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*Research Article*

# Multidrug resistance in *proteus* species isolated from outpatients with urinary tract infections in Minia university hospitals, Egypt

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## Abstract

**Introduction and aim of the work:** *Proteus* species represent an important cause of urinary tract infections (UTIs) both in community and hospital settings. *Proteus* species are more isolated from inpatients especially in catheter associated UTIs while little information is available among outpatients. The current study aims to access prevalence and antimicrobial susceptibility of *proteus* species isolated from outpatients with UTIs. **Subjects and Methods:** 135 outpatients presented with symptoms of UTI from whom midstream urine samples were collected. Urine culture was done on MacConkey agar, colonies more than $10^5$ CFU/ml are further identified for isolation of *proteus* species and antimicrobial susceptibility testing was performed using disk diffusion method. **Results**: *proteus* species were isolated from 11% of outpatients with UTIs; 75% of *proteus* isolates showed multidrug resistance. **Conclusion:** Increased rates of multidrug resistant *proteus* isolated from community acquired urinary tract infections.

**Keywords**: UTI, *proteus*, Multidrug resistant

## Introduction and aim of the work

Over the past years urinary tract infections (UTIs) are known to be among the commonest infections both in the community and hospital settings. Community-acquired UTI (CA-UTI) prevalence is 0.7% over the world while Healthcare-associated UTI (HAUTI) frequency among HCAIs is 12.9, 19.6 and 24% in the United States, Europe and developing countries, respectively[1].

A study over 10 years, following 700,000 community-acquired UTIs, found that *proteus mirabilis* was the causative agent in 5% of cases after *Escherichia coli* (UPEC) and *Klebsiella pneumoniae* [2]. *Proteus mirabilis* is a common cause of complicated UTI in patients with anatomical or functional abnormalities of the urinary tract, particularly in patients with long term indwelling catheters, who may develop catheter-associated UTI[3]. *Proteus* strains which are resistant to antibiotics are increasingly reported, which complicates the treatment of infections caused by *Proteus* species[4].

While *proteus* is known for high rates of catheter associated UTI in hospital settings; little information is available about community acquired UTIs. The current study aims to study *proteus* species isolated from outpatients attending outpatient clinics in Minia university hospitals.

## Materials and Methods

### Study design

This is across sectional study in which urine samples were collected from 135 outpatients attending outpatient clinics in Minia university

hospitals complaining from UTI symptoms as dysuria and increased frequency of urination in the period from July 2021 to April 2022.

**Sample collection**

Midstream urine samples were collected from study patients in sterile screw capped containers and transported within two hours to bacteriology laboratory and processed at once.

**Sample processing**

Urine culture was done from urine samples on MacConkey agar using calibrated loop technique[5]; non-lactose fermenting colonies with colony count more than $10^5$ CFU/ml were further tested for identification of *proteus* isolates by biochemical tests (Indole production test, Methyl red test, Voges proskauer test, citrate and urease tests and $H_2S$ production)[6].

**Antimicrobial susceptibility Testing**

Disk diffusion method was used for antimicrobial susceptibility testing using Muller Hinton agar. Seven antimicrobial agents from Thermo Scientific™ Oxoid, UK were selected for testing according to CLSI guidelines[7]; Amoxicillin/clavulanic acid (AMC) 20/10 µg, Ceftriaxone (CRO) 30 µg, Ciprofloxacin (CIP) 5 µg, Cefoxitin (FOX) 30 µg, Cefazolin (CZ) 30 µg, Gentamicin (CN) 10 µg and Nitrofurantoin (F) 300 µg.

**Statistical analysis**

All data were entered into a Microsoft excel worksheet, and statistical analysis was performed using SPSS for Windows version 19.0 (IBM, USA). Quantitative variables are described in terms of mean, standard deviation (SD) and range. Frequency of qualitative variables are describing as number (no.) and percentage (%).

**Ethical approval**

This research protocol was approved by the Scientific Ethical Committee of faculty of medicine, Minia University. Patient informed consent was fulfilled prior to sample collection.

## Results

Out of 135 outpatients enrolled in the study; urine samples of 109 patients gave positive growth more than $10^5$ CFU/ml which confirmed diagnosis of UTI[8]. *Proteus* species were isolated from 12 patients (11%). Eleven isolates were identified as *proteus mirabilis* and one isolate was identified as *proteus vulgaris.* *Proteus* species were isolated from 6 males and 6 females who had a mean age of 41.8±16.1.

