



Risk Factors for Drug Allergies in Pediatric Palliative Care Patients

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Abstract

Background / aim: Children receiving pediatric palliative care constitute a medically fragile population. Despite this vulnerable clinical profile, data on drug allergy in pediatric palliative care remain scarce. This study aimed to determine the frequency, clinical characteristics, and associated factors of clinically defined drug allergy in children hospitalized in a tertiary pediatric palliative care center.

Methods: This retrospective observational study included all children hospitalized in a tertiary pediatric palliative care center. Drug allergy was clinically defined according to predefined diagnostic criteria, and in vivo and/or in vitro allergy work-up was performed in selected patients. Demographic and clinical characteristics, hospitalization-related variables, and medication burden were compared between patients with and without drug allergy.

Results: A total of 281 hospitalized children were included. Clinically defined drug allergy was identified in 26 patients (9.2%). Antimicrobials were the most frequently implicated drug group (57.7%), followed by antiepileptic drugs (11.5%) and non-steroidal anti-inflammatory drugs (7.7%). Most reactions were immediate (21/26), whereas 5 were non-immediate. One patient developed ranitidine-associated anaphylaxis, and one developed oxybutynin-associated DRESS. In multivariate analysis, older age (OR 1.168; 95% CI 1.036-1.316; p=0.011), longer hospital stay (OR 1.032; 95% CI 1.014-1.050; p<0.001), and a higher number of medications (OR 1.656; 95% CI 1.254-2.189; p<0.001) remained independently associated with drug allergy.

Conclusions: Clinically defined drug allergy was not uncommon among hospitalized children receiving pediatric palliative care. Antimicrobials were the leading culprit drugs, while antiepileptic drugs also represented a notable contributor, likely reflecting the high neurological disease burden of this population. Greater medication exposure and prolonged hospitalization were the strongest correlates of drug allergy.

Keywords: Pediatrics; Palliative Care; Drug Hypersensitivity; Drug Allergy; Polypharmacy

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Çocuk Palyatif Bakım Hastalarında ilaç Alerjileri için risk faktörleri

Öz

Amaç: Pediatrik palyatif bakım alan çocuklar; tıbbi açıdan hassas bir popülasyonu oluşturmaktadır. Bu hassas profile rağmen, pediatrik palyatif bakımda ilaç alerjisine ilişkin veriler sınırlıdır. Bu çalışmanın amacı, üçüncü basamak pediatrik palyatif bakım merkezine yatırılan çocuklarda klinik olarak tanımlanmış ilaç alerjisinin sıklığını, klinik özelliklerini ve ilişkili risk faktörlerini belirlemektir.

Yöntemler: Bu retrospektif gözlemsel çalışmaya, üçüncü basamak pediatrik palyatif bakım merkezine yatırılan tüm çocuklar dahil edildi. İlaç alerjisi, önceden tanımlanmış tanısal kriterlere göre klinik olarak tanımlandı ve seçilmiş hastalarda in vivo ve/veya in vitro alerjik değerlendirme yapıldı. İlaç alerjisi olan ve olmayan hastalar arasında demografik ve klinik özellikler, hastaneye yatışla ilişkili değişkenler ve ilaç yükü karşılaştırıldı.

Bulgular: Toplam 281 çocuk çalışmaya dahil edildi. Klinik olarak tanımlanmış ilaç alerjisi 26 hastada (%9,2) saptandı. En sık suçlanan ilaç grubu antimikrobiyallerdi (%57,7); bunu antiepileptik ilaçlar (%11,5) ve nonsteroid antiinflamatuar ilaçlar (%7,7) izledi. Reaksiyonların çoğu erken tipteydi (21/26), 5'i ise geç tipteydi. Bir hastada ranitidin ile ilişkili anafilaksi, bir hastada ise oksibutin ile ilişkili DRESS gelişti. Çok değişkenli analizde ileri yaş (OR 1,168; %95 GA 1,036-1,316; p=0,011), daha uzun hastanede kalış süresi (OR 1,032; %95 GA 1,014-1,050; p<0,001) ve daha fazla sayıda ilaç kullanımı (OR 1,656; %95 GA 1,254-2,189; p<0,001) ilaç alerjisi ile bağımsız olarak ilişkili bulundu.

