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Infection or Contamination with *Rothia*, *Kocuria*, *Arthrobacter* and *Pseudoglutamicibacter*—a Retrospective Observational Study of Non-*Micrococcus Micrococcaceae* in the Clinic

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ABSTRACT *Rothia*, *Kocuria*, *Arthrobacter*, and *Pseudoglutamicibacter* are bacterial species within the family *Micrococcaceae*. Knowledge of human infections due to these bacteria is limited. This study aimed to examine features of infections caused by non-*Micrococcus Micrococcaceae* (NMM). Findings of NMM from blood cultures and other sterile cultures from 2012 to 2021 were identified from the records of the Department of Clinical Microbiology in Region Skåne, Lund, Sweden. Medical records were retrospectively reviewed. True infection was defined as having signs of infection, no other more likely pathogen, and no other focal infection, together with two positive blood cultures or one positive blood culture and an intravascular device. A total of 197 patients with findings of NMM in blood cultures were included. Among adult patients with bacteremia, 29 patients (22%) were considered to have a true infection. Adults with true infection were significantly more likely to have malignancy (69%), leukopenia (62%), and treatment with chemotherapeutics (66%) compared to patients with contaminated samples (24%, 3%, and 8%, respectively) ($P < 0.001$). A total of 31 patients had findings of NMM in other sterile cultures, and infections were considered true in joints ($n = 4$), a pacemaker ($n = 1$), and peritoneal dialysis fluid ($n = 1$). Infections due to NMM occur but are rare. Growth of NMM in blood cultures should be suspected to be a true infection mainly in immunocompromised patients.

KEYWORDS *Arthrobacter*, bacteremia, bacterial infections, blood culture, catheter-related infections, infectious disease medicine, *Kocuria*, *Micrococcaceae*, *Pseudoglutamicibacter*, *Rothia*

Actinobacteria (or Actinomycetota) make up one of the largest taxonomic units within the bacteria domain. It is a diverse group of Gram-positive bacteria since it contains pathogens, soil inhabitants, and bacteria within the normal flora in humans and animals (1, 2). *Micrococcaceae* is a family within the phylum Actinobacteria, containing, among other genera, *Micrococcus*, *Rothia*, *Kocuria*, *Arthrobacter*, and *Pseudoglutamicibacter* (3).

The bacteria genus *Rothia* was first introduced in 1967 by Georg and Brown (4) and has its natural habitat in the oral cavity of humans. Few case reports are published of human infections due to *Rothia* and have encompassed infective endocarditis, pneumonia, meningitis, and bacteremia. Since *Rothia* is part of the normal flora in humans, findings of *Rothia* from blood cultures may often be considered contamination rather than an invasive infection (5–8).

In 1995, a group of bacteria within the genus *Micrococcus* was reclassified as a separate genus, named *Kocuria* (9). It inhabits the skin and oral cavity of humans and is an uncommon cause of infection. Therefore, it is often dismissed as contamination when there is growth in

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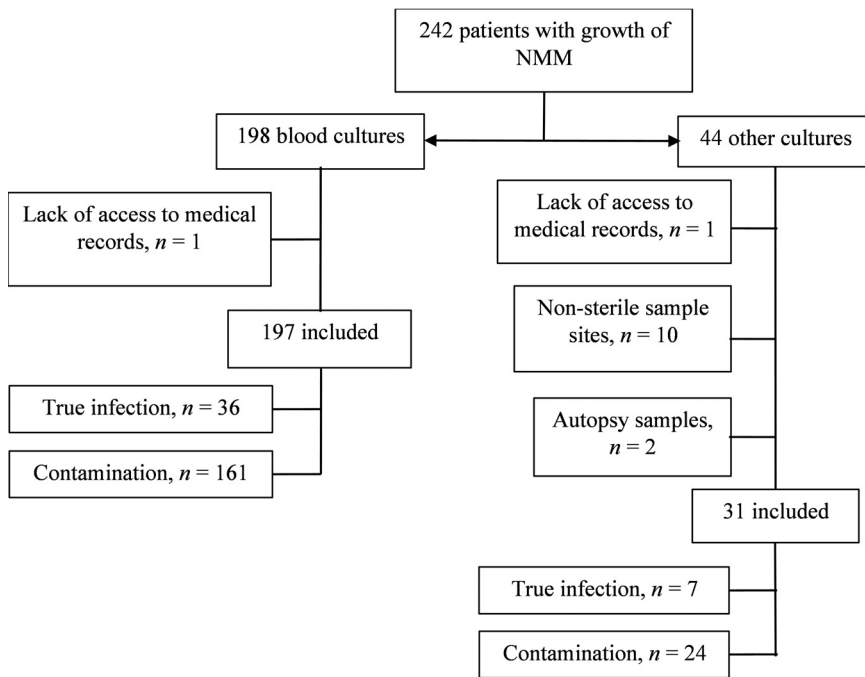


FIG 1 Flowchart of inclusion and exclusion.

blood cultures. Nevertheless, case reports have described infections such as urinary tract infections, peritonitis, and infective endocarditis due to *Kocuria* (10–12). These infections often occurred in patients with predisposing factors such as chronic catheterization, malignancies, and end-stage renal disease with dialysis (13).

