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Major Article

Stenotrophomonas *maltophilia* outbreak originating from a pull-out faucet in a pediatric intensive care unit in Turkey: Insights from clinical records and molecular typing

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Key Words:
Stenotrophomonas *maltophilia* bacteremia
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Faucet aerator
Genotype
Outbreak-investigation

Background: Nosocomial Stenotrophomonas *maltophilia-related* cases are rising and pose a threat to immunocompromised patients. Twelve patients from our pediatric intensive care unit (PICU) presented with S *maltophilia-associated* bloodstream infection.
Methods: This outbreak investigation includes 12 patients from PICU between the ages of 2 months and 4 years (mean 16 months, 7 male). To identify the origin, samples from all possible sources throughout the hospital were collected and ran through DNA isolation and Pulse Field Gel Electrophoresis.
Results: 120 samples were collected during the outbreak. 31 samples (26%) were positive for *S maltophilia.* 30 *S maltophilia* isolates were analyzed, 10 different genotypes were identified. Clustering isolates were grouped into 3 different clusters (tolerance and optimization 1.0, cutoff 90%). The largest cluster was genotype 1, which included 19 isolates, those belong to patients' samples and a sample from a pull-out faucet inside the PICU. The Pull-out faucet was the origin of the bloodstream infection.
Discussion: Pull-out faucets allow biofilm production, due its structure. Pulse Field Gel Electrophoresis identifies the transmission dynamics of the outbreak, with its high discriminatory power.
Conclusions: Water sources should be monitored on a regular basis. Pull-out faucets enable bacterial overgrowth; therefore, we recommend water surveillance during outbreak investigations.

BACKGROUND

Stenotrophomonas maltophilia is the third most common non-fermenting gram-negative rod, which infects humans after *Pseudomonas aeruginosa* and *Acinetobacter spp.*[1,2] In the last few decades *S maltophilia* occurrences have multiplied, making it increasingly recognized as an important cause of nosocomial infections. Therefore, many outbreaks have been reported within the last few years in hospitals and intensive care units (ICUs).[3,4] A study conducted in a European center for pediatric hematology and oncology reported an incidence of 2.3% of *S maltophilia* infections among pediatric patients admitted to the ICU.[5]

S maltophilia presents with minimal invasiveness in immunocompetent individuals, but it can lead to severe even fatal infections in immunocompromised patients. Its high resistance to many antimicrobial agents may result in unsuccessful treatments and a significant mortality rate in patients.[6–8]

METHODS

This is an outbreak investigation, and the project was deemed IRB-exempt.

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Table 1
Demographics and lab findings of the patients

	Patients (n) (%)
Male	*7 (58.3%)*
*Age in months**	*11 (2-48)*
Positive culture after 'n' days in PICU admission	*9.5 (48 h-28 days)*
Known congenital disorder	*10 (83.3%)*
Cardiovascular disease	*6 (50%)*
*Peak C-reactive protein***	*49.9 (5.23-200.89)*
*White blood cell count**	*12.05 (5.5-22.76)*
*Neutrophil count**	*7.01 (2.01-18.61)*
Immunosuppressed	*9 (75%)*
Central venous Catheter presence	*8 (66.6%)*

NOTE. * Median values are calculated ** Fifthpercentile ***peak CRP at the time of BSI.

Subjects

In the PICU of Istanbul Medipol University Mega Hospital, between August 6, 2021, and December 2, 2021, 12 patients between the ages of 2 months and 4 years (mean 16 months, 7 males, 5 female) were diagnosed with bloodstream infection (BSI) due to *S maltophilia*. All patients were positive ≥48 hours of their PICU admission and therefore fulfilled the criteria for hospital-acquired BSI.[9] Each patient was reviewed for their history of known disorders, immunosuppression status, presence of any type on intravenous instruments, peak C-reactive protein, white blood cells, and neutrophil levels at the time of BSI.