Sonuç: Pediatrik palyatif bakım hastalarında klinik olarak tanımlanmış ilaç alerjisi nadir değildir. Antimikrobiyaller en sık suçlanan ilaç grubu iken, antiepileptik ilaçlar da bu popülasyondaki yüksek nörolojik hastalık yükünü yansıtır biçimde dikkate değer bir katkı sağlamıştır. Daha fazla ilaç maruziyeti ve uzun süreli hastanede kalış, ilaç alerjisiyle en güçlü ilişkili faktörler olmuştur.

Anahtar kelimeler: Pediatri; Palyatif Bakım; İlaç Aşırı Duyarlılığı; İlaç Alerjisi; Çoklu İlaç Kullanımı.

INTRODUCTION

Children receiving pediatric palliative care represent a medically complex and vulnerable population. These patients often experience recurrent hospitalizations, prolonged admissions, severe neurological impairment, dependence on medical devices, and substantial exposure to multiple medications. Recent studies in pediatric palliative care and children with medical complexity have shown high rates of polypharmacy, medication burden, and off-label drug use, all of which may increase the risk of drug-related harm^{1,2}.

Drug hypersensitivity reactions in children are an important clinical problem because they may lead to avoidance of first-line therapies, use of broader-spectrum or less effective alternatives, increased healthcare costs, and unnecessary long-term allergy labels. Current pediatric drug hypersensitivity literature indicates that antibiotics, particularly beta-lactams, and non-steroidal anti-inflammatory drugs are among

the most frequently implicated agents³⁻⁵. However, the epidemiology and clinical impact of drug allergy in highly fragile inpatient populations remain insufficiently defined.

The pediatric intensive care literature has demonstrated that adverse drug events are common in critically ill children and may prolong hospitalization, underscoring the broader medication-safety burden in vulnerable pediatric populations⁶⁻⁸. Nevertheless, studies specifically focusing on drug allergy in pediatric palliative care are scarce. In this context, we aimed to determine the frequency and clinical characteristics of clinically defined drug allergy in children hospitalized in a pediatric palliative care unit and to identify factors associated with its occurrence.

In this retrospective observational study, we aimed to evaluate the frequency, culprit drugs,

and clinical features of clinically defined drug allergy in hospitalized pediatric palliative care patients and to investigate the demographic and clinical factors associated with drug allergy in this medically complex population.

METHODS

This retrospective observational study was conducted at the Pediatric Palliative Care Center, İzmir Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital, İzmir, Türkiye. The study included pediatric patients hospitalized between November 2018 and March 2022. The study protocol was approved by İzmir Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital institutional local ethics committee (Approval date: 11.08.2022, approval number: GOA-722). Written informed consent was obtained from the parents and/or legal guardians of all participants prior to enrollment, and assent was also obtained from children whenever appropriate according to age and developmental capacity.

Study population

All children hospitalized in the pediatric palliative care unit during the study period were screened for eligibility. Patients' medical records were reviewed retrospectively. Demographic and clinical data were extracted from hospital records, including age, gender, underlying diagnoses, comorbidities, presence of immobilization, need for mechanical ventilatory support, number of hospitalizations, number of pediatric intensive care unit (PICU) admissions, length of hospital stay, known allergy history, parental atopy, and number of medications used during hospitalization.

