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REVIEW ARTICLE OPEN ACCESS

Revisiting *Kocuria* Infections: A Growing Nosocomial Challenge in Immunocompromised Patients

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Abstract

Nosocomial or hospital acquired infections (NI or HAI) pose significant danger to immunocompromised individuals. Many pathogens involved in NI evade early detection during the initial testing since they are misdiagnosed as contaminants and are also resistant to various first-line antibiotics. Few of the common pathogens that cause NIs or HAIs include various strains of *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella* sp., etc. *Kocuria* sp. previously considered to be an opportunistic pathogen, has recently been identified as the causative agent for a variety of NIs affecting neonates and immunocompromised; cholecystitis, peritonitis, endocarditis, etc. being some of the symptoms caused. Hence, this genus has received more research attention to devise novel strategies for diagnosis and effective treatments of infections. The present review focuses on various features of the genus *Kocuria*, different types of infections caused, case studies highlighting various promising treatment strategies and the antimicrobial resistance shown by the members of this genus.

Keywords: Nosocomial, *Kocuria*, Antibiotic Resistance, Catheter-related Infections, Horizontal Gene Transfer, Biofilm

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INTRODUCTION

Nosocomial or hospital acquired infections (NI or HAI) are those which occur in a patient within 48-72 hours after admission in a hospital, but were not present at the time of entry. Such infections often arise because a patient's immune system is weakened while fighting pre-existing illnesses. The most commonly encountered NI affects the respiratory, urinary, gastrointestinal and circulatory tracts and also surgical sites.[1] The main pathogens which cause NIs include various strains of *Klebsiella* species*, Staphylococcus aureus*, *E. coli, Pseudomonas aeruginosa*, etc. These are notorious as most of them are resistant to many of the commonly used antibiotics.[2] In a global study on the prevalence of NIs in various countries, it was found that they are on the rise, with a global annual rate of increase of 0.06%.[3] *Kocuria* belongs to a bacterial genus which has been observed to cause more NIs recently. They are considered potential pathogens affecting neonates, immunocompromised and those receiving urgent medical attention.[4] The commonly observed symptoms include peritoneal dialysis associated infections, meningitis, skin infections, catheter-associated bacteremia, brain abscess, canaliculitis, cholecystitis, keratitis, peritonitis, endophthalmitis, endocarditis and necrotizing mediastinitis.[5,6] Once considered merely opportunistic pathogens, *Kocuria* species are now known to cause a range of serious infections. This review discusses the different *Kocuria* species, their associated infection types, and the current strategies for disease management.

Nosocomial infections are the leading cause of preventable harm to hospital patients and pose a huge drain on healthcare resources. They are typically caused by several antibiotic-resistant bacteria, and the management of nosocomial infections many a times promotes the development of resistant bacteria. Understanding the intricate interplay of factors that contribute to nosocomial infection is the first step in improving patient outcomes. Most of the *Kocuria* infections reported were from patients who were affected by severe underlying illnesses, such as solid tumors, catheter-related bacteraemia, hematologic malignancies, or metabolic disorders.[7,8] Though many species have been reported in this genus, 5 of them have been found to be opportunistic pathogens.[5] Future research must prioritize understanding *Kocuria* infections, given the lack of significant knowledge gaps in epidemiology.[9]

Features of members of genus *Kocuria*

The word *Kocuria* is adopted from the name of a Slovak microbiologist, Miroslav Kocúr. *Kocuria* spp. are coccoid Actinobacteria that are Gram-positive, coagulase-negative, catalase-positive, belonging to the family *Micrococcaceae,* order Micrococcales and class *Actinomycetes.*[5] They are found to be organized as irregular clusters, in pairs, short chains and tetrads.[5] To date, 26 species of *Kocuria* have been described. Among these, *K. rosea* is a significant representative and *K. coralli* is the most recently discovered.[10] Initially, this bacteria was classified as *Micrococcus*, but taxonomic changes were introduced in accordance with 16S rDNA sequences and composition of amino acids in peptidoglycan, following phylogenetic analysis.[5,11] They are coagulase-negative and catalase-positive in nature, often wrongly identified as coagulase-negative Staphylococci, which might cause misjudgment of the infections caused in patients.[12,13] On nutrient agar, *Kocuria rosea* has pink colonies which are smooth and circular. It is aerobic, non-spore-forming, catalase-positive and oxidase-negative. Also, in blood agar it forms non-hemolytic colonies and is non-capsulated, non-motile, non-spore forming and gives a positive reaction for Voges-Proskauer test and non-acid fast test. Various *Kocuria* species reacts differently to biochemical tests including nitrate reduction, gelatinase, citrate, urease, amylase, phosphate, oxidase, arabinose, and N-acetyl-L-glutamic acid tests.[5] *Kocuria* spp. form round and large colonies with diffusible golden pigmentation on tryptic soy agar (TSA). Menaquinones MK-7(H2) and MK-8(H2): lysine-based A3a-type peptidoglycan, and saturated branched fatty acids are the predominant components that are found in the cell envelopes of *Kocuria.*[11]

The close relationship between *Micrococcus* and *Arthrobacter* species was noted before the results of 16S rDNA sequence analyses became available. In 1974 it was pointed out that "*Micrococcus* species should be regarded

as degenerate forms, locked into the coccoid stage of the Arthrobacter life cycle". The scientist Stackebrandt et al.[5] proposed the genus *Kocuria,* which has 26 species discovered till now. Many members of *Kocuria* species show differences in their biochemical tests and hence identification may not be accurate in many instances. More advanced techniques like 16S rRNA and MALDI-TOF MS could give more precise taxonomic identification of the members of this genus,[14] though many times, taxonomic reframing of species of Kocuria has been observed.[15]

Only three of these known species viz. *K. kristinae, K. rosea,* and *K. rhizophila,* have been

Table 1. Different species of *Kocuria* and their characteristic features

Species of *Kocuria*	Characteristic features
K. rosea	Spherical cells, circular, pink or red and smooth (occasionally rough): obligate aerobe, mesophile or psychrophile based on strain.[5]
K. aegyptia	Pink, circular, opaque colonies, non-motile coccoid cells.[19]
K. carniphila	Coccoid cells, non-acid-fast, non-motile, opaque, colonies of circular shape.[20]
K. rhizophila	Non-endospore-forming, appear as packets measuring radius of 0.5 to 0.75 micrometre, non-acid-fast.[21]
K. palustris	Light-yellowish pigmented colonies. Spherical cells, 0.5 to 0.75 micrometre radii, non-endospore forming, non- acid-fast.[21]
K. kristinae	Spherical cells (radius 0.35-0.55 µm), colonies seen includes smooth or rough.
K. flava	Gram-positive, yellowish colonies, distinguished from *K. turfanensis* by ~6 mol% difference in DNA G+C values.[22]
K. polaris	Isolated from Antarctic cyanobacterial mat, orange colonies, cells are of 0.5-0.75 µm in radius and are coccoid cells.[23]
K. himachalensis	Circular, reddish orange colonies with 0.5-0.75 µm in radius.[24]
K. turfanensis	Gram-positive, yellowish to orange colonies.[22]
K. koreensis	Light orangish colonies which are opaque. Cells are coccoid with a radius of 0.5-0.75 µm.[25]
K. gwangalliensis	Aerobic, non-motile, non-endospore forming, pink–orange pigmented colonies, spherical 0.3-0.6 µm in radius.[26]
K. atrinae	Light yellowish colonies, coccoid cells with a radius of 0.5-0.75 micrometer.[25]
K. halotolerans	Light yellowish colonies, cells are coccoid with 0.3-0.5 µm in radius.[27]
K. dechangensis	Beige-yellow colonies, Gram-positive & coccoid cells (0.4-0.65 µm in radius).[28]
K. indica	Gram-positive, lemon-yellow colonies, aerobic, non-motile coccoid.[29]
K. salsicia	Lemon-yellow colonies, opaque, circular coccoid cells, measuring 0.5-0.75 µm in radius.[30]
K. marina	Halotolerant cells- tolerates upto 16% NaCl, non-motile, aerobic, coccoid cells.[31]
K. varians	Recorded from milk, spherical cells (radius of 0.45-0.75 µm); yellowish colonies, glistening smooth colonies.[5]
K. arsenatis	Arsenic resistant endophyte, aerobic, cells measure 0.1-0.3 µm in radius, non-endospore producing. Opaque, circular, smooth yellow colonies.[19]
K. tytonis	Non-lipophilic, non-motile, elevation is pulvinate, 0.5 mm radius, dry, non-viscous, non-sporulating cocci.[32]
K. pelopila	Mangrove-rhizosphere isolate, Gram-positive, spherical, non-motile, aerobic, measuring approximately 0.5 µm in radius, circular colonies.[33]
K. subflava	Marine sediment isolate, Gram-positive, catalase positive, oxidase negative, aerobic, non-motile cocci, 0.25-0.45 mm in radius.[34]
K. oceani	Coccoid, circular, convex, pinkish orange.[35]
K. salina	Gram-positive, non-motile, oxidase-negative, pastel orange colored colonies, catalase positive, starch hydrolysis positive.[36]
K. coralli	Non-motile, aerobic. Spherical cells with 0.35-0.45 µm in radius, circular colonies, polar lipids include cardiolipin, phosphatidylglycerol.[10]