As a part of the investigation process environmental samples had been swabbed from all possible sources, especially from damp environments, (such as faucets, pull out-faucets, wash trays, water hoses, water reservoirs of humidifiers, ventilators, nebulizers, continuous positive airway pressure machines, nasal cannulas, oxygen masks, tracheostomy tubes, central lines, medicine pumps, nasogastric and gastrostomy tubes, feeding bottles, baby pacifiers, inflatable cuffs, temperature probes, heart monitors, pulse oximeters, hospitals bed head surfaces and sheets, shelving and care trolleys, foley, indwelling catheters). In addition, patient surveillance samples were obtained from endotracheal aspirates, rectal and skin swabs.

Antimicrobial sensitivity tests for Stenotrophomonas maltophilia

Antimicrobial sensitivity tests were conducted on 30 strains of *S maltophilia* using the standard disk diffusion method (Bioanalyze). The tests were performed with 5 different antibiotics: ceftazidime (5 μg), minocycline (30 μg), ciprofloxacin (5 μg), levofloxacin (5 μg), and trimethoprim/sulfamethoxazole (1.25 μg/23 μg). These tests were performed at the Medical Microbiology Research Laboratory of Recep Tayyip Erdogan University, Faculty of Medicine. The results were evaluated according to the EUCAST 2022 (v. 12.0) (European Committee on Antimicrobial Susceptibility Testing) criteria.[10]

DNA isolation and integron gene cassette screening

Total DNA isolation was performed using the boiling method.[11] Integron gene cassettes and resistance genes were screened by protein chain reaction from all bacterial strains using sequences described previously.[12–17]

Pulse field gel electrophoresis (PFGE) protocol

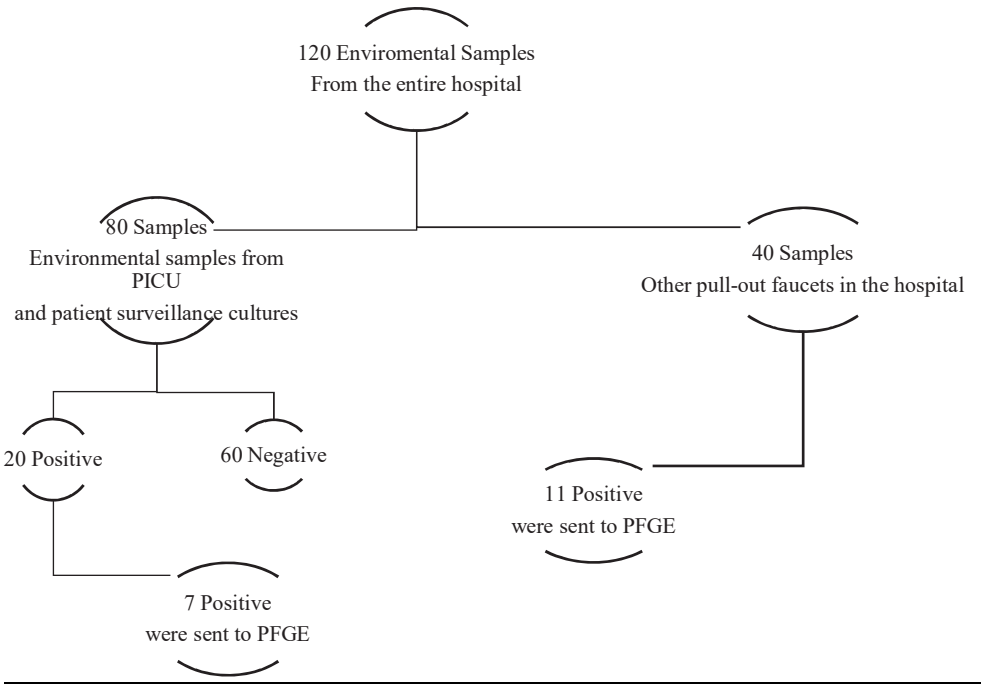
All 30 *S maltophilia* isolates were typed by PFGE according to a protocol published by Durmaz et al with modifications. All strains recovered from patient clinical samples and environmental sources were taken for PFGE study from Medipol Mega hospital in İstanbul. Genotypes were grouped for this outbreak investigation.

