



Retrospective Study

Sequential changes of antibiotic resistances of *Helicobacter pylori* in Taiwan from 2019 to 2024

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Abstract

BACKGROUND

Antibiotic resistance significantly impacts the treatment failure rates of *Helicobacter pylori* (*H. pylori*) infections.

AIM

To investigate the trends in primary antibiotic resistance of *H. pylori* in Taiwan over the past six years.

METHODS

We conducted a retrospective analysis of *H. pylori* isolates from Taiwanese who had not undergone previous treatments ($n = 1408$), collected between January 1, 2019 and December 31, 2024. Susceptibility of these strains to amoxicillin, clarithromycin, levofloxacin, metronidazole, and tetracycline was tested using the Epsilometer test. We analyzed the trends in single and dual resistance profiles over the study period, and compared antibiotic resistance across different regions (northern, southern and eastern areas) of Taiwan.

RESULTS

The overall resistance rates for *H. pylori* to amoxicillin, clarithromycin, metronidazole, tetracycline, and levofloxacin in Taiwan were 1.3%, 18.0%, 31.0%, 0.8%, and 28.7%, respectively. Tetracycline resistance increased significantly from 0% in 2019 to 3.5% in 2024 (P value in χ^2 test for linear trend: < 0.001), while metronidazole resistance declined from 35.5% to 13.0% (P value in χ^2 test for linear trend: < 0.001). No significant changes of amoxicillin, clarithromycin and levofloxacin resistances were observed. The dual resistances to clarithromycin plus tetracycline, and metronidazole plus tetracycline both increased significantly from 0% to 1.7% from 2019 to 2024 (P value in χ^2 test for linear trend: < 0.05). Furthermore, no significant regional differences in resistance frequencies except for levofloxacin were detected.

CONCLUSION

Primary antibiotic resistance to tetracycline in *H. pylori* has increased in Taiwan from 2019 to 2024, while resistance to metronidazole has decreased during the same period. The dual resistance to clarithromycin plus tetracycline and metronidazole plus tetracycline both increased significantly.

Key Words: *Helicobacter pylori*; Resistance; Antibiotic; Amoxicillin; Clarithromycin; Metronidazole; Tetracycline; Levofloxacin

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Core Tip: Antibiotic resistance significantly impacts the treatment failure rates of *Helicobacter pylori* (*H. pylori*) infections. We analyzed the trends in single and dual resistance profiles of *H. pylori* treatment-naïve Taiwanese between January 2019 and December 2024. Primary antibiotic resistance to tetracycline in *H. pylori* has increased in Taiwan from 2019 to 2024, while resistance to metronidazole have decreased during the same period. Additionally, the dual resistance to clarithromycin plus tetracycline and metronidazole plus tetracycline both increased significantly. These changes carry major clinical implications: It threatens the efficacy of bismuth-based quadruple therapy and limit the treatment options.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) infection is associated with chronic gastritis, gastric ulcer, duodenal ulcer, gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue lymphoma[1,2]. The Real-world Practice and Expectation of Asia-Pacific Physicians and Patients in *H. pylori* Eradication Survey indicated that standard triple therapy remains the most commonly prescribed regimen in the Asia-Pacific region[3]. However, its efficacy has declined to below 80% in most countries[4].

Treatment failures, particularly with standard triple therapy, are attributed to factors such as antibiotic resistance, insufficient acid suppression, poor patient compliance[5] and rapid proton pump inhibitor (PPI) metabolism[6]. In response, alternative eradication regimens including bismuth quadruple therapy, non-bismuth quadruple therapies (e.g., sequential therapy, concomitant therapy and hybrid therapy), and high-dose dual therapy have been developed[4,7,8]. The Maastricht VI/Florence Consensus Report[9] recommends using bismuth quadruple therapy, concomitant therapy or hybrid therapy in regions where clarithromycin resistance exceeds 15%, and advocates for culture with antimicrobial susceptibility test for third-line therapies. For second line rescue therapy, levofloxacin-containing triple or quadruple therapy, preferably a 14-day course, is recommended in most consensus reports[9,10]. However, eradication rates for levofloxacin-containing therapies also decline markedly in the presence of levofloxacin-resistant strains.

