First report of CrpP prevalence in a South American country

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Abstract

The presence of *crpP* was established in 201 *Pseudomonas aeruginosa* isolates from 9 Peruvian hospitals. The 76.6% (154/201) of the isolates presented the *crpP* gene. Overall, 123/201 (61.2%) isolates were non-susceptible to ciprofloxacin. The prevalence of *crpP*-possessing *P. aeruginosa* in Peru is higher than in other geographical areas.
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Since first description in 1998 the detection of transferable mechanisms of quinolone resistance (TMQR) has growing worldwide [1]. In 2018, CrpP, a new TMQR was reported [1]. While controversial, CrpP is a phosphorylase which has been proposed to be able to inactivate several quinolones, including ciprofloxacin, resulting in a modest increase in resistance levels [1,2].

Most of the studies describing presence/prevalence of CrpP have been developed in high-income countries or analysing GenBank content [3–5], while data about from low- and middle-income countries, including South American countries, is scarce or absent. This study aimed to determine the prevalence of *crpP* in *P. aeruginosa* clinical isolates from Peruvian hospital settings.

Two-hundred one *P. aeruginosa* isolates from 9 Peruvian hospitals collected in 2016 and 2020-2021 were analysed. Bacterial identification and susceptibility to ciprofloxacin were determined by automated methods and confirmed by disk diffusion. Intermediate and resistant isolates were classified together as non-susceptible isolates.

A 177 bp *crpP* fragment was detected by PCR using previously described primers (5'-CGACCGGTACCGACAAGCTGGAC-3' and 5'-CGAGCTGCTGTTGCTGCTCCTGG-3') [6], and the conditions: 95°C-5min +30x(94°C-30sec, 64°C-30sec and 72°C-30sec) + 72°C-7min). Randomly selected PCR products were recovered and sequenced.

Statistical analysis was performed using the Fisher exact test, with a p value < 0.05 being considered statistically significant.

The *crpP* gene was present in 154/201 (76.6%) isolates, with those collected in 2016 presenting a significantly lower percentage compared to those collected in 2020-2021 (64.9% vs. 83.5%; p = 0.0034).

Overall, 123/201 (61.2%) isolates were non-susceptible to ciprofloxacin, but no significant association between the presence of *crpP* and resistance to ciprofloxacin was observed.

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TABLE 1. Association between CrpP and resistance to ciprofloxacin

					Ciprofloxacin				
					R (N = 123)		S (N = 78)		
Hospital	**City**	**Peru**	**Year**	**N**	**CrpP+**	**CrpP-**	**CrpP+**	**CrpP-**	***p***
HMC	Lima	Center	2016	74	45	3	23	3	NS
HMA	Lima	Center	2021	42	21	1	15	5	BS
HJCH	Piura	Northern	2021	39	21	2	13	3	NS
INMP	Lima	Center	2020-2021	13	6	1	5	1	NS
CD	Lima	Center	2021	13	3	8	1	1	NS
OC	Lima	Center	2021	7	3	1	2	1	NS
OS	Lima	Center	2021	5	3	0	0	2	—
CB	Callao	Center	2021	3	3	0	0	0	—
CM	Piura	Northern	2021	2	1	0	1	0	—
ND [1]	—	—	2021	3	1	0	1	1	—
Overall				**201**	**107**	**16**	**61**	**17**	**NS**
			2016	74	45	3	23	3	NS
			2020-2021	127	62	13	38	14	NS

R: Resistant; S: Susceptible; N: Number; HMC: Hospital Militar Central; HJCH: Hospital Jose Cayetano Heredia; HMA: Hospital María Auxiliadora; INMP: Instituto Nacional Materno Perinatal; CD: Clinica Delgado; OC: Oncocenter; OS: Oncosalud; CB: Clinica Bellavista; CM: Clinica Miraflores; ND: No data recorded; BS: Barely significant ($p = 0.0866$) NS: no significant.
Statistics were only established when $N \geq 10$.
[1] In these 3 cases, data of exact hospital settings were no recorded in database.

Nevertheless, the percentage of isolates carrying the *crpP* gene was clearly higher among ciprofloxacin non-susceptible isolates (86.7% vs 78.2%).(see Table 1).

A study analysing European clinical isolates of *P. aeruginosa* collected between 2000 and 2015, showed that *crpP* was present in 46% of isolates [4]. Along the same line, 58/228 (25.4%) Chinese *P. aeruginosa* isolates collected in 2017-2018 presented *crpP* [5]. Furthermore, a previous study analysing the prevalence of *crpP* among whole *P. aeruginosa* genomes recorded in GenBank showed that 61.9% of these genomes contained a *crpP* gene [5]. The present data show a current higher prevalence of *crpP* in Peru, which might be related to the singularities of circulating *P. aeruginosa* in the area, and suggesting a silent increase in the prevalence of *crpP*-possessing *P. aeruginosa* in the last years.

The non-association between the presence of *crpP* and non-susceptibility to ciprofloxacin while agrees with proposed inability of CrpP to inactivate ciprofloxacin [2], might be related to the sample size the high levels of ciprofloxacin non-susceptibility, and the specificities of isolates from *Clinica Delgado*. Thus, if these isolates were unconsidered, the presence of *crpP* will be significantly higher among ciprofloxacin non-susceptible isolates ($p = 0.0070$).

In summary, the prevalence of *crpP*-possessing *P. aeruginosa* in Peru is higher than that previously observed in other geographical areas or analysing whole GenBank, and increasing in recent years. Further studies in both Peru and other South American countries are needed to establish the regional prevalence of *crpP*-producing *P. aeruginosa*.

Authorship criteria

JR: Conceptualization and design, Formal analysis, Funding acquisition, Writing - original draft, Writing - review & editing. **KO**: Investigation, Writing - review & editing. **GS-J**: Investigation, Resources, Writing - review & editing. **YVR**: Investigation, Writing - review & editing. **ACG**: Investigation, Writing - review & editing. **CV-K**: Investigation, Resources, Writing - review & editing. **ADB-C**: Investigation, Resources, Writing - review & editing. **GS**: Investigation, Resources. **JAP**: Resources, Writing - review & editing. **MR-C**: Resources, Writing - review & editing. **JL**: Resources, Writing - review & editing. **MR**: Investigation, Resources, Writing - review & editing. **MJP**: Conceptualization and design, Investigation, Writing - review & editing.

Declaration of competing interest

The authors declared no conflicts of interest.

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