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Surveillance of *Helicobacter pylori* resistance over 22 Years (2000-2021) in Northern Spain

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ABSTRACT

Objectives: *Helicobacter pylori* gastritis is considered an infectious disease, regardless of symptoms and stage of disease. Most consensus documents recommend empirical therapy based on local antimicrobial susceptibility patterns. We aimed to provide clinically useful information about primary and secondary antimicrobial resistance to antimicrobials commonly prescribed for *H. pylori*.

Methods: Overall, 31,406 gastroduodenal biopsies and 2,641 string tests from patients over 15 years of age were plated on selective media, isolating *H. pylori* in 36.7% of biopsies and 50.7% of string tests. Susceptibility testing could be performed in 96.6% (12,399/12,835) of *H. pylori* isolates. Polymerase chain reaction (PCR) was also used to detect *H. pylori* and its resistance to clarithromycin, providing susceptibility data for 112 patients with negative culture results.

Results: Resistance to amoxicillin and tetracycline was unusual (0.6% and 0.2%, respectively). Rates of primary resistance to clarithromycin and metronidazole remained steady over the 22-year study period, at around 14% for clarithromycin and 30% for metronidazole, while primary resistance to levofloxacin tripled (from 7.6% in 2000 to 21.7% in 2021, $P < 0.001$) and increased with patient age. Notably, 1.8% of isolates were multiresistant to clarithromycin, metronidazole, and levofloxacin. Overall, secondary resistance rates were higher ($P < 0.0001$) than primary resistance rates for clarithromycin (42.5% *vs* 14.1%), metronidazole (40.9% *vs* 32%), and levofloxacin (21.5% *vs* 17.1%).

Conclusion: Determination of susceptibility for *H. pylori* by culture and/or PCR in patients undergoing endoscopy could facilitate the implementation of tailored therapy and guide the choice of empirical therapy when susceptibility testing cannot be performed, potentially helping limit the emergence of antimicrobial resistance.

1. Introduction

Helicobacter pylori (*H. pylori*) has a worldwide distribution, with a high prevalence in Africa, Asia, Latin America, and the Caribbean, while a lower prevalence of infection has been documented in Europe, the USA, and Oceania [1]. *Helicobacter pylori* is a microaerophilic bacterium that infects the gastroduodenal mucosa

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causing gastritis, gastric and duodenal ulcer, gastric cancer, and gastric mucosa-associated lymphoid tissue lymphoma. The infection is also related to extragastrointestinal diseases such as unexplained iron-deficiency anaemia, idiopathic thrombocytopenic purpura, or idiopathic chronic urticaria, among others [2]. The World Health Organization (WHO) warned in 1994 of the oncogenic role of *H. pylori*, and in 2017, highlighted it as one of the resistant bacteria for which there is an urgent need for new treatments at a global level because of its resistance to clarithromycin (CLA) [3].

For the management of the *H. pylori* infection, an important recommendation included in the Kyoto global consensus report, Maastricht VI/Florence Consensus Report, and the 2017 American College of Gastroenterology Clinical guidelines [4–6] is that all infected individuals should be treated and then retested to confirm the successful eradication of the bacteria. For children, the ESPGHAN/NASGHAN guidelines recommend an antimicrobial susceptibility-guided eradication therapy regimen [7]. In contrast, for adults, most consensus recommendations are based on empirical therapy based on local susceptibility patterns, arguing that *H. pylori* culture is troublesome and time-consuming [4,8–10].

Gastroduodenal biopsy culture has a sensitivity of 80–95%; histological diagnosis is the gold standard [11] and has the advantage of allowing susceptibility testing of the infecting strain to any antibiotic, and accordingly, prescribing tailored therapy which helps to achieve an *H. pylori* eradication rate of greater than 90% [7,8]. Molecular methods are an alternative to detect *H. pylori*, showing sensitivity and specificity above 95% [11].

In accordance with the need for monitoring of this pathogen, the primary aim of this study was to provide clinically useful information on rates of primary and secondary resistance of *H. pylori* to CLA, metronidazole (MTZ), and levofloxacin (LEV) over a long period [2000–2021] in an area where culture and susceptibility testing are performed routinely. The secondary aims were to describe the usefulness of performing culture to guide the design of future treatment protocols as well as to investigate the possible impact of this strategy on the pattern of antimicrobial resistance rates.

