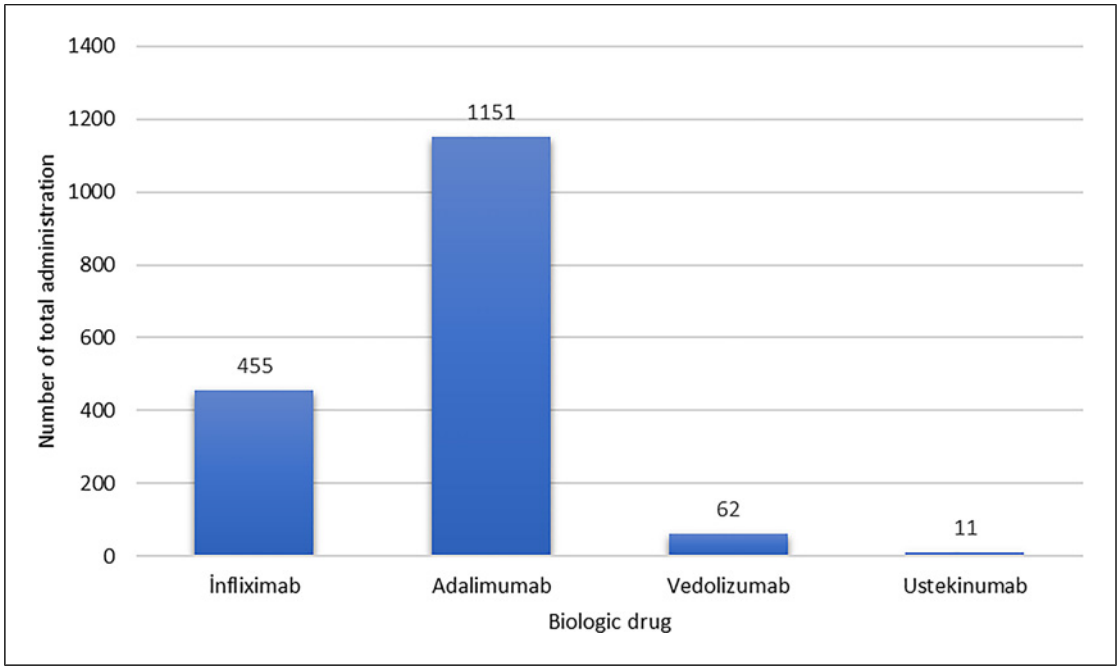


Fig. 2. Number of total administration for each BD.

Discussion

In this study, we evaluated the occurrence of I-HSRs induced by the use of BDs in pediatric IBD patients over 17 years. The frequency of I-HSR per patient is 9.8%, and per administration is 0.36%, and all I-HSRs were noted to be mild to moderate. The presence of any allergic disease increases the development of I-HSRs induced by BD use.

There have been limited studies on BD-HSR in pediatric IBD patients. Results of HSR related to the BD used in IBD have been presented comprehensively along with different disease groups [11]. Most studies focus on an HSR with a single BD type [12–14], while others categorize reactions associated with BDs as "adverse events" or "infusion reactions" [12, 15–17]. In previous studies, immediate and delayed reactions are often combined, leading to reaction frequencies ranging widely from 4.6 to 38.6% [12–14]. Therefore, the frequency of I-HSR in our study aligns with this range. Notably, they reported the highest frequency of 38.6% [12], which they termed "medically significant reactions," including subjective symptoms such as dysphoria, tingling, and numbness. In the study reporting the lowest frequency, we believe that this may be due to the larger patient population [13].

In our study, none of the I-HSRs were severe, consistent with the findings of another pediatric study, which is the only study outside our scope that evaluates severity [17]. It is understood that in this study, unlike ours, patients were given premedication before BD administration. However, the number of patients who received premedication and the content of the premedication remain unclear. Nevertheless, it has been reported that there is no correlation between the development of immediate adverse events and the use of premedication [17]. While other pediatric studies lacked clear severity grade, individual findings suggested the possibility of severe HSRs, including hypotension and hypoxia despite the use of premedication use [12–14]. Moreover, in the study by Jacobstein et al. [13], it was reported that infusion reactions developed more frequently in the group that received premedication compared to those who did not. The role of premedication before the administration of BDs in preventing the development of HSRs remains open to discussion based on these results.