Table 2. Important pathogenic species of the genus *Kocuria* and their clinical manifestations

Name of the pathogen	Disease caused	Manifestation	Symptoms
Kocuria kristinae	Cholecystitis	Inflammation of the gallbladder	Pain in the right upper abdomen and right shoulder, nausea, vomiting, fever.[18]
Kocuria rhizophila	Dacryocystitis	Infection of the lacrimal sac	Pain, redness, and swelling in the inner corner of the eye.[39]
Kocuria marina	Peritonitis	Infection of peritoneum	Abdominal pain, turbid effluent, nausea, mild fever.[40]
Kocuria rosea	Catheter associated bacteremia	Bacteremia originating from an intravenous catheter	Tachycardia, elevated fever and rate of respiration.[41]
Kocuria koreensis	Infectious keratitis	Conjunctival allergic disease with atopic facial dermatitis	Eye redness, blurred vision, eye pain.[42]

recognized to be clinically important infectious agents. All three species are connected to catheter-related bacteremia.[16-18] Some of the important species coming under the genus *Kocuria*, with their characteristic features are listed in Table 1.

Pathogenic species of *Kocuria* and disease symptoms

Scientists describe members belonging to the genus Kocuria as saprophytes since they are commonly found in soil, water, and the atmosphere.[5] Some of them are also found in the human skin epidermis and oral flora.[15,21,37] In 1974, it was initially recognized as an origin of infection of the urinary tract and the name *Micrococcus kristinae* was given.[20] *Kocuria* spp. have been found in the oral cavity, but their pathogenicity is diminished, since, when extracted from clinical specimens, they are usually handled as lab contaminants and given little consideration. The late twentieth century saw a rise in cases of diseases caused by *Kocuria* species. Identification of phenotypes may not be able to distinguish between every member of the species due to the variability of the results of carbon assimilation and biochemical tests in different *Kocuria* species.[38] Some of the important pathogenic species of the genus *Kocuria* and their clinical manifestations are listed in Table 2.

The most common symptoms of *Kocuria* infection include sepsis and enhanced levels of platelets, leucocytes and CRP.[7] Despite the lack of knowledge on the epidemiology and pathogenicity qualities, it has been suggested that biofilms have a role in adhesion, colony formation and infection.[43] Although *K. rosea* is a very uncommon human pathogen and a commensal of the epidermis and oropharynx, its significance in infection may be underappreciated due to probable misidentification and the perception of micrococci as contaminants.[38] These bacteria cause multiple kinds of infections, most of them occurring in immunocompromised hosts with serious underlying diseases.[5,8]

The usage of N-acetyl-L-glutamic acid, inulin, urease, oxidase, amylase, phosphatase and nitrate reduction tests, among other standard biochemical tests, have all been found to cause distinct reactions in different species of *Kocuria*.[8] This may be the cause of the incorrect identification provided by automated and conventional technologies for bacterial identification. But previous studies have shown that *Kocuria* can still be distinguished from *Micrococcus* and *Staphylococcus* with morphology, culture identification and antibiotic discs in the absence of molecular and diagnostic approaches. *Kocuria* spp. are resistant to nitrofurantoin and lysostaphin but sensitive for bacitracin and lysozyme.[44,45]

As an opportunistic pathogen, *K. rosea* was found in many infections of urinary tract, endocarditis and in people receiving peritoneal dialysis, bacteremia, as well as disease related to medical equipment in immunocompetent patients and those with underlying conditions.[18,46,47] *K. kristinae* has also been linked to acute cholecystitis.[18] *K. varians*, another species, was found in a patient with a brain oedema.[48] *K.*

kristinae has been linked to various intravascular diseases in immunocompromised hosts, an illness aggravated by septic pulmonary emboli caused by suppurative thrombosis. In this case, a catheter-related BSI that resulted in such problems was notable.[7]

Nosocomial infections - case studies

The importance of *Kocuria* in transmitting illnesses picked up in hospitals has been addressed.[49] The same study also stated that *Kocuria* spp. should be regarded as possible pathogens in immunocompromised patients, those receiving critical care treatment, and newborns, even though they coexist with people, animals, and the environment. More than 50% of patients in a research involving twelve adolescents who had underlying, severe illnesses such as cancer and were born from preterm delivery developed invasive infections with *Kocuria* spp.[50] There is an increasing trend of reported illnesses brought on by *Kocuria* spp. in previously healthy and immunocompetent people.

A 58 year-old woman with descending necrotizing mediastinitis, who was also taking medication for hypertension and gout, was found to have *K. rosea.*[49] A 10 year-old female patient developed endocarditis from *K. rosea* despite being healthy, although she had undergone surgery to treat congenital heart problems.[51] The strain was collected from a case of peritonitis and tested negative for biofilm formation by *Kocuria* species.[44] The isolation of *K. marina* in a 7 year-old patient on epoprostenol therapy, tolerant to highly alkaline conditions, serves as a warning about the potential of *Kocuria* spp. for opportunistic and nosocomial infections.[46,52]

In a study conducted from June 2019 to June 2021, 7 out of 261 bacteremia positive cases contained *Kocuria* isolates. The study was conducted on pediatric patients between the age of 4 months to 10 years. These patients either had urinary tract related diseases or symptomatic bacteraemia, showing fever within 24 hours of hospitalization. Five cases of *K. kristinae*, one case of *K. rhizophila*, and one case of *K. rosea* were detected. These species exhibited 100% resistance to ceftazidime, gentamicin, and amikacin. The low frequency of *Kocuria* species isolations may possibly be caused by the fact that these species are members of a class of bacteria that are usually overlooked while diagnosing. Additionally, it might be underrated, given how much they resemble coagulase-negative Staphylococci.[53] These results are in line with previous research conducted on *K. kristinae* urinary tract infections.[54-56]

A 55 year-old African American woman with sickle cell pain episodes in her arms, legs, and chest was later diagnosed with a nosocomial infection by *K. rosea.*[57] Standard anti-staphylococcal drugs were ineffective because of the resistance of *Kocuria* to lysostaphin and nitrofurantoin. The infection, which began as a catheter-associated case, progressed to bacteremia.