Antibiotic resistance is one of the most essential factors that determines the eradication success. On the other hand, antibiotic resistance has increased in Taiwan and other countries over time. The clinical decision for optimal eradication regimens should be supported by referring to the relative efficacies stratified by antibiotic resistance and safety profiles. Therefore, continuously monitoring the regional resistance rates was essential. A previous Taiwanese study[11] demonstrated progressively increasing primary resistance rates for clarithromycin and levofloxacin from 2013 to 2019. However, sequential resistance changes beyond 2019 remain unclear. This study aimed to evaluate trends in primary and dual resistance in *H. pylori* across Taiwan over the past six years, and to assess regional differences in resistance rates.

MATERIALS AND METHODS

Ethics statement

This multicenter retrospective study was conducted at Kaohsiung Chang Gung Memorial Hospital, Kaohsiung Medical University and Hospital, Kaohsiung Veterans General Hospital, An Nan Hospital, Buddhist Tzu Chi Hospital, National Taiwan University Hospital, Shin Kong Wu Ho-Su Memorial Hospital, Cathay General Hospital Renai Branch of Taipei City Hospital, Antai Tian-Sheng Memorial Hospital. The study protocol was approved by the Institutional Review Board and the Ethics Committee of An Nan Hospital. The requirement for informed consent was waived, and patient data were anonymized. No minors were included. None of our patients were minors.

Patients and demographic data

We retrospectively analyzed *H. pylori* isolates from treatment-naïve patients ($n = 1408$) between January 1, 2019 and December 31, 2024. Demographic and clinical data, including age, sex, smoking status, and alcohol, coffee, and tea consumption, were obtained from each patient. Smoking was defined as ≥ 1 pack of cigarettes per week, and coffee or tea consumption as ≥ 1 cup per day. Exclusion criteria were prior *H. pylori* treatment, recent antibiotic, PPI, or bismuth use within 4 weeks, prior gastric surgery, severe comorbidities (e.g., decompensated cirrhosis, uremia), pregnancy, or age < 20 years.

Culture and antimicrobial resistance

One antral gastric biopsy specimen was obtained for cultured for *H. pylori*, and susceptibility to amoxicillin, clarithromycin, levofloxacin, metronidazole, and tetracycline was determined by Epsilometer test method (E-test) according to European Committee on Antimicrobial Susceptibility Testing guidelines[12]. All stock cultures were maintained at -80°C

in Brucella broth (Difco, Detroit, MI, United States) supplemented with 20% glycerol. Organisms were identified as *H. pylori* via Gram stain, colony morphology, and positive oxidase, catalase, and urease reactions. The antibiotic susceptibility is tested by E-test (AB Biodisk, Solna, Sweden). Minimum inhibitory concentration value of resistance breakpoints were > 0.5 µg/mL for amoxicillin, > 1 µg/mL for levofloxacin, > 4 µg/mL for tetracycline, > 8 µg/mL for metronidazole, and > 1 µg/mL for clarithromycin.

Statistical analysis

The primary outcome was antibiotic resistance rates for the five antibiotics by the years. Trends over time were assessed using the χ^2 test for linear trends. Dual resistance for combinations excluding levofloxacin were also evaluated. Regional comparisons were made among northern, southern, and eastern Taiwan. Analyses were performed using SPSS v26 (Chicago, IL, United States). A *P* value < 0.05 was considered statistically significant.

RESULTS

Demographic data of study population

The baseline characteristics of the study population are showed in Table 1. The mean age of the patients was 54.96 years. The proportions of male and female patients were 46.0% and 54.0%. With regard to endoscopic findings, showed 71.4% of patients presented with gastritis, 29.8% with gastric ulcer, and 17.3% with duodenal ulcer. The overall primary antibiotic resistance rates of *H. pylori* isolates in Taiwan were 1.3% for amoxicillin, 18.0% for clarithromycin, 31.0% for metronidazole, 0.8% for tetracycline, and 28.7% for levofloxacin.

Sequential changes of antibiotic resistances of *H. pylori* in Taiwan

Table 2 Lists the antibiotic resistances of *H. pylori* from 2019 to 2024 in Taiwan. Tetracycline resistance rates in 2019, 2020, 2021, 2022, 2023 and 2024 were 0%, 0%, 0.6%, 1.0%, 1.2%, 3.5%, respectively. A significant increasing trend was observed in tetracycline resistance from 2019 to 2024 among treatment naïve patients (Figure 1A shows *P* value in χ^2 test for linear trend: < 0.001).