Results

Patients' demographics and lab findings are given in Table 1.

A total of 120 samples were collected from the hospital during the outbreak (80 samples from the PICU and 40 samples from the other pull-out faucets in the hospital) and 31 samples (26%) were positive for *S maltophilia*. In addition to 18 environmental isolates, 12 BSI isolates were analyzed with PFGE (Table 2). Epi-curve for the outbreak is given in Figure 2.

Table 2
Flowchart of the collected environmental samples



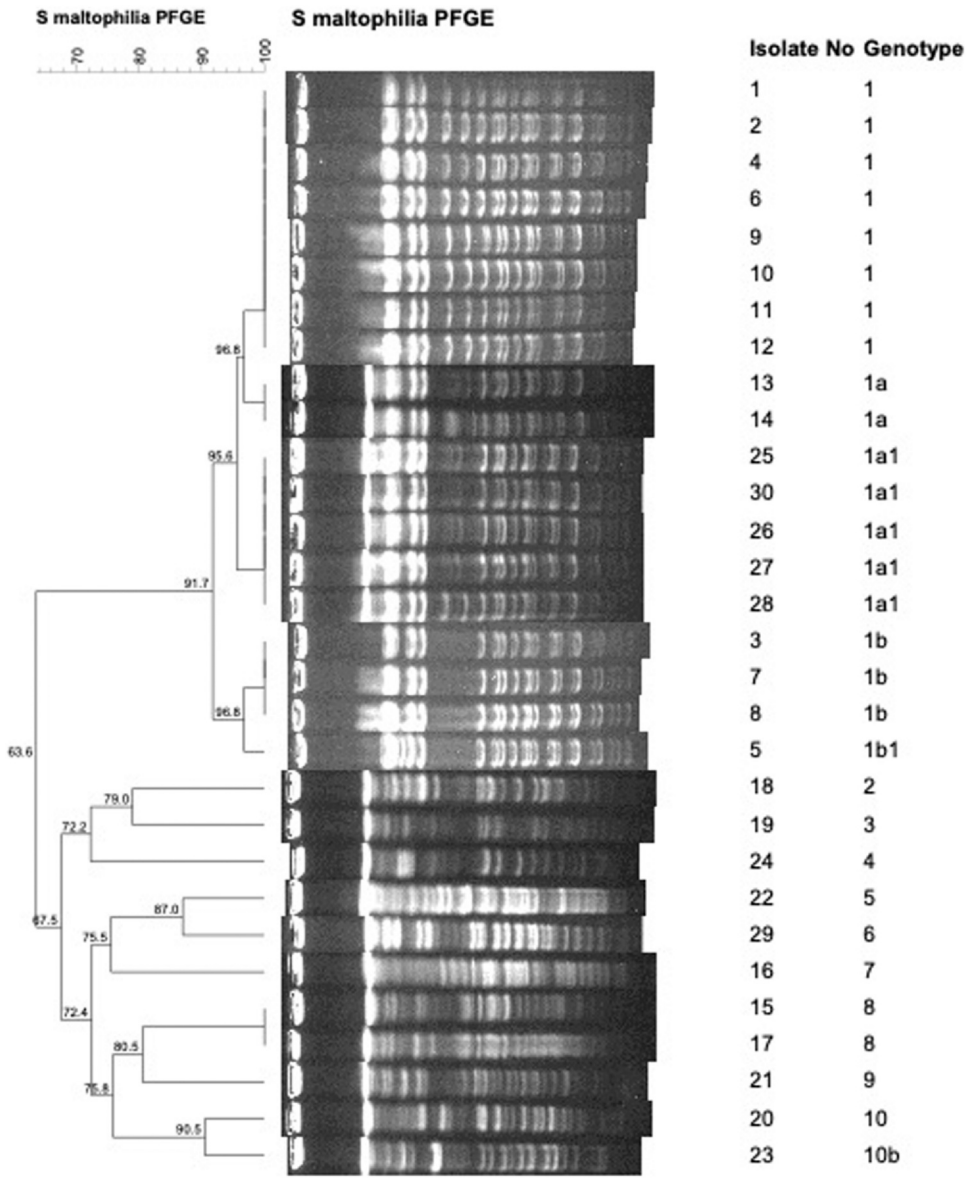


Fig. 1. The PFGE results of 8 environmental and 12 bloodstream infection isolates.

