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Proteus Genus Sensitivity Testing for Various Classes of Antibiotics

Ahmed A. Abdulrraziq and Sami M. Salih

Biology Department, Education Faculty, Omar Al-Mukhtar University, Al-Bayda, Libya.

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A B S T R A C T

Proteus genus has become one of the most common pathogens in Libya, with high antibiotic resistance, which can lead to medical problems in many situations in hospitals. However, there is no comprehensive study of the sensitivity and resistance of Proteus pathogenic to antibiotics in Libya. Therefore, the present study was conducted with the aim to test the sensitivity and resistance of two *Proteus* isolates (UTI and diarrhea) to antibiotics. The Kirby-Bauer (disc diffusion) method was used to investigate the effects of eight Antibiotics, belonging to different classes. Aminoglycosides represented by Gentamicin, Tetracyclins class represented by Doxycycline 30ug, Penicillin class represented by Ampicillin 10ug, Macrolides class represented by (Azithromycin 15ug, Erythromycin 15ug), and Cephalosporins class represented by (Ceftriaxone 30ug, Ceftazidime 30ug, and Cephalexin 30ug). Antibiotic susceptibility results test revealed all proteus isolates to be resistant to most antibiotics, especially the classes (penicillin, Macrolides, Cephalosporins). In contrast, there were no significant differences between the resistance of the protease isolates from the urinary tract and the protease isolated from diarrhea. On the other hand, the antibiotic gentamicin recorded the highest sensitivity to *Proteus* isolates (UTI) and (diarrhea) tested at 46.6% and 39.9%, respectively. This study concludes to new antibiotics must be developed, although aminoglycosides are still effective against *Proteus* genus.

1 Introduction

Libyan society is among the societies using practice self-medication with antibiotics without a physician's prescription, which has led to bacterial resistance to these antibiotics and the emergence of pathological cases, largely unresponsive to drugs (Meerah, 2023; Hosien *et al*., 2022). Since the discovery of antibiotics, Drug manufacturers rely on small molecules derived from microbes, as well improvements in traditional antibiotics have led to the development of various new antibiotics (Shim, 2023), but with the increased antimicrobial resistance, new generations of antibiotics had to be developed more efficiently (Frieri *et al*., 2017). Enterobacteriaceae are important pathogens in nosocomial and community settings, in the last years, antimicrobial resistance in this family has increased dramatically worldwide (Rozwandowicz *et al*., 2018).

Proteus ssp is a gram-negative bacterium, facultatively anaerobic and heterotrophic, usually rod-shaped. It shows a change in shape, is mobile, urease-positive, belongs to Enterobacteriaceae, and is responsible for urinary tract infections. Gustav hauser first described it in 1885 and it is characterized by intensive swarm growth on solid ground. (Mohsin and AL-Rubaii, 2023; Drzewiecka, 2016). These bacteria are found in wastewater and soil, although considered commensals in the digestive system, they also possess many

Corresponding author: E-mail: ahmed.amrajaa@omu.edu.ly

virulence factors that may be relevant to gastrointestinal pathogenicity (Hamilton *et al*., 2018). At first, the genus was divided into two species based on the liquefying gelatin. Lately, new seven species have been detected, the genus *Proteus* thus includes ten species and three unnamed genotypes (Hyun *et al*., 2016; Dai *et al*., 2020), among them were *P.vulgaris* and *P.mirabilis*, the most related causative agents of urinary tract infections (Rozalski *et al*., 1997). Also, they cause various infections, such as wound infections, diarrhea and meningitis in newborns (Phan and Lehman, 2012). High resistance to *Proteus* spp has been reported frequently, by their ability its ability to form crystalline biofilms, in addition, to moving, transferring, adhere, the release of endotoxins and enzymes such as urease, hemolysin, protease and DNase (AL-Dulaimy *et al*., 2023; Jalil *et al*., 2023). Moreover, It was confirmed that this genus has carbapenemase genes that serve to break down the antibiotic and reduce its effectiveness (Al-Nabhani and Shami, 2023), in addition to producing plasmids (Hua *et al*., 2020). In contrast, a recent study found that the synergistic effect of antibiotics could have an antagonistic effect against the growth of these bacteria (Mohsin and AL-Rubaii, 2023). It was found that both the blaTEM and *qnr* genes from *Proteus* spp. involved in conferring resistance to β-lactam and quinolone antibiotics (Bilal *et al*., 2019). However, there is no complete study of the resistance and sensitivity to *Proteus* genus against antibiotics in Libya.

The aim of this study was therefore to provide information on the effectiveness of common antibiotics in combating *Proteus* genus isolates in Libya.

2 Materials and Methods

2.1. Bacterial Isolates

The isolates of *Proteus* spp identified were obtained from an Al-Mejhar laboratory, Al-Bayda City, based on characteristic growth on blood agar, and non-lactose-fermenting colonies on MacConkey's agar media, Fig(1).

