Original Article

Aerococcus-Related Infections and their Significance: A 9-Year Retrospective Study

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Abstract

Introduction: *Aerococcus spp.* is a Gram-positive, catalase- and oxidase-negative, microaerophilic, nonmotile bacteria species rarely associated with human infections such as arthritis, bacteremia, endocarditis, and meningitis. The bacteria are also often confused with streptococci species or treated as a contaminant. **Patients and Methodology:** We conducted a retrospective, observational cohort study on all patients with *Aerococcus spp.* isolates in blood samples from July 2010 to June 2019. All categorical data were presented as counts and proportions, whereas continuous data were presented as median and interquartile ranges. **Results:** A total of 20 *Aerococcus spp.* isolates were identified over the study period of 9 years. Of these, *Aerococcus urinae* was isolated in 10 (50%), *Aerococcus viridans* in 6 (30%), and *Aerococcus spp.* (not speciated) in 4 (20%). The median age was 74.3 years (12 males and 8 females). The two most frequent presentations were fever (15 of 20) and altered mentation (6 of 15). Most of the patients (11 of 15) had at least one predisposing comorbidity related to the urinary tract system (8 with recurrent urinary tract infection, 7 with urinary incontinence, 3 with an indwelling catheter, 2 with renal stones, and 1 each with benign prostatic hyperplasia and a recent cystoscopy). The median white blood cell count was 18,426 cells/mL, median hemoglobin 10.96 g/dL, median platelet count 191,000 cells/μL, median blood urea nitrogen 28.6 mg/dL, and median creatinine 1.54 mg/dL. The urinary tract was the most likely source of bacteremia (10 of 20) based on either imaging findings (5 cases), positive urine culture for *Aerococcus spp.* (4 cases), or instrumentation history (1 case). In the rest, the cause of bacteremia could not be found. Endocarditis was suspected in 9 out of 20 patients. Transthoracic echocardiography/transesophageal echocardiography (TEE) confirmed 3 cases (2 aortic valves, 1 mitral valve and pacemaker). Interestingly, one case had septic emboli causing a right frontal stroke with a normal TEE and normal Doppler study for deep venous thrombosis. Blood cultures were positive in 35% (7 of 20) with polymicrobial growth, 3 with coagulase-negative staphylococci, 2 with *Enterococcus faecalis,* and the other 2 each with *Diphtheroids spp.* and *Proteus mirabilis*. Of the 20 cases, 9 and 10 required intensive care unit level care and vasopressor support, respectively. Most of the patients were treated for 5–14 days except the 3 cases with infective endocarditis (IE). The median hospital stay duration was 6.55 days with 2 fatalities (2 out of 20 patients). **Conclusion:** Old age and underlying urologic conditions are the best-known risk factors for *Aerococcus spp.* infection. Recent advances in diagnostic technology have led to an increase in detection of *Aerococcus spp.*-related infections. The rare occurrence of *Aerococcus spp.* in human infections and resultant lack of randomized control trials have resulted in a significant degree of clinical uncertainty in the management of *Aerococcus spp.* IE.

Keywords: *Aerococcus*, bacteremia, infection

Introduction

Aerococcus spp. can cause invasive and fatal systemic illnesses. Over the last decade, awareness about this species has increased owing to better diagnostic tools. Once considered a contaminant, it is now considered a potential microbe to cause a variety of disorders. This retrospective analysis aims to analyze *Aerococcus spp.*-related bacteremia for the source of infection, complications, treatment given, and outcome at our center.

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Patients and Methodology

Search strategy

This is a retrospective study conducted at Saint Vincent Hospital, Worcester, Massachusetts, United States. The study included all the cases with blood samples reported positive for *Aerococcus spp.* at our microbiology laboratory between July 2009 and June 2019. The study was approved by the institutional review board (IRB # 2019–071).

Selection and inclusion criteria

All adult patients (age >18 years) who had positive *Aerococcus* growth in blood were included in this retrospective analysis.

Data extraction

All selected patients' case records were thoroughly reviewed, and data were extracted and entered in a predefined Excel sheet. For the defined period of the study, age of patients, risk factors for infection, type of *Aerococcus* species, simultaneous growth of other microbes, duration of hospital stay, hemodynamic instability, requirement of vasopressors, requirement of blood products, choice and duration of antibiotics, and outcome were recorded retrospectively.