Among the 30 *S maltophilia* isolates, 10 different genotypes were identified, and the isolates showing clustering were grouped into 3 different clusters (tolerance 1.0, optimization 1.0, cutoff 90%). The largest cluster was genotype 1, which included 19 isolates (Fig 1). It is likely that the isolates within genotype 1 were associated with an outbreak. Isolate numbers 1, 2, 4, 9, 10, 11, 12, 13, 14, 25, 26, and 30 are isolates recovered from patients' blood cultures. Isolate numbers 3, 5, 7, 8, 27, and 28 were environmental isolates. Isolate number 6 was recovered from the pull-out faucet inside the PICU. In Figure 3 the rooms that patients stayed during the outbreak is represented with star sign. Overall, in the PICU, there were 6 faucets (shown with a tap sign) and a pull-out faucet (isolate no: 6, represented with a star sign), which were located in the medicine preparation room. Only the pull-out faucet was positive for *S maltophilia* . When the contaminated pull-out faucet was replaced in December 2021, the outbreak ceased, which clarified the origin. The other clusters were genotype 8 and genotype 10, each containing 2 isolates. 23 out of the 30 *S maltophilia* isolates were included in any of the clusters, with a clustering rate of 76.6%. According to the protein chain reaction results, no gene cassettes were found. All isolates recovered from blood cultures were susceptible to ceftazidime and trimethoprim/sulfamethoxazole. We treated all our patients with trimethoprim/sulfamethoxazole.

DISCUSSION

S maltophilia is frequently recognized as a pathogen that thrives in immunocompromised hosts because of its low virulence and consequent opportunistic nature. According to genomic diversity

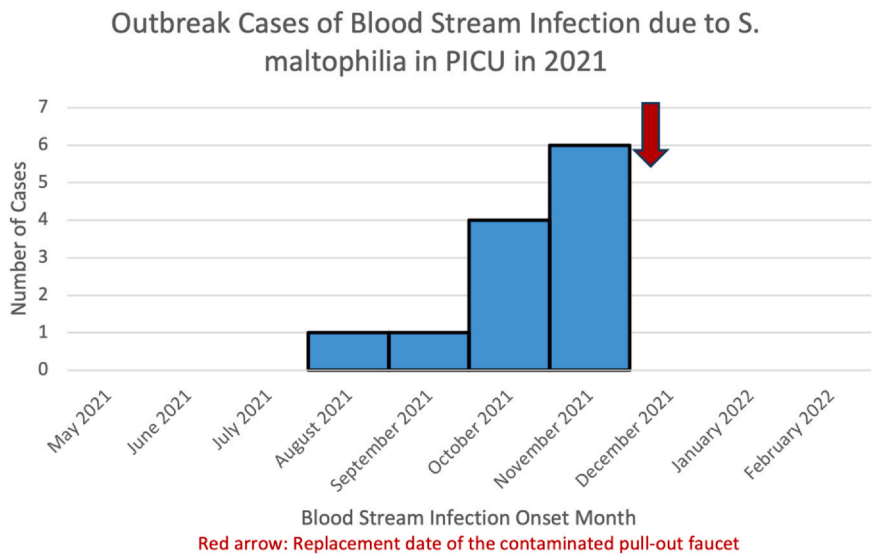


Fig. 2. The epicurve of the outbreak.

