BRIEF RESEARCH COMMUNICATION

A Retrospective Study on UTI by *Myroides* Species: An Emerging Drug Resistant Nosocomial Pathogen

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Received on: 06 February 2024; *Accepted on:* 03 March 2024; *Published on:* 30 March 2024

Abstract

Aim and background: *Myroides (M.)* species are ubiquitous in the environment and cause a variety of infections like urinary tract infections (UTI), sepsis, meningitis, cholecystitis, pneumonia, and soft tissue infections, especially among immunocompromised populations. These are usually resistant to multiple antibiotics. This study aimed to demonstrate the clinical profile, underlying comorbidities, and antimicrobial susceptibility of *Myroides* isolates obtained from nosocomial UTI cases.

Materials and methods: A sudden rise in the isolation of *Myroides* spp. from the repeated urine samples of admitted patients alerted us to conduct this retrospective observational study. Urine cultures that grew *M.* species were included in this study. Antibiotic susceptibility was performed and the patient's clinical data was analyzed.

Results: A total of 14 *Myroides* spp. isolates were obtained from urine culture. The maximum number of cases (71.4%) were from the Nephrology ward and ICUs. The average (mean) age of patients was 46 years (range 2–80 years). All patients were catheterized. All isolates were multidrug resistant. Minocycline and doxycycline were the only drugs found effective in this study.

Conclusions: *Myroides* species are emerging rare pathogens that can cause UTI in immunocompromised and catheterized patients. Minocycline may be used for treating such infections.

Keywords: Multidrug resistance, *Myroides* species, Nosocomial infection, Urinary tract infection.

Indian Journal of Critical Care Medicine (2024): 10.5005/jp-journals-10071-24683

Highlights

This is a retrospective observational study, which was conducted at a Tertiary Care Center in Eastern India. The need for this study arose when a sudden surge of many *Myroides*-positive samples was observed in the urine cultures of patients admitted to the medicine wards and intensive care units (ICUs). Hence, we conducted this study to look for the clinical profile and antibiotic susceptibility of the patients with *Myroides* urinary tract infections (UTI).

Introduction

Nosocomial infections are a rapidly progressing problem in today's modern scenario. They are affecting almost all the hospitals in the world in both developed and developing countries. They tend to occur in almost all areas of healthcare such as long-term care facilities, hospitals, and Outpatient Departments, as well as even after a patient is discharged from the hospital.[1] The major causal agent of UTIs is the uropathogenic *Escherichia coli*, accountable for 40% of hospital-acquired UTI and 80–90% of community-acquired UTIs.[2] These infections can arise due to the bladder–urinary reflux, bladder dysfunction, anatomical defects, prolonged bladder catheterization, and many other risk factors.

An emerging pathogen seen these days is the *Myroides* species, which is otherwise nonpathogenic, but in some cases can give rise to hospital-acquired urinary tract infections. The genus *Myroides* belongs to the family *flavobacteriaceae* and is a group of gram-negative non-motile, non-fermentative, oxidase-positive *bacilli*. *Myroides* is named after the Greek word "Myron" whose literal meaning is perfume owing to its characteristic fruity fragrance. The two most common species infecting humans are *Myroides (M.) odoratimimus* and *Myroides (M.) odoratus*, previously known as *flavobacterium odoratum*. Other species like *Myroides pelagicus, Myroides profundi,* and *Myroides marinus* have been recovered from seawater.[3]

The *Myroides* species, being ubiquitous in the environment, are usually non-pathogenic. However, in recent years, a rising number of cases have been reported as a result of this seemingly avirulent organism. Certain underlying conditions can predispose individuals to *Myroides* infections like diabetes mellitus, foley catheter use, and prolonged ICU stay.[4] Although *Myroides* infections are more severe in the immunocompromised population, they can infect even immunocompetent individuals as well.

Myroides species are notoriously resistant to several antibiotics leading to difficulties in managing infections caused by this organism. Microbiological diagnostics is of great importance in limiting the spread of nosocomial infections. The information on etiological agents of infections and their susceptibility to antibiotics

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How to cite this article: Sahu C, Chaudhary R, Bhartiya C, Patel SS, Bhatnagar N. A Retrospective Study on UTI by *Myroides* Species: An Emerging Drug Resistant Nosocomial Pathogen. Indian J Crit Care Med 2024;28(4):399–403.

