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ORIGINAL RESEARCH

A 5-Year Retrospective Analysis of *Raoultella planticola* Bacteriuria

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Introduction: *Raoultella planticola* is an aerobic gram-negative rod predominantly found in soil and aquatic environments. The typical reservoirs of *Raoultella* spp. include the gastrointestinal tract and the upper respiratory tract. It usually causes pneumonia, biliary tract infections, and bacteremia. Urinary tract infection (UTI) secondary to *R. planticola* is an uncommon entity. Less than 10 cases of *R. planticola*-associated UTIs in adults have been published in the literature to date.

Objective: This is a single institution retrospective study undertaken to identify the epidemiology, patient characteristics, clinical spectrum, predisposing risk factors and the outcome of patients with UTI caused by *R. planticola.*

Results: A total of 37 *R. planticola* isolates were identified in urine samples over a 5-year study period. The mean age of the patient population was 77 years. The most common comorbidity was diabetes mellitus, which was present in 16 patients. Only 3 patients had a history of steroid use, an immunosuppressive condition, or were on chemotherapy. The most common presenting complaint was altered mental status followed by fever. Resistance to ampicillin was found in 35 isolates which seems to be an intrinsic characteristic of *Raoultella* spp. and 2 isolates were multidrug-resistant, but still susceptible to ciprofloxacin. The average length of stay was 3 days, and the average duration of antibiotic administration was 8 days. Ciprofloxacin was the most frequently prescribed antibiotic (9 patients). The severity of infection ranged from simple cystitis in 15 patients to urosepsis in 2 patients and septic shock in 2 patients. There were no mortalities in our cohort.

Conclusion: Our study revealed that patients with *R. planticola* UTI had higher proportion of diabetes mellitus, renal failure compared to the general population. Our study also confirms the intrinsic resistance to ampicillin of *Raoultella* spp., which has been documented previously in the literature.

Keywords: infection, antibiotics, *Raoultella*, urinary tract infection, bacteriuria

Introduction

Infections related to rare pathogens are very challenging to treat due to lack of enough data in the medical literature.[1,2] *Raoultella planticola* is a ubiquitous, non-motile, aerobic gram-negative bacteria. It belongs to the genus *Raoultella* under the *Enterobacteriaceae* family. Two species are clinically important: [1] *Raoultella planticola* and [2] *Raoultella ornithinolytica*. The microbiological identification of *R. planticola* remains a challenge even after 30 years of its identification.[3,4] This is because the conventional phenotypic assessments often misidentify it as *Klebsiella* spp., which is its remarkably close relative in the *Enterobacteriaceae* family. This might be one of the many reasons that the incidence of infections caused by *R. planticola* is underreported.

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The gastrointestinal tract and the upper respiratory tract are the typical reservoirs of *R. planticola*.[5] It commonly causes pneumonia, biliary tract infections, and bacteremia.[6–9] Only a handful of cases of urinary tract infection (UTI) caused by *R. planticola* in adults have thus far been published in the literature.[10–16] Most of the UTIs have been reported in immunocompromised adults, in patients with urinary tract procedures or instrumentation.[11–13,15]

The recent emergence of extended-spectrum β-lactamase (ESBL) producing and carbapenem-resistant nosocomial *R. planticola* infections is a matter of concern. These strains can act as a reservoir for these resistance genes.[17]

Except for a few case reports/series, there has been no published comprehensive review or original study on *R. planticola*-associated UTIs. We conducted a retrospective study to better understand the characteristics of the organism, risk factors for acquisition of infection and to analyze the outcomes associated with UTI caused by *R. planticola*.

Materials and Methods

Search Strategy

This was a retrospective study conducted at a community-based teaching hospital in Massachusetts, United States. The study included data from January 2015 to September 2020 and included all urine cultures positive for *R. planticola* at our institution. The study was approved by our institutional review board (IRB #2020 −142).

Selection and Inclusion Criteria

All adult patients (>18 years) who had a urine culture growing *R. planticola* were included in the study. Primary identification and sensitivities of colonies were done with VITEK® 2 compact automated system and confirmation was done with API 20-E, both from BioMérieux.

Data Extraction

Records of selected patients were reviewed and information including the demographics, clinical symptoms, physical examination findings, laboratory data, radiological parameters and microbiological data were extracted. Further details on hospitalization including the severity of the illness, antibiotics administered, hospital course and outcomes were also obtained. The data extracted was verified by two independent researchers. The data was then entered into a spreadsheet.

