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Kocuria Species: Important Emerging Pathogens in Pediatric Patients

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Abstract

***Kocuria* spp., are frequently documented members of the human microbiota and were formerly thought to be opportunistic bacteria, initiating infection only in immunocompromised patients. This study aimed to determine the prevalence of *Kocuria* species in samples from Iraqi pediatric patients, in addition to their sensitivity pattern. Bacterial identification was performed using a VITEK 2 device, and the Kirby-Bauer disk diffusion method was used to determine antibiotic susceptibility. Of 261 positive cultures, we found *Kocuria* isolates from 7 cases (2.68%). The mean age of the patients was 5.47 years, ranging from 4 months to 10 years; there were 3 males and 4 females. All patients had either urinary tract disease or symptomatic bacteremia. Vitek-2 identification using a gram-positive (GP) card revealed the presence of *Kocuria kristinae* in five cases, *K. rhizophila* in one case, and *K. rosea* in one case. Susceptibility of the *Kocuria* species isolates to amikacin, gentamicin and ceftazidime were demonstrated 100% resistance. In conclusion, *Kocuria* species, which are associated with serious clinical manifestations are an emerging health issue and further attention should be taken for appropriate management of antibiotic treatment as they are intrinsically multi-drug resistant.**

Keywords: *Kocuria, K.rhizophila, K.kristinae, K.rosea,* Pediatric

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INTRODUCTION

In medical society, there have been frequent changes in global health partially due to changes in lifestyle habits. In particular, changes in the composition of bacterial flora and increasingly pathogenic and antibiotic resistant forms are often observed in clinical practice.[1,2] Bacteria initially defined as opportunistic pathogens have shown the ability to produce infections in various systems and organs,[3] one of which being *Kocuria* species which have been collected from innumerable environmental and ecological niches.[4] These are usually considered as non-pathogenic bacteria that are rarely associated with adult infections.[5] In children, infections with *Kocuria* are extremely rare, and only a few cases have been reported.[6]

The genus *Kocuria* which belongs to the family Micrococcaceae, sub-order Micrococcineae, order Actinomycetales, and class Actinobacteria, was named by Miroslav Kocur, a Slovakian microbiologist. They are a Gram-positive cocci organized in pairs, tetrads, short chains, cubical packets of eight and irregular clusters. There are in excess of 18 species of *Kocuria* identified according to previous studies of 16S rRNA phylogenetic analysis.[5,7] These organisms are generally commensal bacteria on the skin and mucous membranes. *Kocuria* have a small genome, are tolerant to a wide range of organic solvents, grow robustly under various conditions.[8]

Kocuria spp. are commonly documented members of the human microbiota.[7,9,10] They were formerly considered an opportunistic bacteria that initiated diverse infections only in immunocompromised hosts.[11,12] Normally, *Kocuria* species are commensal bacteria that mainly colonize sites such as skin, mucous membranes, and oropharynx. *Kocuria* spp. infections have been defined in the last decade as regularly affecting immunocompromised patients who using peritoneal dialysis or intravenous catheters.[7,13,14] However, current evidence has proposed that these bacteria, have pathogenic potential which was formerly undetected because of misidentification via phenotypic analyses as more common bacteria, such as coagulase-negative *staphylococci* (CNS).[5,7]

These bacteria are responsible for various types of infections, generally in immunecompromised patients with serious chronic conditions[5] mainly bacteremia/recurrent sepsis.[3] Notably, immunocompromisation was not shown in all case reports.[15,16] Most pediatric cases initiated via *K. rosea* and *K. kristinae* were defined only in one child so far, with peritonitis.[10,12] Recently, attention has been drawn to clinical aspects of *Kocuria*. This include infections such as endocarditis,[12] pneumonia,[16] sepsis (predominantly in immunocompromised patients),[3] and infections related to implanted foreign bodies such as IV lines and catheters.[17]

The number of confirmed cases of *Kocuria* infections in Iraq is very limited, and its clinical pathogenic potency is still dubious. Moreover, the number of reported patients in the pediatric group is even more limited. Therefore, we performed this study to better comprehend the clinical features of *Kocuria* species in pediatric patients, in addition to considering their sensitivity patterns.