Source of support: Nil

Conflict of interest: None

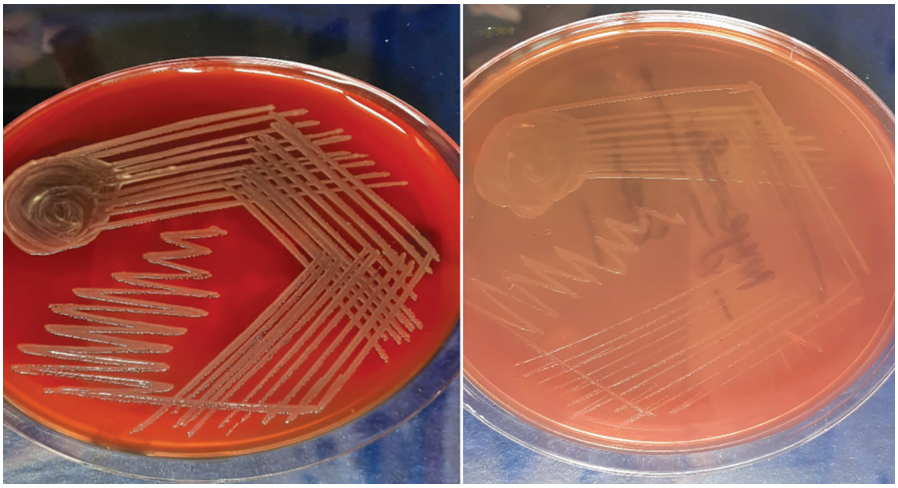

Fig. 1: Colonies of *Myroides* spp. on blood agar (left) and MacConkey agar (right)

enables a quick response in the case of a suspected epidemic outbreak.[5] Hence, clinicians as well as microbiologists should be cognizant of the possibility of infections due to various emerging pathogens such as *Myroides*. Therefore, this study was performed to demonstrate the clinical profile, underlying comorbidities, and the antibacterial spectrum of *Myroides* isolates obtained from nosocomial UTI cases at a Tertiary Care Center.

Study Design

Retrospective Observational Study.

Materials and Methods

This retrospective observational study was conducted at a 1700 bedded Tertiary Care Center spread across 550 acres in Lucknow. The study was approved by the Institutional Ethics Committee, vide letter no. PGI/BE/237/2022 dated 25/04/2022. After the sudden rise of *Myroides* organism in many samples, a retrospective analysis was planned and IEC clearance obtained. Urine samples were cultured on HiChrome agar (HiMedia, Maharashtra) using semi quantitative method and incubation was done overnight at 37°C. Colony count of ≥100 colonies single organism was considered significant. Patients were categorized on the basis of catheter associated urinary tract infections (CAUTI) criteria which includes:[5] catheter in place for more than 2 days, with one of the following-fever, suprapubic tenderness, urinary urgency/frequency/dysuria and one or two organisms isolated from urine with at least one organism of $>10^5$ CFU/mL.

Inclusion Criteria

This study included isolates of *Myroides* identified between August 2021 and December 2021. The first *Myroides* isolate from each urine sample was considered to be a contamination and a repeat sample was requested. Patients in which two or more urine samples grew significant *Myroides* colonies were reported and included in the study. As per laboratory protocol a repeat sample must be cultured if a rare microorganism is isolated before giving its antimicrobial susceptibility. Only the patients fulfilling the case definition for CAUTI criteria were included in our study. All isolates were identified using the VITEK-MS® system (bioMérieux SA, France). Antibiotic susceptibility testing was performed on Mueller Hinton's agar for all the isolates using the Kirby Bauer disc diffusion method.

Exclusion Criteria

Patients in whom repeat culture did not show any growth or in whom sample contamination (≥3 organisms were present) was present, were excluded from our study.

Informed consent was taken from all the patients, or their relatives in case of minor or unconscious patients at the time of admission and their clinical data was obtained from hospital records. Patient's demographic details, underlying comorbid illnesses like diabetes, hypertension, and chronic respiratory, cardiac, or renal illness, presence of an indwelling urinary catheter, etc. were recorded and filled in a proforma. Antimicrobial treatment at the time of culture withdrawal and modified treatment after urine culture and sensitivity report were recorded. Outcomes of patients were also recorded. All the data was entered in Microsoft Excel and analyzed.

Results

A total of 14 *Myroides* spp. isolates were obtained from urine culture during the study period. *Myroides* on blood agar were identified as 2–3 mm, round, smooth, convex, yellow-pigmented colonies with fruity odor as shown in Figure 1. The organism was gram-negative, nonmotile, catalase, oxidase, and gelatinase-positive. They reduce nitrate to nitrite but do not produce indole. Clinical details of all patients with *Myroides* UTI are provided in Table 1. All the samples were received from different wards and ICUs of the hospital. About 35% of the cases were from medicine intensive care unit (MICU) and 14% from the critical care medicine unit. Patients from other units like gastroenterology, gastro-surgery, pediatric surgery, pulmonary medicine and urology were also found to have UTI due to the same species. The commonest comorbid illness was diabetes (28%), followed by chronic kidney disease (CKD) (14%). All 14 patients had indwelling urinary catheters and samples were sent through the sampling port.