Data Analysis

All categorical data were expressed as counts, whereas continuous data were expressed as a mean. The data was analyzed using Google sheets®. No statistical analysis was performed given the small sample size.

Results

Demographic Details

A total of 37 patients had a positive urine culture for *R. planticola*. The demographics of the patients are listed in Table 1. The mean age of our cohort was 77 years (47 years - 91 years). There were 28 females and 9 males in total. Out of our 37 patients, 9 were residents of nursing homes or group homes, and 28 presented from home. The body mass index (BMI) was measured to be <19 kg/m^2 in 3 patients, between 19kg/m^2 to 25 kg/m^2 in 15 patients, between 25 kg/m^2 to 30 kg/m^2 in 10 patients and more than 30 kg/m^2 in 9 patients. The mean BMI was 26.64 kg/m^2.

Risk Factors

We studied the systemic and genitourinary factors in our population that were associated and/or have prognostic significance to our patients with *R. planticola*-associated UTIs (Table 1).

Systemic Characteristics

Alcohol consumption was reported by 5 patients while 32 patients denied it. None of the patients was active smokers with 17 endorsing prior tobacco use. Amongst the 37 patients, 16 patients had a history of diabetes mellitus. Liver dysfunction was present in 7 patients. Chronic corticosteroid and immunosuppressant use were reported by 1 patient each, and chemotherapy by 2 patients.

Genitourinary Characteristics

A history of chronic kidney disease was present in 18 patients. Out of these 18 patients, 5 had an acute on chronic kidney injury. There was a history of a urological procedure or genitourinary instrumentation in 4 patients, with 2 having the procedure within a month of their UTI. An underlying structural abnormality of the genitourinary tract was present in 9 patients as depicted in Figure 1. A history of renal transplantation was present in 1 patient.

Table 1 Patient Demographics and Predisposing Factors

Case No.	Age	Sex	BMI	Living Condition	History of Diabetes	Steroid Use or on Chemotherapy	Renal Failure	Alcohol Use	Smoking	Past Urological Surgery or Procedure	Renal Structural Abnormalities
1	86	F	18.29	Home	No	No	No	No	Never	No	None
2	73	M	24.37	Home	Yes	No	No	No	Never	No	None
3	65	F	19.1	Home	No	No	No	Yes	Never	No	None
4	71	F	29.2	Home	Yes	No	No	No	Never	No	None
5	85	F	21.3	NH	No	No	Chronic	No	Never	No	None
6	90	F	20.5	Home	No	No	Chronic	No	Former	No	None
7	64	F	19.6	NH	No	No	No	No	Former	No	None
8	83	F	29.3	Home	No	No	Chronic	Yes	Never	No	None
9	76	F	32.6	Home	No	No	No	No	Former	No	None
10	91	F	27.9	Home	No	No	No	Yes	Former	No	None
11	63	M	36.6	NH	No	No	No	No	Never	No	None
12	70	M	21.70	Home	No	No	Acute on chronic	No	Never	No	None
13	59	M	21.24	Home	Yes	No	No	No	Never	Yes	None
14	61	F	35.4	Home	No	Yes	Chronic	No	Former	Yes	None
15	47	M	34.4	Home	No	No	No	No	Never	Yes	None
16	74	F	37.6	Home	Yes	Yes	Chronic	Yes	Former	No	None
17	90	F	19.53	Home	No	No	Chronic	No	Never	Yes	None
18	85	F	22.8	Home	Yes	No	Chronic	Yes	Never	No	None
19	85	F	23.17	Home	Yes	No	Acute on Chronic	No	Never	No	None
20	68	M	17.85	Home	Yes	No	No	No	Never	No	None
21	83	M	23.2	Home	No	No	Acute on Chronic	No	Never	No	None

(*Continued*)

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Table 1 (Continued).

