Clonal diversity of *A. baumannii* mediated by carbapenem resistance in Saudi Arabian hospitals

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Objective: To investigate the clonal diversity of multi-drug resistant *A. baumannii* associated with carbapenem resistance in hospitals of Saudi Arabia based in Riyadh city.

Methods: Sixty-two non-repetitive strains of *A. baumannii* from different specimens, collected from King Faisal Specialist Hospital and Research Centre (KFSHRC) in Riyadh were included in the study. The isolates were identified by the Vitek compact II system. Multiplex PCR using primer for bla_{OXA-51} combined with primers for bla_{OXA-23}, $bla_{OXA-24/40}$ and bla_{OXA-58} was employed. The resistance pattern of the tested isolates was determined by Vitek 2 compact system and the minimum inhibitory concentrations of imipenem, meropenem, tigecycline and colistin were determined by Etest strips. The clonal diversity of the isolates was investigated by PFGE.

Results: Carbapenem resistance was considerably high. Sixty-one out of 62 (98.4%) and 58/62(93.5%) were resistant to imipenem and meropenem, respectively. All isolates were susceptible to colistin but resistance to tigecycline was observed in 9/62 (14.5%) (Figure 1). The prevalence of bla_{OXA-23}, $bla_{OXA-24/40}$, bla_{VIM} and bla_{SPM} were 32 (51.6%), 15 (9.3%), 55 (89%) and 37 (60%), respectively (Table 2). None of the isolates had bla_{OXA-58}, bla_{IMP}, bla_{SIM} or bla_{GIM}. IS*Aba1* and IS*Aba2*, were 53 (85%) and 1(1.6%) respectively, while IS*Aba3* and IS*18* were not detected PFGE results showed that the tested isolates were clustered in twenty two groups. Clone 10 and 17 were the dominants clones containing 7 and 9 isolates respectively were from six hospitals followed by clone 14 and 18 containing 5 and 6 isolates respectively were from 6 hospitals (Figure 1).

Conclusion: It is concluded that bla_{OXA-23}, $bla_{OXA-24/40}$, bla_{VIM} and bla_{SPM} were the most prevalent genes in the carbapenem resistant *A. baumannii* isolates under investigation while IS*Aba1* was the most common insertion sequence with bla_{VIM} emerging as the chief culprit. Early recognition of the epidemic clone is very helpful to prevent its dissemination by application of strict infection control measures.

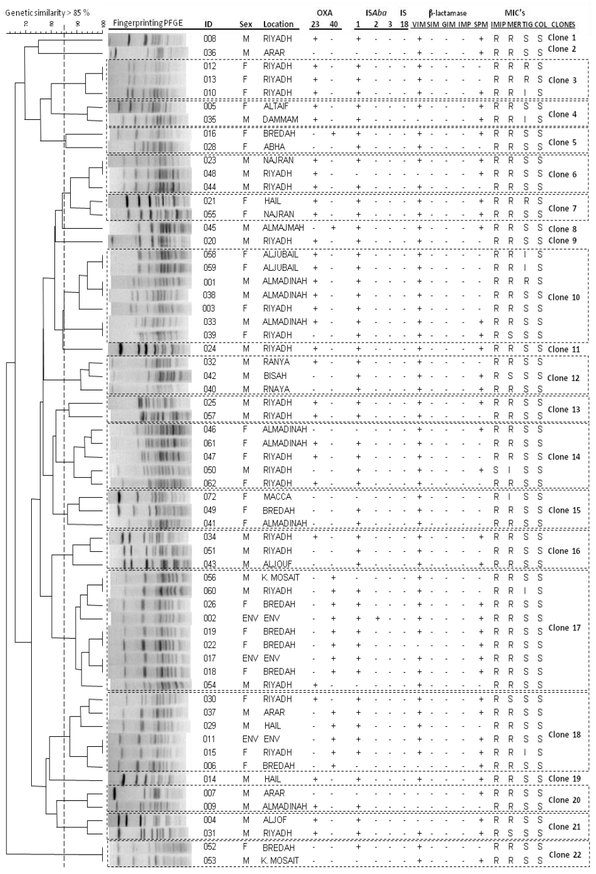

Figure 1. PFGE patterns of *A. baumannii*. Abbreviations: R, resistance; S, susceptible; I, intermediate, IMIP, imipenem; MER, meropenem; TIG, tigecycline; COL, colistin.