Arthrobacter is a heterogenous genus of bacteria species distributed in the environment, especially soil. In contrast to *Rothia* and *Kocuria*, it does not naturally inhabit humans (14). There are only a few case reports describing human infections due to *Arthrobacter*, in which patients with leukemia or injection drug use have been affected (15–17).

Pseudoglutamicibacter was formerly defined as a member of the genus *Arthrobacter*. However, alongside updated taxonomy, the species is now defined as an own genus (18). According to earlier publications, it has low pathogenic potential. There are no cases describing severe infections in humans caused by *Pseudoglutamicibacter*, but there is one case with urinary tract infection (19).

Since there is a lack of studies on the clinical implications of finding these bacteria (henceforth referred to as non-*Micrococcus Micrococcaceae* [NMM]), this study aimed to investigate the microbiological and clinical aspects of infections with *Rothia*, *Kocuria*, *Arthrobacter*, and *Pseudoglutamicibacter* and whether infections due to the bacteria are more likely to occur in certain groups of patients.

MATERIALS AND METHODS

Patients with growth of NMM in blood cultures and other sterile cultures between 2012 and 2021 were identified by searching in the laboratory information system of the clinical microbiology laboratory of Region Skåne, Lund, Sweden. This clinical microbiology laboratory is the only one in the region and serves both public and private clinics (both in- and outpatient), including primary health care and secondary and tertiary hospitals with a covered population of approximately 1.4 million. The medical records were retrospectively reviewed with the inclusion criteria being the presence of the above-mentioned bacteria in cultures. The exclusion criteria were patients who had in-hospital care outside the region and patients whose medical records were unavailable (Fig. 1). Clinical data according to a prespecified protocol involving age, bacterial species, polymicrobial growth, use of immunosuppressive treatment or chemotherapeutics, Charlson Comorbidity Index (20), fever, and leucocytosis within 48 h from when the sample was taken and presence of any intravascular device or joint prosthesis were collected.

The reason for including these specific bacteria (*Rothia*, *Kocuria*, *Arthrobacter*, and *Pseudoglutamicibacter*) is that they are the most commonly found *Micrococcaceae* in our setting, except for *Micrococcus*, which was

TABLE 1 Definition of true infection

Criteria	Definition
In cases with two positive blood cultures	
Criterion 1	Infection confirmed by temp (>38°C) OR hypotension (systolic blood pressure <100 mm Hg) OR chills OR leukocytosis (>12 × 10 ⁹ /L)
Criterion 2	No other more likely pathogen in blood cultures
Criterion 3	No other focal infection
In cases with one positive blood culture	
Criterion 4	Foreign intravascular device ^a present >48 h prior to blood sample AND all of the above
In cases with patients of <18 yrs	
Criterion 5	Infection interpreted as caused by <i>Actinobacteria</i> by treating physician AND all of criteria 1 to 3

^aIntravascular devices include implantable cardioverter defibrillators (ICDs), pacemakers, vascular grafts, central venous catheters, and dialysis catheters.

excluded from the study because it is found so much more often that the inclusion was thought likely to lead to a total domination of statistical analyses.

Nosocomial infection was defined as having a positive microbiological culture after at least 48 h of hospitalization. The definition of a health care-associated infection was reported as stated by Friedman et al. (21), meaning an infection in a patient from a nursing home, who got medical care at home, who had received intravenous therapy, or who had been hospitalized within 90 days before the microbiological culture was taken. To classify sepsis and septic shock, the Sepsis-3 criteria were applied (22) and evaluated using the Sequential Organ Failure Assessment (SOFA) score (23).

Microbiological methods. During the study period, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS: Bruker Daltonics, using the Bruker MBT Compass library version most recent at the time of sample analysis) was used as the main method for bacterial species identification at the clinical microbiology laboratory, with 16S sequencing using Sanger methodology being used as the primary back-up method for some selected cases in which no species identification was possible using MALDI-TOF MS.

The blood culture system used was Bact/Alert 3D (bioMérieux) until December 2012, and Bactec FX (Becton Dickinson) after that, both using a 5-day incubation standard and using both aerobic and anaerobic bottles. For samples taken from sterile sites such as cerebrospinal fluid, joint fluid, or biopsy samples, the standard method used included direct plating samples on blood agar incubated in a CO₂-enriched atmosphere, and fastidious aerobe agar incubated under anaerobic conditions, as well as inoculating a part of the sample in tryptic soy broth and brain heart infusion for samples originating from the central nervous system, incubated in CO₂-enriched atmosphere. All incubations were done at 37°C, with the samples being incubated for a total of 7 days as standard. Additional plates and broth were added at the discretion of the laboratory technicians and clinical microbiologists responsible for the analysis in selected cases and for specific diagnostic needs. Sterile nonblood fluids such as joint fluid were sometimes injected directly into blood culture bottles by the physician taking the sample and were in those cases handled in the same way as blood cultures in the laboratory.

Definition of true infection. To determine true infection, the definition used in this study was based on criteria established for true infection with *Corynebacterium* and *Cutibacterium* (24, 25). In cases with two or more positive blood culture sets the following criteria had to be fulfilled: (i) infection confirmed by fever, hypotension, chills, or leukocytosis; (ii) no other more likely pathogenic bacteria in the bloodstream; and (iii) no other focal infection explaining the symptoms. Other focal infection was defined by two of the following: (i) isolation of a bacteria in the focal site, (ii) infection suggested by imaging results, and (iii) typical symptoms of a focal infection.