among isolates associated with nosocomial cases, there is a strong suggestion of multiple independent environmental sources of transmission.[18,19] *S maltophilia* can attach to and survive on abiotic surfaces within clinical settings via its charged cell wall surface and biofilm production, such as central venous catheters, disinfectant, and handwashing solutions, solutions for hemodialysis, endoscopes, inspiration and expiration circuits of ventilators, nebulizers, tap water, and showerheads.[20–22] Moreover, patient-to-patient transmission has also been reported.[17,18]

E. Sakhnini et al reported 2 infants in a neonatal ICU had *S maltophilia* BSI originating from faucets in the room of one of the patients.[23] Another study from the Netherlands reported 1 *S maltophilia* BSI, which was cultured from tap water from 3 outlets in the neonatal ICU.[24] Data by Weber et al demonstrated that 2 patients were colonized by strains of *S maltophilia* contaminating the faucet aerators in the sink.[25]

WHO has classified *S maltophilia* as one of the leading multidrug-resistant organisms in hospital settings.[19] The risk factors of *S maltophilia* BSI include underlying malignancy (especially hematologic malignancy), organ transplantation, HIV infection, underlying cardiovascular disease, prolonged hospitalization, ICU admission, indwelling catheters (vascular, urinary, and biliary), corticosteroid or immunosuppressive therapy, and prior antibiotic treatment with carbapenem.[21,26–29] Analyzing our patients' profiles, 75% of them were immunocompromised, 50% had underlying cardiovascular disease, and 66.6% had central venous catheters.

We employed various methodologies to assess the contributing factors and identify the transmission patterns. The infection control team observed PICU-staff through the surveillance cameras for 24/7 and weekly meetings were done to give feedback. Our investigation revealed that a pull-out faucet within the PICU and the pipeline attached to it was completely covered with biofilm, which grew *S maltophilia* . Flexible polymeric pipe materials are commonly used as shower hoses or connections to faucets in the last meters of building plumbing. These tend to leach high concentrations of carbon, which may encourage bacterial growth.[30]

There were few theories on how the bacteria located in the pull-out faucet could have caused the outbreak. The theories include a lack of appropriate hand hygiene, incompatible use of medical gloves, asepsis, and cleaning techniques, and not following the isolation rules properly. After pinpointing the outbreak, the hospital's infection control team arranged mandatory training and replaced the pull-out faucet with standard faucets. Training on isolation procedures was provided to resident doctors, whereas new nurses entering the field received training on bedside and mock scenarios. Auxiliary staff were also trained on cleaning procedures.

Our outbreak investigation had several strengths, including access to comprehensive medical records and evaluation of the relevant risk factors. Differentiating true BSI from pseudo-outbreaks due to contamination is crucial for accurate analysis. To address this issue, we used peak C-reactive protein levels as an indicator of true BSI. This approach helped us distinguish genuine infections from contamination-related incidents, thereby enhancing the reliability of our findings. To identify the transmission dynamics of the outbreak, we employed PFGE, which has high discriminatory power. Previous studies conducted in newborns and PICUs have successfully used molecular typing to identify the cross-transmission of *S maltophilia.* [31,32] Furthermore, we took extensive measures to explore all possible sources of contamination by collecting samples from various environmental sources. This comprehensive approach allowed us to thoroughly investigate potential reservoirs and contributing factors within the PICU.

