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EMERGENCY OF NDM-PRODUCING ENTEROBACTERALES ON COMPANION ANIMALS IN ARGENTINA

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Carbapenem-resistant Enterobacterales (CRE) are an emerging risk in many regions of the planet. Reports of CRE are increasing in companion animals and constitute a serious threat to animal health as CRE-associated infections have high mortality and limited treatment options. This study aims to report the emergence of NDM-producing Enterobacterales isolated from clinical samples of companion animals in Argentina.

Between Nov. 2021 and Jul. 2022, 19/3937 Enterobacterales suspected of producing carbapenemases were isolated in Diagnostest Laboratory and referred to the NRL for molecular characterization. Bacterial identification was performed by VITEK2 (BioMérieux) and confirmed by MALDI-TOF (Bruker Daltonics). Antimicrobial susceptibility was determined by VITEK2, E-test strips (BioMérieux) and/or Kirby-Bauer method, and interpreted according to CLSI (M100 or VET01S) and EUCAST. PCR was used to confirm resistance genes. The genetic relatedness among isolates was evaluated by XbaI-PFGE.

Identification was confirmed as *K. pneumoniae* (n=9), *E. coli* (n=6) and *E. cloacae* complex (n=4). Isolates were recovered from nine felines and ten canines (13 ambulatories and 6 hospitalized patients) in ten veterinary hospitals located in Buenos Aires (n=6) and Buenos Aires City (n=13). Isolates were recovered from urine (n=11), abdominal fluid (n=2), bone (n=2), gallbladder (n=2), abscess (n=1) and lung (n=1) samples. Isolates presented resistance to β -lactams, including carbapenems, aminoglycosides, ciprofloxacin and trimethoprim/sulfamethoxazole (Table 1). *bla*_{NDM} was confirmed in all isolates. Additionally, 17 of 19 isolates co-produced *bla*_{CTXM} and *bla*_{CMY} genes. Genetic diversity was observed by PFGE, although some major pulsotypes were observed in *E. coli* and *K. pneumoniae*.

We report the emergence of NDM-producing Enterobacterales in companion animals in Argentina, indicating that the circulation of CRE in our country is no longer limited to humans but also to companion animals. It is necessary to strengthen the tools for diagnosis, surveillance, and control of CRE to prevent the dissemination of these mechanisms in the context of One Health.

Key words: carbapenemase, companion animals, antimicrobial resistance, NDM

Table 1. Epidemiological, phenotypic and genotypic data of Enterobacterales carbapenemase-producing from companion animals

ID	Organism ^a	Host	Source	Jurisdiction ^b	Veterinary Hospital	Isolation date	Hospitalized/ Ambulatory	Xbai-PFGE type	Carbapenemase gene	ESBL/AmpC	Antimicrobial
											resistance profile ^{c,d}
M27828	<i>Ecl</i>	Canine	Gallbladder	Bs. As. City	D	3/26/22	Ambulatory	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, FOS
M27733	<i>Ecl</i>	Feline	Lung	Bs. As. City	J	1/15/22	Ambulatory	B	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, GEN, AMK, SXT, CHL, DOX, MIN, TGC, NIT
M27716	<i>Ecl</i>	Feline	Bone	Bs. As. City	E	12/17/21	Ambulatory	C	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	C3G, IMP, MEM, ETP, ATM, CZA, CIP, GEN, AMK, SXT, CHL
M27897	<i>Ecl</i>	Feline	Urine	Bs. As. City	C	3/4/22	Ambulatory	D	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	C3G, IMP, MEM, ETP, ATM, CZA, CIP, GEN, AMK, SXT, CHL, DOX, MIN
M27974	<i>Eco</i>	Feline	Gallbladder	Bs. As. City	B	4/27/22	Hospitalized	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMP, AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, MIN
M27987	<i>Eco</i>	Feline	Urine	Bs. As.	H	5/4/22	Ambulatory	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMP, AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, MIN
M27788	<i>Eco</i>	Canine	Urine	Bs. As. City	J	2/18/22	Ambulatory	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMP, AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, MIN
M27717	<i>Eco</i>	Canine	Bone	Bs. As.	F	11/30/21	Hospitalized	B	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMP, AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, GEN, AMK, SXT, DOX, MIN
M27739	<i>Eco</i>	Feline	Urine	Bs. As. City	B	1/6/22	Ambulatory	C	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMP, AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK
M27948	<i>Eco</i>	Feline	Abdominal fluid	Bs. As. City	D	4/22/22	Hospitalized	D	<i>bla</i> _{NDM}	<i>bla</i> _{CMY}	AMP, AMC, FOX, C3G, IMP, MEM, ETP, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX
M27738	<i>Kpn</i>	Canine	Urine	Bs. As. City	B	1/15/22	Ambulatory	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, MIN, NIT, FOS
M27715	<i>Kpn</i>	Feline	Urine	Bs. As. City	G	12/3/21	Ambulatory	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, DOX, NIT
M27649	<i>Kpn</i>	Canine	Urine	Bs. As.	I	10/16/21	Hospitalized	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, DOX, NIT
M28114	<i>Kpn</i>	Canine	Urine	Bs. As.	I	6/19/22	Ambulatory	A	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, DOX, NIT
M28115	<i>Kpn</i>	Canine	Abdominal fluid	Bs. As. City	J	7/25/22	Hospitalized	G	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, NIT, FOS
M27789	<i>Kpn</i>	Canine	Urine	Bs. As. City	J	2/8/22	Ambulatory	B	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, ETP, CZA, CIP, GEN, AMK, SXT
M27986	<i>Kpn</i>	Canine	Urine	Bs. As. City	B	5/5/22	Hospitalized	C	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, MIN, NIT
M28019	<i>Kpn</i>	Canine	Abscess	Bs. As.	A	5/21/22	Ambulatory	D	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, CHL, DOX, MIN, NIT
M28018	<i>Kpn</i>	Feline	Urine	Bs. As.	A	5/26/22	Ambulatory	F	<i>bla</i> _{NDM}	<i>bla</i> _{CTXM} + <i>bla</i> _{CMY}	AMC, FOX, C3G, IMP, MEM, ETP, ATM, CZA, CIP, ENR, MAR, GEN, AMK, SXT, DOX, NIT, FOS

^a *Ecl* : *E. cloacae* complex , *Eco*: *E. coli* , *Kpn*: *K. pneumoniae*

^b Bs. As : Buenos Aires

^c Natural resistance to ampicillin in *K. pneumoniae* and to ampicillin, ampicillin/clavulanic acid and cefoxitin in *Enterobacter cloacae* complex have been omitted from the antimicrobial resistance profile.

^d AMP: Ampicillin, AMC: Amoxicillin/Clavulanic acid, FOX: Cefoxitin, C3G: Third generation cephalosporins, IMP : Imipenem, MEM: Meropenem, ETP: Ertapenem, ATM: Aztreonam, CZA:

Ceftazidime/Avibactam, CIP: Ciprofloxacin, ENR: Enrofloxacin, MAR : Marbofloxacin, GEN: Gentamicin, AMK: Amikacin, SXT: Trimethoprim/Sulfamethoxazole, CHL: Chloramphenicol, DOX: Doxycycline, MIN: Minocycline, TGC: Tigecycline, NIT: Nitrofurantoin, FOS: Fosfomicin.