

RESEARCH ARTICLE

Epidemiological and Clinical Features of Healthcare-Associated Infections in Pediatric Inpatient Clinics of a University Hospital; One Year Surveillance

Bir Üniversite Hastanesinin Pediatrik Yataklı Kliniklerinde Sağlık Hizmeti İlişkili Enfeksiyonların Epidemiyolojik ve Klinik Özellikleri; Bir Yıllık Sürveyans

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ABSTRACT

Objective: This study evaluates the characteristics of healthcare-associated infections (HCAIs) among pediatric patients hospitalized in various inpatient units.

Material and Method: All patients admitted to the pediatric ward, pediatric intensive care unit (PICU), and neonatal intensive care unit (NICU) of Suleyman Demirel University Research and Application Hospital who developed HCAIs were prospectively assessed. Infections were classified according to the CDC criteria.

Results: Of 1,291 hospitalized patients, 65 (5.03%) developed 102 infection episodes. These occurred in 16 (24.8%) patients in the pediatric ward, nine (13.8%) in the PICU, and 40 (61.5%) in the NICU. The overall HCAI rate was 7.9%, with an incidence of 9.31 per 1,000 patient-days. Patient-based infection rates were 33.3% in the PICU, 32.3% in the NICU, and 1.74% in the pediatric ward. Bloodstream infections were the most common type (49%), followed by pneumonia and urinary tract infections. Gram-negative bacteria accounted for 52.8% of pathogens, gram-positive bacteria for 28.5%, and fungi for 17.3%. E. coli was among the predominant agents and showed notable antibiotic resistance. The overall HCAI-associated mortality was 7.6%, with a higher rate of 12.5% in the NICU.

Conclusion: HCAIs remain a significant concern in pediatric inpatient care, especially in critical care units. The high frequency of bloodstream infections and predominance of gram-negative and fungal pathogens underscore the need for stringent infection prevention strategies, robust antimicrobial stewardship, and sustained epidemiological monitoring to reduce preventable morbidity and mortality in vulnerable pediatric populations.

Keywords: Healthcare-associated infection, Pediatric inpatients, Antimicrobial Drug Resistances, Mortality Rate, Neonatal Intensive Care Unit.

ÖZET

Amaç: Bu çalışma, hastaneye yatırılan çocuk hastalarda gelişen sağlık hizmeti ile ilişkili enfeksiyonların (SHİE) özelliklerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Süleyman Demirel Üniversitesi Araştırma ve Uygulama Hastanesi'nin çocuk servisi, çocuk yoğun bakım ünitesi (ÇYBÜ) ve yenidoğan yoğun bakım ünitesinde (YYBÜ) takip edilen ve SHİE gelişen tüm hastalar prospektif olarak değerlendirilmiştir. Enfeksiyonlar, CDC (Centers for Disease Control and Prevention) kriterlerine göre tanımlandırıldı.

Bulgular: Toplam 1.291 hastadan 65'inde (%5,03) 102 enfeksiyon atağı gözlenmiştir. Bu hastaların 16'sı (%24,8) çocuk servisinde, 9'u (%13,8) ÇYBÜ'de ve 40'ı (%61,5) YYBÜ'de izlenmiştir. Genel SHİE oranı %7,9, insidans hızı ise 1.000 hasta günü başına 9,31 olarak hesaplanmıştır. Hasta bazında enfeksiyon oranları ÇYBÜ'de %33,3, YYBÜ'de %32,3 ve çocuk servisinde %1,74 olarak bulunmuştur. En sık görülen enfeksiyon tipi %49 ile kan dolaşımı enfeksiyonları olmuştur. Etken mikroorganizmaların %52,8'i gram-negatif, %28,5'i gram-pozitif bakteriler ve %17,3'ü ise mantarlardır. E. coli gibi dirençli suşlar öne çıkmıştır. Tüm klinikler genelinde SHİE ile ilişkili mortalite oranı %7,6 olup,

YYBÜ’de bu oran %12,5’e yükselmiştir.