Case No.	Age	Sex	BMI	Living Condition	History of Diabetes	Steroid Use or on Chemotherapy	Renal Failure	Alcohol Use	Smoking	Past Urological Surgery or Procedure	Renal Structural Abnormalities
22	81	M	28.4	Home	No	No	Acute on Chronic	No	Never	Yes	None
23	88	F	19.01	Home	No	No	No	No	Former	No	Bladder outlet obstruction
24	89	F	17.33	Home	No	No	No	No	Former	No	Abnormal urethra
25	89	F	28.33	NH	Yes	No	Chronic	No	Former	No	None
26	89	F	27.44	NH	Yes	No	Chronic	No	Former	No	Renal cystic disease
27	89	F	26.8	NH	Yes	No	Chronic	No	Former	No	Renal cystic disease
28	89	F	27.1	NH	No	No	No	No	Former	No	Renal cystic disease
29	83	F	44.14	Home	Yes	o	No	No	Former	No	None
30	50	F	34.46	Home	Yes	No	No	No	Former	No	None
31	66	M	37	Home	Yes	No	No	No	Never	No	None
32	81	F	26.9	NH	No	Yes	Chronic	No	Never	No	Renal cystic disease
33	89	F	22.4	Home	Yes	No	Chronic	No	Never	No	None
34	81	F	32.01	Home	Yes	No	Chronic	No	Former	No	None
35	82	F	29.94	Home	Yes	No	Acute on chronic	No	Former	No	None
36	82	F	24.61	Home	No	No	No	No	Former	No	None
37	83	F	24.22	Home	No	No	No	No	Never	No	None

Abbreviation: NH, nursing home.

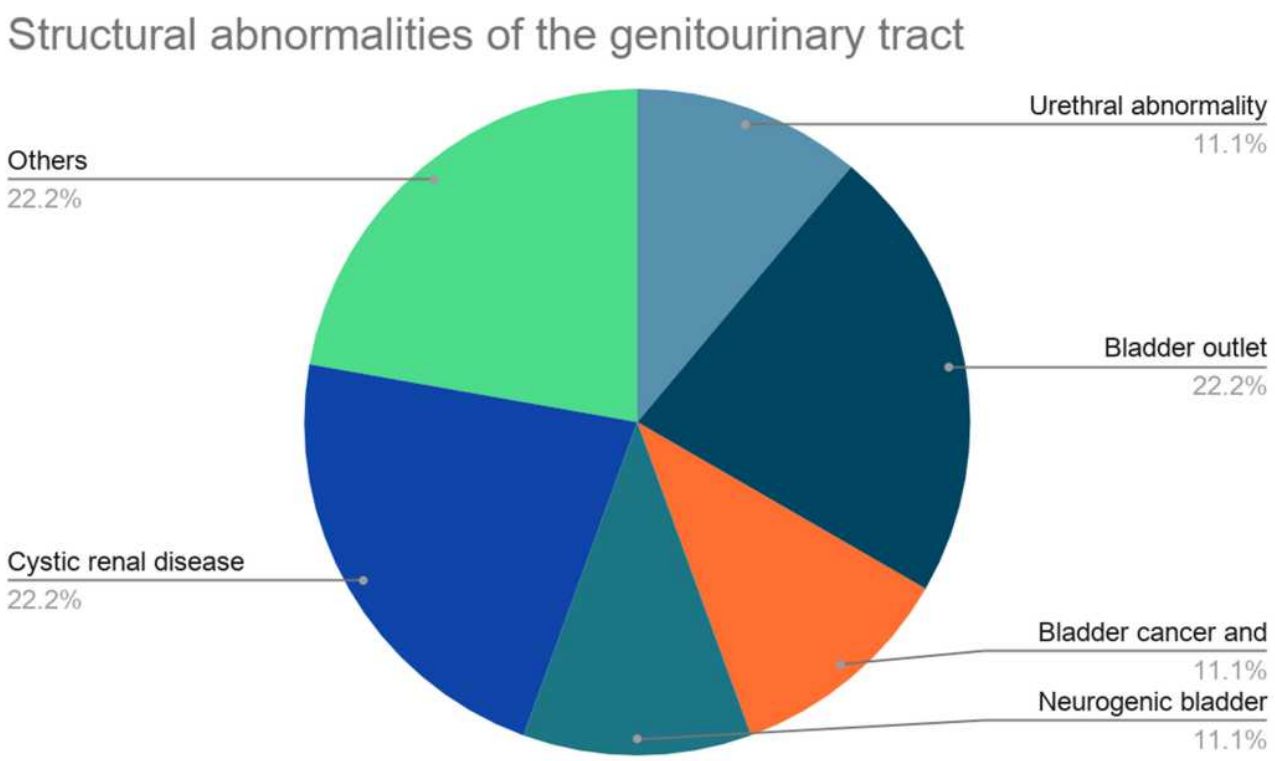

Figure 1 Underlying structural abnormality of the genitourinary tract.