2. Materials and methods

2.1. Ethics statement

This study was undertaken with approval from the Ethics Committee of Donostia University Hospital (MGA-HEL-2022–01).

2.2. Patients and samples

The study was a retrospective analysis of the *H. pylori* culture carried out between 2000 and 2021 in the microbiology laboratory at Donostia University Hospital (HUD), located in Gipuzkoa, Basque Country, northern Spain, which attends a population of ca. 650,000 inhabitants.

The study included all gastroduodenal biopsies (n = 31,406) from patients over 15 years of age who had undergone upper endoscopy prescribed by their physician to rule out *H. pylori* infection as well as all string-test specimens (n = 2,641). Samples from the HUD were received in a container with saline solution, whereas biopsies from outside the HUD (Zumarraga, Mendaro, and Bidasoa regional Hospitals, and Gros and Amara Berri primary care centres) arrived within 24 h of collection in specific transport medium (Portagerm pylori, PORT-PYL, bioMèrieux, Marcy-l'Étoile, France). String-test samples were taken in the microbiology laboratory using the Entero-test (HDC Corp, Mountain View, CA). The string was placed on an empty Petri plate and processed immediately.

2.3. Culture

Gastroduodenal biopsies were cultured immediately on arrival to the laboratory on Brucella agar plates (BBL, Becton Dickinson, Madrid, Spain) supplemented with 5% hemolyzed horse blood and 1% Vitox (Oxoid Ltd, Basingstoke, UK) supplemented with trimethoprim 5 µg/mL and vancomycin 15 µg/mL until 2013 and on marketed selective plates (Pylori Agar; bioMèrieux, Marcy-l'Étoile, France) from 2014–2021. Plates were incubated under microaerophilic conditions (2%H_2, 5% O_2, 7% CO_2, and 86% N_2) at 37°C with 80% humidity for at least 7 days before discarding them as negative. Colonies have been identified as *H. pylori* using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF-MS, MALDI Biotyper®, Bruker Daltonics) since 2015 and previously, based on the morphology of the colony, Gram stain, and catalase, oxidase and urease tests.

2.4. String test

String test was performed in the laboratory when requested by the physician, on some occasions in patients who had previously undergone an endoscopy [12,13]. The end and medium parts of the string were cultured using selective media under the same conditions as the gastroduodenal biopsies. String test was performed using the Entero test kit until 2013 when this kit was taken off the market.

2.5. Polymerase chain reaction (PCR)

From 2015 onwards, nucleic acids were extracted from the same biopsy sample as that used for culture to perform a PCR, which allows partial detection of the 23S rRNA gene of *H. pylori* and sequencing to detect mutations involved in macrolide resistance, as described by Menard et al. [14]. This PCR performed from biopsies was validated in our laboratory by Tamayo et al. [15], who assessed the correlation between the susceptibility data obtained by biopsy culture with susceptibility testing and those obtained by molecular methods using the same gastric biopsy after being plated. In those biopsies in which culture was negative but *H. pylori* was detected by molecular methods (PCR), susceptibility to clarithromycin was assessed by sequencing of the 23S rRNA gene amplicon. The use of *H. pylori* PCR was discontinued in the laboratory in February 2020 because of an overload of molecular methods work associated with the SARS-CoV-2 pandemic and only restarted after the end of the study period.

2.6. E-test susceptibility testing

Helicobacter pylori isolates were obtained from gastroduodenal biopsies or string tests under the culture conditions described above. Antimicrobial susceptibility testing was performed from a McFarland 2.0 *H. pylori* suspension in saline solution using E-test strips (bioMèrieux SA). Plates were incubated for 72 h under the aforementioned conditions. The medium used was Brucella agar plates supplemented with 5% hemolyzed horse blood and 1% Vitox (Oxoid Ltd, Basingstoke, UK) from 2000–2015, and, from 2016–2021, Mueller-Hinton agar plates with 5% sheep blood (Becton Dickinson GmbH, Heidelberg, Germany) was used. Antimicrobial susceptibility was performed for clarithromycin (CLA), levofloxacin (LEV), metronidazole (MTZ), amoxicillin (AMX), and tetracycline (TET). The National Committee for Clinical Laboratory Standards recommended susceptibility breakpoint criteria were followed until 2012 [16], and subsequently, those published by the European Committee on Antibiotic Susceptibility Testing (EUCAST Clinical Breakpoint Tables v.9.0) http://www.eucast.org/clinical_breakpoints/). Isolates with CLA minimum inhibitory concentrations