Sonuç: Bu SHİE’ler, özellikle yoğun bakım ünitelerinde yatan çocuk hastalar için önemli bir sağlık sorunu olmaya devam etmektedir. Kan dolaşımı enfeksiyonlarının yüksek sıklığı, gram-negatif ve mantar etkenlerinin baskınlığı, tedavi zorluklarını artırmaktadır. Bu veriler, enfeksiyon kontrol önlemlerinin güçlendirilmesi, hedefe yönelik antimikrobiyal kullanım ve düzenli sürveyansın önemini vurgulamaktadır.

Anahtar Sözcükler: Sağlık Hizmeti İlişkili Enfeksiyon, Pediatrik Yatan Hastalar, Antimikrobiyal İlaç Dirençleri, Mor-talite Oranı, Yenidoğan Yoğun Bakım Ünitesi.

HHealthcare-associated infections (HCAIs) are infectious diseases of particular concern to all clinical disciplines within a healthcare facility. HCAIs occur while receiving health care, developed in a hospital or other healthcare facility, and first appear 48 hours or more after hospital admission or within 30 days after receiving health care (1). While HCAIs in children share many similarities with those observed in adults, they also exhibit distinctions attributed to age-related host factors and variations in the immune system.

The HCAI rate varies with the patient's age and characteristics, the country's development level, implementation of preventive measures and the hospital's technological capabilities. Varying rates of HCAIs have been reported in different studies, ranging from 3.1% to 14.1% (2). HCAIs are relatively more common in intensive care units than other units providing care to patients with the risk factors (3).

Knowledge regarding the epidemiology of HCAIs is crucial in establishing preventive strategies and implementing effective and reliable plans. In Turkey, like other developing countries, there is little data that specifically focuses on pediatric HCAIs. Epidemiological studies help healthcare policymakers and clinicians improve healthcare. Our results will be used by both our hospital and other health care providers. The incidence, types, responsible microorganisms, antibiotic resistance rates and mortality rates varies between different hospitals. This study aimed to evaluate our clinic in terms of HCAIs and to plan the measures to be taken. In addition, similar studies to be conducted in the following years will determine the effectiveness of planning and precautions. The present study evaluates the HCAIs occurring in the clinics of the Pediatric Department at Suleyman Demirel University Hospital to identify rate and incidence density of HCAI, the causative microorganisms and evaluate antibiotic resistance.

MATERIAL AND METHOD

The pediatric clinic in Suleyman Demirel University Research and Application Hospital comprises a 24-bed pediatric ward, a 6-bed pediatric intensive care unit and a neonatal intensive care unit equipped with nine incubators. This registry-based descriptive study was conducted in Suleyman Demirel University Hospital.

Data were collected prospectively through daily visits to the inpatients. Medical chart reviews, nurse observations, and laboratory parameters, radiological, microbiological and other diagnostic test results were recorded. The form prepared by infection control committee was used. Demographic characteristics, location HCAIs according to site, responsible microorganisms and

antimicrobial resistance were recorded on the forms. The sample size comprised all patients admitted to pediatric clinics for one year. The sampling method was determined by selecting only those diagnosed with HCAI from all patients included in the study for one year. The follow-up of the study participants continued until their discharge, transfer to another facility or death, signifying the conclusion of the patient's stay for any reason. Patients who did not meet the criteria for HCAIs were excluded from the study. HCAIs were defined according to the classification system updated by the Centers for Disease Control and Prevention (CDC) in 2008 (4). The HCAI rate was calculated as the number of HCAIs/number of patients admitted x 100 and HCAI incidence density as the number of HCAIs/patient day x 1,000.

Peripheral and catheter blood cultures were sown on blood culture medium (BD Bactec Peds Plus/F, Becton-Dickinson), other samples were sown on blood agar (Or-Bak), EMB agar (Or-Bak) and chocolate agar (GBL). When growth was observed in blood cultures, they were passaged onto the aforementioned solid media. Blood cultures were incubated for five days and other cultures for two days. Samples with growth were identified by biochemical identification and automated system (Mini Api Biomerieux) according to the type of microorganism and sown on Mueller Hinton (BD, Becton-Dickinson) agar for antibiotic susceptibility testing by Kirby Bauer disc diffusion method. The samples were re-evaluated after 24 hours according to 'Clinical and Laboratory Standards Institute, USA' (CLSI). Antibiotic susceptibility tests were determined by disc diffusion method according to CLSI standards.