K. varians induced central venous catheter (CVC) infection could also be successfully treated with CVC salvage.[58]

In a study of 12 pediatric patients with *Kocuria* infection in blood, one child had acute leukemia and six were premature infants, all of whom had central venous catheters. Fever, hypothermia, apnea, or bradycardia were the symptoms; there was no other evident illness and sepsis treatment was given.[59,60] Such cases call for the need to correctly identify the bacteria to prevent such cases not just in patients with impaired immune systems, but also in healthy people.[61]

Successful treatment strategies for *Kocuria* infections

Given that the infections caused by *Kocuria* species are rare, clinicians may misinterpret and classify them as culture contaminants and hence due care has to be taken in patients with medical implants.[9,62] Even in people with known risk factors, infections by *Kocuria* species are uncommon, yet they can occur in patients without these characteristics as well.[62] The resistance to nitrofurantoin/furazolidone displayed by *Kocuria* species is one of the main requirements for first phenotypic identification. Susceptibility to beta-lactams, quinolones, lincosamides and cotrimoxazole and resistance to kanamycin (among the aminoglycosides) has been observed. Few of the prominent antibiotics used against *Kocuria* and their modes of action are depicted in Figure. Reports of resistance to fusidic acid, rifampicin,

linezolid, or streptogramins have not been reported yet. It is known that Gram-positive bacteria inherit resistance to colistin and polymyxin; however, *Kocuria* species vulnerable to polymyxin are unusual.[38] To assess the susceptibility profile of the Gram-positive *Kocuria* species, a few case studies have been conducted.

In a study of 20 isolates of *K. kristinae,* four patients (3 with catheter-related bacteremia and 1 with infective endocarditis) had implanted catheters. Removal of these catheters helped in reducing the infection. Four *K. kristinae* isolates had MICs up to 4 mg/L for Oxacillin and hence were deemed resistant. One isolate of *K. marina* was also identified in this study.[63]

In a 31 year-old patient who received complete parenteral feeding due to propionic acidemia (via the central venous catheter, CVC) and on hemodialysis, *K. kristinae* was identified in the blood culture. In a situation of uncomplicated CRBSI (Catheter-related bloodstream infection): combination treatment and 10-14 days of antibiotic delivery through the colonized catheter was advised, along with antibiotic lock therapy as advised by the IDSA (Infectious Diseases Society of America) as per the revised guidelines issued in 2011. This was the first successful treatment to preserve the catheter.[64]

A 52 year-old patient with comorbidities was infected with *K. varians* causing brain abscess. After receiving third-generation cephalosporins intravenously for four weeks, the patient was transitioned to taking them orally for two weeks. While erythromycin, amikacin, amoxicillin, ceftriaxone, and cefuroxime were reported to be effective against the majority of *Kocuria* and *Micrococcus* strains, third-generation cephalosporins were utilized due to breach of blood-brain-barrier and penetration of the abscess capsule.[65] In a similar case of brain abscess caused by *K. rosea,* antibiotic therapy with cefepime was administered for four weeks, gradually improving mental capabilities and resulting in a normal neurological evaluation at release. A month later, lesions were no longer present in the brain MRI.[62]

In the case of *Kocuria ocularis* which caused dacrocystitis infection in a patient aged 74 years, the patient was given 1 g amoxicillin and 125 mg clavulanic acid via oral route twice a day combined with topical application of tobramycin dexamethasone ophthalmic ointment (Alcon) and it was observed that the patient's symptoms promptly decreased and did not reappear 15 months post surgery. By disc diffusion analysis, the isolate was found to be sensitive to a wide range of antimicrobials (like benzylpenicillin,

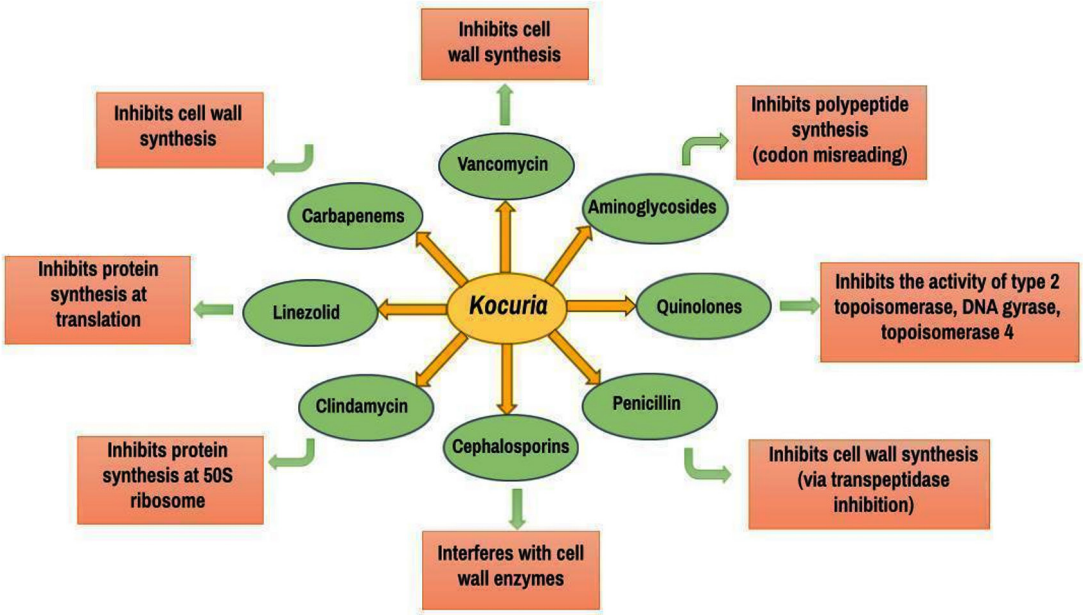

Figure. Mode of action of antibiotics commonly used to treat infections caused by pathogenic species of *Kocuria*

oxacillin, cefoxitin, moxalactam, novobiocin, linezolid, erythromycin, lincomycin, pristinamycin, rifampicin, ofloxacin, vancomycin, teicoplanin, kanamycin, gentamicin, tobramycin, rifampicin, tetracycline, fosfomycin, cotrimoxazole, and fusidic acid) and antibiotics like beta-lactamase (breakpoints of *Staphylococcus* spp. were used).[66]

The first instance of *K. rhizophila* causing bacteremia with infective endocarditis occurred in 2021, recorded in a 81 year-old patient with comorbidities. The strain was sensitive to Cefoxitine, kanamycin, clindamycin, and trimethoprim/sulfamethoxazole but was resistant to erythromycin and norfloxacin (according to the sixth edition of EUCAST-European Committee for Antimicrobial Susceptibility Testing, staphylococcus-species interpretation criteria for the agar disk diffusion assay). Third-generation cephalosporins were administered to the patient in compliance with the EUCAST section "PK/PD (non-species related) breakpoints", sensitivity profile, and categorization rearrangement in order to prevent clinical failure. Currently, *Kocuria* has no established treatment plans or standards for antibiotic susceptibility and hence most often *Staphylococcus* breakpoints are used in most publications.[9]

A recent case was reported on total hip replacement surgery performed on a 74 year old male patient due to pain on the right side of hip. After 6 weeks of surgery he had symptoms like erythema, swelling, tenderness over the wound and problem with weight-bearing. On examination, it was found that debridement and implant retention had to be performed. Further, the patient had to be put on intravenous Vancomycin and Piperacillin-Tazobactam. The culture test revealed 1 out of 5 samples isolated from lesser trochanter as *K. rhizophila* and the patient was put on IV Vancomycin for a period of 12 weeks.[67]

In Nigeria during the COVID-19 pandemic, a 72 year old male presented with symptoms of COVID-19 like cough, loss of taste, sore throat, fever and furthermore respiratory distress and urinary incontinence was later diagnosed with the presence of *S. aureus* and *Kocuria* species (which was earlier misidentified for coagulase-negative Staphylococci) showing 97.87% match to the DNA sequence of *K. rosea.* Both the strains showed high resistance to multiple drugs upon subjecting them to antibiotic susceptibility testing. After 5 days, the patient died while the treatment was ongoing due to certain complications.[68]