Data analysis

Means and percentages were reported for continuous and categorical variables, respectively. Laboratory results, treatment, and outcome are depicted in Tables 1 and 2 and symptomatology and comorbidities in bar graphs [Figures 1 and 2].

Results

Demographic details

The median age of our cohort was 76 years (range: 49–99), comprising 13 males and 7 females [Table 1]. With regard to symptomatology, most of the patients presented with fever (15 cases) and altered mentation (6 cases). Figure 1 mentions the breakdown of symptoms with which each patient presented to our center.

Risk factors

We also studied the local genitourinary and systemic comorbidities in our study population.

Systemic predisposition

Cardiac comorbidities such as hypertension (15 cases), atrial fibrillation (5 cases), valvulopathy (3 cases), and congestive heart failure (CHF) (3 cases) were detected in most of our patients [Figure 2]. Interestingly, two patients also had a pacemaker, of which one was diagnosed with *Aerococcus spp*. endocarditis involving the pacemaker leads. Other comorbidities included type 2 diabetes mellitus (4 patients), chronic obstructive pulmonary disease (COPD) (7 patients), hyperlipidemia (10 patients), HIV under therapy (1 patient), chronic kidney disease stage III or more (5 patients), and substance use disorder (1 case).

Genitourinary predisposition

With regard to local genitourinary comorbidities, we found that more than half of the patients had one or more risk factors for urinary tract infection (UTI) (8/20 patients). The risk factors

Table 1: Details of complete blood count, renal functions, hemodynamics, need of vasopressor support and intensive care unit care, days of hospital stay, and outcome

Case	WBC (cells/mL)	Platelet count (cells/μL)	Hb (g/dL)	Hct (%)	Urea (mg/dL)	Creatinine (mg/dL)	Hemodynamic instability/SIRS	Vasopressors	ICU need	Hospital stay	Outcome
1	10,300	172	8	26	33	2.65	Yes	Yes	1	13	Recovered
2	24,100	189	16.6	51.5	25	1.16	Yes	Yes	1	6	Recovered
3	28,000	74	8.9	28.5	133	5.15	Yes	Yes	1	12	Died
4	13,800	117	7	21	9	0.94	Yes	Yes	1	6	Recovered
5	19,700	231	6.8	22.1	27	1.11	Yes	Yes	1	5	Recovered
6	10,900	300	7.7	22	112	3.08	Yes	Yes	1	1	Died
7	16,800	264	12.8	39.1	30	0.89	Yes	Yes	1	1	Recovered
8	22,900	219	10.5	32.9	22	1.04	Yes	No	1	8	Recovered
9	24,600	146	10.7	33	23	1.86	Yes	No	1	8	Recovered
10	16,700	202	12.8	39	28	1.6	Yes	No	1	5	Recovered
11	12,400	136	12.4	34.9	9	0.58	Yes	No	1	7	Recovered
12	12,500	184	11.7	33.6	15	0.73	Yes	Yes	2	9	Recovered
13	17,400	168	10	29	47	1.44	Yes	No	2	11	Recovered
14	15,800	310	8.9	26.5	14	0.84	Yes	No	2	3	Recovered
15	9500	130	13.6	40	14	1.13	Yes	No	2	4	Recovered
16	25,400	206	10.4	33.4	16	1.24	Yes	No	2	5	Recovered
17	3890	181	10.6	33.2	28	1.81	Yes	No	2	7	Recovered
18	7400	194	13.2	39.4	12	0.89	No	No	2	7	Recovered
19	9100	374	11.6	33.9	10	0.75	No	No	2	5	Recovered
20	8700	210	10	33	11	0.62	No	No	2	8	Recovered

WBC: White blood cell, Hb: Hemoglobin, Hct: Hematocrit, ICU: Intensive care unit, SIRS: Systemic inflammatory response syndrome

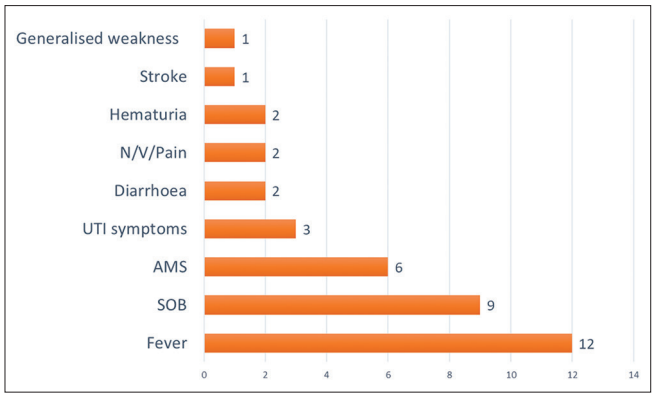

Figure 1: Clinical features of the patients ($n = 20$)

