

MULTIDRUG RESISTANT GRAM NEGATIVE ORGANISMS IN HOSPITALIZED PATIENTS IN AN ITALIAN TERTIARY LEVEL HOSPITAL DURING COVID-19 PANDEMIA: FIRST DETECTION IS MORE FREQUENT IN CLINICAL SAMPLES THAN IN SURVEILLANCE RECTAL SWABS WITH RESPECT TO THE PREVIOUS 14-MONTH PERIOD

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BACKGROUND

- The pandemic of SARS-CoV-2 infection has placed an enormous burden on health authorities in Italy because of the rapid spread of the disease. As of October 2020, SARS-CoV-2 has caused more than 333.940 confirmed cases and the number of hospitalized people continues to rise in the medical department and in the intensive care unit [1].
- Italy has not only one of the highest number of confirmed cases of SARS-CoV-2 infection in Europe, but also the highest burden of infections due to antibiotic-resistant bacteria, with a predominant involvement of the inpatients. Carbapenem-resistant *Enterobacteriaceae* and *Acinetobacter baumannii* have now reached hyper-endemic levels and published data on carbapenemases producing *Klebsiella pneumoniae* (CPKP) diffusion in a tertiary level hospital showed that CPKP detection persisted despite an active monitoring [2].

The aim of this study was to compare the prevalence of multidrug resistant Gram-negative bacteria (MDR-GN) in surveillance rectal swabs (SRS) and in clinical samples (CS) in the period March 1, 2020 – April 24, 2020 with respect to the previous 2-month period and to the previous year, focusing on CPKP and carbapenemase-producing *Acinetobacter baumannii* (CPAB) diffusion. In the index time period, a reorganization of assistance was carried out with the opening of areas dedicated to COVID-19. We described a case series of 9 patients with COVID-19 pneumonia who had MDR-GN isolates detected despite infection control measures.

PATIENTS and METHODS

Epidemiological analysis was performed including the first SRS and the first CS with a MDR-GN isolate detected in the interval January 1, 2019 - April 24, 2020 by comparing three different study periods: January-December 2019, January-February 2020 and March-April 24, 2020: the relative prevalence of SRS and CS was described for each period both as total data and separately for Medical Department (MD), Surgical Department (SD) and the Intensive Care Department (ICD).

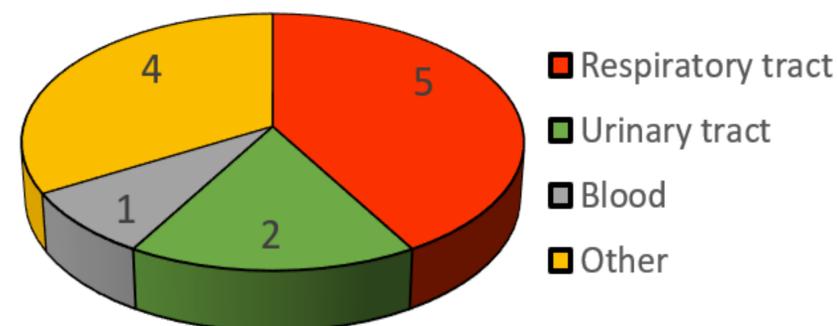


Figure 1. Description of clinical samples detected during COVID-19 pandemic

RESULTS

- 612 MDR-GN were identified (399 SRS and 213 CS): CPKP and CPAB were the most frequent MDR-GN detected in SRS and in CS (Table 1);
- An increasing trend was observed in the frequency of patients with MDR-GN detected in CS respect to those found in SRS in the 3 study periods from January 2019 to April 2020 (32.7% vs 44.5% vs 70.6%, p=0.0005): 5/12 CS detected in the last period were isolated from the respiratory tract (Figure 1);
- Nine patients (median age 69 years, IQR 61-76 years) with SARS-CoV-2 infection had MDR-GN detected in SRS (2 patients), in CS (3 patients) and in SRS and CS at the same time (4 patients). Carbapenemases detected were KPC and OXA-23. All but two patients had a previous negative SRS performed 4 days before (median value, IQR 3-7 days) and the median interval between SARS-CoV-2 positivity and MDR-GN positivity was 7 days (IQR 4-16 days);
- The six patients with CPAB isolation were all hospitalized in the same ward, with partially overlapping hospital stays during the study period. In five of them, CPAB was firstly detected in the respiratory tract (in all cases after a previous negative result). In the sixth subject a blood culture turned positive after a urethral positivity (Table 2).