A 74 year-old man with stomach pain and cloudy peritoneal effluent who has been undergoing peritoneal dialysis for 32 months (previously diagnosed with anuric kidney failure) was found to be infected with *K. salsicia,* which was reported to be sensitive to aminoglycosides, trimethoprim-sulfamethoxazole, erythromycin, clindamycin, linezolid, and glycopeptides but resistant to penicillin, oxacillin, and quinolones. Initially he was treated with intraperitoneal vancomycin (2 g dose given once) and ceftazidime (1 g dose given everyday at overnight exchange) alternatively switching with dialysis 4 times each day. Later due to the unresponsive nature of the infection, the prescribed course of antibiotics was adjusted to include 600 mg of rifampicin taken orally every day, 350 mg of daptomycin, and 50 mg of tobramycin exchanged overnight. No improvement was observed which could possibly be due to the formation of biofilm on the surface of the catheter by the bacteria, the type of strains involved or the type of antibiotics used for the treatment.[69]

Addressing a prospective one-year observational research conducted at a hospital from January 2021-December 2021, samples (10 CSF, pus, peritoneal fluid, extraventricular drainage tip, and BAL) were collected from 14 patients. On examination and confirmation by VITEK 2 and MALDI-TOF, 6 isolates were identified as *K. kristinae* and 6 as *K. rosea* and 2 as *K. rhizophila*. *Kocuria* was not isolated from any of the adult patients throughout the observation period; the antibiograms of these 3 *Kocuria* species also were varied. Given that there are no established guidelines for *Kocuria* in CLSI, utilizing the disc diffusion method, antibiotic susceptibility testing was carried out, and zone interpretation was predicated on *Staphylococcus*.[70]

Another case of single-center retrospective analysis in China, which is considered as the largest case series, a range of diseases in children brought about by the *Kocuria* species was examined. Out of the 36 patients, 29 people contracted the infection from *K. kristinae*, 4 by *K. rosea*, 2 by *K. varians* and 1 by *K. rhizophila*

(bloodstream infection was identified in a total of 26 patients, 6 with pneumonia related to ventilator use, and 1 with urinary tract infection, purulent meningitis, cholangitis and empyema related to catheter use). While most of these patients were immunocompromised, some were immunocompetent; the study set included 4 children too, with early onset before the age of one. While all *Kocuria* species exhibited resistance to oxacillin and penicillin, they were all vulnerable to linezolid, vancomycin, and tigecycline. Majority of the cases were resolved using suitable antimicrobial medications.[71]

Vancomycin (47%):cephalosporins (39.5%):quinolones (36.6%):linezolid (17%):aminoglycosides (14%):penicillin (7.9%):aminopenicillin (6.9%):clindamycin (5.9%):carbapenems (5%): and daptomycin (2%): were the most often used antimicrobials for treating *Kocuria* infections. In 36.6% of cases, surgery was combined with antimicrobial therapy. The overall death rate was 5.9%, of which 4.9% was directly related to the infection.[72] Thus, the treatment strategy to cure *Kocuria* infections depends on a number of factors like accurate and timely diagnosis, resistance profile of the strain, age of patient, comorbidities, days of infection etc.

Antimicrobial resistance, resistance genes and possible mechanisms

Initially members of *Kocuria* species were considered non-pathogenic but recently there has been an increase in the infections with symptoms like endocarditis, peritonitis, meningitis, osteomyelitis, and brain abscess.[65] Due to the limited number of cases reported for infections caused by *Kocuria*, there are no particular therapeutic treatments and administrative measures for this pathogen. At the same time, they show resistance to antimicrobials like ampicillin and erythromycin.[38] Antimicrobial resistance in bacteria poses a huge global problem. Our ability to treat infectious diseases and make improvements in health and medicine is impaired due to the antimicrobial resistance.[5] To avoid the transmission of antimicrobial-resistant bacterial strains, it is important to use antimicrobials more appropriately and wisely.[13]

A French study demonstrated the ability of *Kocuria* spp. to grow even after simultaneous administration of penicillin and oxacillin. *Kocuria* spp. was found to be resistant to erythromycin to which it was earlier sensitive.[73] *Kocuria* genus was found to possess 5 types of ARGs (antibiotic resistance gene) including fosmidomycin (*rosA*):bacitracin (*bacA*):quinolone (*qepA*):MLS (*macB*) and multidrug (*mdtF*, *mexF* and *oprC*).[74] A study conducted on pasteurized milk in Brazil, showed multidrug resistance (MDR) of more than half of the isolates of *Kocuria*. The major resistance was found to be against tetracycline, penicillin and clindamycin.[75]

K. rosea resides on our skin as a normal flora but it is noticed that this gram positive bacteria is capable of causing blood infections associated with the central line in patients who are catheterized and immunocompromised.[61,76] *K. rosea* demonstrated resistance to various classes of antibiotics like macrolides, cephalosporin, fluoroquinolones, ciprofloxacin and ceftriaxone.[76] In a study to detect *mecA* gene in different species of bacteria by PCR, an isolate of *K. rosea* was found with the *mecA* gene, which was previously not reported. On consecutive analysis, it was concluded and confirmed by the NCBI database that the *mecA* gene in *K. rosea* was a result of horizontal gene transfer from *S. aureus*.[77] In a study, from catheter related bacteraemia, though, *K. rosea* was found to be sensitive to vancomycin *in vitro*, no changes in the condition of the patient was noticed after drug administration until the removal of the catheter. According to a hypothesis, the bacteria gained protection against the antibiotics by the formation of biofilm on the device.[41] The index of adhesiveness of *Kocuria* spp. is high, which explains their function in the first stage of biofilm development.[78] The microorganism organizes itself in a three dimensional arrangement with high synergism which helps withstand external hindrances like harsh environmental factors, immune system factors and antimicrobial agents, all these being traits conferred to biofilm forming bacteria.

Isolates of *K. kristinae*, which is another species of *Kocuria* show frequent resistance to penicillins, gentamicin and erythromycin.[79] A recent *in silico* study identified presence of many antibiotic resistance genes in 5 strains of Kocuria.[80] *K. kristinae* were found to be associated with invasive infections in very young children and

Table 3. Important antimicrobial resistance genes in pathogenic bacteria and their mechanisms

Gene	AMR Gene family	Mechanism	Ref.
mecA	Methicillin-resistant PBP2	Antibiotic target replacement- Antibiotic resistance arises from the replacement or substitution of the antibiotic action target (β-lactams). It codes for PBP2a which allows the continuous production of bacterial cell wall due to low affinity of PBP2a to the β-lactam antibiotics like methicillin. Thought to have entered *Kocuria* by HGT from *S. aureus*	91-93
rosA	major facilitator superfamily antibiotic efflux pump	Antibiotic efflux-resistance from antibiotics through transport of antibiotics out of the cell	94
macB	ATP-binding cassette (ABC) antibiotic efflux pump	*macB*-responsible for antibiotic resistance in both Gram-negative and positive bacteria through antibiotic ejection. Genome analysis and resistance phenotypes suggest the presence of direct homologs of these genes in *Kocuria*. The gene is responsible for formation of the *MacA-MacB-TolC* assembly that transports macrolide antibiotics. These antibiotics are responsible for inhibiting protein synthesis in the bacteria.	95-97
ErmX	Erm 23S ribosomal RNA methyl-transferase	Antibiotic target modification-antibiotic resistance was induced by mutational changes or enzymatic modifications. Its methyltransferase activity on 23S ribosomal RNA provides resistance to lincosamides, macrolides and Streptogramin b (MLS_B phenotype).	98,99
bacA	undecaprenyl pyrophosphate	During cell wall biosynthesis, responsible for recycling the undecaprenyl pyrophosphate which provides resistance against bacitracin; also controls bac operon in *P. aeruginosa* which controls biofilm formation.	100
MexF	resistance-nodulation-cell division (RND) antibiotic efflux pump	Antibiotic ejection-resistance to antibiotics by transporting them out of the cell. The gene and the pump is studied in detail when it comes to Gram-negative bacteria. Being an inner membrane protein it is able to throw out the antibiotics using the proton motive force.	101
QepA	major facilitator superfamily (MFS) antibiotic efflux pump	Antibiotic ejection- resistance to antibiotics by transporting them out of the cell. The efflux pumps formed are plasmid born and are responsible for reducing the sensitivity against fluoroquinolone. The pump belongs to the major facilitator super-family (MFS).	102

in patients suffering from malignancies or who are immunocompromised.[81] For the isolate, *K. kristinae_LC*, seven genes were implicated in antibiotic resistance. Furthermore, this isolate also showed resistance to bacitracin. Gene_1280 was identified in the PHI database which produces multidrug-resistance proteins and provides antimicrobial resistance to the bacteria; four genes that encode prevent-host-death proteins were revealed after genome analysis. Overexpression of these genes could have contributed to antibiotic resistance and increased rate of biofilm formation.[82]