MATERIALS AND METHODS

Sample Collection

This study was conducted in the Microbiology Laboratory, Al-Fallujah Teaching Hospital, Fallujah, Iraq, from June 2019 to July, 2021. We estimated the bacteriological profile plus patterns of antibiotic susceptibility for 261 positive bacterial samples from pediatric patients admitted to Fallujah Teaching Hospital for children and women. Patient information such as hospital data including age, sex, underlying disease antibiotic treatment, and hospital indications has been recorded.

Isolation of Bacteria

The collected samples were from pediatric patients with different medical conditions ranging from 6 days to 12 years of age. Over two years, the received positive cultures were sub-cultured on three types of media: Sheep blood, Chocolate, and MacConkey agar. Sheep blood and MacConkey dishes were incubated at 35°C under aerobic conditions, and chocolate agar plates were incubated under microaerophilic condition at the same temperature. All cultured plates were checked for bacterial growth after 24 to 48 h of incubation and results were recorded.

Table 1. Clinical profile of 7 patients with *Kocuria* Species infections

Kocuria Species	Age	Sex	Underlying disease
K. kristinae(1)	6 months	Male	Symptomatic bacteremia
K. kristinae(2)	8 years	Female	Urinary tract diseases
K.rhizophila	9 years	Male	Urinary tract diseases
K. kristinae(3)	4.5 years	Female	Urinary tract diseases
K. kristinae(4)	10 years	Male	Urinary tract diseases
K. rosea	6 years	Female	Symptomatic bacteremia
K. kristinae(5)	4 months	Male	Symptomatic bacteremia

Identification of Bacteria

Pure cultures of *Kocuria* species were obtained from sheep blood agar after incubation at 35 °C for 24 h. Colonies 1-2 mm in size were non-hemolytic, yellow, oxidase-positive, catalase-positive, coagulase-negative, non-capsulated, non-spore forming and non-motile. They were then identified as *Kocuria* by Gram staining and VITEK-2 ID-GPC card (BioMerieux, France) with a more than 95% probability.

Antibiotic Susceptibility Test

This test was performed using the disc-diffusion antibiotic sensitivity method of Kirby-Bauer[18] on Muller-Hilton agar (MHA). All discs were obtained from HiMedia Laboratories (India) in accordance with the Clinical Laboratory Standards Institute (CLSI) guidelines. Ciprofloxacin, gentamicin, vancomycin, trimethoprim, amikacin, clindamycin, ceftazidime, chloramphenicol, erythromycin, and azithromycin were used in this test.

RESULTS

In this study, which was conducted from June 2019 to July 2021, a total of seven *Kocuria* isolates were isolated, out of a total 261 positive cultures (2.68%). The mean age of the pediatric patients was 5.47 years and ranged from 4 months to 10 years of age. Among the pediatric patients there were 3 males (42.85%) and 4 females (57.14%). All patients had either urinary tract diseases (n=4,57.14%) or symptomatic bacteremia (n=3, 42.85%). All pediatric patients had fever after 48 h of hospitalization. Vitek-2 identification revealed the presence of *Kocuria kristinae* in five cases, *K. rhizophila* in one case, and *K. rosea* in one case using the GP card (Table 1).

Overall antibiotic susceptibility to most commonly used antibiotics was found to be good. Susceptibility of the *Kocuria* Species isolates to Amikacin, Gentamicin and Ceftazidime were 100% resistant. While, Trimethoprim and Azithromycin were the most sensitive drugs (100%) susceptibility followed by Vancomycin (85%) as shown in Table 2.

DISCUSSION

Kocuria bacteria uncommon pathogenic organisms in human, especially in children.[17] These bacteria are generally found in the mucosa and skin of humans, but are infrequently found in clinical specimens. Nevertheless, it can cause opportunistic or nosocomial infections in many patients with indwelling devices and acute underlying diseases.[19] *Kocuria* is a member of the Micrococcaceae family and currently encompasses more than 18 species, although only a few species in this genus have been identified as opportunistic pathogens, including *K. kristinae, K. rosea*, and *K. rhizophila*,[20,21] as confirmed in this study.