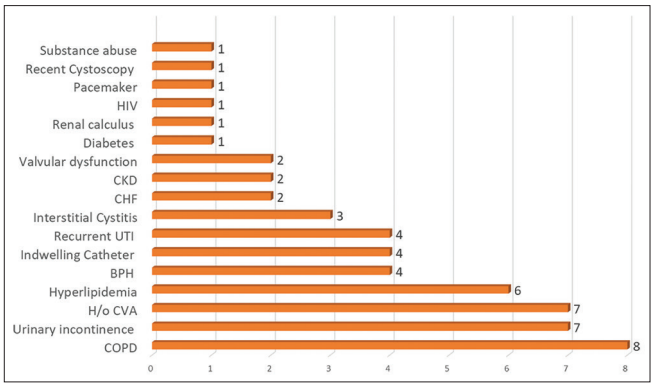

Figure 2: Comorbidities of the patients ($n = 20$)

identified were chronic indwelling catheter (3 patients), recurrent UTI (8 patients), urinary incontinence (7 patients), renal calculus (2 patients), and recent cystoscopy (1 patient).

Significance of *Aerococcus spp.* bacteremia

Based on our review of electronic medical records, we tried to locate the source of *Aerococcus spp.* bacteremia [Table 1]. All patients had consultations from infectious disease consultants. Based on the documentation, we labeled the patients' bacteremia to be either significant (13/20) or a contaminant (7/20). For the 13/20 patients with significant *Aerococcus spp.* bacteremia, we found that most had a genitourinary system source of infection (9/13). Recent instrumentation was the cause of UTI in one case. Of these nine patients, four also underwent computed tomography imaging which showed that three patients had a complicated UTI (pyelonephritis and/or hydroureteronephrosis) and one had renal stones. One case also had an associated cellulitis, presumably *Aerococcus* related.

Out of 7/20 cases of contaminant *Aerococcus spp.* bacteremia, 4 cases had no evidence of any other infection. In the remaining 3 patients, *Acinetobacter spp.*-related colitis, sacral decubitus ulcer, and acute mesenteric syndrome were the primary diagnoses.

Cultures

A total of 20 *Aerococcus spp.* isolates from blood were identified over the 9-year study period. Of these, *Aerococcus urinae* was isolated in 10 (50%), *Aerococcus viridans* in 6 (30%), and *Aerococcus* species (not speciated) in 4 (20%) patients. Seven of 20 (35%) had blood cultures with polymicrobial growth, 3 with coagulase-negative staphylococci, 2 with *Enterococcus faecalis* and the other 3 with *Acinetobacter baumannii, Diphtheroids*, and *Proteus mirabilis* [Table 1]. Of the 20 patients, a urine culture was not done in 2 patients. Of the remaining 18 patients, urine cultures showed no growth in 6 cases. In the remaining 12 urine specimens, only 4 had *Aerococcus spp.* growth (3 cases with *Aerococcus spp.* and 1 with *A. viridans* growth).

Infective endocarditis (IE) was suspected in 9 out of 20 patients. Transthoracic echocardiography/transesophageal echocardiography (TEE) confirmed IE in 3 cases (2 aortic valves, 1 mitral valve and pacemaker). Interestingly, one patient had septic emboli causing a right frontal stroke but with a normal TEE and venous duplex study.

Clinical course, hospital management, and outcome

All patients received antibiotic therapy. The duration of antibiotics included both intravenous and/or oral prescribed during the hospital stay and/or at discharge. 5/20 patients received antibiotics only for less than a week. 13/20 patients received antibiotics for 10–14 days. Out of 3 patients with IE, 2 patients completed 6 weeks of antibiotics, whereas the remaining patient died seconding to worsening sepsis.

Based on systemic inflammatory response syndrome (SIRS) criteria, most of the patients (17/20) were found to have SIRS, with 8 patients receiving vasopressor support. 11/20 patients required ICU level of care of at least a day. The median WBC count was 14,800 cell/mm^3 (range: 3890–28,000). The median platelet count and median hemoglobin levels were 191.5 cells/mm^3 (range: 74–374) and 10.55 g/dL (range: 6.8–16.6), respectively [Table 2]. Only one patient required transfusion.

