Diabetic Patients Are Threatened By "Superbugs" *Acinetobacter baumannii* In Saudi Arabia Hospitals

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Abstract

Objectives:

Aim:
One of the greatest threat to the recent generation of antibiotics is the increasing prevalence of bacterial resistant, specially Gram-negative bacteria. *Acinetobacter baumanni* is one of the most important superbugs becoming increasingly prevalent in patients with diabetes mellitus in Middle East particularly in Saudi Arabia. We have shown that diabetic patients are more susceptible to acquire infections with these type of superbugs than the rest of the population. Carbapenem resistance in *A.baumannii* limits therapeutic options and is largely manifested by β-lactamases and metallo-β-lactamase that play a significant role in mechanisms of drug-resistance in diabetic patients. The aim is to investigate the level of threat of these pathogens to diabetics and the mechanisms of drug-resistance of patients in Saudi Arabia hospitals.

Materials and Methods: A total of 64 non-repetitive, strains collected between 2008 to 2012 from different specimens from diabetic patients from King Faisal Specialist Hospital and Research Centre, Riyadh. All isolates were identified by Vitek system. Multiplex PCR using primers for *bla*$_{OXA-51}$ combined with primers for *bla*$_{OXA-23}$, *bla*$_{OXA-24/40}$ and *bla*$_{OXA-58}$ was employed. PCR was used for detection of β-lactamase and metallo-β-lactamase genes and insertion sequences IS elements. Pulsed-field gel electrophoresis (PFGE) has been preformed. MICs was determined by dilution method.

Results:
Sixty-four clinical isolates of *A. baumannii* having *bla*$_{OXA-51-like}$ gene. All isolates were resistant to imipenem and meropenem (MIC > 16 - 32 mg/L) except four were intermediate (MIC = 8 mg/L) and Six were susceptible (MIC 0.5 - 2 mg/L) to both of them. All isolates were sensitive to tigecycline and colistin (MIC 0.5 - 2 mg/L) except four were resistant (MIC 8 - 32 mg/L) and three were intermediate to tigecycline only (MIC 4 - 8). The cause of resistance was from β-lactamase of OXA-23 and OXA-24/40 and metallo-β-lactamase *bla*$_{VIM}$ and *bla*$_{SPM}$. Fifty-nine isolates were possess the insertion sequence IS*Aba*1. PFGE showed Nine clusters of OXA-51-like enzymes.

Conclusion:
Carbapenem-resistant *Acinetobacter baumannii* is a serious superbugs threaten diabetic patients due to the circulation of β-lactamases and metallo-β-lactamase in Saudi Arabian hospitals. Furthermore, the emergence of tigecycline plus colistin resistance is causing a treatment shortfall for these patients.

to the carbapenem antibiotics specially in immuno-compromised patients [1-3]. This infection can be high world-wide but incredibly in the Middle East [4]. Diabetes mellitus has been shown to be a significant risk factor in the acquisition of serious hospital-acquired infections with *A. baumannii* than the rest of the population [5-6]. *A. baumannii* can become resistant to the carbapenems through a number of mechanisms including expression of OXA-23-like, OXA-40-like, OXA-51-like and OXA-58-like carbapenemases and expression of an acquired metallo-β-lactamase [7]. OXA-51-like, is intrinsic and naturally located in all known strains of *A. baumannii* and carbapenem resistance has sometimes been associated with this gene [8].

Aim

The purpose of this study is to investigate the prevalence of carbapenem resistance in *A. baumannii* in Saudi Arabian hospital.

Materials and Methods

- **A total of 25 non-repetitive, strains were collected between January 2011 and April 2011 from different specimens taken by King Faisal Specialist Hospital and Research Centre (KFSHRC) in Riyadh.**
- **All isolates were identified presumptively by the Vitek compact II system(5).**
- **The similarity of the genospecies group 1 (*A. calcoaceticus*), 2 (*A. baumannii*), 3 and 13TU makes the differentiation between them complex. Therefore, DNA groups 1, 2, 3, and 13TU are referred to as the *A. calcoaceticus-A. baumannii* complex.**
- **The 29 clinical isolates of *A. baumannii* were confirmed by PCR of the intrinsic gene of OXA-51-like b-lactamase by matching the appropriate size of 352bp (6).**
- **PCR was also used to identify the genes encoding the *bla*$_{OXA-23}$ (2).**
- **The MIC of antibiotics was determined by the dilution test according to BSAC guidelines(7).**

Results

Table 2: MIC values and level of resistance among *A. baumannii* isolates

Antibiotics	No. of resistant isolates	MIC range (ml/L)	Resistance
Imipenem	24	16 – 32	96 %
Meropenem	24	16 – 32	96 %
Tigecycline	3	4 – 32	12 %
Colistin	2	8	8 %