Definition of drug allergy

The primary outcome of this study was clinically defined drug allergy. This term was used because drug allergy status was determined using predefined clinical criteria, supported by available *in vivo* and/or *in vitro* allergy

evaluations when feasible, rather than by a complete standardized confirmatory allergy work-up in all patients. Patients with suspected drug hypersensitivity reactions were evaluated according to the predefined "drug allergy diagnostic criteria" developed by Sacerdoti et al. and later validated in children by Özmen et al.^{9,10}. These criteria include: 1- presence of clinical findings compatible with a known adverse effect of the suspected drug, 2- absence of an alternative explanation for the reaction, 3- occurrence of the suspected reaction within the expected time interval for that drug, 4- confirmation that the eruption was not caused by drug overdose, 5- improvement of clinical findings after discontinuation of the drug, and 6- recurrence after rechallenge. Cases fulfilling 1-3 criteria were classified as "possible," those fulfilling 1-5 criteria as "probable," and those fulfilling all 6 criteria as "definite" drug allergy. In the present study, only patients classified as having probable or definite drug allergy were included in the drug allergy group. In these patients, culprit drugs, reaction type, local and systemic findings, and available allergy diagnostic tests were reviewed. In selected patients with suspected beta-lactam allergy, serum specific IgE to penicillin V and penicillin G was measured. When clinically feasible, skin testing was performed, and in some patients the diagnosis was established by graded challenge, consistent with contemporary pediatric approaches in which challenge testing plays a central role in confirming or excluding drug hypersensitivity⁷. In certain patients who were not clinically stable enough or otherwise unsuitable for a complete diagnostic evaluation, graded challenge was performed with a safe alternative drug rather than the suspected culprit agent. Overall, a subset of patients underwent *in vivo* and/or *in vitro* diagnostic evaluation, while in some others the diagnosis was supported by recurrence of symptoms after re-exposure to the suspected or a related drug. Because not all patients underwent a complete

standardized allergy work-up, the outcome of interest was defined as clinically defined drug allergy rather than universally confirmed immunologically proven drug hypersensitivity.

Clinical characterization of drug reactions

For patients classified as having probable or definite drug allergy, the suspected culprit drug, type of allergic reaction, presence of local and systemic findings, and results of diagnostic allergy tests were recorded. Reactions were categorized as immediate or non-immediate according to the timing of symptom onset after drug exposure. Reactions were classified as immediate if they occurred within the first 6 hours after drug administration and as non-immediate if they developed more than 6 hours thereafter.³ Severe presentations, including anaphylaxis and severe cutaneous adverse reactions (SCAR), were also noted.

Statistical analysis

Statistical analyses were performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), as appropriate, and categorical variables as number (percentage). Comparisons between patients with and without drug allergy were performed using the chi-square test or Fisher's exact test for categorical variables and the independent-samples t test or Mann-Whitney U test for continuous variables, as appropriate. Variables associated with drug allergy in univariate analyses were further evaluated using binary logistic regression to identify independent risk factors associated with clinically defined drug allergy. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and a p value <0.05 was considered statistically significant.

RESULTS

During the 3.5-year study period, a total of 281 children hospitalized in the pediatric palliative care unit were included in the analysis. Of these, 170 (60.5%) were male and 111 (39.5%) were

female, with a mean age of 6.5 ± 4.8 years. The most common reason for hospitalization was infection (72.6%), followed by neurologic conditions (7.8%), metabolic disorders (1.4%), and other indications, including patient care and caregiver education (18.1%).

The comorbidity profile of the cohort was predominantly composed of children with neuromotor deficiency (60.9%), followed by inborn errors of metabolism (12.8%), genetic disorders (7.8%), cardiovascular diseases (7.5%), lung diseases (6%), and other conditions (5%), including trauma, primary immunodeficiency, renal, hematological, and gastrointestinal diseases.

According to the diagnostic criteria defined by Sacerdoti et al. and validated by Özmen et al., 26 patients were classified as having probable or definite drug allergy, yielding an overall frequency of 9.2% in the cohort. The available in vivo and/or in vitro allergy work-up findings for these patients are summarized in Table I.