In cases with only one positive blood culture, the criteria above had to be fulfilled, and in addition, an intravascular device 48 h prior to the sample or bacteria cultured from the site of infection must be present. Due to the use of pediatric blood culture bottles with only one bottle used, for patients under 18 years of age, the definition was modified so that only one positive blood culture was needed if the treating physician interpreted it as an infection with the bacteria studied. These criteria are summarized in Table 1. Blood cultures not matching these criteria were classified as probable contamination.

For other sterile cultures, criteria 1 to 3 in Table 1 were used, with the same modification as was made for patients under 18 years of age. If another more likely explanation for the symptoms was found, it was not classified as a true infection.

Statistical analysis. Statistical analyses were made in SPSS Statistics version 28. For categorical data, the 1chi-square test was used. For continuous variables, the Mann-Whitney *U* test was used. A *P* value <0.05 was regarded as statistically significant.

Ethical considerations. Due to the retrospective, observational, nature of the study, the need for patient consent was waived by the Swedish Ethics Authority (approval 2021-03354).

RESULTS

Description of the cohort. A total of 197 cases of findings of NMM from blood cultures and 31 from other sterile cultures were included. Fig. 1 is a flowchart summarizing the inclusion and exclusions of patients.

TABLE 2 Clinical and microbiological features of adult patients with non-*Micrococcus Micrococcaceae* bacteremia^a

Characteristics	Total (n = 152)	True infection (n = 29)	Contamination (n = 123)	P value of difference ^b
Age (yr)	71 (63 to 83)	65 (57 to 75)	72 (66 to 85)	0.005
Women	74 (49)	11 (38)	63 (51)	0.140
Charlson score	2 (1 to 4)	2 (2 to 4)	2 (1 to 4)	0.323
Malignancy	49 (32)	20 (69)	29 (24)	<0.001
Site of acquisition				
Community	70 (46)	3 (10)	67 (55)	<0.001
Nosocomial	33 (22)	15 (52)	18 (15)	<0.001
Health care-associated	49 (32)	11 (38)	38 (31)	0.466
Use of chemotherapy	29 (19)	19 (66)	10 (8)	<0.001
Immunosuppressive therapy	32 (21)	8 (28)	24 (20)	0.337
Sepsis or septic shock ^c	16 (10)	2 (7)	14 (11)	0.479
Intravascular device ^d	51 (34)	23 (79)	28 (23)	<0.001
Days of hospitalization as from blood sample taken	7 (3 to 14)	13 (7 to 22)	7 (3 to 12)	0.003
Fever ^c	102 (67)	25 (86)	77 (63)	0.015
Leukocytosis ^c	64 (42)	2 (7)	62 (50)	<0.001
Leukopenia ^c	22 (15)	18 (62)	4 (3)	<0.001
Mortality				
In hospital	15 (10)	3 (10)	12 (10)	0.924
Within 90 days	18 (12)	4 (14)	14 (11)	0.718
Multiple positive blood cultures	22 (14)	15 (52)	7 (6)	<0.001
Polymicrobial growth	68 (45)	2 (7)	66 (54)	<0.001
Other focal infection	66 (43)	0 (0)	66 (54)	<0.001
Time to positivity (h) ^e	35 (25 to 57)	26 (16 to 36)	44 (31 to 64)	0.002
Genus and species				0.383 (genus), 0.220 (species)
<i>Rothia</i>	108 (71)	24 (83)	84 (68)	
<i>R. dentocariosa</i>	26 (17)	2 (7)	24 (20)	
<i>R. mucilaginosa</i>	53 (35)	16 (55)	37 (30)	
<i>R. aerieae</i>	1 (1)	0 (0)	1 (1)	
<i>Rothia</i> spp. not further specified	28 (18)	6 (21)	22 (18)	
<i>Kocuria</i>	28 (18)	4 (14)	24 (20)	
<i>K. kristinae</i>	2 (1)	0 (0)	2 (2)	
<i>Kocuria</i> spp. not further specified	26 (17)	4 (14)	22 (18)	
<i>Arthrobacter</i>	10 (7)	1 (3)	9 (7)	
<i>Pseudoglutamicibacter</i>	6 (4)	0 (0)	6 (5)	

^aCategorical data are presented as No. (%). Continuous variables are presented as medians (interquartile ranges). For categorical data, the chi-square test is used. For continuous data, the Mann-Whitney *U* test is used. Adults are defined as patients ≥ 18 years of age.

^bDifference between those with true infection and those with contaminated samples.

^cWithin 48 h from when the blood sample was taken.

^dIntravascular devices include implantable cardioverter defibrillators (ICDs), pacemakers, vascular grafts, central venous catheters, and dialysis catheters.

^eOnly for those with monomicrobial growth ($n = 39$).

Clinical features of infections with growth of NMM in blood cultures in adults.