Statistical analysis

This study was conducted following the Principles of the Declaration of Helsinki 2008. It was approved by the ethics committee of Suleyman Demirel University of Medical School (meeting number XVII, no: 08). All statistical analyses were performed using IBM SPSS Statistics (Version 26.0. Armonk, NY: IBM Corp.). All qualitative variables were expressed as count and percent.

RESULTS

A total of 1,291 patients were admitted to the pediatric inpatient clinics of our hospital (pediatric ward (PW), pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU)) in the study period, among which 65 (5.03%) developed a total of 102 episodes of HCAI. Among these patients, 16 (24.8%) were followed up in the PW, nine (13.8%) in the PICU and 40 (61.5%) in the NICU. The total rate of HCAI was

7.9%, and the incidence density of HCAI was 9.31 per 1,000 patient days. An analysis of the HCAI rates of each clinic revealed an HCAI rate of 33.3% in the

PICU, 32.3% in the NICU and 1.74% in the PW (Table 1).

Table 1. Number of inpatients, number of patients with HCAIs, number of HCAI episodes, and the rates and incidences of HCAIs.

Inpatient Clinics										
	Total Number of Inpatients, n	Number of Patients with HCAI, n	Number of HCAI Episodes, n	BSI	NP	NUTI	Other	Patient Days, n	HCAI Rate, %	HCAI Incidence, %
PICU	48	9	16	3	5	8	0	1,422	33.3	11.2
CA*, n (%)				0	3	5	0			
NICU	210	40	68	44	8	3	13	3,699	32.3	18.3
CA*, n (%)				21	6	0	0			
				47.7	75					
Pediatric Ward	1,033	16	18	3	9	5	1	5,833	1.74	3.09
CA*				0	0	0	0			
Total	1,291	65	102					10,954	7.9	9.3

Abbreviation: PICU: Pediatric intensive care unit, NICU: Neonatal intensive care unit, HCAI: Health care-associated infections, BSI: Bloodstream infection, NP: Nosocomial pneumonia, NUTI: Nosocomial urinary tract infections, CA: Catheter associated, Other: Gastrointestinal infection, Central nervous system infection, Soft tissue infection.

Among HCAI subtypes, bloodstream infections (BSIs) were the most common (50 episodes, 49%). The prevalence of different HCAI subtypes was found to vary between different age groups, with BSIs (65%) being most common in the neonatal period, NUTIs (Nosocomial Urinary Tract Infections) (64%) in the 5-12 years age group, and NP (Nosocomial Pneumonia) (54%) in the 1-5 years age group (Figure 1).

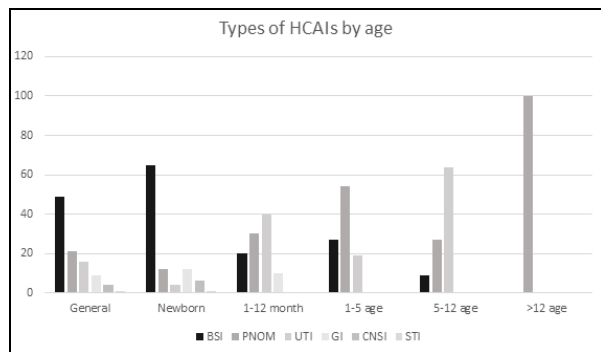


Figure 1. Types of HCAIs (n) by age.

The underlying risk factors of patients with infections were investigated. In NICU, 72.2% of patients with BSI were premature, 66% had catheter use, and all NP patients had mechanical ventilator use. In PICU, 66% of patients with BSI had catheter use and 40% of NP patients had mechanical ventilator use.

The causative agents for HCAIs were gram-positive microorganism in 30%, gram-negative microorganism in 51.4%, and fungi in 17.2%. Among gram-positive bacteria, the most frequently isolated agent was coagulase-negative staphylococci (CoNS), which accounted

for 65% of the total. Among gram-negative bacteria, Klebsiella spp. (12.8%), Acinetobacter baumannii (12.8%) and Escherichiae coli (E. coli) (11.5%) were the most frequently isolated microorganisms. All the isolated fungi was Candida spp. When analyzed by age groups, the predominance of gram-positive microorganisms observed during the neonatal period shifted toward a predominance of gram-negative microorganisms with advancing age (Figure 2).