When we wanted to compare the HSRs to BDs in IBD in terms of frequency, type, and severity with the adult group, we found that most of the data were included in efficacy and safety studies. In these studies, there were heterogeneous definitions such as adverse events, acute infusion reactions or injection site reactions, similar to those in pediatric studies. We could not find any adult studies that exclusively focused on I-HSR and could be directly compared to our study. Nevertheless, considering

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Table 2. Characteristics of patients who developed I-HSR with BD and management

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Subtype of IBD	CD	CD	UC	CD	CD	CD
Duration of IBD, months	52	116	15	54	126	21
Age at development of I-HSR, years	9.2	14.6	12.5	17.5	17.3	16
Culprit BD	IFX	IFX	IFX	ADA	IFX	IFX
Time of I-HSR	10th min	30th min	10th min	15th min	30th min	20th min
I-HSR developing dose	2nd	2nd	2nd	7th	3rd	1st
I-HSR signs and symptoms	Flushing, abdominal pain cough, dyspnea, chest pain hoarseness, tachycardia	Dyspnea, vomiting	Flushing, abdominal pain, dyspnea	Flushing, itching, conjunctivitis	Urticaria, angioedema, chest tightness, tachycardia	Urticaria, flushing, dyspnea
Type of I-HSR	Type 1 non-IgE mediated	IRR	IRR	Type 1 IgE-mediated	Type 1 non-IgE mediated	Type 1
Severity of I-HSR	Moderate	Moderate	Moderate	Mild	Moderate	Moderate
Acute treatment of I-HSR	Infusion discontinued, adrenaline administered	Infusion discontinued	Infusion discontinued, adrenaline and pheniramine administered	Administration discontinued	Infusion discontinued	Infusion discontinued adrenaline administered
Skin tests	Negative	Negative	Negative	Positive (ID test with 1/100 dilution 15×12 mm)	Negative	NA
Non-isotype anti-drug antibody	Positive	Positive	Positive	Negative	Positive	NA
Management of I-HSR	RDD with IFX was applied	Infusion time prolonged	Infusion time prolonged	Treatment changed	Treatment changed	Switching IFX to ADA was planned
Comorbid allergic disease	None	None	Asthma	Penicillin allergy	None	Atopic dermatitis

IBD, inflammatory bowel diseases; CD, Crohn's disease; UC, ulcerative colitis; I-HSR, immediate hypersensitivity reactions; BD, biologic drug; IFX, infliximab; ADA, adalimumab; RDD, rapid drug desensitization; NA, non-applicable.

all these, we can say that the frequency of reactions with BDs in adult patients ranges from 2.3 to 20%, with most being mild, similar to in pediatric IBD [18–21].

Risk factors for HSR to BD include both patients' characteristics, underlying disease to be treated and drug-related factors. In this regard, when assessing hypersensitivity to BDs in IBD, Romeo et al. [16] reported that female gender, starting treatment at the age of 14 or older, and a disease duration of more than 1 year is associated with the development of adverse events. Also, it has been reported that the use of immunomodulators for more than 4 months either prior to or concurrently with the BD

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reduces the development of HSRs [12, 14, 17]. Among the various factors we evaluated, we found that only the presence of any allergic disease is a risk factor for the development of I-HSRs to BDs, in contrast to the findings of D'Arcangelo et al. [17]. Since no other variable that could potentially act as a confounding factor emerged significantly in our study, we evaluated the presence of any comorbid allergic disease as an independent risk factor.