The total duration of hospital stay was 6.5 days (range: 1–13 days). Of the 20 patients, 2 died: 1 due to worsening sepsis from his pacemaker endocarditis and the other due to hemorrhagic shock related to ischemic acute mesenteric syndrome.

Discussion

The *Aerococcus* genus was first described in 1953 as a contaminant sample in air and dust, comprising catalase-negative and Gram-positive cocci that grew in clusters.[1] Initially, *Aerococcus spp.* were considered a fatal disease of lobsters and only a contaminant to humans. However, very soon after, microbiologists started isolating *Aerococcus spp.* from patients suffering from a variety of clinical diseases such as osteomyelitis, septic arthritis, meningitis, endocarditis, and bacteremia.[2] In our case series, apart from the classical UTI symptoms (fever, chills, nausea, vomiting, abdominal pain, altered mentation, and hematuria), patients also presented with atypical clinical

Table 2: Demographics with details of urine, blood culture, antibiotics given with days, and hospital course

Case	Age	Urine culture	Blood culture results	Likely source for *Aerococcus* bacteremia	TTE/TEE	Antibiotic regimen	Days of antibiotics	Hospital course, assessment, and management
1	99	No growth	*A. viridans* Coagulase-negative *S. aureus*	Contaminant	No vegetation	Vancomycin, ceftazidime, metronidazole	10	Had exploratory laparotomy and right-sided incarcerated hernia repair 3 days before admission, postoperative period complicated by hypoxemia, hypotension followed by intubation and vasopressor support Positive modified barium study for aspiration requiring PEG tube *Aerococcus* was considered as a contaminant infection
2	84	*Aerococcus*, unspecified *E. faecalis*	*A. urinae*	UTI	No vegetation	Ampicillin	14	Developed sepsis requiring pressure support, developed rapid ventricular rate transiently requiring dose increment of metoprolol
3	81	*P. aeruginosa*	*A. urinae* *E. faecalis*	Pacemaker lead endocarditis, UTI	AV vegetation, right atrial pacer lead vegetation	Vancomycin	10	Developed worsening sepsis despite being on antibiotics, he was planned for removal of infected pacemaker but deteriorated and expired
4	55	No growth	*A. urinae* *E. faecalis* (Group D)	UTI, renal stones	No vegetation	Piperacillin and tazobactam	10	CT showed large hematoma formation within the bladder, no hydroureteronephrosis, multiple small stones in both kidneys He underwent bladder irrigation with one unit of blood transfusion
5	87	*Aerococcus*, unspecified	*A. urinae*	UTI	Not done	Vancomycin, piperacillin, and tazobactam f/b amoxicillin	5	Had hypotension initially, required pressure support and ICU care Two-unit PRBCs for anemia
6	81	*P. aeruginosa*	*A. viridans*	Contaminant	Not done	Piperacillin and tazobactam	1	A patient came with massive gastrointestinal bleed Her repeat urine culture grew *P. aeruginosa* Had hemorrhagic shock possibly due to acute mesenteric syndrome and died within 6 h of arrival
7	87	*A. viridans*	*A. viridans*	Unknown	Normal	Vancomycin, piperacillin and tazobactam	1	Developed septic shock with hypoxic respiratory failure Family opted for hospice care
8	72	*Streptococcus* (1000-10,000 col/ml)	*A. urinae*	Instrumentation-related UTI	Not done	Ertapenem	14	Postlithotripsy and right ureteral stent, he developed fever, hypotension Found to have *Aerococcus* bacteremia
9	72	No growth	*A. urinae*	Cystitis	No vegetation	Vancomycin f/b amoxicillin	10	CT abdomen showed evidence of nonobstructive hydroureteronephrosis with bladder wall thickening
10	90	Mixed Gram-positive growth (10,000-50,000 col/ml)	*A. viridans* *P. mirabilis*	Complicated UTI, right urolithiasis, hydroureteronephrosis	Not done	Ceftriaxone f/b sulfamethoxazole and trimethoprim	14	CT abdomen showed right urolithiasis with hydroureteronephrosis. She underwent cystoscopy and stent placement for decompression of ureteral system, improved with antibiotics

Contd...

Table 2: Contd...