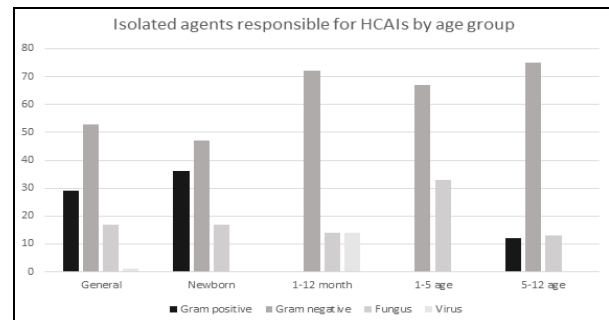


Figure 2. Isolated agents responsible for HCAIs (n) by age group.

The antibiotic resistance patterns of certain isolated agents responsible for HCAIs were investigated. For P. aeruginosa, the resistance rates were as follows: 100% resistance to cefepime and 66.6% resistance to piperacillin-tazobactam, while no resistance to carbapenems or aminoglycosides was identified. Table 2 presents the results of antibiotic susceptibility tests for microorganisms responsible for HCAIs, exhibiting an isolation rate higher than 5%.

Table 2. Antibiotic resistance status (%) of microorganisms responsible for HCAs with an isolation rate higher than 5%.

	CoNS	<i>P.aeruginosa</i>	<i>A.baumannii</i>	<i>Klebsiella</i> species	<i>E.coli</i>	<i>Enterococcus</i> spp
Amikacin	-	0	87.5	0	0	33.3
Amoxicillin-Clavulanate	-	-	-	71.4	100	-
Ampicillin-Sulbactam	-	-	0	14.2	28.5	85.7
Aztreonam	-	100	-	57.1	85.7	-
Dalfopristin	46.1	-	-	-	-	-
Doripenem	-	-	75	-	-	-
Erythromycin	69.2	-	-	-	-	-
Gentamycin	38.4	0	87.5	14.2	0	-
Imipenem	-	0	0	14.2	0	-
Clindamycin	61.5	-	-	-	-	-
Colistin	-	-	37.5	-	-	-
Levofloxacin	-	0	87.5	-	-	-
Linezolid	0	-	-	-	-	0
Meropenem	-	0	87.5	14.2	0	-
Metronidazole	-	-	-	85.7	-	-
Mezlocillin	-	-	87.5	-	-	-
Minocycline	-	-	12.5	-	-	-
Netilmicin	-	0	87.5	-	-	-
Ofloxacin	100	0	-	-	-	-
Oxacillin	100	-	-	-	-	-
Penicillin	100	-	-	-	-	-
Piperacillin-Tazobactam	-	66.6	62.5	14.2	28.5	-
Rifampin	100	-	-	42.8	-	-
Cefepime	-	100	100	71.4	57.1	-
Cefoperazone-sulbactam	-	33.3	25	28.5	0	-
Cefotaxime	-	-	-	71.4	85.7	-
Ceftazidime	-	100	87.5	71.4	85.7	-
Ceftriaxone	-	-	87.5	71.4	85.7	-
Cefuroxime	-	-	-	57.1	85.7	-
Ciprofloxacin	69.2	0	87.5	14.2	0	42.8
Cefazolin	-	-	-	71.4	85.7	-
Cefalotin	-	-	-	42.8	85.7	-
Cefixime	-	-	-	14.2	85.7	-
Teicoplanin	7.6	-	-	0	-	0
Ticarcillin-clavulanic acid	-	66.6	50	-	-	-
Trimethoprim-sulfamethoxazole	69.2	-	0	28.5	57.1	-
Tobramycin	-	-	12.5	-	-	-
Vancomycin	0	-	-	-	-	0

The overall mortality rate was 3.1% among all pediatric inpatients, and 24.6% for patients diagnosed with

HCAs. The overall mortality associated with HCAI was 7.6%. All mortality rates are presented in table 3.

Table 3. Mortality Rates.