In contrast, metronidazole resistance rates in 2019, 2020, 2021, 2022, 2023 and 2024 were 35.5%, 35.8%, 32.7%, 28.8%, 30.1%, 13.0%, respectively. There was a statistically significant decreasing trend from 2019 to 2024 (Figure 1A shows *P* value in χ^2 test for linear trend: < 0.001). No significant changes were observed in the resistance rates for amoxicillin, clarithromycin, or levofloxacin during the same period.

Sequential changes of dual resistances of *H. pylori* in Taiwan

Table 3 displays the dual resistance of *H. pylori* from 2019 to 2024 in Taiwan. The dual resistance to clarithromycin plus tetracycline and metronidazole plus tetracycline both increased significantly from 0% to 1.7% during the study period (*P* value in χ^2 test for linear trend: < 0.05). There were no significant changes in dual resistance for amoxicillin plus clarithromycin, amoxicillin plus metronidazole, or clarithromycin plus metronidazole (*P* value were 0.720, 0.543, 0.208 respectively). No cases of dual resistance to amoxicillin plus tetracycline were detected (Figure 1B shows *P* value in χ^2 test for linear trend: < 0.001).

Regional differences of antibiotic resistances of *H. pylori* in Taiwan

Table 4 demonstrated antibiotic resistance rates of *H. pylori* according to different regions in Taiwan. The antibiotic resistance rates for levofloxacin in northern, southern and eastern Taiwan were 26.5%, 30.9%, 20.2%, respectively. The antibiotic resistance rate for levofloxacin in southern Taiwan was significantly higher than that in eastern and north Taiwan (*P* < 0.05). No significant regional differences in antibiotic resistance rates for amoxicillin, clarithromycin, metronidazole, tetracycline were observed among northern, southern, and eastern Taiwan.

DISCUSSION

Antibiotic resistance remains a major cause of *H. pylori* eradication failure and the observed resistance rates direct impact on treatment choices. In prior Taiwanese study (2013-2019) discussing the trend of changes in antibiotic resistance in *H. pylori*[11] reported rising primary resistance to clarithromycin, levofloxacin, and metronidazole. In contrast, our current surveillance of primary resistance rate in *H. pylori* from 2019 to 2024 found clarithromycin and levofloxacin resistance rates remained no significant changes, while metronidazole resistance decreased significantly.

In our large multicenter survey, we observed a notable emergence of tetracycline resistance (from 0% to 3.5%) in Taiwanese *H. pylori* isolates, in contrast to its historically negligible prevalence in Taiwan and globally (< 2%-5%)[11,13-15]. One possible explanation is that tetracycline is widely used in medicine, aquaculture, livestock industry in early Taiwan, and still residual tetracyclines been detected in aquaculture environments and animal food products[16]. On the other hand, the abrupt emergence in tetracycline resistance likely reflects genetic changes in *H. pylori*. Tetracycline binds the bacterial 30S ribosome at a 16S rRNA target[17]. In *H. pylori*, tetracycline resistance arises from mutations in the 16S rRNA gene that block tetracycline binding. Point mutations cause low-level tetracycline resistance, whereas high-level resistance requires multiple mutations in the 16S rRNA binding site[18,19]. For example, a triple-base substitution (AGA965-967TTC) in the 16S rRNA has been directly linked to high-level resistance[18]. In addition, expression of *hefA*

Table 1 Baseline characteristics of study population, *n* (%)

Variables	Patient characteristics (<i>n</i> = 1408)
Age (years), IQR	54.96 (46-65)
Gender	
Male	648 (46.02)
Female	760 (53.98)
Cigarette smoking	233 (16.5)
Alcohol drinking	198 (14.1)
Ingestion of coffee	558 (39.6)
Ingestion of tea	569 (40.4)
Endoscopic findings	
Gastritis	1005 (71.4)
Gastric ulcer	420 (29.8)
Duodenal ulcer	244 (17.3)
Antibiotic resistance	558 (39.6)
Amoxicillin resistance	18 (1.3)
Clarithromycin resistance	253 (18.0)
Metronidazole resistance	437 (31.0)
Tetracycline resistance	11 (0.8)
Levofloxacin resistance	404 (28.7)

IQR: Interquartile range.

gene attributing to upregulation of the efflux pump[18,20], which can lower intracellular tetracycline concentration and increased drug efflux. These suggest new tetracycline-resistant *H. pylori* in Taiwan have likely evolved through multiple ribosomal mutations (and/or accompanying efflux).