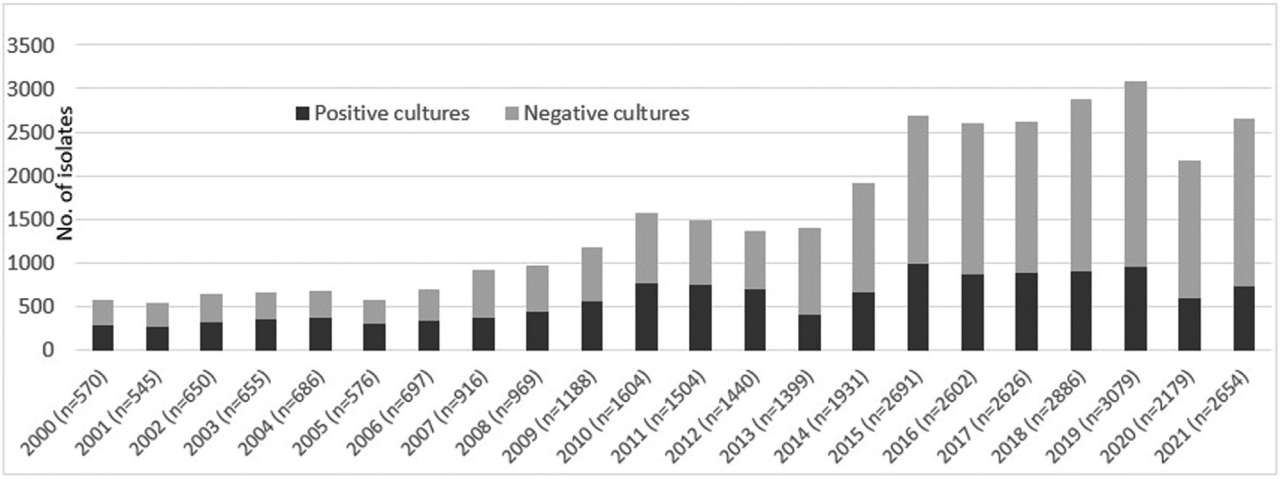

Fig. 1. *Helicobacter pylori* cultures performed between 2000 and 2021 (n = 34,047).

(MICs) >0.5 mg/L, LEV MIC >1 mg/L, MTZ MIC >8 mg/L, AMX MIC >0.125 mg/L, and TET MIC >1 mg/L were considered resistant.

Primary resistance (R-1) was estimated considering the first gastroduodenal biopsy or string test from patients who had not undergone any previous diagnostic tests for *H. pylori* diagnosis in our laboratory (naïve patients). Secondary resistance (R-2) was estimated including data from biopsies and string tests performed on patients who had a previous *H. pylori*-positive test result, assuming they had undertaken an eradication therapy prior to the collection of the second or subsequent samples.

2.7. Statistical analysis

Categorical data were compared with χ^2 tests using Prism version 9.4.1 GraphPad software. Differences were statistically significant when *P* values were below 0.05.

3. Results

Over the 22-year study period, 34,047 samples from 25,626 patients were cultured, obtaining a positive *H. pylori* culture in 37.7% (n= 12,835) of the samples. Out of these, 31,406 were gastroduodenal biopsies obtained from 23,658 patients and 2,641 were string tests obtained from 1,998 patients. A total of 36.7% (n = 11,495) of biopsy specimens and 50.7% (n = 1,340) of string tests yielded a positive result. The number of samples received for *H. pylori* culture showed an increasing trend up until 2020 when it decreased because of the SARS-CoV-2 pandemic. The percentage of positive cultures was around 50% until 2012; since 2013, it has remained at 30% (Fig. 1).

