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P049

Does drug consumption has an influence on plasmids diffusion in CZA-resistant *Klebsiella pneumoniae* isolates?

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Introduction

Carbapenem-resistant *Klebsiella pneumoniae* strains emerged as an important cause of health care-associated infections in the last decade. Ceftazidime/avibactam (CZA) was introduced in Italy for the treatment of multi-drug-resistant gram-negative bacteria since 2018, and isolation of CZA-resistant strains of *K. pneumoniae* has been observed. Based on data on CZA consumption, the aim of this study was to analyze whether CZA-resistance could be related to the circulation of bla_{KPC} in plasmids from 2019 to 2021 in a tertiary care University Hospital.

Material and methods

CZA-resistant *K. pneumoniae* were isolated in 2019-2021 from patients admitted to the Policlinico Umberto I of Rome (Italy). The strains (n=37) were analyzed with RT-PCR (GeneXpert, Cepheid, USA), MLST and WGS (Illumina and Nanopore Technologies). CZA consumption was expressed in DDD/1000 admission.

Results

28 bla_{KPC}, with different variants, and 9 bla_{NDM} genes were detected in CZA-resistant *K. pneumoniae* isolates (Table 1.). The CZA-resistant strains belonged to different Sequence Type: ST512, ST307, ST101, ST111, ST15, ST37 (Figure 1). They acquired bla_{KPC} via identical pKpQIL plasmids, with a huge variability between the *Klebsiella* genome. In ST512 and ST111, pKpQIL was the most common plasmid; in ST307, bla_{KPC} was located on the pKpQIL-pKPN plasmid fusion; in ST101 a portion of the pKpQIL plasmid was transferred on plasmids carrying the FIA(HI1)-R replicons; in ST37 bla_{KPC} were detected on pKpQIL and pKpN (1); in ST15 bla_{NDM} were identified on IncC plasmid (2). Several strains showed increased plasmid copy number and amplification of bla_{KPC} copies. The CZA consumption expressed in DDD/1000 admissions was constantly increasing, with values ranging from 198.1 to 323.5 DDD*1000 admissions, in the period 2018-2021 (Figure 2). Since 2018, there has been a positive trend in CZA consumption.

Table 1. CZA-resistant *K. pneumoniae* strains.

Strain	Ward	ST	KPC variant	Year	Sample	MIC CZA (mg/L)	Plasmid (copy number per cell)	WGS
2	ICU	512	KPC-67	2019	BC	48	pKpQIL	Yes
4	ICU	512	KPC-49	2019	BC	12	pKpQIL (0.47x)	Yes
5	ICU	512	KPC-66	2019	BC	12	pKpQIL	Yes
6	ICU	512	KPC-29	2019	BC	24	pKpQIL (0.73x)	Yes
7	ICU	512	KPC-3	2019	BC	12	pKpQIL(0.58x)+ColRNAI (1.62x)	Yes
8	ICU	512	KPC-67	2019	BC	24	pKpQIL	
9	ICU	512	KPC-31	2019	BC	32	pKpQIL	Yes
10	ICU	101	KPC-68	2019	BC	32	FIIk-FIA(HI1)-R	Yes
11	ICU	512	KPC-67	2019	BC	16	pKpQIL	
13	ICU	512	KPC-67	2019	UR	32	pKpQIL	
14	MED	307	KPC-31	2019	RS	12	pKpQIL -pKPN	
16	ICU	101	KPC-39	2019	BC	24	FIIk-FIA(HI1)-R	Yes
17	MED	307	KPC-31	2019	BC	12	pKpQIL	Yes
18	SU	512	KPC-67	2019	UR	24	pKpQIL	
19	SU	101	KPC-66	2019	AF	12	FIIK-R + chromosome	Yes
20	ICU	512	KPC-67	2019	BC	12	pKpQIL (0.7x)	Yes
21	MED	101	KPC-31	2019	UR	>256	FIIk-FIA(HI1)-R +ColRNAI	Yes
23	HEM	307	KPC-31	2019	RS	12	pKpQIL -pKPN (1.71x)	Yes
24	HEM	512	KPC-66	2019	RS	12	pKpQIL (0.67x)	Yes
26	HEM	307	KPC-31	2019	RS	12	pKpQIL -pKPN	
27	ICU	512	KPC-67	2019	UR	24	pKpQIL	
29	ICU	512	KPC-67	2019	RS	24	pKpQIL	
30	HEM	307	KPC-31	2020	UR	12	pKpQIL -pKPN	
31	ICU	101	KPC-68	2020	BC	32	FIIk-FIA(HI1)-R	Yes
20-2	ICU	512	KPC-67	2020	UR	24	pKpQIL -pKPN (1.74x)	Yes
32	MED	512	KPC-70	2020	RTS	>256	pKpQIL (0.67x)	Yes
34	MED	111	KPC-69	2020	RS	8	pKpQIL (0.68x)	Yes
24-2	ICU	512	KPC-67	2020	WS	16	pKpQIL (0.45x)	Yes
831	ICU	15	NDM-1	2020	RTS	>256	IncC	Yes
8471	PNE	15	NDM-1	2020	RS	>256	IncC	
917	ICU	15	NDM-1	2020	RS	>256	IncC	
921	ICU	15	NDM-1	2020	RS	>256	IncC	
1017	PNE	15	NDM-1	2020	RS	>256	IncC	
1009	ICU	15	NDM-1	2020	RTS	>256	IncC	Yes
1021	PNE	15	NDM-1	2020	RTS	>256	IncC	Yes
1027	PNE	15	NDM-1	2020	RTS	>256	IncC	Yes
9065	ICU	15	NDM-1	2020	RS	>256	IncC	Yes