Case	Age	Urine culture	Blood C/S	Likely source for *Aerococcus* bacteremia	TTE/TEE	Antibiotic regimen	Days of antibiotics	Hospital course, assessment, and management
11	49	Mixed Gram-positive organisms (>100,000 col/ml)	*A. urinae* *A. baumannii* Coagulase-negative *S. aureus*	Contaminant	Not done	Ceftriaxone, IV	5	A patient came for abdominal pain, CT showed evidence of colitis and *Acinetobacter*-related bacteremia
12	62	No growth	*A. viridans*	Contaminant	Not done	Vancomycin and ceftazidime, IV	10	Was treated for aspiration pneumonia and HCAP as he was a nursing home resident
13	80	*Aerococcus*, unspecified (>100,000 col/ml)	*A. urinae*	IV drug abuse (bloodstream infection) leading IE, UTI	Mass (0.5 cm × 0.5 cm) on mitral anterior leaflet	Vancomycin, IV	14	Presented with right middle cerebral infarct, toxicology was found positive for cocaine abuse, mitral valve vegetations Both urine and blood culture grew *A. urinae*, a patient had a significant neurological deficit, underwent PEG tube placement, and discharged to rehabilitation services
14	87	Mixed Gram-positive growth (10,000-50,000 col/ml)	*A. urinae*	Unknown	No vegetation	Vancomycin, IV	42	Found to have right frontal stroke, TTE-normal Vancomycin×6 weeks planned for presumed IE, discharged to rehabilitation services
15	64	Alpha-hemolytic *Streptococcus*	*Aerococcus*, unspecified Diphtheroids	Contaminant	Not done	Levofloxacin, IV	10	Fever and dysuria at presentation, was treated with levofloxacin
16	51	Not sampled	*A. viridans*	Contaminant	Not done	Vancomycin, PO	14	Fever and diarrhea were worked up and found to have C. difficile-related diarrhea
17	78	No growth	*A. urinae*	Penile cellulitis, bilateral pyelonephritis	Not done	Vancomycin, IV	14	Was septic at presentation, likely source penile cellulitis, pyelonephritis
18	68	No growth	*Aerococcus*, unspecified	Unknown	Not done	Vancomycin f/b ceftriaxone, IV	14	A patient came for altered sensorium which responded to antibiotics and supportive management
19	72	Not sampled	*Aerococcus*, unspecified	IE	AV vegetation	Ceftriaxone, IV	42	TEE confirmed AV endocarditis, treated with 6 weeks of ceftriaxone
20	74	*Lactobacillus*	*Aerococcus*, unspecified Coagulase-negative *S. aureus*	Contaminant	Not done	None	0	A patient had decubitus ulcer for which he underwent local debridement

A. viridans: *Aerococcus* viridans, *S. aureus*: *Staphylococcus aureus*, *E. faecalis*: *Enterococcus faecalis, A. urinae*: *Aerococcus* urinae, UTI: Urinary tract infection, *P. aeruginosa*: *Pseudomonas aeruginosa*, CT: Computed tomography, *P. mirabilis*: *Proteus mirabilis, A. baumannii: Acinetobacter baumannii*, IV: Intravenous, *C. difficile: Clostridium difficile*, AV: Aortic valve, PO: per oral, TTE: Transthoracic echocardiogram, TEE: Transesophageal echo, PEG: Percutaneous endoscopic gastrostomy, PRBCs: Packed red blood cells, IE: Infective endocarditis, HCAP: Health care associated pneumonia, f/b: Followed by

features such as shortness of breath (9), diarrhea (1), and stroke (1).

The most crucial challenge is the similarity of *Aerococcus spp*. with *Streptococcus spp*. (colonic morphology) and *Staphylococcus spp.* (microscopic appearance), which often leads to an incorrect diagnosis. Earlier in the 1990s, a PCR-based test was developed for identification of *Aerococcus spp.* using oligonucleotide primers which were based on highly specific small subunit (16S) rRNA sequencing.[2] Subsequently, with increased awareness of this rare species and the introduction of more advanced technique – matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) – now, *Aerococcus spp.* species are increasingly being recognized as a potential threat of many lethal complications.