Tetracycline has been a cornerstone of bismuth-based quadruple therapy (PPI-bismuth-tetracycline-metronidazole) because of traditionally low resistance rates[13]. The sudden rise of tetracycline-resistant strains is therefore a significant clinical concern, as it could undermine the efficacy of the bismuth quadruple therapy, that is widely recommended as first-line therapy in regions with elevated clarithromycin resistance[21]. Notably, international guidelines[9] (e.g., Maastricht VI) now endorse optimized bismuth quadruple therapy as the preferred empiric regimen when clarithromycin resistance exceeds 15%. Our findings suggest that in Taiwan, the new incidence of tetracycline resistance may decrease the high success rates historically with quadruple regimens, potentially necessitating alternative or susceptibility-guided therapies. In particular, the emergence of dual-resistant strains containing tetracycline in combination with another drug (e.g., metronidazole or levofloxacin) is worrisome, as these dual resistances dramatically limit effective options. By contrast, some prior work showed that bismuth quadruple therapy performs well even in the face of dual clarithromycin/metronidazole resistance[13], but rising tetracycline resistance could challenge this advantage. Furthermore, the rising resistance to tetracycline in Taiwan could also compromise the effectiveness of vonoprazan-tetracycline dual therapy in patients with penicillin allergy. In summary, the new 3.5% resistance rate serves as a warning sign: It is far above Taiwan's prior baseline (approximately 0%) and approaches the upper end of expected rates internationally, signaling that continued surveillance and alternative strategies may soon be needed.

In parallel, we observed a decline in metronidazole resistance over the study period. This is striking given that global and regional data document very high rates of metronidazole resistance (often 30%-60% or more)[13,14,22]. The downward trend in metronidazole resistance is encouraging, since metronidazole is a key component of bismuth quadruple therapy. Lower resistance to metronidazole may help preserve the efficacy of bismuth quadruple therapy, even as we face new challenges with tetracycline resistance. Overall, the rising resistance to tetracycline and the declining resistance to metronidazole observed in Taiwan may have implications for the effectiveness of bismuth quadruple therapy, although the clinical significance remains to be determined.

By contrast, clarithromycin resistance (13.7%-24.3%) remained relatively stable throughout 2019-2024 in our cohort, with just slightly risen from past Taiwanese baseline (approximately 15%). These findings differ from many global reports of steadily rising clarithromycin resistance; for example, recent Asian data report primary clarithromycin resistance around 30%[22], mainland China (approximately 50%), Japan (approximately 30%)[15] and Europe (approximately 23%)[13]. However, our results may reflect local practice patterns. Since clarithromycin-based triple therapy has been used sparingly in Taiwan in recent years, and this may have contained further increases in clarithromycin resistance.

Table 2 Antibiotic resistances in *Helicobacter pylori* treatment-naïve patients from 2019 to 2024 in Taiwan

	Year	Patient number	Proportion, % (95%CI)	P value (χ^2 test for linear trend)
Amoxicillin	2019	0/256	0.0 (0.0-0.0)	0.289
	2020	7/330	2.1 (0.6-3.7)	
	2021	4/159	2.5 (0.1-5.0)	
	2022	1/299	0.3 (0.0-1.0)	
	2023	1/249	0.4 (0.0-1.2)	
	2024	5/115	4.3 (0.6-8.1)	
Clarithromycin	2019	37/256	14.5 (10.1-18.8)	0.514
	2020	65/330	19.7 (15.4-24.0)	
	2021	33/159	20.8 (14.4-27.1)	
	2022	56/299	18.7 (14.3-23.3)	
	2023	34/249	13.7 (9.4-17.9)	
	2024	28/115	24.3 (16.4-32.3)	
Metronidazole	2019	91/256	35.5 (29.6-41.4)	0.000
	2020	118/330	35.8 (30.5-41.0)	
	2021	52/159	32.7 (25.3-40.1)	
	2022	86/299	28.8 (23.6-33.9)	
	2023	75/249	30.1 (24.4-35.9)	
	2024	15/115	13.0 (6.8-19.3)	
Tetracycline	2019	0/256	0.0 (0.0-0.0)	0.000
	2020	0/330	0.0 (0.0-0.0)	
	2021	1/159	0.6 (0.0-2.0)	
	2022	3/299	1.0 (0.0-2.3)	
	2023	3/249	1.2 (0.0-2.8)	
	2024	4/115	3.5 (0.1-7.2)	
Levofloxacin	2019	81/256	31.6 (25.9-37.3)	0.269
	2020	91/330	27.6 (22.7-32.4)	
	2021	57/159	35.8 (28.3-43.4)	
	2022	76/299	25.4 (20.5-30.4)	
	2023	64/249	25.7 (20.2-31.2)	
	2024	35/115	30.4 (21.9-39.0)	