- **Twenty-five clinical isolates were identified as *A. baumannii* by having the intrinsic of *bla*$_{OXA-51-like}$ gene.**
- **Twenty-four were resistant to Imipenem (MIC > 16mg/L) and meropenem, (MIC > 32mg/L), one isolate was resistant while two were intermediate to tigecycline.**
- **Two isolates were resistant to colistin (MIC > 8mg/L).**
- **Most isolates were β-lactam antibiotics resistant.**
- **The OXA-23 β-lactamase was the cause of imipenem and meropenem-resistance in 12 strains,**
- **Ten isolates were resistant to carbapenems because of OXA-40 β-lactamase, three of which were either intermediate or resistant to tigecycline and two were also colistin resistant.**
- **Two resistant isolates had neither β -lactamase and carbapenem resistance derived from the intrinsic OXA-51 enzyme.**

Table 1: The clinical data, OXA β-lactamases group and resistant str

NO	Sex	Age	Body Site	Location	OXA's 51	OXA's 23	OXA's 40	OXA's 58	MIC IMP	MIC MER	MIC TRG	MIC CLS
1	M	2	trachea	ALMADINAH	+	+	-	-	R ≥16	R=32	S=2	S=125
2	M	10	trachea	ALMADINAH	+	+	-	-	R ≥16	R=32	S ≤ 0.5	S ≤ 0.5
3	M	18	trachea	RIYADH	+	-	-	-	S ≤ 0.5	S ≤ 0.5	S ≤ 0.5	S ≤ 0.5
4	M	23	throut	RIYADH	+	+	-	-	R ≥16	R=32	S ≤ 0.5	S ≤ 0.5
5	M	25	left- nare	KAMIS MOSAIT	+	-	-	-	R ≥16	R=32	S ≤ 0.5	S ≤ 0.5
6	F	25	trachea	RIYADH	+	-	+	-	R ≥16	R=32	S=2	S ≤ 0.5
7	F	25	abdomen	RIYADH	+	-	+	-	R ≥16	R=32	S=2	S ≤ 0.5
8	F	25	trachea	RIYADH	+	-	+	-	R ≥16	R=32	S=2	R=8
9	F	25	abdomen	RIYADH	+	-	+	-	R ≥16	R=32	S=2	S ≤ 0.5
10	F	25	trachea	RIYADH	+	-	+	-	R ≥16	R=32	I =4	S ≤ 0.5
11	F	25	mouth	RIYADH	+	-	+	-	R ≥16	R=32	S=1	R=8
12	M	30	trachea	RIYADH	+	+	-	-	R ≥16	R =32	S=1	S ≤ 0.5
13	F	32	abdomen	BREEDA	+	+	-	-	R ≥16	R ≥32	S= 2	S ≤ 0.5
14	F	35	trachea	KAMIS MOSAIT	+	+	-	-	R ≥16	R=32	S ≤ 0.5	S=1
15	F	39	trachea	RIYADH	+	+	-	-	R ≥16	R=32	S=2	S ≤ 0.5
16	F	40	trachea	ALQASEEM	+	-	-	-	R ≥16	R=32	S ≤ 0.5	S ≤ 0.5
17	M	40	left-thigh	RIYADH	+	+	-	-	R ≥16	R=32	S=2	S ≤ 0.5
18	M	40	trachea	RIYADH	+	+	-	-	R ≥16	R=32	S=2	S ≤ 0.5
19	M	40	urine-cath	RIYADH	+	+	-	-	R ≥16	R=32	S=2	S ≤ 0.5
20	M	40	abdomen	RIYADH	+	+	-	-	R ≥16	R=32	S=2	S ≤ 0.5
21	M	42	abdomen	ANAK	+	+	-	-	R ≥16	R=32	S=2	S ≤ 0.5
22	F	50	trachea	RIYADH	+	-	+	-	R ≥16	R>32	S=2	S ≤ 0.5
23	F	50	trachea	RIYADH	+	-	+	-	R ≥16	R>32	S ≤ 0.5	S ≤ 0.5
24	F	50	throut	RIYADH	+	-	+	-	R ≥16	R =32	I =4	S ≤ 0.5
25	F	50	central cath-cvc	RIYADH	+	-	+	-	R ≥16	R>32	R =32	S ≤ 0.5

IMP – Imipenem, MER – meroper … R – Resistant, I – Intermediate, S –

Conclusion

- **We show for the first time that diabetic patients with an *A. baumannii* infection are more likely than non-diabetic patients to carry a carbapenem-resistant isolate. With the prevalence of diabetes increasing, this represents a real healthcare problem as it amplifies the risk posed to diabetics from infection with *A. baumannii* [13].**
- **The increased level of carbapenems multi-resistance in *A. baumannii* responsible for infection of diabetic patients due to the circulation of the OXA-23 and OXA-40 β-lactamases, in comparable numbers, in Saudi Arabian hospitals. Furthermore, the emergence of tigecycline plus colistin resistance is causing a treatment shortfall for these patients.**
- **Further investigation would be needed to verify the genome content in such isolates.**

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