A. viridans was the first the subspecies to be detected. Later in 1989, Christensen *et al*. described separate urinary pathogen *Aerococcus spp*.-like organisms from patients suffering from IE and UTI.[3] These were later labeled as *Aerococcus urinae*.[4] Apart from *A. urinae* and *A. viridans*, another subspecies – *Aerococcus sanguinicola* – was found responsible for many human infections. *Aerococcus christensenii* and *Aerococcus urinaehominis* are the other subspecies very rarely associated with human pathologies.[5,6]

Challenges in diagnosis

Based on the morphological appearance of the hemolysis, *Aerococcus spp.* produces alpha-hemolysis (semi-transparent colonies), thereby posing similarity with streptococcal species.[7] Due to the higher prevalence, any alpha-hemolytic pattern in the blood agar might suggest either *Streptococcus viridans or pneumoniae*. Similarly, on Gram stain, the microscopic appearance of *Aerococcus* is like that of *Staphylococcus* (both appear as Gram-positive cocci in clusters). Other patterns of microscopic evidence are pair form or tetrads, but, unlike staphylococci, *Aerococcus spp.* are catalase negative.[1] The growth of atypical organisms always poses a challenge in diagnosis and thereby delay in diagnosis.[8]

Intraspecies diagnosis among *Aerococcus spp.* is also one of the challenges. Lawson *et al*. proposed a scheme of biochemical reactions to differentiate between *Aerococcus* species. Grude *et al*. screened over 4000 urine samples at their center and studied 24 species of A-hemolytic nonenterococcal bacterial isolates with a newer diagnostic technique – the BBL-Crystal-GP system.[9] Similarly, there are few other commercially available systems: the API system and Vitek 2 system. Unlike the Vitek 2 system, the API system and BBL-Crystal-GP readily identify *A. urinae*. Both the API and Vitek systems tend to misread A. *sanguinicola* as A. *viridans*.[10,11] These are the few pitfalls of the biochemical reaction-based techniques. Because of the above complexities while using the biochemical technologies, nowadays the genetic encoding using the 16S rRNA sequencing method is the gold standard method for species determination of *Aerococcus spp*.[6,12] The disadvantage of 16S rRNA is that it is time-consuming and hence practically less useful. Recently, a newer modality based on MS, MALDI-TOF MS, has shown good sensitivity and high specificity in practical settings.[13] At our center, we use the Vitek system for species identification.

Discrepancies can occur between growths in urine versus blood. There have been ample reports where cases of *Aerococcus spp.* bacteremia with classical UTI symptoms lacked growth of *Aerococcus spp.* in the urine culture. It is postulated that this discrepancy could be related to urine cultures not usually processed in an all CO2 atmosphere which favors the growth of aerococci. Similarly, in a few cases, the exact cause of *Aerococcus spp.* bacteremia remains obscured despite diligent microbiological workup.[14,15] In our case series, the cause of bacteremia could not be elicited in two patients.

Another challenge is the polymicrobial growth and the significance of *Aerococcus spp.* in such cases. There are not much data with regard to the polymicrobial growth either in urine or in blood. Narayanasamy *et al*. reported Foley microbial growth in 35% of their cases of *Aerococcus spp.* bacteriuria (14 out of 40 cases).[16] The most common growth in addition to *Aerococcus spp.* was *Escherichia coli,* followed by other Gram-negative enteric flora and *Enterococcus faecalis*. In our series of *Aerococcus spp.* bacteremia, polymicrobial growth in addition to *Aerococcus* species was detected in seven samples of blood and one sample of urine [Table 1].

Infections and associated complications

As mentioned above, for a long time, *Aerococcus spp.* was considered a contaminant. Gradually with increased awareness and advancement in diagnostic tools, *Aerococcus* species are no more routinely considered a contaminant.

Aerococcus spp. is considered as an uncommon pathogen for UTI. Overall, the isolation rate of aerococci from urine has been reported as 0.2%–0.8% of urine cultures sent to various laboratories.[17,18] In a Netherlands-based study involving two national medical microbiology laboratories, Schuur *et al*. reported the incidence of *A. urinae*-related UTI to be only 0.31 and 0.44%, respectively. They found old age and local genitourinary comorbidities as the most common predisposing factor. They also found significant systemic comorbidities such as diabetes mellitus, malignancy, and dementia (67.5%) in their study population. Most of the patients (97.5%) reported classic UTI symptoms. In our case series as well, there were one or more local comorbidities in most of the patients: urinary incontinence (7), recurrent UTI (4), prolonged indwelling catheters (4), interstitial cystitis (3), renal stones (1), and recent cystoscopy (1). Similar to the Schuur *et al*. study, systemic illnesses such as diabetes, dementia, Parkinson's disease, Alzheimer's disease, stroke, CHF, or COPD were also seen in our patient series.[19] Immunocompromised statuses such as HIV, tuberculosis, cancers, and diabetes increase the susceptibility to variety of the unusual microbes which are difficult to diagnose and treat.[20-24]