Among patients with drug allergy, antimicrobials were the most frequently implicated drug group, accounting for 57.7% of cases, followed by antiepileptic drugs (11.5%) and non-steroidal anti-inflammatory drugs (7.7%). When culprit drugs were examined in more detail, beta-lactams were the leading agents within the antimicrobial group ($n=10$), followed by glycopeptides ($n=3$), clindamycin ($n=1$), and fluconazole ($n=1$) (Figure-1). Among antiepileptic drugs, vigabatrin, rufinamide, and valproic acid were each implicated in one patient. Ibuprofen was the only non-steroidal anti-inflammatory drug identified and accounted for two patients. Other culprit drugs included allopurinol, oxybutynin, ursodeoxycholic acid, amlodipine, ranitidine, and N-acetylcysteine, each reported in one case. Regarding reaction timing, 21 patients had immediate reactions, whereas 5 had non-immediate reactions. Anaphylaxis occurred in 1 patient after ranitidine exposure, and 1 patient developed SCAR, specifically DRESS, associated with oxybutynin. The individual characteristics of

patients with clinically defined drug allergy, including underlying diagnoses, suspected culprit drugs, reaction types, and available in vivo and/or in vitro allergy work-up results, are summarized in Table I.

Table I: Demographic and clinical characteristics of patients with clinically defined drug allergy

	Sex	Diagnosis	Suspected drug	Reaction	Allergy work-up
P1	F	Lennox-Gastaut Syndrome	Rufinamide	Urticaria	Graded challenge +
P2	F	Refractory Epilepsy	Vigabatrin	MPE	Drug provocation test +
P3	F	RETT Syndrome	Meropenem	MPE	Skin prick test+
P4	F	CP/ Epilepsy	N-acetylcysteine	MPE	Graded challenge+
P5	F	SMA type 1	Ceftriaxone	Urticaria	Sp IgE+
P6	F	SMA type 1	Ibuprofen	MPE	Drug provocation test+
P7	F	CP/MMR	Ranitidine	Anaphylaxis	Skin prick test+
P8	M	CP /MMR /Epilepsy	Ibuprofen	Angioedema	N/A
P9	M	CP / MMR	Vancomycin	Angioedema	Skin prick test+
P10	M	CP / MMR /Epilepsy	Piperacillin-tazobactam	MPE	N/A
P11	M	CP / MMR /Epilepsy	Piperacillin-tazobactam	MPE	N/A
P12	M	CP / MMR	Ceftriaxone	Urticaria	Skin prick test+
P13	M	CP / MMR /Epilepsy	Clindamycin	MPE	Graded challenge+
P14	M	CP / MMR /Epilepsy	Amlodipine	Urticaria	N/A
P15	M	CP / MMR /Epilepsy	Vancomycin	Facial erythema	Graded challenge+
P16	M	SMA type 1	Ertapenem	Generalized erythema	N/A
P17	F	SMA type 1	Piperacillin-tazobactam	Generalized erythema	Sp IgE+
P18	M	CP / MMR /Epilepsy	Vancomycin	Facial erythema	Graded challenge+
P19	F	Inborn errors of neurometabolism	Valproic acid	Urticaria, MPE	N/A
P20	F	GM2 activator protein deficiency	UDCA	Urticaria	N/A
P21	M	Inborn errors of neurometabolism	Ceftriaxone	MPE	Drug provocation test+
P22	M	Mitochondrial DNA depletion syndrome	Allopurinol	MPE	N/A
P23	M	Down syndrome/AVSD	Ampicillin	Generalized erythema	Sp IgE+
P24	F	Diffuse axonal damage	Ampicillin-clavulinate	MPE	Drug provocation test+
P25	F	Spinal cord injury	Fluconazole	Urticaria, angioedema	Graded challenge+
P26	M	Spinal cord injury	Oxybutynin	DRESS	N/A

Abbreviations: F, female; M, male; CP, cerebral palsy; MMR, mental motor retardation; SMA, spinal muscular atrophy; AVSD, atrioventricular septal defect; MPE, maculopapular exanthema; DRESS, drug reaction with eosinophilia and systemic symptoms; Sp IgE, serum specific immunoglobulin E (penicillin V/G-specific IgE); N/A, not available; UDCA, ursodeoxycholic acid.