Isolates of *K. varians* were collected in Spain from cheese samples made out of raw milk. Two isolates were highly resistant to oxacillin and furazolidone and showed resistance to more than five antibiotics.[83] Meletis et al. reported the resistance of *K. varians* to levofloxacin in a patient receiving continuous ambulatory peritoneal dialysis (CAPD).[43] An isolate of *K. rhizophila* from a 3 year-old patient with a catheter showed resistance to erythromycin and ciprofloxacin.[84] *K. rhizophila* isolated from the blood of another pediatric sepsis patient was found to be resistant only to norfloxacin.[17] The genome of *K. rhizophila* strain DC2201 revealed the presence of 13 proteins that are likely to be involved in a multidrug efflux mechanism. These proteins facilitate the active transport of various unrelated molecules from the cytoplasm to the extracellular environment. It is presumed that during this process, the toxic organic compounds are transported outside. Interestingly, one of these 13 efflux proteins shows homology with *Xanthomonas albilineans* pump, which is a plant pathogen. This could be possibly due to some evolutionary association of the similar niches shared by these 2 bacterial ancestors. The extent of efflux activity on providing drug resistance and affecting drug sensitivity is still unclear.[76]

Recent research on antibiotic resistance of *Kocuria* has thrown light on some serious pointers as indicated by infective endocarditis caused by *K. kristinae,*[85] relapsing dialysis associated peritonitis due to *K. rhizophila*[86] and catheter associated bacteremia in a pediatric cancer patient.[87] In a recent study on clinical samples collected from 2 countries viz. Egypt and Iraq, macrolide resistance of *K. kristnae* was very evident.[88] An even more pertinent problem lies in the spread of these resistant *Kocuria* in the environment. In a recent study, raw milk samples have been shown to harbour multidrug-resistant (Lindamycin and Ampicillin) *Kocuria* with biofilm forming ability.[89] Hence measures should be initiated to have in depth studies on the environmental spread of such resistant strains and their impact on public health.

When compared to major Gram-positive (*S. aureus* and *Clostridium difficile*) and Gram-negative (*Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter, Acinetobacter baumannii*) nosocomial pathogens, the number of cases and severity of infections caused by *Kocuria* are lower, with catheter related sepsis in immunocompromised and post surgery patients being a major event in multiple cases; mostly resulting in peritonitis, endocarditis and colitis.[41,84,87]

The genome of *Kocuria indica* DP-K7 was sequenced via k-mer-based method in PATRIC platform; the genome was found to carry antimicrobial resistance genes like *rpoB, folA, gyrA, fabL-like, dxr, S10p, efG, Iso-tRNA, fabG, gyrB, folP, rho, efTu, dfr, alr, htdX, gidB, kasA, mtrA, rpoC, erm(X):mtrB, ddl, pgsA, GgdpD, murA* and *lpqB.*[90] Table 3 elaborates the prominent AMR mechanisms of few important pathogenic bacterial species.

CONCLUSION

Kocuria spp., owing to its potential pathogenicity to cause a range of infections including urinary tract infections, endocarditis, meningitis, etc., has gained attention in recent years as a nosocomial pathogen. Species such as *K. kristinae*, *K. rosea,* etc. have been identified to be a threat to people who are immunocompromised and those with underlying medical conditions. Treatment methods vary, including surgical interventions and the use of antibiotic cocktails. However, the identification of the species has remained quite tricky due to its morphological similarities with other closely related species. This has in turn led to the initiation of inappropriate treatment approaches for the diseases associated with the pathogen. *Kocuria* species show resistance to several classes of antibiotics such as penicillin, erythromycin, cephalosporin

and fluoroquinolones, making the treatment excessively difficult. Due research focus should be on biofilm mechanisms and ways of tackling them, genome characterization to identify virulence and resistance genes, identifying HGT events and also to pinpoint nosocomial transmission routes. Hence, it is important to prevent the transmission of such strains of bacteria by understanding the mode of disease transmission, enabling improved and early identification, enhanced patient care and by the use of appropriate antibiotics.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

SS conceptualized the study. SS, AG, LRP, KD and MG wrote the manuscript. SS reviewed the manuscript. All authors read and approved the final manuscript for publication.

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DATA AVAILABILITY

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

ETHICS STATEMENT

Not applicable.

REFERENCES

1. Hazard D, von Cube M, Kaier K, Wolkewitz M. Predicting Potential Prevention Effects on Hospital Burden of Nosocomial Infections: A Multistate Modeling Approach. *Value Health.* 2021;24(6):830-838. doi: 10.1016/j.jval.2021.02.002
2. Irek EO, Amupitan A, Obadare TO, Aboderin AO. A systematic review of healthcare-associated infections in Africa: An antimicrobial resistance perspective. *Afr J Lab Med.* 2018;7(2):796. doi: 10.4102/ajlm.v7i2.796
3. Raoofi, S, Kan FP, Rafiei S, et al. Global prevalence of nosocomial infection: A systematic review and meta-analysis. *PloS One.* 2023;18(1):e0274248. doi: 10.1371/journal.pone.0274248
4. Napolitani M, Troiano G, Bedogni C, Messina G, Nante N. Kocuria kristinae: An emerging pathogen in medical practice. *J Med Microbiol*. 2019;68(11):1596-160
5. Stackebrandt E, Koch C, Gvozdiak OR, Schumann P. Taxonomic Dissection of the Genus *Micrococcus*: *Kocuria* gen. nov, *Nesterenkonia* gen. nov, *Kytococcus* gen. nov, *Dermacoccus* gen. nov, and *Micrococcus Cohn* 1872 gen. emend. *Int J Syst Bacteriol.* 1995;45(4):682-692. doi: 10.1099/00207713-45-4-682
6. Dotis J, Printza N, Stabouli S, Papachristou F. Kocuria species peritonitis: although rare, we have to care. *Perit Dial Int*. 2015;35(1):26-30. doi: 10.3747/pdi.2013.00138
7. 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
8. Kiraz A, Durmaz S, Baykan A, Perçin D. Endocarditis and Bacteremia due to *Kocuria rosea* Following Heart Valve Replacement. *Eur J Basic Med Sci*. 2013;3(4):93-5. doi: 10.15197/sabad.2.3.18
9. 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
10. Li J, Zhang S. *Kocuria coralli* sp. nov, a novel actinobacterium isolated from coral reef seawater. *Int J Sys Evol Microbiol.* 2020;70(2):785-789. doi: 10.1099/ijsem.0.003825
11. Stackebrandt E, Frederiksen W, Garrity GM, et al. Report of the ad hoc committee for the re-evaluation of the species definition in bacteriology. *Int J Sys Evol Microbiol*. 2002;52(3):1043-1047. doi: 10.1099/00207713-52-3-1043
12. Kandi V, Palange P, Vaish R, Bhatti AB, Kale V, Kandi MR, Bhoomagiri MR. Emerging Bacterial Infection: Identification and Clinical Significance of *Kocuria* Species. *Cureus*. 2016; 10;8(8):e731. doi: 10.7759/cureus.731
13. Organji SR, Abulreesh HH, Elbanna K, Osman GEH, Almalki MHK. Diversity and characterization of *Staphylococcus* spp. In food and dairy products: a foodstuff safety assessment. *J Microbiol Biotechnol Food Sci*. 2018;7(6):586-593. doi: 10.15414/jmbfs.2018.7.6.586-593
14. Parte AC, Carbasse JS, Meier-Kolthoff JP, Reimer LC, Goker M. List of Prokaryotic names with Standing in Nomenclature (LPSN) moves to the DSMZ. *Int J Syst Evol Microbiol.* 2020;70(11):5607-5612. doi: 10.1099/ijsem.0.004332
15. Quadri SR. Survival Strategy, Metabolic Potential and Taxonomic Reframe of *Kocuria polaris. J Pure Appl Microbiol*. 2024;18(3):1620-1626. doi: 10.22207/JPAM.18.3.11
16. Basaglia G, Carretto E, Barbarini D, et al. Catheter-Related Bacteremia Due to *Kocuria kristinae* in a Patient with Ovarian Cancer. *J Clin Microbiol.* 2002;40(1):311-313. doi: 10.1128/jcm.40.1.311-313.2002