Previously, the presence of atopy was not considered a risk factor for drug HSRs; instead, it was thought to contribute to more severe allergic reactions [22]. However, a recent study showed that determinants of atopy were predictors of immediate-type beta-lactam allergy in the Spanish population [23]. Additionally, atopy was found to be a risk factor for NSAID hypersensitivity in another recent study, including both adults and children [24]. Therefore, it is evident that further studies are needed to elucidate the impact of comorbid atopic diseases on the development of HSRs, both in other drug groups and with BDs. From this perspective, the diagnosis of comorbid allergic diseases is primarily based on history, and atopy was evaluated in history-positive patients; in other patients, we did not check for the presence of atopy with skin tests.

Specific factors related to the drug, also play a significant role in the development of HSR with BDs [9]. Hypersensitivity reactions to BDs are less common for fully human or humanized BD that elicits lower immunogenic responses [25]. In support of this, despite a higher frequency of ADA administration compared to IFX, a lower frequency (3.8% vs. 11.4% per patient) of I-HSR was observed in our study. This is due to the higher level of humanization in ADA compared to IFX, which is a chimeric IgG1 monoclonal antibody. In all patients except one who developed I-HSR with IFX, non-isotype antidrug antibodies were found to be positive despite negative skin tests. These antibodies may be associated with I-HSRs, although we could not test for the presence of these antibodies in the group without I-HSR. Furthermore, we did not detect I-HSR with VDZ and UST. We attribute this finding not only to their humanized nature but also to the lower number of administered patients and doses. On the other hand, although the safety profiles of UST and VDZ are reported to be good, cases of hypersensitivity with both have been reported in both children and adults [26–28]. Additionally, the relationship between disease-specific variables and the development of I-HSR with BD has been reported in children diagnosed with rheumatological diseases [29]. In order to determine disease-specific risk factors, we compared variables such as age at diagnosis, duration of IBD, subtype of IBD, and presence of accompanying extra-intestinal manifestations between the groups. However, aside from the presence of any comorbid allergic disease, we did not find any significant differences.

The main limitation of our study is its relatively small patient population, which might restrict the generalizability of our findings. Additionally, its retrospective design could potentially lead to data loss and hinder our ability to identify other risk factors such as atopy, disease activity, and anti-drug antibodies in the development of I-HSR. Although comorbid allergic diseases were correlated with I-HSR development in univariate analyses, the lack of significant differences compared to other variables precluded conducting multivariate analyses.

The strengths of the study are its exclusive focus on the pediatric age group, its evaluation of all types of BDs used in pediatric IBD, its accurate classification of I-HSRs according to current criteria, and its completion of the allergic diagnostic workup. Moreover, we attempted to identify risk factors that could be associated with the development of I-HSR with BDs.

In conclusion, the frequency of I-HSRs to BDs in children with IBD is not rare but not severe in the long term. The presence of any comorbid allergic disease is a risk factor for the development of I-HSRs.

Statement of Ethics

This study protocol was reviewed and approved by the Ethics Committee of Gazi University, Approval No. [2022-942]. Written informed consent was obtained from participants' parents for both participation in the study and the publication of their medical details.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Sinem Polat Terece, H. Ilbilge Ertoy Karagol, and Arzu Bakirtas designed of the work. Sinem Polat Terece, Gizem Koken, Demet Teker Duztas, Hakan Ozturk, Odul Egritas Gurkan, Sinan Sari, and Buket Dalgic interpreted the data for the work. Sinem Polat Terece, Gizem Koken, Demet Teker Duztas, Hakan Ozturk, Odul Egritas