Characteristics of adult patients and their infections are listed in Table 2. Using the criteria in Table 1, 26 of these patients (19%) were classified as having a true infection. Adult patients having a true infection were found to be younger but also had a higher portion of malignancy (69%), leukopenia (62%), use of chemotherapeutics (66%), and nosocomial infections (52%) compared to patients who were considered to have a contamination (24%, 3%, 8%, and 15%, respectively; $P < 0.001$).

Looking at the number of positive blood cultures, 22 patients (15%) had more than one positive blood culture. Of these, 14 were infected with some species of *Rothia*. The 22 patients with multiple positive blood cultures were found to have a higher incidence of malignancy (68%), leukopenia (50%), use of chemotherapeutics (55%), and nosocomial infections (45%) compared those patients with growth of NMM in only one culture (26%, 8%, and 13% [$P < 0.001$] and 18% [$P = 0.003$], respectively).

TABLE 3 Clinical and microbiological features of children with non-*Micrococcus Micrococcaceae* bacteremia^a

Characteristics	Total (n = 45)	True infection (n = 7)	Contamination (n = 38)	P value of difference ^b
Age (yr)	1 (0 to 5)	3 (0 to 8)	1 (0 to 3)	0.362
Women	22 (49)	3 (43)	19 (50)	0.728
Charlson score	0 (0 to 2)	2 (0 to 2)	0 (0 to 0)	0.010
Malignancy	8 (18)	5 (71)	3 (8)	<0.001
Site of acquisition				
Community	14 (31)	0 (0)	14 (37)	0.053
Nosocomial	16 (36)	5 (71)	11 (29)	0.031
Health care-associated	15 (33)	2 (29)	13 (34)	0.771
Use of chemotherapy	8 (18)	5 (71)	3 (8)	<0.001
Immunosuppressive therapy	8 (18)	2 (29)	6 (16)	0.416
Sepsis or septic shock ^c	0 (0)	0 (0)	0 (0)	
Intravascular device ^d	6 (13)	2 (29)	4 (11)	0.197
Days of hospitalization as from blood sample taken	5 (2 to 8)	6 (4 to 15)	5 (2 to 8)	0.126
Fever ^c	28 (62)	6 (86)	22 (58)	0.163
Leukocytosis ^c	14 (31)	0 (0)	14 (37)	0.053
Leukopenia ^c	7 (16)	5 (71)	2 (5)	<0.001
Mortality				
In hospital	2 (4)	1 (14)	1 (3)	0.169
Within 90 days	3 (7)	2 (29)	1 (3)	0.011
Multiple positive blood cultures	0 (0)	0 (0)	0 (0)	
Polymicrobial growth	12 (27)	2 (29)	10 (26)	0.901
Other focal infection	21 (47)	0 (0)	21 (55)	0.007
Time to positivity (h) ^e	31 (20 to 49)	25 (14 to 38)	35 (21 to 51)	0.126
Genus and species				0.466 (genus), 0.050 (species)
<i>Rothia</i>	38 (84)	7 (100)	31 (82)	
<i>R. dentocariosa</i>	9 (20)	0 (0)	9 (24)	
<i>R. mucilaginosa</i>	21 (47)	7 (100)	14 (37)	
<i>Rothia</i> spp. not further specified	8 (18)	0 (0)	8 (21)	
<i>Kocuria</i>	6 (13)	0 (0)	6 (16)	
<i>Arthrobacter</i>	1 (2)	0 (0)	1 (3)	

^aThe categorial data are presented as No. (%). Continuous variables are presented as medians (interquartile ranges). For categorial data, the chi-square test was used. For continuous data, the Mann-Whitney *U* test was used. Children are defined as patients <18 years of age.

^bDifference between those with true infection and those with contaminated samples.

^cWithin 48 h from when the blood sample was taken.

^dIntravascular devices include implantable cardioverter defibrillators (ICDs), pacemakers, vascular grafts, central venous catheters, and dialysis catheters.

^eOnly for those with monomicrobial growth (*n* = 19).

Clinical features of infections with growth in blood cultures of NMM in children.

Characteristics of patients < 18 years of age and their infections are listed in Table 3. Among these, 7 patients (16%) were classified as having a true infection, and 38 (84%) had a contaminated blood sample. Children with a true infection were found to have higher Charlson score ($P = 0.010$), a higher incidence of malignancy (71%), use of chemotherapeutics (71%), leukopenia (71%), and nosocomial infections (71%) compared to those children with a contaminated blood cultures (8%, 8%, 5%, and 29%, respectively; $P < 0.001$).

Microbiological features of infections with growth of NMM in blood cultures.

Rothia was the most common genus, with *R. mucilaginosa* being the most common species, both among true infections ($n = 23$, 64%) and in total ($n = 74$, 38%). *R. mucilaginosa* was also the most pathogenic species, with 31% of the positive blood cultures being defined as true infections.

Median time to positivity (TTP) was statistically significantly shorter in patients who were considered to have a true infection compared with those who had contamination, 26 h (interquartile range [IQR], 16 to 36) versus 44 h (IQR, 31 to 64) ($P < 0.001$) (Table 2).