Table 1. Description of CPKP, CPAB and of other MDR-GN strains isolated in SRS (a) and in CS (b) from Jan 1, 2019 to Dec 31 (period A) from Jan 1, 2020 to Feb 29, 2020 (period B) and from Mar 1, 2020 to Apr 24, 2020 (period C). Data are reported by absolute numbers and percentage respect to the total number of isolates detected in SRS or in CS in the specific department.

a) Surveillance rectal swabs	Medical Department			Surgery Department			Intensive Care Department			Total		
	Period A	Period B	Period C	Period A	Period B	Period C	Period A	Period B	Period C	Period A	Period B	Period C
All patients, n	108	11	1	161	10	0	95	9	4	364 (60/bimes ter, mean)	30	5
<i>Acinetobacter baumannii</i> , n	36 (33.3)	0	0	30 (18.6)	1 (10)	0	36 (37.9)	8 (88.9)	1 (25)	102 (28)	9 (30)	1 (20)
<i>Klebsiella pneumoniae</i> , n	51 (47.2)	10 (90.9)	1 (100)	106 (65.8)	7 (70)	0	44 (46.3)	1 (11.1)	3 (75)	201 (55.2)	18 (60)	4 (80)
<i>Pseudomonas aeruginosa</i> , n	11 (10.2)	1 (9.1)	0	14 (8.7)	1 (10)	0	7 (7.4)	0	0	32 (8.8)	2 (6.7)	0
Others, n	10 (9.3)	0	0	11 (6.8)	1 (10)	0	8 (8.4)	0	0	29 (8)	1 (3.3)	0

b) clinical samples	Medical Department			Surgery Department			Intensive Care Department			Total		
	Period A	Period B	Period C	Period A	Period B	Period C	Period A	Period B	Period C	Period A	Period B	Period C
All patients, n	70	10	3	33	7	2	74	7	7	177 (29/bimes ter, mean)	24	12
<i>Acinetobacter baumannii</i> , n	32 (45.7)	6 (60)	0	4 (12.1)	2 (28.6)	0	27 (36.5)	4 (57.1)	7 (100)	63 (35.6)	12 (50)	7 (58.3)
<i>Klebsiella pneumoniae</i> , n	14 (20)	2 (20)	2 (66.7)	11 (33.3)	3 (42.9)	1 (50)	33 (44.6)	1 (14.3)	0	58 (32.8)	6 (25)	3 (25)
<i>Pseudomonas aeruginosa</i> , n	15 (21.4)	1 (10)	1 (33.3)	17 (51.5)	2 (28.6)	1 (50)	11 (14.9)	2 (28.6)	0	43 (24.3)	5 (20.8)	2 (16.7)
Others, n	9 (12.9)	1 (10)	0	1 (3)	0	0	3 (4.1)	0	0	13 (7.3)	1 (4.2)	0

Table 2. Description of the characteristics of the carbapenemase producing *Klebsiella pneumoniae* (CPKP), carbapenemase producing *Acinetobacter baumannii* (CPAB) and of other MDR-GN strains detection in patients with COVID-19 pneumonia

Patient	Isolates	Dept	Site of the first MDR-GN detection	Interval between COVID-19 detection and MDR-GN isolation	Interval between previous negative SRS and first MDR-GN detection	Interval between previous negative CS and first MDR-GN detection in the same site	Other positive sites of MDR-GN
Pt 1 (M, 62 y)	CPAB (OXA-23)	ICD	SRS + Upper respiratory tract	9 days	7 days	7 days	Lower respiratory tract + Blood
Pt 2 (M, 54 y)	CPKP (OXA-23)	ICD	SRS	4 days	Not tested	Not applicable	Upper and lower respiratory tract + Urinary tract
Pt 3 (M, 62 y)	CPAB (OXA-23)	ICD	SRS + Upper and lower respiratory tract	7 days	4 days	4 days	-
Pt 4 (M, 78 y)	CPKP (KPC)	ICD	SRS	2 days	Not tested	Not applicable	-
Pt 5 (M, 76 y)	CPAB (OXA-23)	ICD	SRS + Lower respiratory tract	13 days	4 days	4 days	Blood
Pt 6 (M, 69 y)	CPAB (OXA-23)	ICD	Urethral swab	25 days	2 days	Not tested	SRS + Blood
Pt 7 (F, 60 y)	CPAB (OXA-23)	ICD	Lower respiratory tract	4 days	5 days	4 days	SRS + Blood
Pt 8 (M, 71 y)	CPAB (OXA-23)	ICD	SRS + Lower respiratory tract	31 days	12 days	8 days	Urethral swab
Pt 9 (M, 82 y)	PSAE	MD	Skin	6 days	1 day	Not tested	-

CONCLUSION

The first detection of MDR-GN in CS and the nosocomial MDR-GN acquisition despite cohorting due to COVID-19 infection and strict droplet and contact precautions underline the need to reinforce infection control measures, even within these dedicated areas, in a high prevalence country.

The decrease observed in MDR-GN detection from March 1, 2020 was possibly not due to an attention shift, but to the reorganization and reduction of other healthcare-related activities.

A correct antimicrobial policy urged because most patients with COVID-19 infection received antimicrobial therapy. Furthermore, MDR-GN infection could play a role in the negative outcome of these patients.

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