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Gurkan, Sinan Sari, Buket Dalgic, Arzu Bakirtas, and Dilek Yapar drafted the work. Dilek Yapar analyzed the data. H. Ilbilge Ertoy Karagol and Sinem Polat Terece reviewed it critically for important intellectual content. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Corica D, Romano C. Biological therapy in pediatric inflammatory bowel disease: a systematic review. J Clin Gastroenterol. 2017;51(2):100–10. https://doi.org/10.1097/MCG.0000000000000696
2 Conrad MA, Kelsen JR. The treatment of pediatric inflammatory bowel disease with biologic therapies. Curr Gastroenterol Rep. 2020;22(8):36. https://doi.org/10.1007/s11894-020-00773-3
3 World Health Organization. Evaluation of certain veterinary drug residues in food. Seventy-eighth report of the Joint FAO/WHO expert committee on food additives. World Health Organ Tech Rep Ser. 2014(988):1–266.
4 Mori F, Saretta F, Bianchi A, Crisafulli G, Caimmi S, Liotti L, et al. Hypersensitivity reactions to monoclonal antibodies in children. Medicina. 2020;56(5):232. https://doi.org/10.3390/medicina56050232
5 Isabwe GAC, Garcia Neuer M, de Las Vecillas Sanchez L, Lynch DM, Marquis K, Castells M. Hypersensitivity reactions to therapeutic monoclonal antibodies: phenotypes and endotypes. J Allergy Clin Immunol. 2018;142(1):159–70.e2. https://doi.org/10.1016/j.jaci.2018.02.018
6 Levine A, Koletzko S, Turner D, Escher JC, Cucchiara S, de Ridder L, et al. ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. J Pediatr Gastroenterol Nutr. 2014;58(6):795–806. https://doi.org/10.1097/MPG.0000000000000239
7 Lichtenstein L, Ron Y, Kivity S, Ben-Horin S, Israeli E, Fraser GM, et al. Infliximab-related infusion reactions: systematic review. J Crohns Colitis. 2015;9(9):806–15. https://doi.org/10.1093/ecco-jcc/jjv096
8 Brown SG. Clinical features and severity grading of anaphylaxis. J Allergy Clin Immunol. 2004;114(2):371–6. https://doi.org/10.1016/j.jaci.2004.04.029
9 Bavbek S, Pagani M, Alvarez-Cuesta E, Castells M, Dursun AB, Hamadi S, et al. Hypersensitivity reactions to biologicals: an EAACI position paper. Allergy. 2022;77(1):39–54. https://doi.org/10.1111/all.14984
10 Puchner TC, Kugathasan S, Kelly KJ, Binion DG. Successful desensitization and therapeutic use of infliximab in adult and pediatric Crohn's disease patients with prior anaphylactic reaction. Inflamm Bowel Dis. 2001;7(1):34–7. https://doi.org/10.1097/00054725-200102000-00005
11 Yilmaz Topal O, Kose V, Acar B, Bayrakci US, Ozyoruk D, Hizal G, et al. Evaluation of hypersensitivity reactions in pediatric patients using biological drugs. Int Arch Allergy Immunol. 2021;182(9):844–51. https://doi.org/10.1159/000515500
12 Crandall WV, Mackner LM. Infusion reactions to infliximab in children and adolescents: frequency, outcome and a predictive model. Aliment Pharmacol Ther. 2003;17(1):75–84. https://doi.org/10.1046/j.1365-2036.2003.01411.x
13 Jacobstein DA, Markowitz JE, Kirschner BS, Ferry G, Cohen SA, Gold BD, et al. Premedication and infusion reactions with infliximab: results from a pediatric inflammatory bowel disease consortium. Inflamm Bowel Dis. 2005;11(5):442–6. https://doi.org/10.1097/01.mib.0000158166.88238.ea
14 El-Matary W, Dykes DMH, Bauman L, El-kadri A, Carroll MW, Izaguirre MR, et al. Rapid infliximab infusion in children with inflammatory bowel disease: a multicenter North American experience. Inflamm Bowel Dis. 2017;23(12):2104–8. https://doi.org/10.1097/MIB.0000000000001259
15 Bodini G, Demarzo MG, Saracco M, Coppo C, De Maria C, Baldissarro I, et al. High anti-TNF alfa drugs trough levels are not associated with the occurrence of adverse events in patients with inflammatory bowel disease. Scand J Gastroenterol. 2019;54(10):1220–5. https://doi.org/10.1080/00365521.2019.1666914