Clinical Features

As shown in Table 2, most of the patients were asymptomatic at the time of presentation. The symptomatic patients presented with the following symptoms altered mental status (6 patients), generalized fatigue (5 patients), fever (4 patients), dysuria (2 patients), flank pain (1 patient), the combination of fever, suprapubic pain, and increased frequency (1 patient), flank pain and turbid urine (1 patient), and altered mental status and increased urinary frequency (1 patient).

Table 2 Clinical Features of Patients with *R. planticola*-Associated UTIs

Symptom	Number of Patients (Total:37)	Percentage
Asymptomatic Bacteriuria	16	43.24%
Altered sensorium	7	18.92%
Fatigue	5	13.51%
Fever	5	13.51%
Dysuria	2	5.41%
Flank pain	2	5.41%
Increased frequency	2	5.41%
Suprapubic pain	2	5.41%
Turbid urine	1	2.7%

Four patients were bradycardic, and 8 patients were tachycardic at the time of presentation. Only 8 patients were febrile (>100.4^{O} F) at the time of presentation. Hypotension was present in 1 patient and the rest of the patients had systolic blood pressure greater than 90 mm Hg.

Laboratory Data

The laboratory results of the patients are depicted in Table 3. The mean white blood cell count was 8.96 x 10^9/L (2.3 × 10^9/L - 20.5 × 10^9/L), platelet count was 246 x10^9/L (52 × 10^9/L - 599 × 10^9/L), glucose was 152 mg/dL (49 mg/dl - 684 mg/dL), creatinine was 1.31 mg/dL (0.53 mg/dl - 6.3 mg/dL), and GFR was 56.87 mL/min (5.7 mL/min - 111.6 mL/min). A glycated hemoglobin level was measured only in 12 patients and the mean was 8.39% (5.3%- 13.7%). An elevated lactate level was present in 3 patients.

Culture, Coexisting Organism, and Antibiotic Sensitivity

The microbiological data are detailed in Table 4. Resistance to ampicillin was found in 35 isolates, which seems to be an intrinsic character of the *Raoultella* spp., and 2 isolates were multidrug-resistant, but still susceptible to ciprofloxacin. Concomitant growth of other organisms was found in 9 urine

Table 3 Laboratory Results

Case No.	WBC (Cells/mL)	Platelets (Cells/µL)	Hemoglobin A1C (%)	Blood Sugar at Presentation (mg/dl)	Creatinine (mg/dl)	Glomerular Filtrataion Rate (mL/min)	Lactic Acid (mmol/L)
1	11.7	430	Not done	110	0.84	63.4	1.2
2	14.4	231	6.5	171	0.87	85.6	1.4
3	12.7	599	Not done	116	0.6	95.7	1.8
4	7.7	277	8.5	213	1.07	52.6	Not done
5	6.5	285	Not done	99	0.81	66.7	Not done
6	10.2	199	5.9	96	1.38	33.6	Not done
7	4.6	87	Not done	106	0.53	100.3	Not done
8	8.2	269	Not done	49	1.16	43.5	Not done
9	18.9	567	Not done	93	1.35	44.1	Not done
10	12.7	253	Not done	119	1.73	29.6	1.8
11	5.6	118	5.3	111	0.98	81.7	0.8
12	12.8	330	Not done	126	1.63	42.1	1.5
13	6.6	184	9	156	111.6	1	2.5
14	10.6	259	7.2	95	1.55	36.1	2.1
15	2.3	257	Not done	117	1.13	77	Not done
16	8.3	400	8.8	216	1.32	39.6	1.2
17	7	240	Not done	95	1.08	45.2	Not done
18	9	52	6.2	235	1.23	46.3	Not done
19	9.9	88	Not done	285	3.36	11.9	Not done
20	7.3	270	13.7	684	0.81	92	1.8
21	20.5	147	Not done	121	1.98	30.6	1.4
22	19.5	199	Not done	123	1.57	40.7	2.3
23	8	182	Not done	122	0.86	59.1	Not done
24	6.4	183	Not done	115	0.84	60.3	Not done
25	7.7	200	5.4	131	1.32	35.7	Not done
26	7.1	214	Not done	225	1.35	34.7	1.9
27	8.7	201	Not done	123	1.42	38.5	1.5
28	8.2	321	Not done	148	0.54	84.3	0.7
29	5.8	109	Not done	176	0.63	83.5	Not done
30	5.4	168	Not done	142	0.72	98.3	Not done
31	6.2	225	Not done	129	1.01	77.1	Not done
32	6.2	61	Not done	85	6.3	5.7	0.5
33	3.3	75	Not done	124	1.75	25.4	Not done
34	8.3	227	11.1	117	1.27	39.5	Not done
35	12.1	243	13.2	251	1.83	25.2	Not done
36	6.3	451	Not done	98	0.68	81.5	Not done
37	5	503	Not done	104	0.59	85.4	Not done