	OVERALL (n =1291)	NICU (n =210)	PICU (n =48)	PW (n =1,033)
Overall Mortality, n (%)	41 (3.1%)	24 (11.4%)	17 (35.4%)	-
HCAIs-related Mortality, n (%)	5 (0.4%)	5 (2.4%)	-	-
Non-HCAIs-related Mortality, n (%)	25 (1.9%)	17 (8.1%)	8 (16.6%)	-
Other causes, n (%)	11 (0.8%)	2 (0.9%)	9 (18.8%)	-
	OVERALL-HCAIs* (n =65)	NICU-HCAIs* (n =40)	PICU-HCAIs* (n =9)	PW-HCAIs* (n =16)
Overall Mortality, n (%)	16 (24.6%)	12 (30%)	4 (44.4%)	-
HCAIs-related Mortality, n (%)	5 (7.6%)	5 (12.5%)	-	-
Non-HCAIs-related Mortality, n (%)	11 (16.9%)	7 (17.5%)	5 (55.6%)	-

Abbreviation: PICU: Pediatric intensive care unit, NICU: Neonatal intensive care unit, HCAI: Health care-associated infections, BSI: Bloodstream infection, NP: Nosocomial pneumonia, NUTI: Nosocomial urinary tract infections, CA: Catheter associated.

DISCUSSION

Studies carried out worldwide have reported a broad spectrum of HCAI rates among pediatric inpatients, ranging from 0.7% to 17% (5-7). In the present study, the HCAI rate was 7.9%, with an incidence of 9.31 per 1,000 patient days. The results are consistent with the literature.

When the clinics were examined separately, the HCAI rate in PICUs abroad was found to be 6-26.5% (8-11). Studies show that HCAs for PICUs in our country are still in limited number. In studies conducted on this subject, the PICU rate varies between 11.7% and 31.4% (12-14). In our study, the HCAI rate in the PICU was found to be 33.3%. The reason for the high result may be due to the small sample size.

In studies conducted in other countries, the rate of HCAs among NICU patients has been reported to vary between 1.8% and 74.3% (15-18). In studies conducted in two different centers in our country, it was reported as 28.1% in Istanbul University and 42.3% in Uludağ University (14, 19). The rate of HCAs among NICU patients observed in the present study (32.3%) is higher than the average rate of those reported from developed countries, but comparable to rates reported from other countries and those reported in previous studies conducted in Turkey.

The ranking of frequently observed infections varies when HCAs are analyzed based on the affected body system. In a study conducted by Raymond et al. (17), BSIs, NP and NUTIs were identified as the most commonly observed HCAs, supporting in part the findings of another study reporting NP and NUTIs as the most common HCAs (20). In a multicenter European study, BSIs were identified as the most common HCAI, followed by NP with rates of 44.6% and 22.2%, respectively (21). In a study covering all pediatric clinics in a hospital in Iran, the most common type of HCAs was found to be BSI (36.34%) (22). In a similar study conducted in Istanbul, BSI rate was 26.5% and NP rate was 20.4% (14). The most common HCAs observed in the present study were BSIs, NP and NUTIs, with rates of 49%, 21% and 16%, respectively. The results were consistent with the literature. BSI rate was found to be the highest in the neonatal intensive care unit. This result increased the overall average.

The pathogenic agents responsible for HCAs vary between studies of adult populations and those conducted with children. In a study conducted by Raymond et al. (17) of pediatric inpatient clinics of all kinds, gram-positive bacteria were identified as the most common agent responsible for HCAs with a rate of 37.2, followed by CoNS with a rate of 24.1%, and gram-negative bacteria were identified at a rate of 47.9%. In a 4-year surveillance study conducted in Turkey spanning the period from 2016 to 2020, the most common causes of HCAs were identified as gram-positive bacteria, gram-negative bacteria and fungi, with rates of 23.4%, 64.9% and 11.7%, respectively (23). In a study conducted at Istanbul University, the most common causative agent of HCAI was gram-negative bacteria with 32% (14). In the present study, the causative

agents for HCAs were gram-positive bacteria in 30%, gram-negative bacteria in 51.4% and fungi in 17.2%. The most frequently detected microorganisms were 18.5% CoNS, 17.3% *Candida* spp, 12.8% *Klebsiella* spp, 12.8% *Acinetobacter* spp and 11.5% *E. coli*. In our study, we found that gram-negative agents were lower and fungal agents were higher than the national average, but our rates were similar to those found in other countries. The high rate of fungal infections may be related to long-term multiple antibiotics and central catheter use.