TABLE 4 Clinical and microbiological features of patients with non-*Micrococcus Micrococcaceae* growth from joint fluid and bone tissue^a

Characteristics	Total (n = 13)	True infection (n = 4)	Contamination (n = 9)	P value of difference ^b
Age (yr)	67 (45 to 81)	60 (37 to 71)	76 (43 to 83)	0.315
Women	5 (38)	1 (25)	4 (44)	0.506
Charlson score	1 (0 to 1)	1 (0 to 1)	1 (0 to 1)	0.488
Malignancy	0 (0)	0 (0)	0 (0)	
Site of acquisition				
Community	9 (69)	1 (25)	8 (89)	0.021
Nosocomial	0 (0)	0 (0)	0 (0)	
Health care-associated	4 (31)	3 (75)	1 (11)	0.021
Immunosuppressive therapy	4 (31)	2 (50)	2 (22)	0.317
Sepsis or septic shock ^c	0 (0)	0 (0)	0 (0)	
Intravascular device ^d	3 (23)	1 (25)	2 (22)	0.913
Joint prosthesis	5 (38)	1 (25)	4 (44)	0.506
Days of hospitalization as from blood sample taken	1 (0 to 10)	9 (2 to 10)	0 (0 to 7)	0.329
Fever ^c	4 (31)	3 (75)	1 (11)	0.021
Leukocytosis ^c	2 (15)	2 (50)	0 (0)	0.021
Leukopenia ^c	0 (0)	0 (0)	0 (0)	
Mortality	0 (0)	0 (0)	0 (0)	
Polymicrobial growth	4 (31)	0 (0)	4 (44)	0.109
Genus and species				0.853 (genus), 0.375 (species)
<i>Rothia</i>	7 (54)	2 (50)	5 (56)	
<i>R. dentocariosa</i>	3 (23)	0 (0)	3 (33)	
<i>R. mucilaginosa</i>	3 (23)	2 (50)	1 (11)	
<i>Rothia</i> spp. not further specified	1 (7)	0 (0)	1 (11)	
<i>Kocuria</i>	6 (46)	2 (50)	4 (44)	
<i>K. kristinae</i>	1 (7)	0 (0)	1 (11)	
<i>Kocuria</i> spp. not further specified	5 (38)	2 (50)	3 (33)	

^aThe categorial data are presented as No. (%). Continuous variables are presented as medians (interquartile ranges). For categorial data, the chi-square test is used. For continuous data, the Mann-Whitney *U* test is used.

^bDifference between those with true infection and those with contaminated samples.

^cWithin 48 h from when the blood sample was taken.

^dIntravascular devices include implantable cardioverter defibrillators (ICDs), pacemaker, vascular graft, central venous catheter, dialysis catheter.

Identification was performed using MALDI-TOF in all cases except for four, where 16S sequencing using Sanger methodology was used.

Severe infection with bacterial growth of NMM in blood cultures. One patient was diagnosed with infective endocarditis caused by *R. mucilaginosa*, which was isolated in three sets of blood cultures, as well as on tissue from his prosthetic cardiac valve. Transthoracic echocardiogram showed a vegetation on the aortic prosthetic valve measuring 13 mm, with a suspicion of a root abscess. The patient was initially treated conservatively but then, after a cardiac arrest, underwent acute surgery, with a successful outcome after continued treatment with benzylpenicillin and gentamicin, with vancomycin being used before blood culture results were finished.

Infections with NMM identified by cultures other than blood cultures. A total of 31 cultures were taken from locations other than the bloodstream, with joint fluid being the most common. In total, 7 cases of true infection were found among these patients. Characteristics of patients with growth of NMM in joint fluid and bone tissue are listed in Table 4, and the characteristics of patients with growth of NMM in samples other than blood, joint fluid, and bone are listed in Table 5.

Four patients had growth of NMM in joint fluid and were diagnosed with septic arthritis. All patients had risk factors for infection: recent knee surgery ($n = 1$), knee prosthesis ($n = 1$), and immunosuppressive treatment ($n = 2$). The bacteria causing infections in joints were *Kocuria* sp. and *R. mucilaginosa*.

A pacemaker infection caused by *Kocuria* sp. was found in one patient, and peritonitis was found in one patient. One patient was classified as having an infection with isolation

TABLE 5 Clinical and microbiological features of patients with non-*Micrococcus Micrococcaceae* growth from other locations than blood, joint fluid, and bone tissue^a

Characteristics	Total (n = 18)	True infection (n = 3)	Contamination (n = 15)	P value of difference ^b
Age (yr)	64 (43 to 74)	74	62 (35 to 69)	0.313
Women	9 (50)	2 (67)	7 (47)	0.527
Charlson score	2 (2 to 5)	2	1 (0 to 5)	0.501
Malignancy	5 (28)	0 (0)	5 (33)	0.239
Site of acquisition				
Community	7 (39)	1 (33)	6 (40)	0.829
Nosocomial	5 (28)	0 (0)	5 (33)	1.000
Health care-associated	6 (33)	2 (67)	4 (27)	0.180
Immunosuppressive therapy	3 (17)	0 (0)	3 (20)	0.396
Sepsis or septic shock ^c	0 (0)	0 (0)	0 (0)	
Intravascular device ^d	8 (44)	3 (100)	5 (33)	0.034
Days of hospitalization from blood sample taken	5 (0 to 18)	16	1 (0 to 10)	0.150
Fever ^c	4 (22)	1 (33)	3 (20)	0.612
Leukocytosis ^c	4 (22)	0 (0)	4 (27)	0.310
Leukopenia ^c	0 (0)	0 (0)	0 (0)	
Mortality	1 (6)	0 (0)	1 (7)	0.645
Polymicrobial growth	0 (0)	0 (0)	0 (0)	
Genus and species				0.105 (genus), 0.206 (species)
<i>Rothia</i>	9 (50)	0 (0)	9 (60)	
<i>R. dentocariosa</i>	3 (17)	0 (0)	3 (20)	
<i>R. mucilaginosa</i>	2 (11)	0 (0)	2 (13)	
<i>Rothia</i> spp. not further specified	4 (22)	0 (0)	4 (27)	
<i>Kocuria</i>	8 (44)	3 (100)	5 (33)	
<i>K. kristinae</i>	2 (11)	0 (0)	2 (13)	
<i>Kocuria</i> spp. not further specified	6 (33)	3 (100)	3 (20)	
<i>Arthrobacter</i> spp.	1 (6)	0 (0)	1 (7)	