Overall, 25,656 samples were obtained from naïve patients and 8,391 were second or subsequent samples from the same patient. The median age of patients who underwent upper endoscopy was 50 years (range 15–96 years), without any age group that stood out for a greater intervention. The median age of the patients who underwent the string test was 48 years (range 15–88 years). Antimicrobial susceptibility testing was successful for 96.6% (12,399/12,835) of *H. pylori* isolates, 11,056 of them being obtained from naïve patients and 1,343 from second or subsequent gastroduodenal samples (biopsy or string test) from the same patient. *H. pylori* took between two and five days to grow from biological samples (biopsy or string test) depending on the amount of bacteria present in the sample. The subcultures, necessary to obtain enough of the bacteria to carry out susceptibility testing, took 2 days to grow. As the plates with the E-test strips must be incubated for 72 h, it took on average 10–14 days to report the antimicrobial susceptibility of *H. pylori* from the time the patient's sample arrived at the microbiology laboratory.

Between 2015 and February 2020, *H. pylori* PCR was performed on 13,694 samples, 4,376 testing positive. In 249 biopsy samples, culture was negative and *H. pylori* was diagnosed by PCR. In 112 of these cases, susceptibility to CLA was determined by sequencing.

3.1. Primary resistance (R-1)

Overall, 49.3% (n = 5,448) of all *H. pylori* isolates were resistant to one or more of the antimicrobials tested. Primary resistance to one of the studied antibiotic classes was observed in 36.9% of *H. pylori* isolates, dual resistance in 10.5%, and multiresistance to three antibiotics (CLA, MTZ, LEV) in 1.8% (Tab. 1). On the other hand, primary resistance to amoxicillin and tetracycline was unusual, with rates of just 0.6% and 0.2%, respectively.

Annual rates of primary resistance to CLA, MTZ, and LEV are shown in Figure 2. CLA and MTZ primary resistance rates remained steady throughout the 22 years of the study, at around 14% and 30%, respectively. In contrast, the LEV primary resistance rate tripled from 7.6% in 2000 to21.7% in 2021 (Chi-square for trend $P < 0.001$). Among CLA-resistant isolates, 55% were simultaneously resistant to an antimicrobial of another class (Table 1).

By age group, primary resistance to CLA was higher in the youngest (24.2%) and oldest (17.1%) age groups ($P = 0.07$), contrary to the pattern found for MTZ which showed the lowest primary resistance data in the same groups (rates of 20.4% and 18.9% respectively, $P < 0.001$). The primary resistance to LEV increased with age, being 1% in the 15–19 age group and reaching 37.5% in those >80 years (χ^2 test for trend $P < 0.001$) (Table 2).

3.2. Secondary resistance (R-2)

Overall, 10.8% (1,343/12,399) of isolates were obtained from second or subsequent samples from the same patient. Specifically, 814 isolates were from second samples and 529 from third or subsequent samples. Clarithromycin and MTZ secondary resistance rates were above 40% and the LEV secondary resistance rate was 21.5% (Tab. 1). Rates of secondary resistance to amoxicillin and tetracycline were also higher than rates of primary resistance: 1% vs. 0.6% in AMX and 0.4% vs. 0.2% for TET. No trend was observed in secondary resistance rates over the study period for any of the antibiotics studied (Fig. 3).

Overall, rates of single CLA, MTZ, and LEV secondary resistance, as well as the dual or triple secondary resistance to these antimi-

Table 1
Primary and secondary resistance of *Helicobacter pylori* (n = 12,399) to clarithromycin, metronidazole, and levofloxacin between 2000 and 2021.

Year	No. *H. pylori* (first sample)	No. *H. pylori* (≥second sample)	Resistance % to													
			CLA*		MTZ		LEV		CLA/MTZ		CLA/LEV		MTZ/LEV		CLA/MTZ/LEV	
			R-1	R-2	R-1	R-2	R-1	R-2	R-1	R-2	R-1	R-2	R-1	R-2	R-1	R-2
2000–2004	1,475	103	14.0	44.7	29.4	39.8	10.2	9.7	4.7	18.4	1.6	1.9	2.2	1.0	1.0	3.9
2005–2009	1,796	173	14.1	42.8	32.2	38.7	15.6	15.0	4.5	17.3	2.4	4.0	4.0	2.9	1.7	4.6
2010–2014	2,768	373	14.0	47.2	36.8	43.2	17.3	24.7	4.2	12.6	1.8	6.7	5.8	4.3	2.1	10.2
2015–2019	3,875	562	13.9	40.3	29.9	40.2	18.9	22.8	3.0	13.5	2.7	6.2	4.5	4.8	1.8	5.2
2020–2021	1,142	132	15.4	36.8	30.5	40.9	21.6	25.0	3.9	15.9	2.4	6.8	5.5	4.5	2.1	4.5
Total	11,056	1,343	14.1	42.5	32.0	40.9	17.1	21.5	3.8	14.4	2.2	5.8	4.5	4.1	1.8	6.3

