Sinks at the ICU are reservoirs of antimicrobial resistance: a putative risk for critically ill patients?

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Background

Antimicrobial resistance (AMR) threatens public health and healthcare around worldwide. Especially extended-spectrum β-lactamase- (ESBL-) and carbapenemase-producing Enterobacterales (CPE) compromise clinical treatment and have been identified as priority pathogens by the WHO[1]. Dissemination of AMR genes via horizontal gene transfer (HGT) could increase the number and level of resistant bacteria. Previously, a genetic resistance element (GRE) was identified where 14 AMR genes associated with each other in a 48kb region, conferring resistance to seven classes of antibiotics and causing multiple hospital outbreaks[2, 3]. Presence of AMR bacteria and genes in the environment could pose a threat to vulnerable patients. Therefore, possible environmental reservoirs of AMR bacteria and genes in the hospital should be investigated to mitigate the spread of AMR and maintain safe healthcare.

Objective

Investigate possible reservoirs of antimicrobial resistance in the clinical environment of the intensive care unit (ICU) and the risk for vulnerable patients.

Conclusions

- Sink drains form reservoirs for AMR bacteria with stable presence of ESBL-containing isolates over time.
- The complete GRE was absent at the ICU, indicating a limited risk patient health.
- Environmental reservoirs include bacteria of potential clinical origin, while no direct spread from reservoir to patient has been observed on the ICU.
- Acquisition of AMR genes could result in additional resistances, creating isolates that could form putative risks. Therefore, future research should investigate the case with clonal ESBL and CPE isolates and elucidate the possibility of HGT within bacterial reservoirs.

Methods

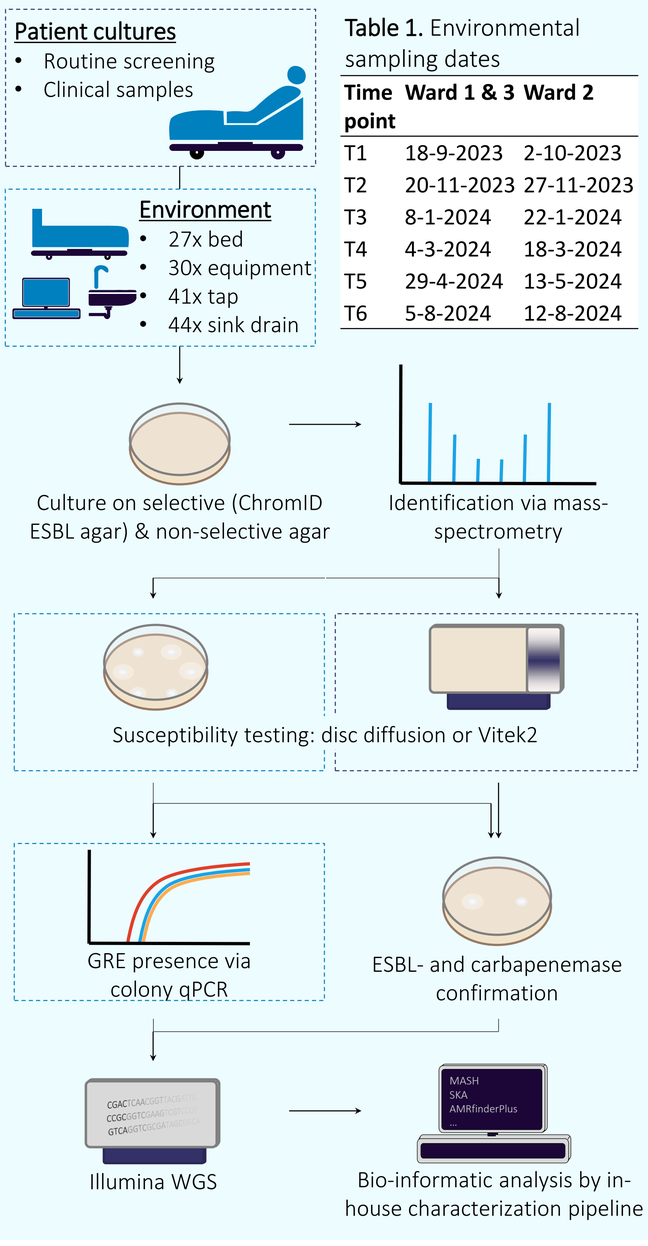

Table 1. Environmental sampling dates

Time point	Ward 1 & 3	Ward 2
T1	18-9-2023	2-10-2023
T2	20-11-2023	27-11-2023
T3	8-1-2024	22-1-2024
T4	4-3-2024	18-3-2024
T5	29-4-2024	13-5-2024
T6	5-8-2024	12-8-2024