Antibiotic resistance continues to be a potential threat. In studies carried out in various pediatric wards in Turkey, the rate of methicillin resistance ranged from 50% to 66.6% in *S. aureus* strains, and 87.5% for CoNS strains. Extended-spectrum beta-lactamase (ESBL) positivity was identified in 31.8-73% of *E. coli* strains and 46-66% of *Klebsiella* strains (24, 25). In another study, methicillin resistance rate was found to be 50% in *S. aureus* strains and 86.2% in CoNS strains, while ESBL positivity rate was 55.6% in *E. coli* strains and 61.9% in *Klebsiella* strains (14). In the present study, the rate of methicillin resistance was 33.3% in *S. aureus* strains and 100% in CoNS, whereas the rate of ESBL positivity was 75% in *E. coli* strains and 55.5% in *Klebsiella* strains. Recent studies have reported an increase in the frequency of methicillin-resistant *S. aureus* strains, reaching rates as high as 57% (23). No vancomycin resistance was found in enterococci. In the present study, although resistance rates were comparable to those reported in local publications, the rate of ESBL positivity was high (75%) for *E. coli* strains, which can be attributed to the limited number of reproduced strains and irrational antibiotic use. CoNS and *E. coli* had a high resistance rate compared to the literature. These microorganisms may cause more significant problems in the future, especially in pediatric patients receiving intensive care treatment. Attention should be paid to hand hygiene and contact isolation.

The highest resistance rates to the *Klebsiella* species were observed for amoxicillin-clavulanate, cefepime, cefotaxime, ceftriaxone and cefazolin (71.4%), and the rates of susceptibility were 85.8% for piperacillin-tazobactam, 85.8% for carbapenem and 85.8% for ciprofloxacin. Due to comparable susceptibility profiles, these antibiotics can be used for empirical therapy and as second-line treatment options. It is worthy of note in the present study that the rate of carbapenem resistance in *Klebsiella* strains was 14.2%, while the NHAISN (National Healthcare-Associated Infections Surveillance Network) 2021 report indicated a rate of 48.9% that was updated to 63.57% in the NHAISN 2022 report (26).

Addressing the issue of mortality linked to HCAs, a retrospective study conducted in France of patients who had died within the previous year found HCAs to be the underlying cause of death in 4.4% of cases (27). The rate of deaths attributable to HCAs in NICUs was reported to be 12.7% in an Italian study and 10.3% in a Japanese study (28, 29). In a study conducted in Turkey, the rate of mortality associated with HCAs was

reported in the range of 16–24.4% (19). The present study's overall mortality rate in NICU patients was 11.4% (24/210). The rate of HCAI-related mortality was 12.5% (5/40) in newborns diagnosed with HCAs. The mortality rates observed in the present study were consistent with those reported in the literature. No HCAI-related mortality was observed in the pediatric ward or PICU. Mortality due to HCAI is currently seen especially in the NICU. Therefore, infection control measures should be paid more attention to in the NICU.

We found that hospitalized children in NICU and PICU wards are the most susceptible to HCAs. In Suleyman Demirel University Hospital, BSIs, NP, and NUTIs were the most frequent infections, and CoNS, *Candida* spp, *Klebsiella* spp, and *Acinetobacter* spp were the most commonly detected microorganisms. ESBL positivity was found to be high in *E. coli* strains. The antibiotic resistance status of the identified causative agents allowed us to update the appropriate empirical antibiotic selection. It was concluded that implementing surveillance, education on this subject and frequent and careful application of isolation methods will

reduce the incidence of HCAs and the mortality and morbidity caused by them.

Determining the frequency, types, causative microorganisms and bacterial resistance rates of HCAI can guide clinicians in empiric antibiotic selection and measures to prevent infections.

Limitations

The limitations of our study include the sample size, the number of patients, the number of beds, the low number of inpatients, the short duration of the research and the need for comparative data from previous years in the exact center. Other limiting features include the lack of a burn unit, immunology unit, transplant unit and hematology-oncology unit in our hospital and therefore the inability to follow immunocompromised patients. In addition, our patients had some risk factors. These increase the incidence of HCAI. In our study, 72.2% of patients with BSI in NICU were premature, 66% were using central catheters, and all patients with NP were receiving mechanical ventilator support. No panel tests were conducted for viral infections that caused HCAI.

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