culture samples; namely, *Escherichia coli* (5 cultures), carbapenem-resistant *Pseudomonas aeruginosa* (1 culture), *Enterococcus* sp. (1 culture), *Group B Streptococcus* (1 culture), and mixed gram-positive organisms (1 culture). None of the patients had positive blood cultures.

Clinical Course, Hospital Management, and Outcome

The severity of illness varied widely ranging from asymptomatic bacteriuria to septic shock as depicted in Table 5. Antibiotics were administered to 24 patients

Table 4 Microbiological Characteristics

Case No.	Antibiotic Sensitivity Profile*	Blood Cultures	Mode of Urine Collection	Other Organisms#
1	Resistant to ampicillin	Negative	Clean catch	None
2	Resistant to ampicillin	Not done	Clean catch	None
3	Resistant to ampicillin	Not done	Clean catch	<50,000 Group B *Streptococcus*
4	Resistant to ampicillin	Not done	Clean catch	None
5	Resistant to ampicillin, cefazolin, ceftazidime, gentamicin. Intermediate sensitivity to tobramycin.	Not done	Clean catch	*Escherichia coli*
6	Resistant to ampicillin.	Not done	Clean catch	None
7	Resistant to ampicillin	Negative	Clean catch	*Escherichia coli*
8	Resistant to ampicillin	Not done	Clean catch	*Escherichia coli*, 50,000–100,000 CFU mixed gram positive orgnisms
9	Resistant to ampicillin	Not done	Clean catch	None
10	Resistant to ampicillin	Not done	Clean catch	None
11	Resistant to ampicillin	Not done	Clean catch	None
12	Resistant to ampicillin	Not done	Nephrostomy tube	*Enterococcus fecalis*
13	Resistant to ampicillin, cefazolin, ceftazidime, cefoxitin, gentamicin, trimethoprim-sulfamethoxazole, aztreonam, meropenem, piperacillin-tazobactam. Intermediate sensitivity to tobramycin;	Negative	Foley catheter	CRE *Pseudomonas aeurogenosa*.
14	Resistant to ampicillin	Negative	Clean catch	None
15	Resistant to ampicillin	Negative	Clean catch	*Escherichia coli*
16	Resistant to ampicillin	Not done	Foley catheter	*Escherichia coli*
17	Resistant to ampicillin	Not done	Clean catch	None
18	Resistant to ampicillin	Not done	Straight catheterization	None
19	Resistant to ampicillin	Not done	Clean catch	None
20	Resistant to ampicillin	Negative	Clean catch	None
21	Resistant to ampicillin	Negative	Straight catheterization	None
22	Resistant to ampicillin	Negative	Clean catch	50,000–100,000 CFU Mixed gram positive and gram negative.
23	Resistant to ampicillin	Not done	Clean catch	None
24	Resistant to ampicillin	Not done	Clean catch	None
25	Resistant to ampicillin	Negative	Clean catch	None

(*Continued*)

Table 4 (Continued).

Case No.	Antibiotic Sensitivity Profile*	Blood Cultures	Mode of Urine Collection	Other Organisms#
26	Resistant to ampicillin	Not done	Clean catch	None
27	Resistant to ampicillin	Not done	Foley catheter	None
28	Resistant to ampicillin	Not done	Clean catch	None
29	Resistant to ampicillin	Not done	Straight catheterization	None
30	Resistant to ampicillin	Not done	Clean catch	None
31	Resistant to ampicillin	Not done	Foley catheter	None
32	Resistant to ampicillin	Negative	Clean catch	None
33	Resistant to ampicillin	Negative	Clean catch	None
34	Resistant to ampicillin	Not done	Clean catch	None
35	Resistant to ampicillin	Negative	Foley catheter	None
36	Resistant to ampicillin	Not done	Clean catch	None
37	Resistant to ampicillin	Not done	Clean catch	None