Results

Sink drains contain multidrug-resistant bacteria with ESBL and carbapenemase genes.

Table 2. The number of environmental isolates with confirmed ESBL, carbapenemase production, or GRE presence according to culture, WGS, and PCR (3/3 PCR targets) per time point and as total with the percentage of ESBL and carbapenemase genes present in the WGS data. No sequenced isolates contained all GRE genes, lacking *aac(6')-Ib-cr* and *aph(3')-Ib* in 99% of the isolates.

		T1	T2	T3	T4	T5	T6	Total
ESBL	# isolates cultured	11	22	20	21	18	25	117
	# isolates sequenced	4	14	9	12	12	18	69
	% *blaCTX-M-15*	*33,3*	*47,6*	*25,0*	*47,8*	*12,5*	*38,1*	*34,2*
	% *blaCTX-M-9*	*16,7*	*0,0*	*12,5*	*0,0*	*25,0*	*4,8*	*9,4*
	% *blaOXY* (1, 2, 5, 6)	*50,0*	*52,4*	*37,5*	*43,5*	*41,7*	*52,4*	*46,2*
Carbapenemase	# isolates cultured	1	2	7	7	10	6	32
	# carbapenemase containing isolates (WGS)	0	1	3	6	9	4	23
	% *blaNDM*(-7)	*0,0*	*0,0*	*33,3*	*33,3*	*66,7*	*75,0*	*52,2*
	% *blaOXA*(-48 & -427)	*0,0*	*0,0*	*0,0*	*33,3*	*0,0*	*25,0*	*13,0*
	% *blaVIM2*	*0,0*	*0,0*	*66,7*	*33,3*	*33,3*	*0,0*	*30,4*
GRE	#PCR+	3	12	4	11	3	8	41

Clonal environmental isolates persist over time in sample sink drains

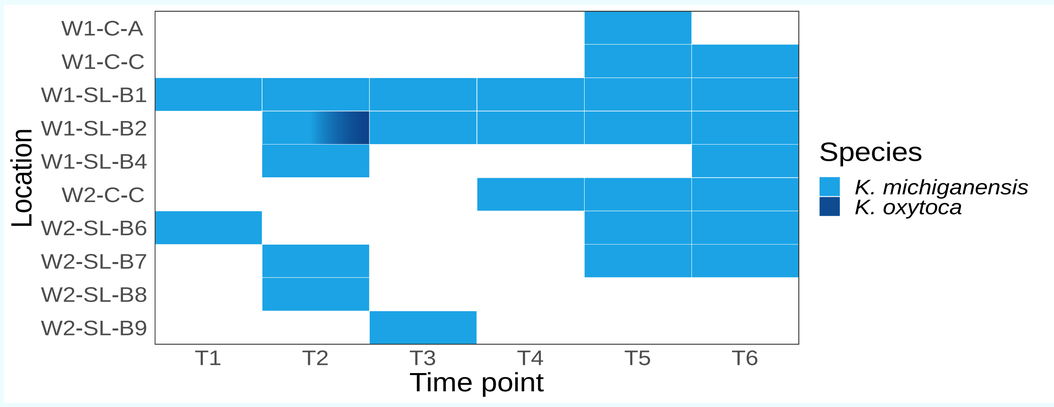

Figure 1. Prevalence of a cluster of clonal ESBL *Klebsiella* spp. (<20 SNPs) in sink drains on two wards (W1, W2), in the central (C) or sluice room (SL) in different sink drains (-A, -C) or patient rooms (B). Five other environmental clusters also showed clonality between various sample locations and time points.