^aThe categorial data are presented as No. (%). The continuous variables are presented as medians (interquartile ranges). For the categorial data, the chi-square test is used. For continuous data, the Mann-Whitney *U* test is used.

^bDifference between those with true infection and those with contaminated samples.

^cWithin 48 h from when the blood sample was taken.

^dIntravascular devices include implantable cardioverter defibrillators (ICDs), pacemakers, vascular grafts, central venous catheters, and dialysis catheters.

of *Kocuria* sp. in material from an aortic pseudoaneurysm; cultures were taken perioperatively, but the patient did not have any clear signs of infection before surgery.

DISCUSSION

While previous case reports have identified single cases of infection with *Kocuria* and *Arthrobacter*, this study, to our knowledge, represents the first systematic effort to describe what characterizes infection and contamination with these bacteria. Bacteremia with *Rothia* has been described in a case series (26), but this is, to our knowledge, the largest case series to date and the first to describe invasive infections outside the bloodstream. None of the patients with findings of *Pseudoglutamicibacter* from cultures turned out to have a true infection, but since this study only covered six cases, it is difficult to draw any conclusions about whether they can cause infections or not. Patients with malignancy seem to be more vulnerable to infections with the studied bacteria. An association between malignancy and *Rothia* infections has been shown in previous studies, but not in infections with *Kocuria* and *Arthrobacter* (26). Even when applying multiple positive blood cultures as the definition of a true infection, the results are similar.

According to this study, findings of *Rothia* in blood cultures accounted for true infection in 22% of the cases. How often growth of *Rothia* in a blood culture represents true infection was also analyzed in 2014 by Ramanan et al. (27), describing 67 cases. In that study, a true infection was classified as having multiple positive blood cultures. *Rothia* grew in multiple blood cultures in 37% of the patients, and leukemia was identified as a risk factor

for infection. The proportion of *Rothia* bacteremia with growth in multiple blood cultures in our material was lower at 13%. Region Skåne, Sweden, had an average of 1.3 million inhabitants between 2012 and 2021, indicating that true bacteremia with the studied bacteria has an incidence of 2.8 cases per 1 million inhabitants per year and that the total incidence of invasive infections is 3.3 cases per 1 million inhabitants per year.

Since many of the studied bacteria are found on the skin, drawing blood from venous catheters, as opposed to directly from the vein, might be more likely to result in contamination (as is the case for other skin contaminants). Information on the method used to draw the blood in individual instances was not available, but the recommendation throughout the study period has been to draw the blood directly from the vein.

TTP was shorter in cultures representing true infection compared with contaminated samples. Former studies have shown that in some bacteria species, a shorter TTP can be an indication of severe infection due to higher bacterial concentration in blood (28, 29). This study shows that shorter TTP in cultures with the studied bacteria is correlated with a higher risk of true infection, but any correlation between TTP and the severity of infection was not possible to confirm.

Regarding the identification of the studied bacteria in locations other than blood, seven cases with true infection were found, including septic arthritis caused by *R. mucilaginosa* and arthritis, peritonitis, and pacemaker infection caused by *Kocuria* spp. Except for *Kocuria* peritonitis, these infections have previously been identified although only published in a few case reports, with each making these findings among the first published (30–34). The adjustments for pediatric blood cultures and for infections outside the bloodstream are somewhat less robust than the ones used for adults with bloodstream infection. However, not taking this into consideration would probably result in a definition with which true infection was overestimated.

A strength of this study compared with other studies is that the cultures were collected at a central laboratory covering all inpatient and outpatient care in the whole region. This makes the result more representative for the population in general compared to a hospital-based design. This is one of the first studies looking at the clinical implications of finding *Rothia* in cultures in a systematic way and the first systematic study of the clinical implications of finding *Kocuria*, *Arthrobacter*, or *Pseudoglutamicibacter*. This study also has several limitations, mainly due to its retrospective design. Data regarding specific clinical sign were sometimes missing in the medical records, and the amount of blood collected was not documented. The fact that several bacterial species were grouped and analyzed together causes a risk that differences between them are missed. However, the individual species (except for some *Rothia* species) had few cases despite the long study period, making it difficult to perform statistical analyses on them separately.