Notes: *The antibiotics for which the sensitivities were analyzed were ampicillin, cefoxitin, cefazolin, ceftazidime, gentamicin, ciprofloxacin, nitrofurantoin, trimethoprim-sulfamethoxazole (Bactrim), aztreonam, meropenem, piperacillin-tazobactam. Due to lack of space, only the resistance pattern has been documented in the table It is implied that the isolate was sensitive to other antibiotics mentioned above. #All the organisms in the urine culture were greater than 10^5 colony forming units unless specified.
Abbreviation: CFU, colony forming units.

while 13 patients did not receive any antibiotics. The mean duration of antibiotic administration was 7.54 days. Ciprofloxacin was the most commonly used antibiotic and was administered to 9 patients. Ceftazidime/avibactam was used in the UTI caused by drug-resistant isolates. All patients responded to treatment. The mean length of stay was 3.18 days.

Discussion

Urinary tract infections can range from simple asymptomatic bacteriuria to complicated ascending tract infections leading to bacteremia and sepsis.[18] The risk of complications is more pronounced in diabetics, elderly people with indwelling catheters, and immunocompromised individuals.[19–21] *Raoultella planticola* has been rarely reported to be significantly associated with UTI. To the best of our knowledge, this is the first review of the clinical characteristics of *R. planticola*-associated UTIs.

R. planticola UTI seems to occur approximately three times more common in females in our study population, which mirrors the gender distribution for UTIs with other organisms.[22]

Advanced age, immunocompromised condition like cancer, diabetes mellitus and impaired renal function were noted to be significant risk factors for developing *R. planticola* UTI, similar to the risk factors in UTIs due to other organisms.[23,42] The mean age of our study population was 77 years. A diagnosis of diabetes mellitus was present in 43.24% (16/37) of the patients and 21% (8/37) had a glycated hemoglobin (HbA1C) >6%.

A BMI of greater than 25 kg/m^2 was present in 51.35% (19/37) of patients and the mean BMI of this cohort was 26.64 kg/m^2. Our study was underpowered to determine if obesity was an independent risk factor.

A large study of UTI in diabetics, done in Germany, has suggested that a GFR of less than 60 mL/min increases the risk of UTI.[23] However, it is unclear if chronic renal insufficiency is a risk independent of age and diabetes mellitus.[24] Twenty-three patients (including one patient who was post-renal transplant) in our study population had chronic kidney disease (GFR < 60 mL/min). In the subset of patients with chronic renal insufficiency, 52% (12/23) did not have a diagnosis of diabetes mellitus. Therefore, it is likely that impaired renal function

Table 5 The Clinical Course of the Patients with *R. planticola*-Associated UTIs

Case No.	Severity of Illness	Antibiotic Administered	Length of Stay	Duration of Antibiotics	Outcome
1	Acute cystitis	Ciprofloxacin	2	7	Discharged home
2	Acute cystitis	Ciprofloxacin	3	7	Discharged home
3	Asymptomatic bacteriuria	None	4	–	Discharged home
4	Asymptomatic bacteriuria	None	2	–	Discharged home
5	Asymptomatic bacteriuria	None	5	–	Discharged back to NH.
6	Acute cystitis	Ciprofloxacin	3	5	Discharged home
7	Acute cystitis	Ciprofloxacin	5	7	Discharged back to NH.
8	Acute cystitis	Ciprofloxacin	5	5	Discharged home
9	Asymptomatic bacteriuria	Nitrofurantoin	6	10	Discharged home
10	Acute cystitis	Levofloxacin, Cefdinir	4	1	Discharged home
11	Acute cystitis	Cephalexin	0		Left against medical advice from the ED.
12	Asymptomatic bacteriuria	Ampicillin	7	3	Discharged home
13	Septic shock	Ceftazidime/Avibactam	8	14	Discharged home
14	Asymptomatic bacteriuria	Ampicillin + ceftazidime	4	3	Discharged home
15	Asymptomatic bacteriuria	None			Discharged home
16	Acute cystitis	Ciprofloxacin	4	10	Discharged home.
17	Acute cystitis	None	0		Left against medical advice from the ED.
18	Asymptomatic bacteriuria	None	0		Discharged home from the ED
19	Asymptomatic bacteriuria	None	4	0	Discharged home
20	Sepsis	Ceftriaxone	3	7	Discharged home
21	Sepsis	Ceftazidime	6	14	Discharged home
22	Acute cystitis	Ceftazidime for 3 days then ciprofloxacin.	3	10	Discharged to short term rehab
23	Asymptomatic bacteriuria	None	2	0	Discharged home

(*Continued*)

Table 5 (Continued).