Clinical and environmental isolates can be clonally related, with and without clear epidemiological links

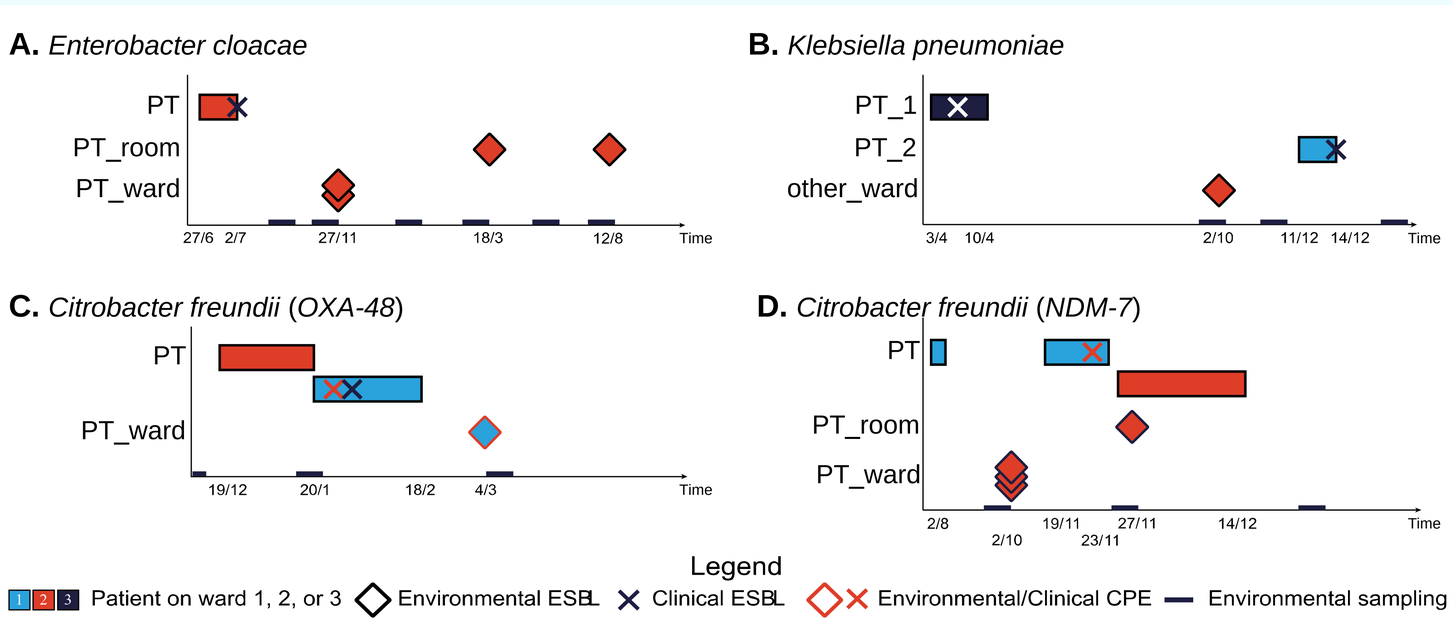

Figure 2. Time of patient (PT) admission with dates of environmental sampling and culture of clinical and environmental isolates carrying ESBL (black or white outline) or CPE genes (orange outline) with location of origin on ward 1, 2, and 3 and patient room (PT_room). Two clusters (A,C) demonstrate environmental contamination after patients admission, while two clusters (B,D) show no direct epidemiological link. Moreover, environmental *CTXM-15*-containing ESBL isolates clustered with a *NDM-7*-containing clinical CPE isolate (D).

References

1. WHO, *WHO Bacterial Priority Pathogens List, 2024*. 2024, Geneva: World Health Organization.
2. Jamin, C., *The molecular-matryoshka phenomenon: peeling the layers of spread of antimicrobial resistance genes*. 2023, Maastricht: Maastricht University.
3. Van der Zwet, WC., *Role of the environment in transmission of Gram-negative bacteria in two consecutive outbreaks in a haematology-oncology department*. 2022, Maastricht.

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