The antibiotic susceptibility pattern of all 14 *Myroides* isolates is given in Table 2. All *Myroides* isolates were extremely drug-resistant and showed resistance to amikacin, aztreonam, cefoperazone-sulbactam, levofloxacin, ceftazidime, piperacillin-tazobactam, imipenem, meropenem, trimethoprim-sulfamethoxazole as well as to the last resort antibiotic fosfomycin. Only 3 isolates were susceptible to colistin. The only effective drugs against all isolates were minocycline and doxycycline. All but three patients recovered from UTI after the change of antibiotics to minocycline, the remaining

Table 1: Clinical details of 14 patients with *Myroides* urinary tract infection

S. No	Age (yrs)/ Sex	Ward	Diagnosis	Duration of hospital stay (days)	Comorbidity	Foley's catheter in situ	Antibiotics given for Myroides infection	Outcome
1.	49/M	MICU	Acute pancreatitis	39	Diabetes	Yes	Minocycline, piperacillin-tazobactam	Death
2.	65/F	Gastro-surgery	Cholecystitis	37	None	Yes	Minocycline, ceftriaxone	Recovered
3.	29/M	CCM	AKI, Community acquired pneumonia	42	COPD	Yes	Minocycline, ceftazidime-avibactam	Death
4.	68/M	Urology	CKD, Ca Urinary bladder	9	CKD	Yes	Minocycline, cotrimoxazole	Recovered
5.	36/M	MICU	AKI, ARDS	22	Diabetes, CLD	Yes	Minocycline, imipenem	Death
6.	18/M	Pulmonary Medicine	Cavitatory pneumonia	35	None	Yes	Colistin, ceftazidime-avibactam	Recovered
7.	37/M	Nephrology	CKD, post renal transplant	25	CKD	Yes	Minocycline, ceftriaxone	Recovered
8.	80/F	Pulmonary medicine	Interstitial lung disease	22	Diabetes	Yes	Minocycline, ceftazidime-avibactam	Recovered
9.	60/M	MICU	Acute pancreatitis	50	Diabetes	Yes	Minocycline, meropenem	Recovered
10.	67/M	CCM	AKI, RTA	86	None	Yes	Minocycline, cefoperazone-sulbactam	Recovered
11.	2/M	Urology	Vesicoureteral reflux	37	None	Yes	Colistin, levofloxacin	Recovered
12.	66/F	MICU	Dengue shock syndrome	15	Renal failure	Yes	Minocycline, imipenem	Death
13.	34/M	Gastroenterology	Acute pancreatitis, AKI	57	None	Yes	Colistin, ceftazidime	Recovered
14.	33/M	MICU	CKD, Renal transplant	29	CKD	Yes	Minocycline, piperacillin-tazobactam	Recovered

Ca, carcinoma; CCM, critical care medicine; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; F, female; M, male; MICU, medicine intensive care unit; RTA, road traffic accident

Table 2: Antibiotic susceptibility pattern of 14 *Myroides* isolates from urine samples using Kirby Bauer disc diffusion method

Antibiotic	Sensitive (%)	Intermediate (%)	Resistant (%)
Amikacin	0	0	14 (100)
Aztreonam	0	0	14 (100)
Ceftazidime	0	0	14 (100)
Imipenem	0	0	14 (100)
Meropenem	0	0	14 (100)
Levofloxacin	0	0	14 (100)
Cefoperazone-sulbactam	0	0	14 (100)
Piperacillin-tazobactam	0	0	14 (100)
Ticarcillin-clavulanate	0	0	14 (100)
Fosfomycin	0	0	14 (100)
Trimethoprim-sulfamethoxazole	0	0	14 (100)
Doxycycline	14 (100)	0	0
Minocycline	14 (100)	0	0
Colistin	3 (21.4)	0	11 (78.6)

three were prescribed colistin and they responded positively. Four patients (28.6%) expired, owing to severe underlying illnesses.