In conclusion, *Rothia*, *Kocuria*, and *Arthrobacter* can cause infections and approximately 9 to 22% of all positive blood cultures with these bacteria represent true infections. Growth of NMM in blood cultures should be considered true infections foremost in immunocompromised patients. However, a large proportion of the patients whose charts were reviewed in this study and had a true NMM infection had neither immunosuppressive treatment nor a diagnosed malignancy, showing the importance of combining clinical information and microbiological information such as short TTP in blood culture and lack of other identified likely pathogens when finding uncommon bacteria such as these. These infections seem most often to be subacute, and cases have a favorable prognosis.

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REFERENCES

- Barka Essaid A, Vatsa P, Sanchez L, Gaveau-Vaillant N, Jacquard C, Meier-Kolthoff JP, Klenk H-P, Clément C, Ouhdouch Y, van Wezel GP. 2015. Taxonomy, physiology, and natural products of *Actinobacteria*. *Microbiol Mol Biol Rev* 80:1–43.
- Oren A, Garrity GM. 2021. Valid publication of the names of forty-two phyla of prokaryotes. *Int J Syst Evol Microbiol* 71. <https://doi.org/10.1099/ijsem.0.005056>.
- Nouioui I, Carro L, García-López M, Meier-Kolthoff JP, Woyke T, Kyrpides NC, Pukall R, Klenk H-P, Goodfellow M, Göker M. 2018. Genome-based taxonomic classification of the phylum *Actinobacteria*. *Front Microbiol* 9:2007. <https://doi.org/10.3389/fmicb.2018.02007>.
- Georg LK, Brown JM. 1967. *Rothia*, gen. nov. an aerobic genus of the family actinomycetaceae. *Int J System Bacteriol* 17: <https://doi.org/10.1099/00207713-17-1-79>.
- Franconieri F, Join-Lambert O, Creveuil C, Auzou M, Labombarda F, Aouba A, Verdon R, de La Blanchardière A. 2021. *Rothia* spp. infective endocarditis: a systematic literature review. *Infect Dis Now* 51:228–235. <https://doi.org/10.1016/j.medmal.2020.10.021>.
- Lee AB, Harker-Murray P, Ferrieri P, Schleiss MR, Tolar J. 2008. Bacterial meningitis from *Rothia mucilaginosa* in patients with malignancy or undergoing hematopoietic stem cell transplantation. *Pediatr Blood Cancer* 50:673–676. <https://doi.org/10.1002/pbc.21286>.
- Cho E-J, Sung H, Park S-J, Kim M-N, Lee S-O. 2013. *Rothia mucilaginosa* pneumonia diagnosed by quantitative cultures and intracellular organisms of bronchoalveolar lavage in a lymphoma patient. *Ann Lab Med* 33: 145–149. <https://doi.org/10.3343/alm.2013.33.2.145>.
- Fatahi-Bafghi M. 2021. Characterization of the *Rothia* spp. and their role in human clinical infections. *Infect Genet Evol* 93:104877. <https://doi.org/10.1016/j.meegid.2021.104877>.
- Stackebrandt E, Koch C, Gvozdzik O, Schumann P. 1995. 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* 45:682–692. <https://doi.org/10.1099/00207713-45-4-682>.
- Mashouf RY, Babalhavaeji H, Yousef J. 2009. Urinary tract infections: bacteriology and antibiotic resistance patterns. *Indian Pediatr* 46:617–620.
- Lee JY, Kim SH, Jeong HS, Oh SH, Kim HR, Kim YH, Lee JN, Kook J-K, Kho W-G, Bae IK, Shin JH. 2009. Two cases of peritonitis caused by *Kocuria marina* in patients undergoing continuous ambulatory peritoneal dialysis. *J Clin Microbiol* 47:3376–3378. <https://doi.org/10.1128/JCM.00847-09>.
- Moreira JS, Riccetto AG, Silva MT, Vilela MM. 2015. Endocarditis by *Kocuria rosea* in an immunocompetent child. *Braz J Infect Dis* 19:82–84. <https://doi.org/10.1016/j.bjid.2014.09.007>.
- Kandi V, Palange P, Vaish R, Bhatti AB, Kale V, Kandi MR, Bhoomagiri MR. 2016. Emerging bacterial infection: identification and clinical significance of *Kocuria* species. *Cureus* 8:e731.
- Funke G, Hutson RA, Bernard KA, Pfyffer GE, Wauters G, Collins MD. 1996. Isolation of *Arthrobacter* spp. from clinical specimens and description of *Arthrobacter cumminsii* sp. nov. and *Arthrobacter woluwensis* sp. nov. *J Clin Microbiol* 34:2356–2363. <https://doi.org/10.1128/jcm.34.10.2356-2363.1996>.
- Hsu CL, Shih LY, Leu HS, Wu CL, Funke G. 1998. Septicemia due to *Arthrobacter* species in a neutropenic patient with acute lymphoblastic leukemia. *Clin Infect Dis* 27:1334–1335. <https://doi.org/10.1093/clinids/27.5.1334>.
- Esteban J, Bueno J, Perez-Santonja JJ, Soriano F. 1996. Endophthalmitis involving an *Arthrobacter*-like organism following intraocular lens implantation. *Clin Infect Dis* 23:1180–1181. <https://doi.org/10.1093/clinids/23.5.1180>.