Regarding antimicrobial susceptibility testing (table 1); none of *proteus* isolates were sensitive to cefazolin nor nitrofurantoin while they were all sensitive to gentamicin. They exhibit moderate resistance to both of amoxicillin-clavulanic acid (58.3%) and ciprofloxacin (50%). They showed high sensitivity to ceftriaxone (83.8%) and cefoxitin (75%), Multidrug resistant strains represents 75% of isolated *proteus* strains; MDR was defined as antimicrobial resistance to at least one antimicrobial drug in three or more antimicrobial categories[9].

**Table 1: Antimicrobial resistance pattern among *proteus* study isolates**

| Antimicrobial agent | Sensitive | | Resistant | |
|---|---|---|---|---|
| | N | % | N | % |
| **Amoxicillin- clavulanic (AMC)** | 5 | 41.7% | 7 | 58 % |
| **Ceftriaxone** | 10 | 83.3% | 2 | 16.7% |
| **Ciprofloxacin** | 6 | 50% | 6 | 50% |
| **Cefoxitin** | 9 | 75% | 3 | 25% |
| **Cefazolin** | 0 | 0% | 12 | 100% |
| **Gentamicin** | 12 | 100% | 0 | 0% |
| **Nitrofurantoin** | 0 | 0% | 12 | 100% |

## Discussion

*Proteus* isolates represent 11% of the study isolated uropathogens from outpatients, this is relatively higher than reported in other studies. In a previous study in the same hospital, *proteus* species were isolated from 7.8% of outpatients presenting with UTI[10]. Lower rates among outpatients were also reported by Muhammad el al, 2020[11] and Salm et al, 2022[12] who reported prevalence of 2.1% and 9.2% respectively.

High sensitivity rates were reported in the Current study to gentamicin, ceftriaxone and cefoxitin; probably because they are not usually prescribed on outpatient basis in which most of cases are simple uncomplicated UTI. *Proteus* isolates showed absolute resistance to nitrofurantoin whish is a first line drug in treatment of uncomplicated cystitis[13] and commonly prescribed in the locality which matches with fact that P. mirabilis and P. vulgaris are naturally resistant to nitrofurans[14]; high resistance to nitrofurantoin was also reported in Egypt (98.3%) [15] and Jordan (88.2%) [16]. Our finding reported absolute resistance against cefazolin (100% resistance). This agreed with Lin et al., who found ninety-six percent of the collected isolates were not susceptible to cefazolin[17]. Another study was done in Egypt but its result disagreed with our finding as it reported 36.6% resistance to cefazolin[18].

Also ciprofloxacin showed a moderate resistance rate (50%) which is one of first line drugs in uncomplicated pyelonephritis[13] and also commonly prescribed in the locality. Mishu et al., reported very high resistance to ciprofloxacin (70.5%) **[19],** lower resistance rates were reported by Tabatabaei et al., (19%)[20], Shaaban et al., in Egypt (25.9%)[21] and Musa et al., (13.3%)[22]

Regarding amoxicillin-clavulanic acid resistance in our study, 58.3% of *Proteus* isolates show resistance to AMC. Our finding agreed with a study in Egypt by Salama et al., who found 45% resistance[15]. Other studies in Egypt reported less percentage as Shaaban et al., (22.4%)[21] and Zakeer et al., (33.3%) [18]. Mirzaei et al., reported 22.5% resistance [23]. On the other hand, G Ali et al., in Egypt reported 93.9% resistance [24] and Al-Ezzy et al., reported 100% resistance [25].

In the current study, high rate of multidrug resistance of *proteus* isolates is observed (75%) may be due to non-indicated, random and excessive use of these antibiotics in UTI therapy. This was close to the result obtained by Salama et al., in Egypt (73.3%) [15] and the result reported by Mirzaei et al., (82.5%) [23].

## Conclusion

The current study revealed increased rates of *proteus* species isolated from community acquired urinary tract infection which showed high resistance rate to commonly prescribed antimicrobial agents as nitrofuratoin and ciprofloxacin with high rate of MDR strains (75%). These findings spots light on revising antimicrobial polices in the locality and avoidance of extensive and non- indicated use of antimicrobial agents.

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