CLA, clarithromycin; LEV, levofloxacin; MTZ, metronidazole; R-1, primary resistance; R-2, secondary resistance.
* For CLA, 112 additional isolates were tested by molecular techniques (2015–2019: 84 isolates from first samples and 13 isolates from ≥second samples; 2020–2021: 11 isolates from first samples and 4 isolates from ≥second samples).

Table 2
Helicobacter pylori culture positivity and primary resistance to clarithromycin, metronidazole, and levofloxacin by age group

Age group (years)	No. of first samples	Positive samples		No. of *H. pylori* isolates with susceptibility test results*	Primary resistance to		
		No.	%		CLA	MTZ	LV
15–19	243	104	42.8	98	24.2%	20.4%	1.0%
20–29	1,592	712	44.7	690	15.3%	31.6%	8.8%
30–39	3,052	1,558	51.0	1,511	15.3%	38.6%	12.6%
40–49	4,815	2,469	51.3	2,381	13.5%	36.3%	14.5%
50–59	5,427	2,653	48.9	2,564	12.7%	34.0%	15.4%
60–69	5,173	2,192	42.4	2,126	14.2%	28.3%	20.9%
70–79	3,930	1,320	33.6	1,277	15.2%	22.9%	25.1%
≥80	1,328	357	26.9	344	17.1%	18.9%	37.5%
Unknown	96	64	66.7	62	8.1%	27.4%	3.2%

CLA, clarithromycin; LEV, levofloxacin; MTZ, metronidazole.
* No. of *H. pylori* isolates including those tested by molecular techniques for CLA resistance were: 15–19=99, 20–29=698, 30–39=1526, 40–49=2400, 50–59=2581, 60–69=2146, 70–79=1286, and ≥80=350.

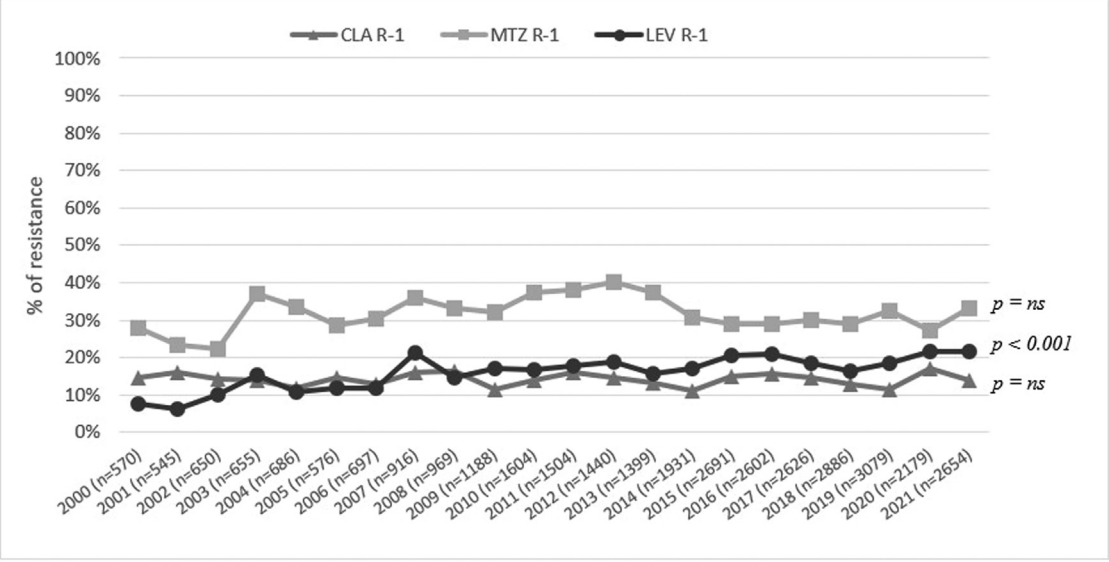

Fig. 2. Pattern of primary resistance of *Helicobacter pylori* to clarithromycin, metronidazole, and levofloxacin between 2000 and 2021.

crobials, were significantly higher than rates of primary resistance ($P < 0.001$), excepting those for dual resistance to MTZ and LEV (Tab. 1). Clarithromycin, MTZ, and LEV resistance rates showed a significant increasing trend from first to second and subsequent samples (χ^2 test for trend, $P < 0.001$) (Fig. 4).