In the present study, the prevalence of *Kocuria* spp. was 7 out of total 261 positive cultures (2.68 %). One explanation for small number of isolations could be due to *Kocuria* spp. belonging to a category of bacteria which are usually ignored by clinical microbiologists.[22] In addition, it might be underestimated considering their close similarity to coagulase negative *Staphylococci*.[7,23] The automated diagnosis by the Vitek 2 database allows for better identification of *Kocuria* in the recent times.[13] mainly in pediatric patients. In addition, documented cases of pediatric infections in Iraq which initiated via *Kocuria* species are very restricted. Most of these infections have been observed in hospitalized patients with underlying

Table 2. Antibiotic susceptibility pattern of *Kocuria* Species

Kocuria Species	Vancomycin	Clindamycin	ceftazidime	Trimethoprim	Amikacin	Chloramphenicol	Ciprofloxacin	Erythromycin	Azithromycin	Gentamicin
K.kristinae(1)	+	-	-	+	-	=	+	+	+	-
K.kristinae(2)	=	-	-	+	-	-	+	+	+	-
K.rhizophila	+	+	-	+	-	+	-	+	+	-
K.kristinae(3)	+	=	-	+	-	-	-	=	+	-
K.kristinae(4)	+	+	-	+	-	+	+	+	+	-
K.rosea	+	+	-	+	-	-	-	-	+	-
K.kristinae(5)	+	+	-	+	-	+	=	+	+	-
Resistant Percentage	85	57	100	0	100	42	42	71	0	100

- : Resistant =: Intermediate +: Sensitive

diseases, indwelling devices or suppressed immunity.[24]

Furthermore, we found that 5 out of 7 *Kocuria* isolates belonged to *K. kristinae*, which were collected from pediatric patients with symptomatic bacteremia and urinary tract diseases. The other two *Kocuria* isolates belonged to *K. rosea* and *K. rhizophila*, in patients with urinary tract disease and symptomatic bacteremia, respectively. This result is in accordance with reported cases by Tewari et al,[24] who recorded an unusual case of a *K. kristinae* urinary tract infection, Kandi et al[22] and Wojno et al.[25]

This finding coincides with those of previous studies worldwide like Hassan et al.[21] who reported the first case from Egypt with *Kocuria kristinae* bacteremia and Manzoor et al.[19] who discussed a uncommon case of bacteremia caused by *K. kristinae* in a 46-year-old male patient. Also, Bernshteyn et al[16] presented a unique case report on community-acquired pneumonia and systemic bacteremia caused by *K. kristinae* in the USA. There is a study of infective endocarditis caused by *K. rosea* in a 10 year old immune competent female in Brazil by Moreira et al,[12] and Pierron et al[26] have described a case of catheter-related bacteremia with *K. rhizophila* in an 81 years old diabetic patient. These case reports on *Kocuria* spp. involved suppressed immunity similar to our patients, but no cases have been described in children with symptomatic bacteremia or urinary tract diseases.

Because of the limited number of pediatric cases reported, there are no precise strategies for the increasing *Kocuria* infections or Clinical Laboratory Standards Institutes (CLSI) breakpoint interpretations for *in vitro* susceptibility testing of *Kocuria* isolates.[27] All the tested isolates were susceptible to trimethoprim and azithromycin, followed by vancomycin, and this treatment was highly efficient. Meanwhile, amikacin, gentamicin and ceftazidime were the most resistant antibiotics tested.

Treatment with vancomycin, piperacillin/tazobactam, oxacillin, or ciprofloxacin and combination therapy with teicoplanin and vancomycin, Ciprofloxacin and clindamycin, ceftriaxone and ofloxacin have been used effectively in case reports.[7,9,20,28,29] An interesting finding in our study was that the majority of *Kocuria* isolates were resist to many common antibiotics, which could be a serious problem.

Our study has a number of limitations. First, the number of Iraqi published studies of pediatric cases with invasive *Kocuria* spp infections is relatively small. In addition, most of the current studies lack vital information about the sensitivity of *Kocuria* spp. to antibiotics.