- *Proteus* (UTI): isolate from urine tract infection.

- *Proteus* (D): isolate from diarrhea.

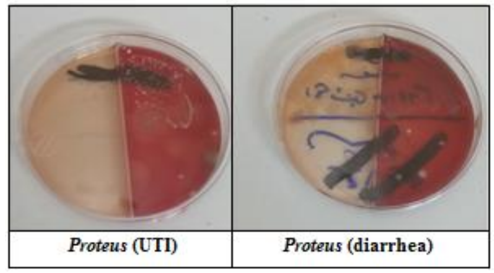

Figure (1): *Proteus* isolates on MacConkey's and blood agar media.

2.2 Antimicrobial Susceptibility Test

The media were sterilized in an autoclave at 121 °C for 15 minutes, and the bacteria were grown on Mueller—Hinton Agar. A routine antimicrobial susceptibility test was performed by the Kirby–Bauer disk diffusion method against *Proteus* spp. For screening, a disc antibiotic was placed on the surface of the inoculated bacterial medium. The dishes were incubated at 37°C for 20–24 hours in triplicate per dish. The zone of inhibition diameter minus the disc diameter was measured. This study used 8 types of commonly used antibiotics including: Doxycycline (DO) 30µg, Gentamicin (CN) 10µg, Ampicillin (AMP) 10µg, Azithromycin (AZM) 15µg, Cephalexin (CL) 30µg, Ceftriaxone (CTR) 30µg, Ceftazidime (CAZ) 30µg, Erythromycin (ERY) 10µg (Abdulrraziq and Salih, 2022).

Statistical Analysis

The study experiences tense designed according to the complete random design (CRD). Statistical analysis was performed using Minitab 17 program and ANOVA variance analysis tables. The averages were compared using Tukey's test at P <0.05 (Abdulrraziq *et al*., 2023).

3 Results

Table (1) and Fig. (2, 3 and 4). The results represent of antibiotic susceptibility testing of Proteus spp. isolates against 8 types of commonly used antibiotics, which showed a wide variation in their antibiotic resistance.

3.1. Sensitivity of *Proteus* isolates (UTI) to antibiotics

The highest was percentage of sensitivity to the antibiotic Gentamicin at a diameter of (5.9mm) by (39.3%), followed by Doxycycline at a diameter of (4.6mm) by (30.6%), while middle-sensitivity to Erythromycin and Ceftriaxone by (20.0 and 15.0%) respectively. The isolate showed high resistance to the rest, antibiotics, including (Ampicillin and Ceftazidime), were recorded sensitivity (6.0%), and Azithromycin by (3.0%). Finally, the highest percentage of resistance to the antibiotic Cephalexin was 100%.

Table(1): Effect of various antibiotics against *Proteus* isolate (UTI).

Class \ Antibiotic	Isolate		Urine tract infection (UTI)		
			Zone inhibition (mm)	Sensitivity (%)	Resistance (%)
Tetracyclins	Doxycycline (DO)	30	4.6+0.3	30.6	69.4
Aminoglycoside	Gentamicin (CN)	10	5.9+0.5	39.3	60.7
Penicillin	Ampicillin (AMP)	10	1.0+0.0	6	94
Macrolides	Azithromycin (AZM)	15	0.5+0.0	3.3	96.7
	Erythromycin (ERY)	15	3.0+0.1	20	80
Cephalosporins	Ceftriaxone (CTR)	30	2.3+0.0	15.3	84.7
	Ceftazidime (CAZ)	30	1.0+0.0	6	94
	Cephalexin (CL)	30	0.0+0.0	0	100

3.2. Sensitivity of *Proteus* isolates (Diarrhoea) to antibiotics

Proteus isolate showed maximum sensitivity to gentamicin (46.6%), which was the highest sensitivity ratio recorded in this study, while antibiotics (Ceftriaxone, Ampicillin, Ceftazidime, Erythromycin and Doxycycline) recorded sensitivity ranged between (10-20%). On the other hand, it was found that Proteus isolate showed maximum resistance (100.0%) to two antibiotics; Cephalexin and Azithromycin.

Table(2): Effect of various antibiotics against *Proteus* isolate (diarrhea).

Class \ Antibiotic	Isolate		Diarrhea		
			Zone inhibition (mm)	Sensitivity (%)	Resistance (%)
Tetracyclins	Doxycycline (DO)	30	3.0+0.3	20	80
Aminoglycoside	Gentamicin (CN)	10	7.3+1.0	46.6	53.4
Penicillin	Ampicillin (AMP)	10	1.8+0.2	12	88
Macrolides	Azithromycin (AZM)	15	0.0+0.0	0	100
	Erythromycin (ERY)	15	2.3+0.2	15.3	84.7
Cephalosporins	Ceftriaxone (CTR)	30	1.5+0.0	10	90
	Ceftazidime (CAZ)	30	2.2+0.3	14.6	85.4
	Cephalexin (CL)	30	0.0+0.0	0	100