Case No.	Severity of Illness	Antibiotic Administered	Length of Stay	Duration of Antibiotics	Outcome
24	Asymptomatic bacteriuria	None	0 (ED)	0	Discharged home
25	Acute cystitis	Ceftazidime for 3 days then cefpodoxime	4	7	Discharged back to NH
26	Acute cystitis	Nitrofurantoin	0 (ED)	7	Discharged back to NH
27	Acute cystitis	Ceftazidime for 3 days then cefpodoxime	3	10	Discharged back to NH
28	Asymptomatic bacteriuria	Ciprofloxacin	4	5	Discharged back to NH
29	Acute cystitis	Ceftazidime for 4 days then cefpodoxime	5	10	Discharged to short term rehab.
30	Acute cystitis	Ciprofloxacin	0(ED)	7	Discharged home
31	Asymptomatic bacteriuria	None	2	0	Discharged to short term rehab.
32	Septic shock	Ceftazidime	4	7	Discharged back to NH.
33	Asymptomatic bacteriuria	None	4	0	Discharged home.
34	Asymptomatic bacteriuria	None	3	0	Discharged home.
35	Acute cystitis	Ceftazidime for 3 days then cefpodoxime.	3	7	Discharged home.
36	Asymptomatic bacteriuria	None	2	0	Discharged home.
37	Acute cystitis	Cefpodoxime	4	7	Discharged home.

Abbreviations: NH, nursing home; ED, emergency department.

increases the risk of *R. planticola*-associated UTIs. However, our study was not powered to make that determination.

In our study, the most common presentation was asymptomatic bacteriuria (16/37, 43.24%). However, 4 patients (10.81%) in the study population fulfilled the SIRS criteria for sepsis. Of those, 2 patients (5.4%) went into septic shock requiring aggressive intravenous fluid therapy and/or pressor support. Levy et al found that approximately 9–31% of all cases of sepsis can be attributed to urinary tract infection (depending on the geographical region).[25] Based on studies, *Klebsiella* spp. is responsible for 15% of all cases of urosepsis.[26,27] Due to its close similarity to *Klebsiella* spp., it is possible that many of those could have been due to *R. planticola* and may have been misdiagnosed in the past. There have been a few case reports of *Raoultella* bacteremia.[6–9,28,29] No cases of bacteremia secondary to UTI were observed in our study. With the increasing use of techniques such as Matrix-Assisted Desorption Ionization–Time of Flight Mass Spectrometry (MALDI-TOF MS), *R. planticola* is being detected more frequently than in the past.[28,29]

Multiple studies have demonstrated that UTIs present differently in the elderly.[30,31] A study performed by D'Agata et al in-nursing home residents showed that altered mental status is by far the commonest presentation (approximately 40%). The classical UTI symptoms of

dysuria (3.8%), costovertebral tenderness (2.3%), urinary frequency (1.5%), urgency (0%) and suprapubic pain (0%) are much less common in adults greater than 65 years.[30] Our study demonstrated similar findings.

As mentioned above, due to phylogenetic similarities, it is difficult to differentiate between *Klebsiella* spp. and *Raoultella* spp. by microscopy. The biochemical tests to differentiate *Raoultella* spp. from *Klebsiella* spp. such as ornithine decarboxylase activity, histamine or D-melezitose utilization, is not routinely available in commercial test kits.[26,27] MALDI-TOF MS has emerged, in recent years, as a faster technique to identify *Raoultella* spp. and its reliability has been proven by multiple studies.[5,32–34] It essentially involves taking a sample from a bacterial colony, absorbing the lysed bacterial proteins onto a matrix, followed by ionizing and desorbing it with a laser. The resultant plume is analyzed through mass spectrometry to detect the signature pattern that identifies the bacteria. An additional advantage is the rapid detection of resistant strains. This technique is very effective in gram-negative bacteria, even with microcolonies.[35] One limitation is the need for pure colonies; mixed colonies can lead to erroneous results.