Discussion

Myroides spp. was first isolated by Stutzer et al. in 1923 and was initially classified in the genus *flavobacterium*, family *bacteriaceae*, and tribe c*hromobacteriaceae*. This genus comprises two clinically relevant species of typically *opportunistic aerobic, gram-negative non-motile bacilli*, which includes *M. odoratus* and *M. odoratimimus*.[3] Although it is ubiquitous in soil and marine environments, this species have been implicated in 52 documented infections since the 1920s when *F. odoratum* was first identified.[2,3] While typically found in immunocompromised patients, few cases have been documented in immunocompetent individuals.[4] In 1996, a new genus *Myroides* was created due to the distinctive phenotypic properties of *F. odoratum* like lack of gliding motility, halotolerance, high capacity of growth at 37°C and many differences in the fatty acid profile. The new genus comprises of *M. odoratum* (previously *F. odoratum*) and *M. odoratimimus*.[6]

Irrespective of the immune status, *Myroides* spp. are frequently multi-drug resistant with incompletely understood mechanisms of resistance.[7] Members of *Myroides* spp. are usually considered of low virulence, however, several case reports have reported their association with a variety of clinical infections. In 2013, Deepa et al.

reported a case of *m. odoratus* causing pneumonia in a diabetic female with pulmonary tuberculosis.[8] Thomas et al. reported a case of acalculous cholecystitis due to *Myroides* spp.[9]

In our study, all 14 *Myroides* isolates were obtained from urine samples of catheterized patients. Similar to this study, Agrawal et al. reported 16 cases of *Myroides* UTI from catheterized patients admitted to ICUs.[10] However, in our study, half of the patients were from MICUs and critical care medicine units, and the other half were from various wards, namely gastroenterology, gastro-surgery, pediatric surgery, pulmonary medicine, and urology. The most common comorbidity associated with the patients in our study was diabetes (28%) followed by CKD (14%), in contrast to other studies where most of the *Myroides* UTI patients were diabetic.[11,12] The association of *Myroides* infections with Foley's catheters is due to their propensity to form biofilms. The ubiquitous nature and tendency for autoaggregation and coaggregation to form strong biofilms may be responsible for their ability to cause infections in immunosuppressed patients with prolonged hospitalization and catheterization.[13] A urinary tract infection must be differentiated from mere bacterial detection in the genito-urinary tract. This is known as asymptomatic bacteriuria, and is quite common and does not require any treatment, especially in a patient with an indwelling urinary catheter.[14]

There are numerous cases where quinolones and trimethoprim-sulfamethoxazole were found to be effective and the clinical cure was achieved using these drugs. In this study, the only effective antibiotics against all *Myroides* isolates were doxycycline and minocycline. Anti-pseudomonal agents like third-generation cephalosporin ceftazidime, piperacillin-tazobactam, β-lactam–β-lactamase inhibitor combinations, carbapenems like imipenem and meropenem, cefoperazone-sulbactam, as well as fosfomycin were ineffective against these isolates. In our study, 78.6% of isolates were even resistant to the last resort antibiotic colistin. Another Indian study analyzing 16 patients of *Myroides*-associated UTI, also reported 100% sensitivity to minocycline and resistance to all other antibiotics, including colistin.[10] A case series of five patients of catheter-associated urinary tract infections also reported high sensitivity towards the same drug.[12]

Worldwide we see a different picture. A study conducted in Western Romania reported a good response towards tigecycline.[15] Synergistic efficacy of ciprofloxacin (CIP), meropenem (MEM), and colistin (CT) was checked against biofilm and planktonic forms of *M. odoratimimus* bacterial isolates, in a study in Turkey, and it was found that combinations of CT/CIP and CT/MEM are synergistic towards all strains, whereas CIP/MEM combination has an additional effect. As per the biofilm inhibition result, all three antibiotics were able to inhibit biofilm formation.[16] Different strategies can be applied regarding the appropriate management of this extensively drug-resistant nosocomial pathogen, depending upon the antibiotic susceptibility results.

Conclusion

In conclusion, clinicians should be aware of this emerging pathogen as a causative agent of urinary tract infections, especially in immunocompromised and catheterized patients. It is imperative to note that repeated positive urine cultures must be considered in these patients due to the presence of such multidrug-resistant microorganisms. According to our knowledge, no such study with such a high incidence of *Myroides*-associated UTIs has been reported from Eastern Uttar Pradesh and hence it is important to consider this pathogen in cases where patients are not responding to the conventional UTI treatment regimens.

Author Contributions

Nidhi Bhatnagar: Conception and design of the work, the acquisition, analysis, and interpretation of data for the work, drafted the work and revised it critically for important intellectual content, approval of final version of manuscript to be published; Chinmoy Sahu: The acquisition of data for the work, drafted the work, approval of final version of manuscript to be published; Radhika Chaudhary: The acquisition, analysis, and interpretation of data for the work, approval of final version of manuscript to be published; Chitra Bhartiya: Acquisition of the data, approval of final version of manuscript to be published, conception and design of the work, the acquisition, analysis, and interpretation of data for the work, drafted the work and revised it critically for important intellectual content; Sangram Singh Patel: Acquisition of the data, approval of final version of manuscript to be published.

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