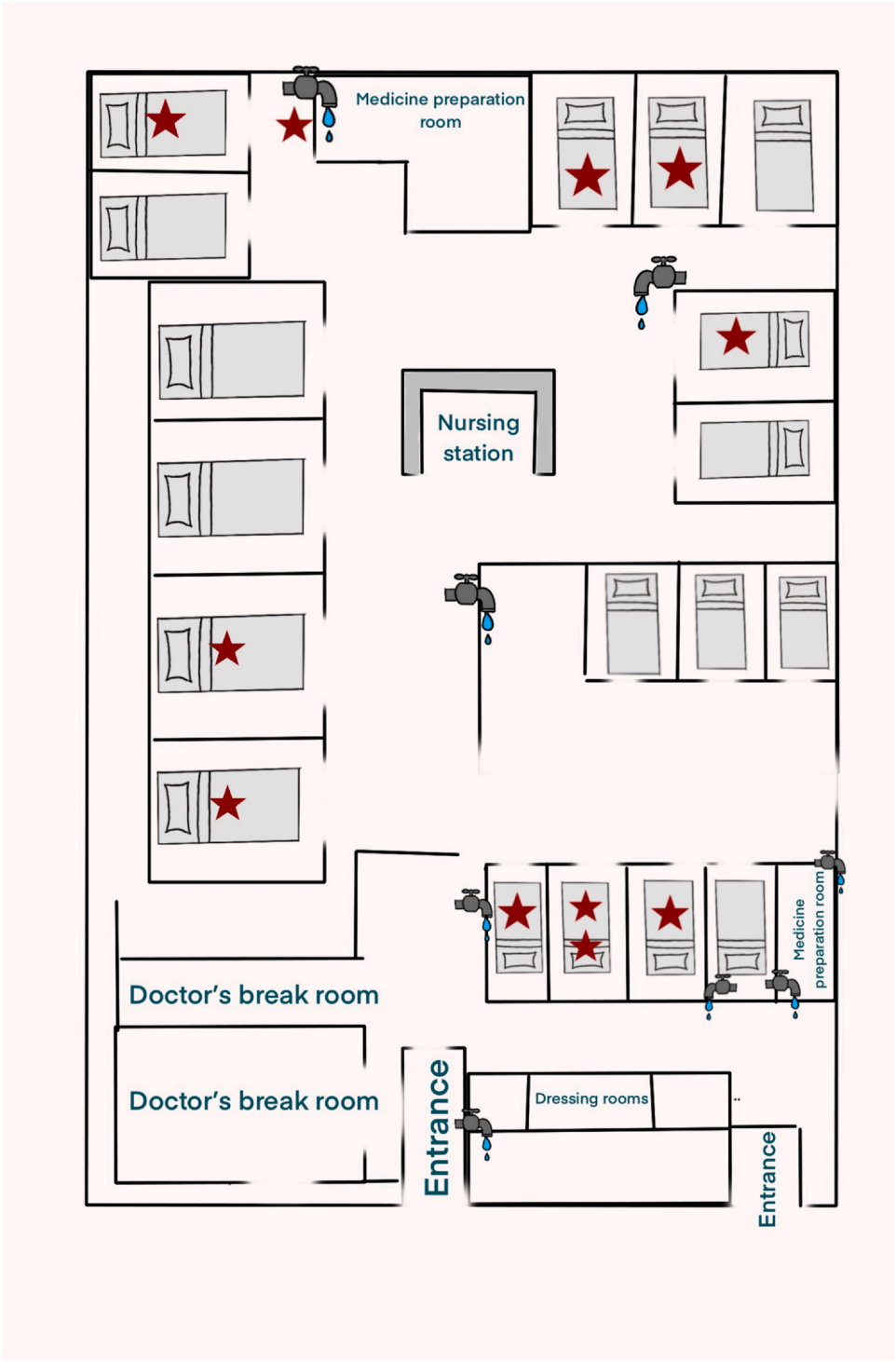


Fig. 3. The map of the pediatric intensive care unit during the outbreak.

CONCLUSIONS

Our outbreak investigation highlights a significant positive link between waterborne *S maltophilia* prevalence rates in PICU patients and tap water supply contamination. The molecular correlation between pull-out faucet originating *S maltophilia* and clinical strains isolated from vulnerable patients was a remarkable finding. Even though pull-out faucets allow easier access to water, it is susceptible to biofilm formation. Therefore, we do not recommend the use of pull-out faucets inside the PICU. Our research highlights the importance of mandating the use of sterile water in PICUs, training hospital staff to spot breaks in sterilization techniques, and including water surveillance during outbreak investigations.

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