4. Discussion

Heliobacter pylori culture from gastric biopsy specimens is a sensitive technique that allows for the isolation of most strains, facilitating antimicrobial susceptibility testing as well as phenotypic and genotypic studies. *Heliobacter pylori* can be isolated by culture from gastroduodenal biopsies; laboratories should strive to do this routinely and gastroenterologists should request susceptibility testing for *H. pylori* from laboratories. Considering the growth requirements of *H. pylori* (2–5 days from a biological sample and 48 h from a subculture), microbiological results including susceptibility data will generally be available in 10 to 14 days, often enabling the tailoring of the antibiotic treatment before the patient's next appointment with the doctor. In our geographical area, sending

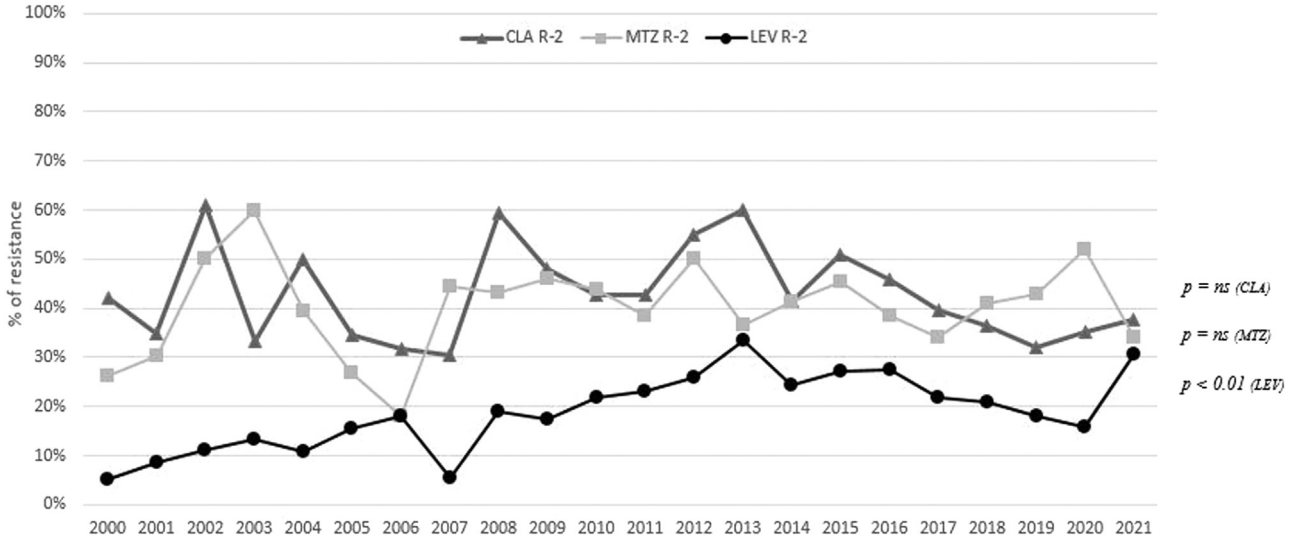

Fig. 3. Pattern of secondary resistance of *Helicobacter pylori* to clarithromycin, metronidazole, and levofloxacin between 2000 and 2021.