In conclusion, pediatric infections caused by *Kocuria* spp. are rare, And we report the first confirmed Iraqi pediatric cases of *Kocuria* spp. The associated serious clinical manifestations are an emerging health concern, and further care should be taken for proper administration of antibiotic

treatment, as they are intrinsically multi-drug resistant.

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DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This article does not contain any studies with human participants or animals performed by any of the authors.

REFERENCES

1. Manzi P, Lenzi D, Messina G, et al. Healthcare-associated infections and antimicrobial use: Siena 2012. *Eur J Public Health.* 2013;23(1):285. doi: 10.1093/eurpub/ckt124.118
2. Holst J. Global Health - Emergence, hegemonic trends and biomedical reductionism. *Global Health.* 2020;16(1):42. doi: 10.1186/s12992-020-00573-4
3. Napolitani M, Troiano G, Bedogni C, Messina G, Nante N. *Kocuria kristinae*: An emerging pathogen in medical practice. *J Med Microbiol.* 2019;68(11):1596-1603. doi: 10.1099/JMM.0.001023
4. Park EJ, Kim MS, Roh SW, Jung MJ, Bae JW. *Kocuria atrinae* sp. nov., isolated from traditional Korean fermented seafood. *Int J Syst Evol Microbiol.* 2010;60(4):914-918. doi: 10.1099/ijs.0.014506-0
5. Kandi V, Palange P, Vaish R, et al. Emerging Bacterial Infection: Identification and Clinical Significance of *Kocuria* Species. *Cureus.* 2016;8(8):e731. doi: 10.7759/cureus.731
6. Grama A, Sirbe C, Fufezan O, Pop TL. *Kocuria varians* meningitis in a child with chronic granulomatous disease. *Turk Arch Pediatr.* 2021;56(3):278-279. doi: 10.5152/TurkArchPediatr.2021.20228
7. Savini V, Catavitello C, Masciarelli G, et al. Drug sensitivity and clinical impact of members of the genus *Kocuria. J Med Microbiol.* 2010;59(12):1395-1402. doi: 10.1099/jmm.0.021709-0
8. Sheerin Aa, Anand A, Mukherjee B. *Kocuria rhizophila* dacryocystitis: Report of a rare causative organism in a common clinical condition. *TNOA Journal of Ophthalmic Science and Research*. 2022;60(1):57-59. doi: 10.4103/tjosr.tjosr_113_21
9. Chen HM, Chi H, Chiu NC, Huang FY. *Kocuria kristinae*: A true pathogen in pediatric patients. *J Microbiol Immunol Infect.* 2015;48(1):80-84. doi: 10.1016/j.jmii.2013.07.001
10. Oncel EK, Boyraz MS, Kara A. Black tongue associated with *Kocuria* (*Micrococcus*) kristinae bacteremia in a 4-month-old infant. *Eur J Pediatr.* 2012;171(3):593. doi: 10.1007/s00431-011-1573-8
11. Amadeo-Oreggioni GP, Ortiz-Ramirez GY, Baquero-Ospina P, Salcedo-Villanueva G, Fromow-Guerra JJ, Velez-Montoya R. *Kocuria Endophthalmitis*: Clinical Spectrum and Long-term Outcomes. *Ocul Immunol Inflamm.* 2021:1-7. doi: 10.1080/09273948.2021.1951304
12. Moreira JS, Riccetto AGL, da Silva MTN, Vilela MM dos S. Endocarditis by *Kocuria rosea* in an immunocompetent child. *Braz J Infect Dis.* 2015;19(1):82-84. doi: 10.1016/j.bjid.2014.09.007
13. Dave VP, Joseph J, Pathengay A, Pappuru RR. Clinical presentations, management outcomes, and diagnostic dilemma in *Kocuria endophthalmitis*. *J Ophthalmic Inflamm Infect.* 2018;8(1):21. doi: 10.1186/s12348-018-0163-6
14. Citro R, Prota C, Greco L, et al. *Kocuria kristinae* endocarditis related to diabetic foot infection. *J Med Microbiol.* 2013;62(Pt 6):932-934. doi: 10.1099/jmm.0.054536-0
15. Zaric RSZ, Pejcic AV, Jankovic SM, et al. Antimicrobial treatment of *Kocuria kristinae* invasive infections: Systematic review. *J Chemother.* 2019;31(3):109-119. doi: 10.1080/1120009X.2018.1542551
16. Bernshteyn M, Kumar PA, Joshi S. *Kocuria kristinae* pneumonia and bacteremia. *Proc (Bayl Univ Med Cent).* 2020;33(4):608-609. doi: 10.1080/08998280.2020.1792749
17. Mathew A, Nath JR, Modaweb A, Lone R, Abuhammour W. A Rare Case of Pediatric Central Venous Catheter-Related Bloodstream Infection With *Kocuria Varians. Cureus.* 2021;13(9):e18200. doi: 10.7759/cureus.18200
18. Hudzicki J. Kirby-Bauer Disk Diffusion Susceptibility Test Protocol Author Information. *American Society For Microbiology.* 2012:1-13. https://www.asm.org/Protocols/Kirby-Bauer-Disk-Diffusion-Susceptibility-Test-Pro.
19. Manzoor MAP, Shabeena KS, Mujeeburahiman M, Khan A. Indwelling J ureteral stents associated asymptomatic bacteraemia caused by multidrug resistant strain of *Kocuria kristinae*. *J Clin Diagn Res.* 2018;12(5):PD15-PD16. doi: 10.7860/JCDR/2018/35083.11522
20. Purty S, SaranathanR, Prashanth K, et al. The expanding spectrum of human infections caused by *Kocuria* species: a case report and literature review. *Emerg Microbes Infect.* 2013;2(10):e71. doi: 10.1038/emi.2013.71
21. Hassan RM, Bassiouny DM, Matar Y. Bacteremia Caused by *Kocuria kristinae* from Egypt: Are There More? A Case Report and Review of the Literature. *Case Rep Infect Dis.* 2016;2016:18064. doi: 10.1155/2016/6318064
22. Kandi V, Palange P, Vaish R, Kale V, Kandi MR, Bhoomagiri MR. A case of urinary tract infection caused by Kocuria species and identified by conventional methods. *Perspectives in Medical Research.* 2016;4(2):64-66.
23. Ali AM, Waseem GR, Arif S. Rare case report of infective endocarditis due to *Kocuria kristinae* in a patient with ventricular septal defect. *Access Microbiol.*