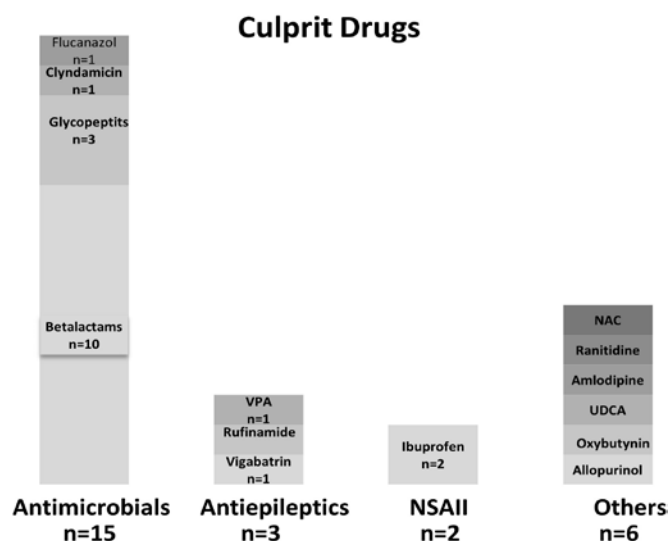


Figure 1. Distribution of culprit drugs in patients with clinically defined drug allergy

Abbreviations: VPA, valproic acid; UDCA, ursodeoxycholic acid; NAC, N-acetylcysteine; NSAIDs, non-steroidal anti-inflammatory drugs.

When patients with and without drug allergy were compared, those with drug allergy were significantly older (9.8 ± 4.2 vs 6.2 ± 4.7 years, $p < 0.001$) (Table II). They also had a higher mean number of hospitalizations (6.9 ± 4.7 vs 4.4 ± 2.7 , $p < 0.001$), longer hospital stay (73.2 ± 90.5 vs 16.1 ± 18.2 days, $p < 0.001$), a greater number of medications used (7.2 ± 2.8 vs 3.7 ± 1.9 , $p < 0.001$), and more PICU admissions (1.6 ± 1.5 vs 0.8 ± 0.9 , $p < 0.001$). In contrast, gender distribution and known drug allergy history did not differ significantly between the groups.

Additionally, gastrostomy, tracheostomy, and immobilization were significantly more frequent in patients with drug allergy than in those without drug allergy (26.9% vs 5.1%, $p = 0.001$; 42.3% vs 22.7%, $p = 0.033$; and 100% vs 72.9%, $p < 0.001$, respectively).

Table II: Comparison of demographic and clinical characteristics between patients with and without drug allergy

Variables	No DA (n=255)	DA group (n=26)	p
Age, years, mean $\pm$ SD	6.2 $\pm$ 4.7	9.8 $\pm$ 4.2	<0.001
Gender, % male	156 (61.2)	14 (53.8)	0.466
Known DA history, n (%)	15 (5.9)	4 (15.4)	0.085
Number of hospitalizations	4.4 $\pm$ 2.7	6.9 $\pm$ 4.7	<0.001
Length of stay in hospital	16.1 $\pm$ 18.2	73.2 $\pm$ 90.5	<0.001
Number of medications	3.7 $\pm$ 1.9	7.2 $\pm$ 2.8	<0.001
Number of PICU admissions	0.8 $\pm$ 0.9	1.6 $\pm$ 1.5	<0.001
Presence of gastrostomy, n(%)	13 (5.1)	7 (26.9)	0.001
Presence of tracheostomy, n(%)	58 (22.7)	11 (42.3)	0.033
Immobilization, n(%)	186 (72.9)	26 (100)	<0.001

Abbreviations: DA, drug allergy; SD, standard deviation; PICU, pediatric intensive care unit.