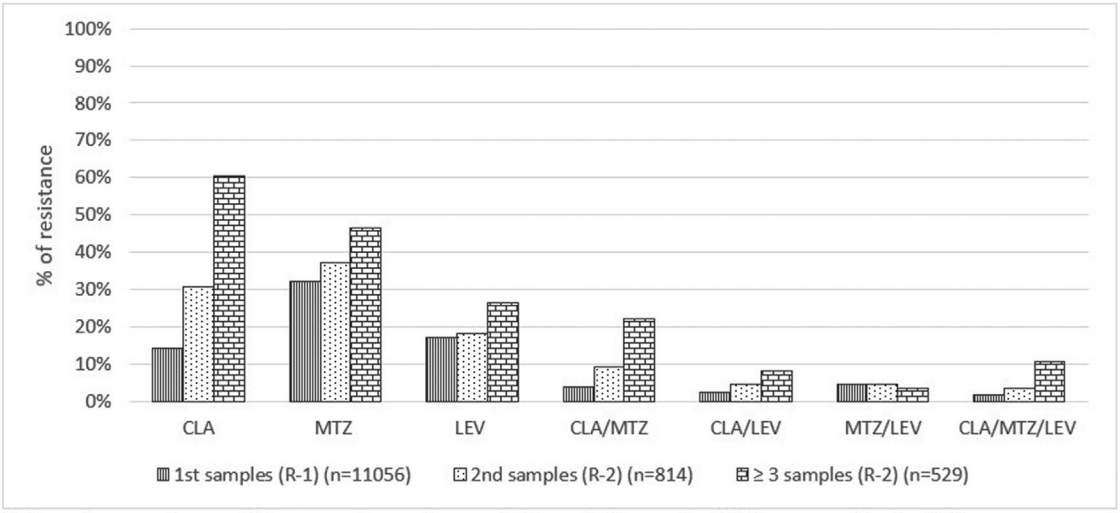

Fig. 4. Single, dual and triple *Helicobacter pylori* primary and secondary resistance to clarithromycin, metronidazole, and levofloxacin by sample groups.

gastric biopsies obtained from patients with symptoms compatible with *H. pylori* infection to the microbiology laboratory to screen for this pathogen has become standard practice. Moreover, in a survey conducted in Spain in 2017, gastric biopsy culture was the most used technique in microbiology laboratories for *H. pylori* infection diagnosis [18]. Increasing resistance of *H. pylori* to various antimicrobials has become a global concern and challenge for the treatment of *H. pylori* infection, and has led the WHO to consider it a 'high priority pathogen' to be monitored for clarithromycin resistance [3]. Moreover, *H. pylori* is involved in 85% of gastric cancers occurring worldwide and its successful and timely eradication is of crucial importance to prevent the development of gastric cancer, long-term complications like peptic ulcer disease, and recurrence of the disease, besides curing gastritis [17]. In this context, tailored therapy is the most suitable option as it may reduce rates of treatment failure [18].

In Gipuzkoa, the rate of primary resistance to CLA was 14.1%, with no significant changes over the years. Only five countries in Europe (Denmark, Latvia, Norway, the Netherlands, and Lithuania) have reported CLA primary resistance rates lower than those observed in this study [19]. Rates of primary and secondary resistance to CLA, as well as to MTZ and LEV, are higher than 15% in most WHO regions [5,20]. Nonetheless, in Gipuzkoa, rates of primary resistance to the three most used antimicrobials for *H. pylori* infection were lower than those reported for other countries [20–23]. This could be, at least in part, due to the performing of culture of *H. pylori* followed by antibiogram in all isolates obtained from biopsies, and accordingly the prescribing of susceptibility-guided therapy. Some authors have demonstrated higher eradication rates with culture-guided therapy than empirical treatment [24,25], showing tailored therapy to be the most cost-effective strategy [18,24]. Nyssen et al. also obtained better efficacy results for first-line therapy with a susceptibility-guided strategy, but this benefit could not be demonstrated when quadruple regimens were prescribed [25]. Indeed, it is important to consider the risks of prescribing empirical quadruple therapy in rela-

tion to selecting resistant *H. pylori* strains and their impact on gut microbiota.

The rate of LEV primary resistance increased progressively from 7.6% in 2000 to 16.2% in 2018, similar to findings for Spain reported by Megraud et al. [19], increasing up to 21.2% in 2021. This increase in LEV resistance has also been reported in other regions, such as southern Italy, with an increase from 10% to 37.8% between 2017 and 2020 [26], and the Asian-Pacific region, with an increase from 2% before 2000 to 27% between 2011 and 2015 [21]. Moreover, consistent with Mosites et al. [27], we observed that rates of LEV resistance increased significantly with age (P <0.001) and, hence, LEV would not be a good choice for empirical therapy in adults in Gipuzkoa. Quinolones are widely used to treat other pathologies, especially respiratory and urinary diseases, and this could explain the increase in their rates of resistance with increasing age. Megraud et al. found a positive correlation between consumption of macrolides and quinolones in the community with resistance in *H. pylori* in European countries [19].