In an interesting comparison between *Aerococcus spp.* bacteriuria versus non-A*erococcus* bacteriuria, Senneby *et al*.

found that when compared to *E. coli* bacteriuria, patients with *Aerococcus* bacteriuria were significantly older and more likely to be male.[25] Our study group also had similar results with a median age of 76 years (range 49–99) and comprised 13 males and 7 females.

Initial reports suggested a higher incidence of *Aerococcus spp.-related* IE.[15,26] However, more recent studies have indicated that IE is a rare presentation of an *Aerococcus spp.* bacteremia.[27,28] In general, IE is a devastating complication of bacteremia as it not only requires prolonged duration of antibiotics but could also have valvular complications.[29-31] In our series of 20 patients, two patients had evidence of IE, of which one succumbed to his illness. Sunnerhagen *et al*. conducted a 12-year retrospective study on *Aerococcus spp.*-related IE reported to the Swedish Registry of Infective Endocarditis. In total, they found 16 *Aerococcus spp.*-related IE cases, of which 14 were *A. urinae* related and only two with *A. sanguinicola*. Interestingly, 7/16 of the patients had severe sepsis at presentation, but ICU level of care was required only in 1 patient, and no deaths were reported. Valve surgery was undergone by 4/16, and septic embolization was seen in three patients. In our series, 17 patients fulfilled the SIRS criteria, 11 required intensive level care, and 8 required vasopressor support. Only one patient had embolization related to *Aerococcus spp.*-related IE. Apart from urinary tract and heart valves, rarely other focuses such as vertebral bones, joints, peritoneum, and dialysis port could be a site of nidus.[32,33]

Just like any other bacteria, antimicrobial susceptibility testing (AST) of isolates guides therapy for *Aerococcus spp.* bacteremia. Unfortunately, due to poor understanding, lack of studies, and rarity of infection, none of the infectious disease societies including the Infectious Diseases Society of America, the Clinical and Laboratory Standards Institute, and the European Committee on Antimicrobial Susceptibility Testing worldwide are currently able to firmly lay down antibiotic breakpoints for *Aerococcus spp.* Various methods of AST can be employed, including broth microdilution, E-test, and agar dilution methods. The antibiotic susceptibility is variable in different subspecies of *Aerococcus spp*. In general, *Aerococcus spp.* are sensitive to β-lactam antibiotics (penicillin and ampicillin) with modal minimum inhibitory concentrations (MICs) (range of 0.03–0.06 mg/L).[34,35] In contrast, the MIC for cephalosporins is considerably higher (but less than beta-lactams) and for meropenem and imipenem is low with only a few exceptions. Unfortunately, our center did not have an adequate facility for assessing the AST for *Aerococcus spp.* Patients were treated based on various ID physicians' discretion and expertise. Schuur *et al*. reported that 100% of *Aerococcus spp.* isolates tested in their study were susceptible to penicillin, amoxicillin, and nitrofurantoin, and the majority were treated with amoxicillin, amoxicillin with clavulanic acid, or norfloxacin.

Limitations of this study

All limitations which are applicable for a retrospective study were present in this study. Due to lack of data on the antibiotic sensitivity pattern of the *Aerococcus spp.* isolates, we cannot comment on the choice of antibiotics in individual cases. Due to rarity of the disease, the number of patients is not enough for any significant statistical output.

Conclusion: What is in the future? Upcoming challenges

With more laboratories upgrading to improved diagnostic tools such as MALDI-TOF MS, the incidence of detection of *Aerococcus spp.* in blood and urine is expected to increase significantly.[36] On the one hand, this will help us to understand the role of *Aerococcus spp.* as normal flora and help us in understanding the prognosis of *Aerococcus spp.*-related infections. However, this will bring more challenges in terms of clinical decision-making and choosing the right antibiotics. This will need large operation-based studies involving multiple centers across the globe to understand the immune evasion mechanism, pattern of antibiotic resistance, and predisposition to *Aerococcus spp.*

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Conflicts of interest

There are no conflicts of interest.

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