17. Becker K, Rutsch F, Uekotter A, et al. *Kocuria rhizophila* Adds to the Emerging Spectrum of Micrococcal Species Involved in Human Infections. *J Clin Microbiol.* 2008;46(10):3537-3539. doi: 10.1128/jcm.00823-08
18. Ma ES, Wong CL, Lai KT, Chan EC, Yam WC, Chan AC. *Kocuria kristinae* infection associated with acute cholecystitis. *BMC Infect Dis*. 2005;5:60. doi: 10.1186/1471-2334-5-60
19. Li W, Zhang Y, Schumann P, et al. *Kocuria aegyptia* sp. nov, a novel actinobacterium isolated from a saline, alkaline desert soil in Egypt. *Int J Sys Evol Microbiol.* 2006;56(4):733-737. doi: 10.1099/ijs.0.63876-0
20. Tvrzova L, Schumann P, Sedlacek I, et al. Reclassification of strain CCM 132, previously classified as *Kocuria* varians, as *Kocuria carniphila* sp. nov. *Int J Sys Evol Microbiol.* 2005;55(1):139-142. doi: 10.1099/ijs.0.63304-0
21. Kovacs GM, Burghardt J, Pradella S, Schumann P, Stackebrandt E, Marialigeti K. *Kocuria palustris* sp. nov. and *Kocuria rhizophila* sp. nov, isolated from the rhizoplane of the narrow-leaved cattail (*Typha angustifolia*). *Int J Sys Evol Microbiol.* 1999;49(1):167-173. doi: 10.1099/00207713-49-1-167
22. Zhou G, Luo X, Tang Y, et al. *Kocuria flava* sp. nov. and *Kocuria turfanensis* sp. nov, airborne actinobacteria isolated from Xinjiang, China. *Int J Sys Evol Microbiol.* 2008;58(6):1304-1307. doi: 10.1099/ijs.0.65323-0
23. Reddy GSN, Prakash JSS, Prabahar V, Matsumoto GI, Stackebrandt E, Shivaji S. *Kocuria polaris* sp. nov, an orange-pigmented psychrophilic bacterium isolated from an Antarctic cyanobacterial mat sample. *Int J Sys Evol Microbiol.* 2003;53(1):183-187. doi: 10.1099/ijs.0.02336-0
24. Mayilraj S, Kroppenstedt RM, Korpole S, Saini HS. *Kocuria himachalensis* sp. nov, an actinobacterium isolated from the Indian Himalayas. *Int J Sys Evol Microbiol.* 2006;56(8):1971-1975. doi: 10.1099/ijs.0.63915-0
25. Park E, Roh SW, Kim M, Jung MH, Shin K, Bae J. *Kocuria koreensis* sp. nov, isolated from fermented seafood. *Int J Sys Evol Microbiol.* 2010;60(1):140-143. doi: 10.1099/ijs.0.012310-0
26. Seo YB, Kim D, Kim G, et al. *Kocuria gwangalliensis* sp. nov, an actinobacterium isolated from seawater. *Int J Sys Evol Microbiol.* 2009;59(11):2769-2772. doi: 10.1099/ijs.0.008482-0
27. Tang S, Wang Y, Lou K, et al. *Kocuria halotolerans* sp. nov, an actinobacterium isolated from a saline soil in China. *Int J Sys Evol Microbiol.* 2009;59(6):1316-1320. doi: 10.1099/ijs.0.006627-0
28. Wang K, Zhang L, Liu Y, et al. *Kocuria dechangensis* sp. nov, an actinobacterium isolated from saline and alkaline soils. *Int J Sys Evol Microbiol*. 2015;65(Pt-9):3024-3030. doi: 10.1099/ijs.0.000372
29. Dastager SG, Tang S, Krishnamurthi S, Lee J, Li W. *Kocuria indica* sp. nov, isolated from a sediment sample. *Int J Sys Evol Microbiol.* 2014;64(Pt-3):869-874. doi: 10.1099/ijs.0.052548-0
30. Yun J, Roh SW, Jung MH, et al. *Kocuria salsicia* sp. nov, isolated from salt-fermented seafood. *Int J Sys Evol Microbiol.* 2011;61(2):286-289. doi: 10.1099/ijs.0.021469-0
31. Kim SB, Nedashkovskaya OI, Mikhailov VV, et al. *Kocuria marina* sp. nov, a novel actinobacterium isolated from marine sediment. *Int J Sys Evol Microbiol.* 2004;54(5):1617-1620. doi: 10.1099/ijs.0.02742-0
32. Braun MS, Wang E, Zimmermann S, Wagner H, Wink M. *Kocuria tytonis* sp. nov, isolated from the uropygial gland of an American barn owl (*Tyto furcata*). *Int J Sys Evol Microbiol.* 2019;69(2):447-451. doi: 10.1099/ijsem.0.003170
33. Hamada M, Shibata C, Tamura T, et al. *Kocuria pelophila* sp. nov, an actinobacterium isolated from the rhizosphere of a mangrove. *Int J Sys Evol Microbiol.* 2016;66(9):3276-3280. doi: 10.1099/ijsem.0.001186
34. Jiang Z, Zhang WH, Yuan CG, et al. *Kocuria subflava* sp. nov, isolated from marine sediment from the Indian Ocean. *Antonie van Leeuwenhoek*. 2015;108(6):1349-1355. doi: 10.1007/s10482-015-0587-z
35. Zhang L, Xi L, Ruan J, Huang Y. *Kocuria oceani* sp. nov, isolated from a deep-sea hydrothermal plume. *Int J Sys Evol Microbiol.* 2017;67(1):164-169. doi: 10.1099/ijsem.0.001599
36. Camacho M, Redondo Gomez S, Rodriguez-Llorente I, et al. *Kocuria salina* sp. nov, an actinobacterium isolated from the rhizosphere of the halophyte *Arthrocnemum macrostachyum* and emended description of *Kocuria turfanensis*. *Int J Sys Evol Microbiol.* 2017;67(12):5006-5012. doi: 10.1099/ijsem.0.002401
37. Kloos WE, Tornabene TG, Schleifer KH. Isolation and Characterization of Micrococci From Human Skin, Including Two New Species: *Micrococcus lylae* and *Micrococcus kristinae. Int J Syst Bacteriol.* 1974;24(1):79-101. doi: 10.1099/00207713-24-1-79
38. 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
39. Ajeeba SA, Anand AR, 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
40. Brandle G, L'Huillier AG, Wagner N, Gervaix A, Wildhaber BE, Lacroix L. First report of *Kocuria marina* spontaneous peritonitis in a child. *BMC Infect Dis.* 2014;14(1). doi: 10.1186/s12879-014-0719-5
41. Altuntas F, Yildiz O, Eser B, Gundoan K, Sumerkan B, Cetin M. Catheter-related bacteremia due to *Kocuria rosea* in a patient undergoing peripheral blood stem cell transplantation. *BMC Infect Dis.* 2004;4(1):62. doi: 10.1186/1471-2334-4-62
42. Inada N, Shoji J, Yamagami S. Atopic keratoconjunctivitis complicated by *Kocuria koreensis* keratitis: the first case. *Allergy Asthma Clin Immunol.* 2017;13(1):6. doi: 10.1186/s13223-017-0178-9
43. Meletis G, Gogou V, Palamouti M, et al. Catheter-related relapsing peritonitis due to *Kocuria varians* in a patient undergoing continuous ambulatory peritoneal dialysis. *Nefrologia.* 2012;32(4):541-542. doi: 10.3265/nefrologia.pre2012.apr.11471
44. Purty S, Saranathan R, Prashanth K, et al. The expanding spectrum of human infections caused by

