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Dissemination of Integron Class 1 among XDR isolates of *P. aeruginosa* in Najaf City

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Integrons are gene capture systems observed in chromosomes, plasmids, and transposons, where identified and capture multiple gene cassettes. Integerons are consists of 3 elements: the initial is integrase gene (*int1)* encoding integrase enzyme (*int1*), which is essential to insertion or deletion of specific site. The second element is *attI as* integron-connected recombination site. The 3rd element is promoter (Pc), which is required in the expression of cassette-connected genes.
Aim of the Study: This thesis designed to examine the occurrence of integron class one genes among XDR isolates of *P. aeruginosa*.

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Methods: An overall of 79 specimens were isolated from patients during the period of study and the specimens were carried to the laboratory. By monoplex PCR assay, the 19 XDR isolates of *P. aeruginosa* were investigated for the presence of integrons class one using intI1primer.
Results: This result found that 8 isolates are isolated from burns, 7 isolates are from urine, 4 isolates are from wounds. The PCR results show that 17 (89.5%) of the isolates harbored integrase (*intI1*) gene, while two isolate (10.5%) was negative for *intI1* gene. .
Conclusions: Present result showed elevated occurrence of integrons class one among XDR isolates of *P.aeruginosa*.

Keywords: Pseudomonas aeruginosa; integrons; plasmids; transposons; Class 1 integrons, gene cassettes; XDR; MDR; ESBL; CLSI; VITEK-2 compact system.

1. INTRODUCTION

1.1 Integrons

Integrons are gene capture systems observed in chromosomes, plasmids, and transposons, where identified and capture multiple gene cassettes. A gene cassette is a genetic element containing site-specific recombination has capable of integrating, expressing, and exchanging specific DNA elements [1]. This gene cassette contains one or occasionally two genes, often genes of antibiotic resistance, and a backbone element, which had called an integrin [2]. As a result, integrons were described as a major site of antimicrobial resistance genes in the microbial community also thought to be a reservoir for these genes [3].

Integerons are consists of 3 elements: the initial is integrase gene (*int1)* encoding integrase enzyme (*int1*), which is essential to insertion or deletion of specific site. The second element is *attI as* integron-connected recombination site. The 3rd element is promoter (Pc), which is required in the expression of cassette-connected genes [4]. Gene cassettes received are considered as a major source of new genes for antibiotic resistance, and multiple cassettes can remain together within the integron and therefore provide resistance to more than one antibiotic [5].

There are 2 main kinds of integrons were defined as mobile integron and chromosomal integron. Chromosomal type is found in chromosomes of different bacterial species, where called super integrons that can hold up to 250 cassettes that mainly express unknown functional proteins. While, mobile integrons are not known to be self-transposible factors but found on motile inherited factor like plasmid and transposons that facilitate spread among different bacterial species [3]. To date, ten classes of integrons whose identification have identified any class by variations in the sequence of integrase genes [6].

Integrons of class one are the major prevalent and are present in a large number of bacterial Gram-negative [7]. These integrons are widespread and their significant association with the *Enterobacteriaceae* multi-resistance phenotype [8] Fluit and Schmitz, [7]. Cassettes in integrons of class one are connected with genes that encode resistance enzymes like chloramphenicol acetyltransferases, β-lactamases, and aminoglycoside-modifying enzymes; they can also have recently been correlating with genes that mediate resistance to quinolones and rifampin, as well as genes that encode ESBL and carbapenemases [9]. Integrons of class one are common and widely showed in *Enterobacteriacae* producing ESBL, ensuring *K. pneumoniae* [10,11].

2. MATERIALS AND METHODS

2.1 Collecting of Samples

This cross sectional study was conducted in 2 major hospitals in Najaf City (General Hospital of Al-Hakeem and Medical City of Al-Sadder) through the period of September 2023 to December 2023. A total of 79 samples (burns, urine, wound) were obtained from patients during the period of study and the samples were carried to the laboratory.

2.2 Isolation and identification of *P. aeruginosa*

Microbiological standard diagnostic criteria were used to isolate and identify *P.aeruginosa* clinical isolates, which included colony morphology, Gram stain, and conventional biochemical tests. The VITEK-2 automated system has been utilized to diagnose *P.aeruginosa*.

2.3 Class I integrons Molecular Screening

This thesis was carried out to discover the dissemination of the integrons class one genes in the XDR *P.aeruginosa* isolates collected from two hospitals of Najaf during 4 months period. The early detection of class I integrons genes may inactivate the dissemination of these XDR isolates on the future.

3. RESULTS

3.1 Frequency of Integrons Class one

By monoplex PCR assay, the 19 XDR isolates of *P.aeruginosa* were observed for detection integrons of class one using int11 primer. Class I integrons was found to be predominant among the test isolates. This result found that 8 isolates are isolated from burns, 7 isolates are isolated from urine, 4 isolates are isolated from wounds. The PCR results show that 17 (89.5%) of the isolates harbored integrase (*intI1*) gene, while two isolate (10.5%) was negative for *intI1* gene (Fig. 1). However, the characteristics of XDR isolates and the detection integrons of class one are shown in Table (1).