- Bernasconi E, Valsangiacomo C, Peduzzi R, Carota A, Moccetti T, Funke G. 2004. *Arthrobacter woluwensis* subacute infective endocarditis: case report and review of the literature. *Clin Infect Dis* 38:e27–e31. <https://doi.org/10.1086/381436>.
- Chaves BL, Gómez-Camarasa C, Illescas LM, Chueca PN, Rojas-García LL. 2022. Unusual isolation of *Pseudoglutamicibacter cumminsii* in urine culture. *Rev Esp Quimioter* 35:95–96. <https://doi.org/10.37201/req/088.2021>.
- Funke G, Pagano-Niederer M, Sjöden B, Falsen E. 1998. Characteristics of *Arthrobacter cumminsii*, the most frequently encountered *Arthrobacter* species in human clinical specimens. *J Clin Microbiol* 36:1539–1543. <https://doi.org/10.1128/JCM.36.6.1539-1543.1998>.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. 1987. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 40:373–383. [https://doi.org/10.1016/0021-9681\(87\)90171-8](https://doi.org/10.1016/0021-9681(87)90171-8).
- Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, Lamm W, Clark C, MacFarquhar J, Walton AL, Reller LB, Sexton DJ. 2002. Health care-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. *Ann Intern Med* 137:791–797. <https://doi.org/10.7326/0003-4819-137-10-200211190-00007>.
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Cooper-Smith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. 2016. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 315:801–810. <https://doi.org/10.1001/jama.2016.0287>.
- Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart CK, Suter PM, Thijs LG. 1996. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 22:707–710. <https://doi.org/10.1007/BF01709751>.
- Rasmussen M, Mohlin AW, Nilson B. 2020. From contamination to infective endocarditis—a population-based retrospective study of *Corynebacterium* isolated from blood cultures. *Eur J Clin Microbiol Infect Dis* 39:113–119. <https://doi.org/10.1007/s10096-019-03698-6>.
- Boman J, Nilson B, Sunnerhagen T, Rasmussen M. 2022. True infection or contamination in patients with positive *Cutibacterium* blood cultures—a retrospective cohort study. *Eur J Clin Microbiol Infect Dis* 41:1029–1037. <https://doi.org/10.1007/s10096-022-04458-9>.
- Poyer F, Friesenbichler W, Hutter C, Pichler H, Dworzak M, Peters C, Mann G, Indra A, Attarbaschi A. 2019. *Rothia mucilaginosa* bacteremia: a 10-year experience of a pediatric tertiary care cancer center. *Pediatr Blood Cancer* 66:e27691. <https://doi.org/10.1002/pbc.27691>.
- Ramanan P, Barreto JN, Osmon DR, Tosh PK. 2014. *Rothia* bacteremia: a 10-year experience at Mayo Clinic, Rochester, Minnesota. *J Clin Microbiol* 52:3184–3189. <https://doi.org/10.1128/JCM.01270-14>.
- Krus D, Kahn F, Nilson B, Sunnerhagen T, Rasmussen M. 2022. Blood culture time to positivity in non- β -hemolytic streptococcal bacteremia as a predictor of infective endocarditis—a retrospective cohort study. *Eur J Clin Microbiol Infect Dis* 41:325–329. <https://doi.org/10.1007/s10096-021-04339-7>.
- Bläckberg A, Svedevall S, Lundberg K, Nilson B, Kahn F, Rasmussen M. 2022. Time to blood culture positivity—an independent predictor of mortality in *Streptococcus pyogenes* bacteraemia. *Open Forum Infect Dis* 9:ofac163. <https://doi.org/10.1093/ofid/ofac163>.
- Kohli U, Hazra A, Shahab A, Beaser AD, Aziz ZA, Upadhyay GA, Ozcan C, Tung R, Nayak HM. 2021. Atypical pathogens associated with cardiac implantable electronic device infections. *Pacing Clin Electrophysiol* 44: 1549–1561. <https://doi.org/10.1111/pace.14311>.
- Daoub A, Ansari H, Orfanos G, Barnett A. 2021. *Rothia mucilaginosa*: a case of septic arthritis in a native knee and review of the literature. *BMJ Case Rep* 14:e237015. <https://doi.org/10.1136/bcr-2020-237015>.
- Dotis J, Printza N, Stabouli S, Papachristou F. 2015. *Kocuria* species peritonitis: although rare, we have to care. *Perit Dial Int* 35:26–30. <https://doi.org/10.3747/pdi.2013.00138>.
- Bhatnagar N, Poojary A, Maniar A, Contractor A, Rohra S, Kumar G. 2019. *Mycobacterium wolinskyi*: a rare strain isolated in a persistent prosthetic knee joint infection: a case report. *JBJS Case Connect* 9:e0315. <https://doi.org/10.2106/JBJS.CC.18.00315>.
- Horino T, Shimamura Y, Ogata K, Inoue K, Terada Y. 2016. *Kocuria kristinae* septic arthritis associated with infectious endocarditis in a hemodialysis patient with diabetes mellitus: a case report and literature review. *Renal Replacement Ther* 2:32. <https://doi.org/10.1186/s41100-016-0041-3>.