Kocuria species: a case report and literature review. *Emerg Microb Infect.* 2013;2(10):e71. doi: 10.1038/emi.2013.71

45. Ben-Ami, R, Navon-Venezia S, Schwartz D, Carmeli Y. Infection of a Ventriculoatrial Shunt with Phenotypically Variable *Staphylococcus epidermidis* Masquerading as Polymicrobial Bacteremia Due to Various Coagulase-Negative Staphylococci and Kocuria varians. *J Clin Microbiol*. 2003a;41(6):2444-2447. doi: 10.1128/jcm.41.6.2444-2447.2003
46. Dotis J, Printza N, Stabouli S, Papachristou F. *Kocuria* Species Peritonitis: Although Rare, we Have to Care. *Perit Dial Int.* 2015;35(1):26-30. doi: 10.3747/pdi.2013.00138
47. Srinivasa KH, Agrawal N, Agarwal A, Manjunath CN. Dancing vegetations: *Kocuria rosea* endocarditis. *BMJ Case Reports.* 2013;2013:bcr2013010339. doi: 10.1136/bcr-2013-010339
48. Saldaña-Ruiz MA, Chávez-García JM, Ortiz-Alonso F, Ortiz-Arce CS, Espinosa-Mora JE, Cortés-Cárdenas JR. Kocuria kristinae neuroinfection in an immunocompetent patient: a case report and review of the literature. *IJID Reg*. 2023;9:117-119. doi: 10.1016/j.ijregi.2023.10.006
49. Lee MK, Choi SH, Ryu DW. Descending necrotizing Mediastinitis caused by *Kocuria rosea*: a case report. *BMC Infect Dis.* 2013;13:475. doi: 10.1186/1471-2334-13-475
50. 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
51. Moreira JS, Riccetto AGL, da Silva MTN, dos Santos Vilela MM. 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
52. Horiuchi A, Kubota N, Hidaka E, et al. Notable alkaline tolerance of *Kocuria marina* isolate from blood of a pediatric patient with continuous intravenous epoprostenol therapy. *J Infect Chemother.* 2015;21(9):680-686. doi: 10.1016/j.jiac.2015.06.004
53. Taher NM. *Kocuria* Species: Important Emerging Pathogens in Pediatric Patients. *J Pure Appl Microbiol*, 2022;16(4):2874-2879. doi: 10.22207/JPAM.16.4.60
54. 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
55. Kandi V. A case of urinary tract infection caused by *Kocuria* species and identified by conventional methods. *Perspectives in Medical Research*. 2016;4(2):64-66.
56. 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
57. Nudelman BG, Ouellette T, Nguyen KQ, Schmaus WH, Chokshi RR. *Kocuria rosea* Bacteremia in a Sickle Cell Patient: A Case Report. *Cureus.* 2022;14(9):e28870. doi: 10.7759/cureus.28870
58. 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
59. Goldstein BGB, Giroir B, Randolph A. International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med.* 2005;6(1):2-8. doi: 10.1097/01.PCC.0000149131.72248.E6
60. Haque KN. Definitions of bloodstream infection in the newborn. *Pediatr Crit Care Med.* 2005;6(3 Suppl):S45-9. doi: 10.1097/01.PCC.0000161946.73305.0A
61. Hecht SM, Ardura MI, Yildiz VO, Ouellette CP. Central Venous Catheter Management in High-risk Children With Bloodstream Infections. *Pediatr Infect Dis J*. 2020;39(1):17-22. doi: 10.1097/INF.0000000000002495
62. Montoya JEM, Moran MAM, Ardila JAB, Henao PGC, Rodriguez EEM, Meza GAM. Brain abscess by *Kocuria rosea*: Case report and literature review. *Interdiscip Neurosurg.* 2017;7:59-61. doi: 10.1016/j.inat.2016.11.007
63. Lai C, Wang JY, Lin SH, et al. Catheter-related bacteremia and infective endocarditis caused by *Kocuria* species. *Clin Microbiol Infect.* 2011;17(2):190-192. doi: 10.1111/j.1469-0691.2010.03211.x
64. Kimura M, Kawai E, Yaoita H, Ichinoi N, Sakamoto O, Kure S. Central Venous Catheter-Related Blood stream Infection with *Kocuria kristinae* in a patient with Propionic Acidemia. *Case Rep Infect Dis.* 2017;2017(1):1254175. doi: 10.1155/2017/1254175
65. Tsai C-Y, Su S, Cheng Y-H, Chou Y, Tsai T-H, Lieu A-S. *Kocuria varians* infection associated with brain abscess: a case report. *BMC Inf Dis*. 2010;10(102):102. doi: 10.1186/1471-2334-10-102
66. Domont F, Fleche-Mateos AL, Bremond-Gignac D, Hamdad F. *Kocuria dacryocystitis* infection, caused by *Kocuria ocularis* sp. *JMM Case Reports*. 2014;1(2):1-4. doi: 10.1099/jmmcr.0.002022
67. McAleese T, Ahmed A, Berney M, O'Riordan R, Cleary M. *Kocuria rhizophila* prosthetic hip joint infection. *J Surg Case Rep.* 2023;(8):rjad484. doi: 10.1093/jscr/rjad484
68. Fowora MA, Omolopo IA, Aiyedogbon A, et al. Multidrug-Resistant and Methicillin-Resistant Co-Infection in a Nigerian Patient with COVID-19: A Case Report. *Am J Case Rep.* 2023;24:e938761. doi: 10.12659/AJCR.938761
69. Giron FF, Ramos JO, Martin JMS, Numancia GMT, Chaparro CG, Diez ID. *Kocuria salsicia* peritonitis in a peritoneal dialysis patient. *Ren Fail.* 2023;45(1):2210683. doi: 10.1080/0886022X.2023.2210683
70. Biswal D, Kaur R, Satija S, Seth A, Rathi A, Kant L.. The Expanding Spectrum of Human Infections Caused By *Kocuria* Species In Pediatric Patients: One Year Observational, Prospective Hospital-Based Study. *Science Direct.* 2023;130(Suppl 2):S64. doi: 10.1016/j.ijid.2023.04.160
71. Zhang Y, Hu Q, Li Z, Kang Z, Zhang L. *Kocuria* species: an underappreciated pathogen in pediatric patients-a single-center retrospective analysis of

10 years' experience in China. *Diagn Microbiol Infect Dis*. 2023;107(4):116078. doi: 10.1016/j.diagmicrobio.2023.116078