16 Romeo AC, Ventimiglia M, Dipasquale V, Orlando A, Citrano M, Pellegrino S, et al. Effectiveness and safety of biologics in pediatric inflammatory boweldisease: real-life data from the Sicilian Network. Clin Res Hepatol Gastroenterol. 2020;44(2):223–9. https://doi.org/10.1016/j.clinre.2019.05.008
17 D'Arcangelo G, Distante M, Raso T, Rossetti D, Catassi G, Aloi M. Safety of biological therapy in children with inflammatory bowel disease. J Pediatr Gastroenterol Nutr. 2021;72(5):736–41. https://doi.org/10.1097/MPG.0000000000003044
18 Lichtenstein GR, Feagan BG, Cohen RD, Salzberg BA, Safdi M, Popp JW Jr, et al. Infliximab for Crohn's disease: more than 13 Years of real-world experience. Inflamm Bowel Dis. 2018;24(3):490–501. https://doi.org/10.1093/ibd/izx072
19 D'Haens G, Reinisch W, Panaccione R, Satsangi J, Petersson J, Bereswill M, et al. Lymphoma risk and overall safety profile of adalimumab in patients with Crohn's disease with up to 6 Years of follow-up in the pyramid registry. Am J Gastroenterol. 2018;113(6):872–82. https://doi.org/10.1038/s41395-018-0098-4
20 Colombel JF, Sands BE, Rutgeerts P, Sandborn W, Danese S, D'Haens G, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. Gut. 2017;66(5):839–51. https://doi.org/10.1136/gutjnl-2015-311079
21 Verstockt B, Deleenheer B, Van Assche G, Vermeire S, Ferrante M. A safety assessment of biological therapies targeting the IL-23/IL-17 axis in inflammatory bowel diseases. Expert Opin Drug Saf. 2017;16(7):809–21. https://doi.org/10.1080/14740338.2017.1338273
22 Joint Task Force on Practice Parameters American Academy of Allergy, Asthma and Immunology American College of Allergy, Asthma and Immunology Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010;105(4):259–73. https://doi.org/10.1016/j.anai.2010.08.002
23 Cornejo-García JA, Guéant-Rodriguez RM, Torres MJ, Blanca-Lopez N, Tramoy D, Romano A, et al. Biological and genetic determinants of atopy are predictors of immediate-type allergy to betalactams, in Spain. Allergy. 2012;67(9):1181–5. https://doi.org/10.1111/j.1398-9995.2012.02867.x
24 Blanca-López N, Cornejo-García JA, Plaza-Serón MC, Doña I, Torres-Jaén MJ, Canto G, et al. Hypersensitivity to nonsteroidal anti-inflammatory drugs in children and adolescents: cross-intolerance reactions. J Investig Allergol Clin Immunol. 2015;25(4):259–69.
25 Picard M, Galvão VR. Current knowledge and management of hypersensitivity reactions to monoclonal antibodies. J Allergy Clin Immunol Pract. 2017;5(3):600–9. https://doi.org/10.1016/j.jaip.2016.12.001
26 Schneider AM, Weghuber D, Hetzer B, Entenmann A, Müller T, Zimmermann G, et al. Vedolizumab use after failure of TNF-α antagonists in children and adolescents with inflammatory bowel disease. BMC Gastroenterol. 2018;18(1):140. https://doi.org/10.1186/s12876-018-0868-x
27 Sunny J, Fonseca AG, Crim AM, Goyal A, Felipez LM. Hypersensitivity reaction to Ustekinumab in pediatric and young adult inflammatory bowel disease patients: a case series. JPGN Rep. 2022;3(2):e205. https://doi.org/10.1097/PG9.0000000000000205
28 Xie Y, Li H, Zhou L, Tian F. A case of vedolizumab-induced acute allergic reaction in a patient with refractory ulcerative colitis. Inflamm Bowel Dis. 2022;28(7):e103. https://doi.org/10.1093/ibd/izac008
29 Soyer O, Demir S, Bilginer Y, Batu ED, Sonmez HE, Arıcı ZS, et al. Severe hypersensitivity reactions to biological drugs in children with rheumatic diseases. Pediatr Allergy Immunol. 2019;30(8):833–40. https://doi.org/10.1111/pai.13114

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