In multivariate logistic regression analysis, older age, longer hospital stay, and a higher number of medications remained independently associated with clinically defined drug allergy. The odds ratio was 1.168 (95% CI, 1.036-1.316; $p=0.011$) for age, 1.032 (95% CI, 1.014-1.050; $p<0.001$) for length of hospital stay, and 1.656 (95% CI, 1.254-2.189; $p<0.001$) for number of medications.

DISCUSSION

In this retrospective cohort of hospitalized children receiving pediatric palliative care, clinically defined drug allergy was identified in 9.2% of patients. Antimicrobials were the leading culprit drugs, followed by antiepileptic drugs and non-steroidal anti-inflammatory drugs, while older age, longer hospitalization, and greater medication exposure emerged as independent predictors of drug allergy. These findings suggest that drug allergy is a clinically relevant medication-safety issue in pediatric palliative care, a population characterized by medical complexity, repeated healthcare exposure, and substantial pharmacologic burden.

In comparison with published pediatric data, the frequency of clinically defined drug allergy observed in our cohort was higher than that reported for general pediatric inpatients. While self- or clinician-reported drug hypersensitivity in children ranges from 1% to 10.2%, only a minority of these labels are ultimately confirmed after formal diagnostic evaluation, and the incidence of suspected drug hypersensitivity among hospitalized children has been reported to be approximately 1.1%.^{3,11,12} By contrast, pediatric intensive care studies have consistently demonstrated a high burden of medication-related harm, including adverse drug events and drug-related problems, underscoring the vulnerability of children with severe illness and intensive medication exposure⁶⁻⁸. In this context, the relatively high frequency observed in our pediatric palliative care cohort is not unexpected, given the marked polypharmacy, prolonged hospitalization, and recurrent healthcare exposure in this population. Recent studies by Zanin et al. and Mengato et al. have shown that polypharmacy, medication burden, and off-label prescribing are highly prevalent in children with medical complexity and in pediatric palliative care populations^{1,2}. However, given the retrospective nature of the study and the absence of definitive allergy testing in all patients, the findings should be interpreted cautiously, as some reactions may have been overestimated or misclassified. For instance, vancomycin infusion-related reactions, including red neck syndrome, may be difficult to distinguish clinically from urticarial eruptions associated with concurrent infection¹³. For this reason, our findings are best interpreted as reflecting clinically defined drug allergy rather than confirmed drug hypersensitivity. Future prospective studies using standardized diagnostic pathways will be essential to determine the true prevalence and spectrum of drug hypersensitivity in pediatric palliative care.

The pediatric intensive care literature provides a useful parallel framework for interpreting our findings. A multicenter prospective PICU study by Alghamdi et al. showed that adverse drug events were common and a significant proportion were preventable⁸. Previous studies by Silva et al. similarly demonstrated that drug side effects were frequent in the PICU and associated with prolonged hospital stay⁶. More recently, Shirzad-Yazdi et al. reported that drug-related problems affected 57% of children in the PICU, with treatment safety issues and drug-drug interactions being major contributing factors¹⁴. Importantly, while drug side effects, drug-related problems, and drug allergies are not interchangeable concepts, all three reflect the high drug burden of these vulnerable children who are medically hospitalized.

The predominance of antimicrobials in our cohort is consistent with contemporary pediatric drug hypersensitivity literature. Current evidence, including the 2025 WAO Statement and recent pediatric reviews, identifies antibiotics, particularly beta-lactams, as the leading culprit drugs in children^{3,15}. In our cohort, this distribution is clinically understandable, given that infection was the most common indication for hospitalization and likely resulted in repeated exposure to broad-spectrum antimicrobial agents. The contribution of antiepileptic drugs in our study is likewise unsurprising given the neurological complexity of the pediatric palliative population. Many children in palliative care have severe neurodevelopmental impairment, epilepsy, or neurometabolic disease requiring long-term anticonvulsant treatment, and antiepileptic drugs are well recognized causes of both maculopapular exanthems and severe delayed hypersensitivity reactions^{16,17}. This background may explain why antiepileptic drugs represented the second most frequent drug class in our cohort. Similarly, the presence of an oxybutynin-associated DRESS case

highlights that, although uncommon, severe cutaneous adverse reactions may occur even with drugs not classically regarded as the most frequent culprits, especially in medically complex children receiving multiple concomitant therapies.