4. DISCUSSION

4.1 Integrons of Class one among XDR *P.aeruginosa*

The spreading of XDR *P. aeruginosa* harboring integrons of class 1 is concerned in the possible dissemination of XDR isolates. Little information is available on the distribution of integron class I and their relation to MDR in *P. aeruginosa* isolates in Najaf. Because the integrons are significant in the dissemination of antibiotic resistance, this cross-sectional thesis was also designed to examine the frequency of integrons class one among XDR *Pseudomonas aeruginosa* isolates in Najaf hospitals. Also, this result reported there was an important association between the presence of integrons class one and XDR isolates. Out of 19 XDR isolates, 17 (89.5%) were positive for integrons of class one by amplification the gene *intI1* (Table 1). The elevated rate of integrons class 1 may be a possible reason for dissemination of XDR in Najaf hospitals. Higher frequency of class 1 integrons was reported in recent study in Najaf where all (100%) carbapenem resistant *P. aeruginosa* isolates contained integrons

Table 1. Incidence of integron gene among 19 XDR isolates of *P.aeruginosa*

intl1 gene positive No. (%)	Isolate code No.	Hospital	sources	Hospitalization
17 (89.5)	Pa16	Al-Sadder	Burn	Inpatient
	Pa14	Al-Sadder	Burn	Inpatient
	Pa10	Al-Hakeem	Urine	Inpatient
	Pa8	Al-Sadder	Wound	Inpatient
	Pa4	Al-Sadder	Burn	Inpatient
	Pa12	Al-Hakeem	Urine	Inpatient
	Pa9	Al-Sadder	Wound	Inpatient
	Pa3	Al-Hakeem	Urine	Outpatient
	Pa1	Al-Sadder	Burn	Inpatient
	Pa17	Al-Hakeem	Urine	Inpatient
	Pa6	Al-Sadder	Burn	Outpatient
	Pa13	Al-Sadder	Wound	Outpatient
	Pa2	Al-Sadder	Burn	Inpatient
	Pa5	Al-Hakeem	Urine	Inpatient
	Pa11	Al-Hakeem	Urine	Inpatient
	Pa18	Al-Sadder	Burn	Inpatient
	Pa19	Al-Hakeem	Urine	Inpatient
intl1 negative 2 (10.5)	Pa7	Al-Hakeem	burn	Inpatient
	Pa15	Al-Sadder	Wound	Outpatient

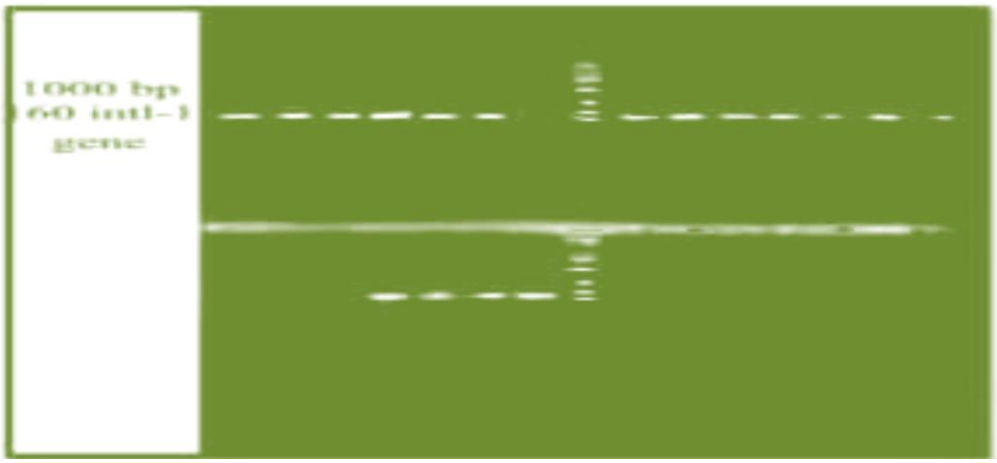

Fig. 1. Gel of agarose with red save stained of mono-plex PCR amplified product isolates DNA of isolates with intI1primer. The electrophoresis used for 120 min at 65 volt. Lane (L) is marker of DNA molecular size (10,000 –bp ladder). Lanes 2, 1, 4, 5, 3, 6, 11, 10, 12, 9, 8, 14, 13, 17, 16, 19, 18, show positive results with *intI-1* gene (160 bp)

class 1 Al-Janahi, [12]. However, several results showed that MDR has strong relationship with the spread of integrons class 1 among the isolates of *P.aeruginosa* Gu*et al*., [13] Budak *et al*., [14] Khosravi *et al*., [15] Liu *et al*., [16]. Numerous genes associated resistance are carried in integrons of class one found in the *P.aeruginosa* and the family members of *Enterobacteriaceae* Fonseca *et al.,* [17]. The detection of numerous antibiotic resistant genes in this result may be reflects the new presence XDR in isolates of this bacteria as result of the wide spreading capacity observed by these genes that happen frequently as portion of class 1 integrons structures on mobile transferable genetic factors Rojo-Bezares *et al*., [18]. Several studies reported that carbapenemases are mostly encoded in class 1 integrons along with the AMEs, are likely the transferable determinants recently having the large effect on antimicrobial therapy in the hospitals worldwide [19,20,21]. Finally, present finding observed the wide occurrence of integrons class one among XDR *P. aeruginosa* isolates in Najaf hospitals. Moreover, connection between resistance to antibiotic and the dissemination of *intI1* gene in the XDR isolates suggested integrons of class one might by important for the spreading of genes confer resistance to antibiotic among XDR isolates.

5. CONCLUSIONS

Present result showed elevated occurrence of integrons class one among XDR isolates of *P.aeruginosa*. This study has identified for the first time 17 (89.5%) isolates co-harbors *intI1* gene of integrons class one XDR *P. aeruginosa* isolates in Iraq.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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