Gene	Number of isolates (%)
bla_{OXA-23}	32 (51.6)
bla_{OXAcc}	15 (24.2)
bla_{VIM}	55 (88.7)
bla_{SPM}	37 (59.6)
bla_{SIM}	0 (0)
bla_{IMP}	0 (0)
bla_{GIM}	0 (0)

Table 2
Prevalence of different carbapenemases in the tested isolates

Table 3
Prevalence of bla_{OXA} genes in Saudi Arabia
ND: Not Determined

Reference	Number of isolates (%) harboring		
	bla_{OXA-23}	$bla_{OXA-24/40}$	bla_{OXA-58}
Al-Arfaj et al. (2011)[12]	29/40 (72.5)	18/40 (45)	15/40 (37.5)
Ribeiro et al. (2012)[22]	16/27 (46.3)	1/27 (3.7)	ND
Shehata et al. (2012)[20]	45/118 (38)	ND	ND
Present study	32/62 (51.6)	15/62 (24.1)	0/62 (0)

Table 4
Relation between location and gender with the prevalence of different components

Variables	Location			Gender		
	Chi-square value	df	P-value	Chi-square value	df	P-value
OXA-23	29.86	16	**0.019**	1.224	1	0.269
OXA-24/40	34.24	16	**0.005**	1.740	1	0.187
IS*Aba1*	26.15	16	0.052	0.661	1	0.488
VIM	16.9	16	0.392	2.278	1	0.205
SPM	22.95	16	0.115	0.680	1	0.410
Imipenem resistance	1.665	16	1	0.858	1	1
Meropenem resistance	47.1	32	**0.042**	0.048	2	0.976
resistance	35.97	32	0.287	2.917	2	0.185

Discussions

- High level of carbapenem resistance among *A. baumannii* isolates was observed (96% against imipenem versus 93% against meropenem). Studies on carbapenem resistant *A. baumannii* in Saudi Arabia have also cited extremely high percentage resistance[1].
- Four strains (14%) were also resistant to tigecycline. Recent studies have reported an increased resistant to this antibiotic which has further narrowed down the therapeutic options.[2] The incidence of OXA type β-lactamase mediated carbapenem resistance among *A. baumannii* has been rising and several different types of OXA-like genes have been identified until now.[3]
- The prevalence of bla_{OXA-23} gene in Saudi Arabia has been in the range of 38-72.5%. The genetic clone has disseminated considerably in this country as shown in Table 3 *A. baumannii* strains bearing OXA-23 gene has also been reported to be the chief cause of carbapenem resistant worldwide[4] .
- OXA-24/40 family of OXA genes could be seen in 41% isolates in this study. OXA-24/40 in clinical isolates of *A. baumannii* has been reported in significant number.[5] Previous studies in Saudi Arabia have also documented the presence of *A. baumannii* strains carrying this gene as show in Table 4.
- Chi-square test was used to compare the locations and OXA-23, OXA-40 among them and the value of chi-square to both were significant value.
- The clonal diversity revealed two types of clones that cause an epidemic: monoclonal and polyclonal. The polyclonal is the most common clone appears in 9 of 17 cities in the Kingdom. Riyadh and Bredah affected by 12 different clones of 17, both cities were affected an explosive outbreak however at different times.
- The monoclonal model has affected eight cites of Saudi Arabia and each of these cities had only one clone that could reflect the coexistence of sporadic and epidemic clones[6] too all of these cities might have low levels of hospital infection control that may help in these outbreaks
- Henceforth, this study has pointed out that the transmission of an existing clone from one hospital to another could originate a new outbreak at these hospitals and that eventually affects health care workers. And during transmission, the possibility of *A. baumannii* transmission is highly recognized[7] that reflects the reappearance of certain clones within these hospitals. Consequently, it reinforces persistence of endemic from this pathogen in patients, hospital and environments, which, could be a major risk factor in future outbreas.

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