In our study, the rate of secondary resistance to CLA being alarmingly higher than the primary resistance rate (42.5% vs. 14.1%), as well as the marked differences observed in the cases of MTZ (40.9% vs. 32%) and LEV (21.5% vs. 17.1%), add to concerns regarding growing resistance; furthermore, a worrying rate of dual secondary resistance to CLA and MTZ (14.4%) was observed. This increase in antimicrobial resistance may be due to the use of these antimicrobials in previous *H. pylori* eradication therapy as well as their use to treat other diseases.

The choice of the most appropriate diagnostic test (culture, PCR, urea breath test, or stool antigen test) will depend on the availability of the laboratory and the patient's clinical symptomatology. We believe that whenever an endoscopy is performed on a patient with suspected *H. pylori* infection, either because of the patient's symptoms or age ≥50 years, a culture should be performed and, if positive, this should be followed by antimicrobial susceptibility testing. In this study, 63.6% (19,960/31,406) of cultured biopsies were obtained from patients ≥50 years old. Once an upper endoscopy has been performed, it would be better to culture the biopsies than to perform the rapid urease test, which, though it has high specificity and sensitivity [28], does not allow for antimicrobial susceptibility testing. Performing susceptibility testing more routinely will provide knowledge about local susceptibility patterns on which to base empirical therapy for patients in whom an upper endoscopy is not indicated.

Polymerase chain reaction has a sensitivity and specificity above 95% for detecting *H. pylori* [11] and, hence, it is very useful for diagnosis. Moreover, PCR allows for the detection of CLA and LEV resistance [29,30]. The amplification of the 23S gene of *H. pylori* and subsequent sequencing allowed us to determine CLA susceptibility in 112 patients with negative cultures. As in this study, Gallardo et al. used PCR to detect only resistance to CLA [28,31] and in combination with culture, as the performance of two or more tests increases sensitivity [28,31,32]. While the mutations in the 23S rRNA gene that confer resistance to CLA and the mutations in the *gyrA* and *parC* genes that confer resistance to quinolones are well defined, the same is not true for the molecular mechanisms involved in resistance to MTZ and AMX in *H. pylori*. Hulten et al. compared culture with antimicrobial susceptibility testing in *H. pylori* with next-generation sequencing (NGS) using *H. pylori* strains and concluded that NGS has a fair consistency for MTZ and AMX [33]. Nonetheless, molecular tests are currently available for detecting *H. pylori* resistance to macrolides and quinolones but not yet its resistance to MTZ and AMX [29,30].

Finally, the string test was very useful for recovering *H. pylori* and is less invasive than biopsy but, unfortunately, it has been off the market since 2013. Specifically, this test allows the isolation by culture and/or detection of *H. pylori* by PCR from the gastric juice of infected patients, without the need for endoscopy [12,34]. In this study, it was performed on patients without severe signs or experiencing eradication failure among whom the probability of isolating *H. pylori* was very high, and this would explain the high percentage of positive results from string tests in this study (50%).

One limitation of the study concerns the classification of patients undergoing first biopsies as 'naïve' without checking their medical records. Some patients might have been treated empirically prior to the reception of the initial samples at the laboratory, although it is unlikely because clinical practice in our region, in the event of symptomatic and older patients, includes sending samples to the laboratory for culture. Moreover, the CLA primary resistance rate was similar to the rate of 12.1% obtained by Fernández-Reyes et al. for the same geographical area [35] in 102 naïve patients between 2014 and 2017, which lends validity to our assumption.

Tailored therapy for *H. pylori* probably contributed to the fact that rates of primary resistance to clarithromycin remained constant throughout the 22 years of study at figures <15%. Rates of secondary resistance to clarithromycin, metronidazole, and levofloxacin were very high and, therefore, future protocols should place emphasis on the need for susceptibility testing using culture and/or molecular techniques before treating patients if eradication has previously failed and whenever there is a biopsy sample for culture. Knowledge of antimicrobial susceptibility allows physicians to carry out more accurate management of *H. pylori* infections.

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