72. Ziogou A, Giannakodimos I, Giannakodimos A, Baliou S, Ioannou P. *Kocuria* Species Infections in Humans-A Narrative Review. *Microorganisms.* 2023;11(9):2362. doi: 10.3390/microorganisms11092362
73. Perrin-Guyomard A, Soumet C, Leclercq R, Doucet-Populaire F, Sanders P. Antibiotic susceptibility of bacteria isolated from pasteurized milk and characterization of macrolide-lincosamide-streptogramin resistance genes. *J Food Prot*. 2005;68(2):347-352. doi: 10.4315/0362-028x-68.2.347
74. Liang H, Wang F, Mu R, et al. Metagenomics analysis revealing the occurrence of antibiotic resistome in Salt Lakes. *Sci Total Environ.* 2021;790:148262. doi: 10.1016/j.scitotenv.2021.148262
75. Machado MAA, Ribeiro WA, Toledo VS, Ramos GLPA, Vigoder HC, Nascimento JS. Antibiotic resistance and biofilm production in catalase-positive gram-positive cocci isolated from Brazilian pasteurized milk. *Journal of Food Quality and Hazards Control*. 2020;7(2):67-74. doi: 10.18502/jfqhc.7.2.2886
76. Takarada H, Sekine M, Kosugi H, et al. Complete genome sequence of the soil actinomycete *Kocuria rhizophila*. *J Bacteriol*. 2008;190(12):4139-4146. doi: 10.1128/jb.01853-07
77. Abdulla Z, Barzani K. Characterization and detection of *mecA* gene in different species of *Staphylococcus, Streptococcus* and *Kocuria* which isolated from thalassemia patients in Erbil City. Proceedings of the 4th International Scientific Conference of Cihan University-Erbil on Biological Sciences. 2017.
78. Stykova E, Nemcova R, Valocky I, Novotny F, Guba P. Adherence of bacteria to mucus collected from different parts of the reproductive tract of heifers and cows. *Can J Microbiol.* 2013;59(11):720-725. doi: 10.1139/cjm-2013-0542
79. Liebl W, Kloos WE, Ludwig W. Plasmid-borne macrolide resistance in *Micrococcus luteus* GenBank accession number for the sequence reported in this paper is AF462611. *Microbiology.* 2002;148(8):2479-2487. doi: 10.1099/00221287-148-8-2479
80. Pleshko EM, Zhurina MV. Distribution of Antibiotic Resistance Genes in *Kocuria* Species. *Antibiotics,* 2025;14(10), 1041. doi: 10.3390/antibiotics14101041
81. Robles-Marhuenda A, Romero-Gomez MP, Garcia-Rodriguez J, Arnalich-Fernandez F. Native valve endocarditis caused by *Kocuria kristinae*. *Enfermedades Infecciosas y Microbiologia Clinica*. 2016;34(7):464-465. doi: 10.1016/j.eimc.2015.09.008
82. Meng X, Chen F, Xiong M, Hao H, Wang K-J. A new pathogenic isolate of *Kocuria kristinae* identified for the first time in the marine fish *Larimichthys crocea. Front Microbiol.* 2023;14:1129568. doi: 10.3389/fmicb.2023.1129568
83. Rodriguez-Alonso, P, Fernandez-Otero C, Centeno JA, Garabal JI. Antibiotic resistance in lactic acid bacteria and *micrococcaceae/staphylococcaceae* isolates from artisanal raw milk cheeses, and potential implications on cheese making. *J Food Sci.* 2009;74(6):M284-93. doi: 10.1111/j.1750-3841.2009.01217.x
84. Moissenet D, Becker K, Merens A, Ferroni A, Dubern B, Vu-Thien H. Persistent bloodstream infection with *Kocuria Rhizophila* related to a damaged central catheter. *J Clin Microbiol*. 2012;50(4):1495-1498. doi: 10.1128/jcm.06038-11
85. Poyser TA, Gbadebo D, Krebs J, Brock JM, Robinson E. *Kocuria kristinae* Induced Infective Endocarditis: Unveiling an Emerging Threat in Clinical Practice. *Cureus.* 2024;16(4):e58979. doi: 10.7759/cureus.58979
86. Nakata M, Kuji H, Toishi T, et al. Relapsing peritoneal dialysis associated peritonitis due to *Kocuria rhizophila*: A case report. *Case Rep Nephrol Dial.* 2024;14(1):10-14. doi: 10.1159/000534765
87. Kachhwaha A, Gupta A, Kumar K, Omar BJ, Nath UK. Infection Control Challenge: *Kocuria rhizophila* Bacteremia from A Peripherally Inserted Central Venous Catheter in A Pediatric Oncology Patient. *Mathews Journal of Cancer Science.* 2024;9(1):49. doi: 10.30654/MJCS.10049
88. Al-Khamesi MB, Ibrahim MK, El-Shatoury EH, El-Kholy IMA, Mikawye EE, Tolba STM. Antibiotic resistance and molecular characteristics of upcoming pathogenic Kocuria spp. isolated from Iraq and Egypt. *Baghdad Science Journal.* 2024;22(6):1560-1567. doi: 10.21123/bsj.2024.11601
89. Mathew M, Athulya B, Chaithanya MV, et al. Antibiotic resistance and biofilm formation of thermoduric *Kocuria* and Micrococci isolated from the milk samples of healthy cows. *Proc Indian Natl Sci Acad.* 2025. doi: 10.1007/s43538-025-00409-y
90. Kumaran S, Ngo ACR, Schultes FPJ, Tischler D. Draft genome sequence of *Kocuria indica* DP-K7, a methyl red degrading actinobacterium. *3 Biotech.* 2020;10(4):175. doi: 10.1007/s13205-020-2136-3
91. Deurenberg RH, Stobberingh EE. The evolution of *Staphylococcus aureus*. *Infect Genet Evol*. 2008;8(6):747-763. doi: 10.1016/j.meegid.2008.07.007
92. Cuny C, Layer, F, Strommenger B, Witte W. Rare occurrence of methicillin-resistant *Staphylococcus aureus* CC130 with a novel mecA homologue in humans in Germany. *PloS One*. 2011;6(9):e24360. doi: 10.1371/journal.pone.0024360
93. Khosravi AD, Hoveizavi H, Farshadzadeh Z. The Prevalence of Genes Encoding Leukocidins in *Staphylococcus aureus* Strains Resistant and Sensitive to Methicillin Isolated from Burn Patients in Taleghani Hospital, Ahvaz, Iran. *Burns.* 2012;38 (2):247-51. doi: 10.1016/j.burns.2011.08.002
94. Bengoechea JA, Skurnik M. Temperature-regulated efflux pump/potassium antiporter system mediates resistance to cationic antimicrobial peptides in Yersinia. *Mol Microbiol*. 2000;37(1):67-80. doi: 10.1046/j.1365-2958.2000.01956.x
95. Xu Y, Sim SH, Nam KH, et al. Crystal structure of the periplasmic region of MacB, a noncanonic ABC transporter. *Biochemistry.* 2009;48(23):5218-5225. doi: 10.1021/bi900415t
96. Fitzpatrick AWP, Llabres S, Neuberger A, et al. Structure of the MacAB-TolC ABC-Type Tripartite Multidrug Efflux Pump. *Nat Microbiol.* 2017;2:17070. doi: 10.1038/nmicrobiol.2017.70
97. Kobayashi N, Nishino K, Hirata T, Yamaguchi A.

Membrane topology of ABC-type macrolide antibiotic exporter MacB in *Escherichia coli. FEBS Letters.* 2003;546(2-3):241-246. doi: 10.1016/s0014-5793(03)00579-9

98. Roberts MC, Sutcliffe J, Courvalin P, Jensen LB, Rood J, Seppala H. Nomenclature for Macrolide and Macrolide-Lincosamide-Streptogramin B Resistance Determinants. *Antimicrob Agents Chemother.* 1999;43(12): 2823-30. doi: 10.1128/aac.43.12.2823
99. Rosato AE, Lee BS, Nash KA. Inducible macrolide resistance in *Corynebacterium jeikeium*. *Antimicrobial agents and chemotherapy,* 2001;45(7):1982-1989. doi: 10.1128/AAC.45.7.1982-1989.2001.
100. Shaaly A, Kalamorz F, Gebhard S, Cook GM. Undecaprenyl pyrophosphate phosphatase confers low-level resistance to bacitracin in Enterococcus faecalis. *The Journal of antimicrobial chemotherapy,* 2013;68(7):1583-1593. doi: 10.1093/jac/dkt048
101. Köhler T, Epp SF, Curty LK, Pechère JC. Characterization of MexT, the regulator of the MexE-MexF-OprN multidrug efflux system of *Pseudomonas aeruginosa. Journal of bacteriology,* 1999;181(20), 6300–6305 doi: 10.1128/JB.181.20.6300-6305.1999.
102. Yamane K, Wachino J, Suzuki S, Kimura K, Shibata N, Kato H, Shibayama K, Konda T, Arakawa Y. New plasmid-mediated fluoroquinolone efflux pump, QepA, found in an Escherichia coli clinical isolate. *Antimicrobial agents and chemotherapy,* 2007;51(9): 3354-3360. doi: 10.1128/AAC.00339-07