ICU, intensive care unit; MED, medical clinic; HEM, hematology ward; SU, surgical unit; BC, blood culture; UR, urine; RS, rectal swab; WS, wound swab; RTS, respiratory tract sample; AF, ascitic fluid; WGS, whole-genome sequencing.

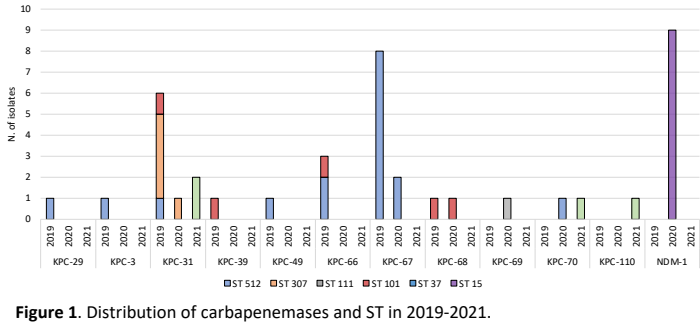

Figure 1. Distribution of carbapenemases and ST in 2019-2021.

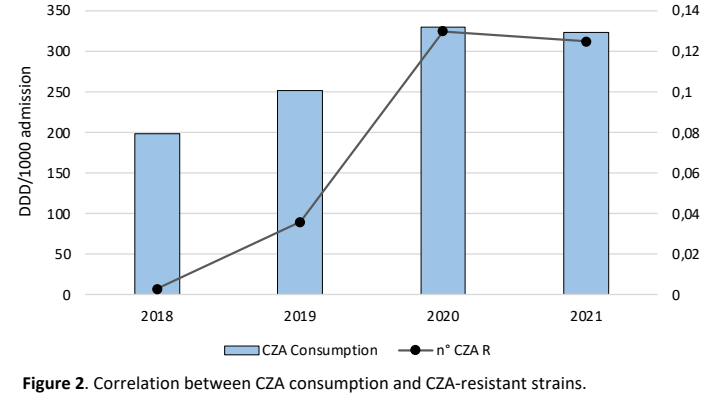

Figure 2. Correlation between CZA consumption and CZA-resistant strains.

Conclusions

In a high KPC endemicity nosocomial setting, CZA-resistance seemed to be supported by the horizontal gene transfer of pKpQIL that was highly conserved apart for the different bla_{KPC} mutated genes isolated in the observation period. Drug consumption data evidenced an intensive use of CZA during the study period inducing a constant selective pressure and most probably facilitating the emergence of CZA-resistant strains.

References

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