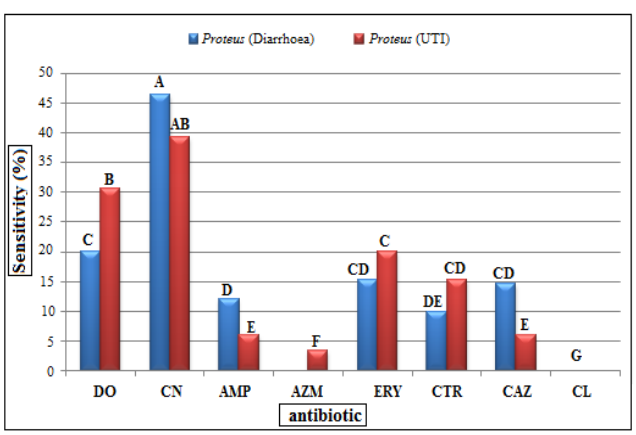

Figure (2): Sensitivity of *Proteus* isolates to antibiotics.

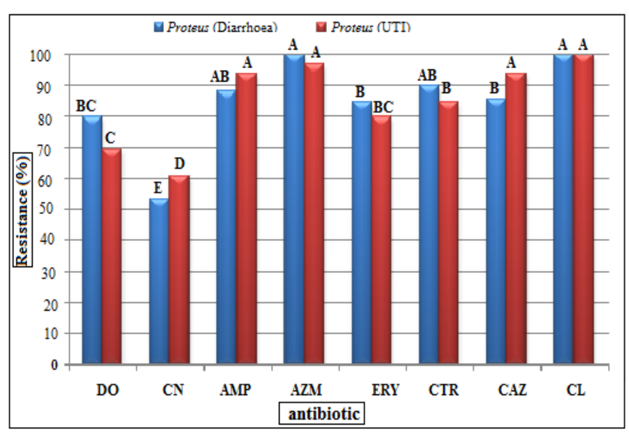

Figure (3): Resistance of *Proteus* isolates to antibiotics.

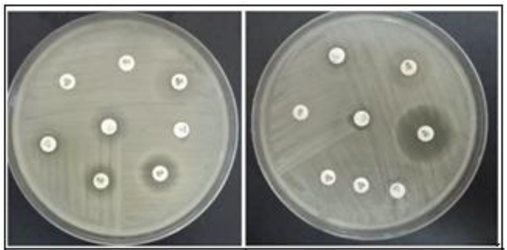

Figure (4): Effect of various antibiotics against *Proteus* isolate (UTI and diarrhea).

4 Discussion

The characterization and dissemination of antimicrobial resistance profiles provide useful details on the potential challenges in treating bacteria (Jalil *et al*., 2023). In this study, the high percentage sensitivity of *Proteus* spp isolates to Gentamicin 46.6 and 39.3%. This result is similar to the study that was reported by Flamerz *et al*. (2023). It was supported by McMurtry *et al*. (2021) who noticed that aminoglycosides effectiveness against negative gram bacteria, where this group of antibiotics binds to disrupt protein translation, leading to widespread cell damage and bacterial cell death (Webster and Shepherd, 2023). Also, the group of tetracyclins antibiotics represented by Doxycycline had reasonable activity against Proteus isolates, This result agrees with (Alqani *et al*., 2023), a study also pointed to the possibility of re-treating and advancing the three generations of the tetracyclins class in treating bacterial infections (LaPlante *et al*., 2022), by binding tetracycline particles to 16S rRNA using the ribosomal subunit of bacteria (Chukwudi, 2016), As for the penicillin represented by Ampicillin, the percentage of sensitivity of the isolates against this antibiotic in the current study was between (6-12%), This means that the resistance rate is about 90%. The penicillin class of antibiotics is known to be effective in treating both infectious and non-infectious diseases, however, biofilm formation by *Proteus* species can impede the action of these antibiotics (Li *et al*., 2022). As for the sensitivity of class antibiotics Macrolides (Erythromycin and Azithromycin), bacterial isolates resistance was high, between (80 -100%), These results agree with (ALjeelizy *et al*., 2022). Finally, the highest rates of resistance were against class Cephalosporins antibiotics represented by (Ceftriaxone, Ceftazidime, and Cephalexin) in this study. This result is consistent with a study, which reported a decrease in the clinical effect of cephalosporins series with frequent use (Shipitsyna and Osipova, 2022).

5 Conclusion

Generally, In the present study, all Proteus ssp isolates were shown to be multi-antibiotic resistant. There were no significant differences between the resistance of protease isolated from the urinary tract and those isolated from diarrhea. In addition, aminoglycosides are still effective in combating Proteus bacteria. Although, the development of generations of drugs, it should be that noted self-medication and long-term antibiotic therapy can lead to the emergence of resistant isolates.

Conflict of Interest: The authors declare that there are no conflicts of interest**.**

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