2020;2(1):acm00076. doi: 10.1099/acmi.0.000076

24. Tewari R, Dudeja M, Das AK, Nandy S. *Kocuria kristinae* in catheter associated urinary tract infection: A case report. *J Clin Diagn Res.* 2013;7(8):1692-1693. doi: 10.7860/JCDR/2013/6077.3247
25. Wojno KJ, Baunoch D, Luke N, et al. Multiplex PCR Based Urinary Tract Infection (UTI) Analysis Compared to Traditional Urine Culture in Identifying Significant Pathogens in Symptomatic Patients. *Urology.* 2020;136:119-126. doi: 10.1016/j.urology.2019.10.018
26. Pierron A, Zayet S, Toko L, Royer PY, Garnier P, Gendrin V. Catheter-related bacteremia with endocarditis caused by *Kocuria rhizophila. Infect Dis Now.* 2021;51(1):97-98. doi: 10.1016/j.medmal.2020.09.007
27. Bhavsar SM, Hamula CL, Dingle TC. Report of two paediatric cases of central line infections caused by species of the genus *Kocuria. JMM Case Reports.* 2016;3(3):e005040. doi: 10.1099/jmmcr.0.005040
28. Dunn R, Bares S, David MZ. Central Venous Catheter-Related Bacteremia Caused by *Kocuria Kristinae*: Case Report and Review of the Literature. *Ann Clin Microbiol Antimicrob.* 2011;10:31. doi: 10.1186/1476-0711-10-31
29. Lai CC, Wang JY, Lin SH, et al. Catheter-related bacteraemia and infective endocarditis caused by Kocuria species. *Clin Microbiol Infect.* 2011;17(2):190-192. doi: 10.1111/j.1469-0691.2010.03211.x