One of the key findings of our study was that drug allergy remained independently associated with older age, longer hospitalization, and a higher number of medications. This observation is consistent with recent pediatric literature showing that age, chronic underlying disease, polypharmacy, repeated or high-dose exposure, and host-related factors all contribute to the risk of drug hypersensitivity in children^{18,19}. A similar pattern has also been reported in the broader pediatric medication-safety literature, where prolonged hospital stay, multiple drug exposure, and treatment for comorbid conditions have been linked to a greater likelihood of drug-related side effects and medication-related problems in hospitalized children²⁰. In our cohort, prolonged hospital stay can reasonably be interpreted as an indicator of cumulative drug exposure, likely reflecting an overall treatment burden and a high risk of re-exposure. Likewise, the association with older age may indicate longer disease duration, more frequent prior treatment courses, and a greater chance of previous sensitization.

The observation that gastrostomy, tracheostomy, and immobilization were more frequent in the drug allergy group in our study also deserves comment, even though these variables were not retained as independent predictors in multivariable analysis. Although similar variables have not been specifically established as direct risk factors for drug allergy in pediatric palliative care, they likely identify a subgroup with greater medical complexity, recurrent infections, and more frequent healthcare contact²¹. In such children, repeated

hospitalizations and cumulative pharmacologic exposure may plausibly increase the likelihood of both true drug hypersensitivity and clinically suspected drug allergy. In addition, in selected device-dependent subgroups, particularly those with congenital neurologic or urologic disorders and repeated procedural exposure, latex sensitization may represent another relevant consideration, as repeated medical interventions are a recognized risk factor for latex allergy in children^{22,23}. However, this issue was not systematically evaluated in the present study.

This study has several notable strengths. To our knowledge, it is the first to specifically investigate drug allergy in hospitalized children receiving pediatric palliative care. It also addresses a clinically relevant but understudied setting, uses predefined diagnostic criteria to identify probable and definite cases, and includes both descriptive and multivariable analyses. In addition, the detailed presentation of culprit drugs and available allergy work-up data increases the clinical value of the findings. However, some limitations should be acknowledged. The study was retrospective and single-center, which may limit generalizability. Moreover, not all patients underwent complete standardized allergy evaluation with the culprit drug, and in some cases the diagnosis relied on rechallenge or challenge with an alternative drug rather than full confirmatory testing. Finally, given the medical complexity of the study population, the effects of underlying disease severity and medication exposure may not be fully separable.

In conclusion, our findings indicate that drug allergy is not uncommon among hospitalized children receiving pediatric palliative care. Antimicrobials were the most frequent culprit drugs, while antiepileptic drugs also emerged as a notable drug class, likely reflecting the high neurological disease burden of this population. Greater medication exposure and prolonged

hospitalization were the most consistent factors associated with clinically defined drug allergy. These results support increased awareness of clinically defined drug allergy in pediatric palliative care, and consideration of formal allergy assessment whenever clinically feasible. Future prospective multicenter studies using standardized diagnostic pathways are needed to determine the true incidence of confirmed drug hypersensitivity in pediatric palliative care and to clarify how drug allergy labels affect drug choice, symptom management, and overall healthcare utilization.

Ethics Committee Approval: The study included pediatric patients hospitalized between November 2018 and March 2022. The study protocol was approved by İzmir Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital Hospital institutional local ethics committee (Approval date: 11.08.2022, approval number: GOA-722).

Conflict of Interest: The author(s) declare that there is no financial conflict of interest related to this article.

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