**Kocuria Species: Important Emerging Pathogens in Pediatric Patients**

Noor M. Taher

Department of Microbiology, College of Medicine, University of Fallujah, Iraq.

**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*
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 Micrococccaceae, 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 immune compromised patients with serious chronic conditions5 mainly bacteremia/recurrent sepsis.3 Notably, immunocompromise 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.
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\(^\text{18}\) 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.\(^\text{17}\) 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.\(^\text{19}\) *Kocuria* is a member of the Micrococaceae 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*,\(^\text{20,21}\) 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.\(^\text{22}\) In addition, it might be underestimated considering their close similarity to coagulase negative *Staphylococci*.\(^\text{7,23}\) The automated diagnosis by the Vitek 2 database allows for better identification of *Kocuria* in the recent times.\(^\text{13}\) 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 1. Clinical profile of 7 patients with *Kocuria* Species infections

<table>
<thead>
<tr>
<th><em>Kocuria</em> Species</th>
<th>Age</th>
<th>Sex</th>
<th>Underlying disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>K. kristinae</em> (1)</td>
<td>6 months</td>
<td>Male</td>
<td>Symptomatic bacteremia</td>
</tr>
<tr>
<td><em>K. kristinae</em> (2)</td>
<td>8 years</td>
<td>Female</td>
<td>Urinary tract diseases</td>
</tr>
<tr>
<td><em>K. rhizophila</em></td>
<td>9 years</td>
<td>Male</td>
<td>Urinary tract diseases</td>
</tr>
<tr>
<td><em>K. kristinae</em> (3)</td>
<td>4.5 years</td>
<td>Female</td>
<td>Urinary tract diseases</td>
</tr>
<tr>
<td><em>K. kristinae</em> (4)</td>
<td>10 years</td>
<td>Male</td>
<td>Urinary tract diseases</td>
</tr>
<tr>
<td><em>K. rosea</em></td>
<td>6 years</td>
<td>Female</td>
<td>Symptomatic bacteremia</td>
</tr>
<tr>
<td><em>K. kristinae</em> (5)</td>
<td>4 months</td>
<td>Male</td>
<td>Symptomatic bacteremia</td>
</tr>
</tbody>
</table>
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., who recorded an unusual case of a K. kristinae urinary tract infection, Kandi et al. and Wojno et al.

This finding coincides with those of previous studies worldwide like Hassan et al. who reported the first case from Egypt with Kocuria kristinae bacteremia and Manzoor et al. who discussed a uncommon case of bacteremia caused by K. kristinae in a 46-year-old male patient. Also, Bernshteyn et al. 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. and Pierron et al. 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. 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. 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.

<table>
<thead>
<tr>
<th>Table 2. Antibiotic susceptibility pattern of Kocuria Species</th>
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<tr>
<td><strong>Kocuria Species</strong></td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td>K.kristinae(1)</td>
</tr>
<tr>
<td>K.kristinae(2)</td>
</tr>
<tr>
<td>K.rhizophila</td>
</tr>
<tr>
<td>K.kristinae(3)</td>
</tr>
<tr>
<td>K.kristinae(4)</td>
</tr>
<tr>
<td>K.rosea</td>
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<tr>
<td>K.kristinae(5)</td>
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</tbody>
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Resistant Percentage: 85 57 100 0 100 42 42 71 0 100
- : Resistant    =: Intermediate    +: Sensitive
treatment, as they are intrinsically multi-drug resistant.

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FUNDING
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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