In our laboratory, we used the VITEK® 2 compact automated system microbial identification (ID) and antibiotic susceptibility testing (AST) card for identification of organisms. The VITEK® 2 compact automated system uses 47 biochemical tests on a compact card specifically designed to identify gram-negative bacilli and their sensitivity. This technique usually identifies the organisms within 10 hours.[36] A frequently encountered problem with the system is the misidentification of *Raoultella* spp. as *Klebsiella* spp.[32] To avoid such errors, Analytical Profile Index-20E (API-20E) was used to differentiate between members of the *Enterobacteriaceae* family in our laboratory. This technique uses a miniaturized version of 20 biochemical tests. The positive and negative results are compiled to obtain a unique profile code used to identify the organism. The sensitivity for identification of *Raoultella* spp. is 93.3% in VITEK® 2 compact automated system, and 97.4% in the MALDI-TOF MS method. Though MALDI-TOF is better than VITEK® 2 compact automated system in terms of sensitivity, both systems detect *Raoultella* spp. with a high degree of accuracy and the high initial cost of the MALDI-TOF system has restricted its use mostly to higher centres.

R. planticola is intrinsically resistant to ampicillin due to the over-expression of chromosomally encoded class-A β-lactamase.[31,32] The other two major groups of resistance genes seen in *Raoultella* spp. are extended-spectrum β-lactamase (ESBL) and carbapenemase genes. Due to the ubiquitous nature of *Raoultella* spp, there is a very high risk of them acting as environmental reservoirs for resistance genes, such as carbapenemase.[37,38] An analysis of sewage water from a tertiary centre in Spain revealed the presence of multiple carbapenemases producing *Raoultella* spp.[39] These resistance genes can then be carried on mobile genetic elements like transposons and plasmids which are capable of transforming naive bacteria. In our study population, 2 patients had multidrug-resistant *R. planticola*-associated UTI. Both of these strains were resistant to ceftazidime which is routinely used in our institution to cover urinary gram-negative bacteria as per our hospital antibiogram. Though not reported, we can assume that this isolate probably had ESBL resistance gene/genes. Out of these two patients, one had a hospital-acquired catheter-associated UTI with a coexisting carbapenem-resistant *Pseudomonas aeruginosa*. The other patient had a coexisting *Escherichia coli* infection.

In addition to this, another 9 patients had a concomitant growth of a second organism found on urine culture. This is particularly concerning as mobile genetic elements, especially plasmids (chiefly IncF, IncI, IncA/C, IncL, IncN, and IncH plasmids) can transmit resistance genes between *Enterobacteriaceae*.[40,41]

Limitations of the Study

Due to the low prevalence of *R. planticola*-associated UTIs in general, the sample size was small in our study. We were not able to establish the statistical significance of our findings as a result of the small sample size. As this was a retrospective study, we encountered missing data. For example, not all patients had glycated hemoglobin levels analyzed during their hospitalization. Information on whether a urinary catheter was placed during the current hospitalization or whether it was chronic was not documented in many patient's charts. This left us unable to determine whether some of the UTIs were true infections or colonization that was discovered incidentally. Similarly, details on the structural abnormalities of the genitourinary tract and outpatient urological procedures were missing sometimes. The samples were analyzed by VITEK® 2 compact automated system microbial identification (ID) and antibiotic susceptibility testing (AST) card which is less accurate than a MALDI-TOF MS.

Conclusion

Our study revealed that patients with *R. planticola* UTI had higher proportion of diabetes mellitus, renal failure compared to the general population. Unlike prior case reports, most of the infections occurred in immunocompetent patients. Our study also confirms the intrinsic resistance to ampicillin of *R*. species, which has been documented previously in the literature. Surprisingly, *Escherichia coli* seems to coexist with *Raoultella* spp. in a significant number of cultures. A worrying finding was the presence of multidrug-resistant isolates, one of which was associated with multidrug-resistant *Pseudomonas aeruginosa*, which raises concern for the transmission of resistance genes. This raises concern for the transmission of resistance genes. As our study was limited by relatively small sample size and the retrospective nature of the analysis, larger studies would help us further define the observations noted in this study.

Ethical Statement

The article doesn't contain the participation of any human being and animal. As per our IRB, we did not require to take patient consent for the retrospective study for the electronic chart review. The study team ensured to maintain the patient data confidentiality and also was compliant with the Declaration of Helsinki.

Institutional Approval

IRB approval taken for this project from our hospital research approval team (MetroWest Medical Centre Institutional Review Board, IRB #2020 −142).

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

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Authors have no conflicts of interest to declare.

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