CI: Confidence interval.

This result approaches the 15% threshold which clarithromycin-based triple therapy is no longer recommended as first-line therapy in Taiwan by Maastricht VI and other consensus guidelines[9]. Similarly, levofloxacin resistance, which is known to reduce the efficacy of quinolone-containing regimens[21], did not climb appreciably in our data. Importantly, both drugs remain moderately resistant at present, reinforcing that empiric use of clarithromycin or levofloxacin without prior sensitivity testing would not achieve reliable cure rates. Our findings support the replacement of conventional clarithromycin-based triple therapy with bismuth quadruple therapy or concomitant therapy for empiric first-line treatment in Taiwan.

The trend of dual resistance also warrants emphasis. We noted an increase in strains resistant to two antibiotics simultaneously, especially those combinations involving tetracycline (*e.g.*, tetracycline + metronidazole or tetracycline + levofloxacin), that reflected the truth of increasing primary resistance of tetracycline. Dual resistance is clinically important because it corresponds to very low eradication rates with standard regimens. For example, dual clarithromycin/metronidazole resistance is known to reduce eradication success to around 50%[21], necessitating use of salvage therapies. To date, no first line eradication regimen including clarithromycin plus tetracycline. In contrast, although

Table 3 Dual resistances in *Helicobacter pylori* treatment-naïve patients from 2019 to 2024 in Taiwan

	Year	Patient number	Proportion, % (95%CI)	P value (χ^2 test for linear trend)
Amoxicillin + clarithromycin	2019	0/256	0 (0.0-0.0)	0.720
	2020	2/330	0.6 (0.0-1.0)	
	2021	0/159	0 (0.0-0.0)	
	2022	1/299	0.3 (0.0-1.1)	
	2023	0/249	0 (0.0-0.0)	
	2024	1/115	0.9 (0.0-2.9)	
Amoxicillin + metronidazole	2019	0/256	0 (0.0-0.0)	0.543
	2020	5/330	1.5 (0.3-3.0)	
	2021	2/159	1.3 (0.0-3.2)	
	2022	1/299	0.3 (0.0-1.1)	
	2023	0/249	0.0 (0.0-0.0)	
	2024	1/115	0.9 (0.0-2.9)	
Amoxicillin + tetracycline	2019	0/256	0.0 (0.0-0.0)	0
	2020	0/330	0.0 (0.0-0.0)	
	2021	0/159	0.0 (0.0-0.0)	
	2022	0/299	0.0 (0.0-0.0)	
	2023	0/249	0.0 (0.0-0.0)	
	2024	0/115	0.0 (0.0-0.0)	
Clarithromycin + metronidazole	2019	20/256	7.8 (4.5-11.1)	0.208
	2020	23/330	7.0 (4.2-9.7)	
	2021	10/159	6.3 (2.5-10.1)	
	2022	21/299	7.0 (4.1-9.9)	
	2023	14/249	5.6 (2.7-8.5)	
	2024	5/115	4.3 (0.6-8.1)	
Clarithromycin + tetracycline	2019	0/256	0.0 (0.0-0.0)	0.013
	2020	0/330	0.0 (0.0-0.0)	
	2021	0/159	0.0 (0.0-0.0)	
	2022	2/299	0.7 (0.0-1.7)	
	2023	1/249	0.4 (0.0-1.3)	
	2024	2/115	1.7 (0.0-4.5)	
Metronidazole + tetracycline	2019	0/256	0.0 (0.0-0.0)	0.007
	2020	0/330	0.0 (0.0-0.0)	
	2021	1/159	0.6 (0.0-2.1)	
	2022	2/299	0.7 (0.0-1.7)	
	2023	3/249	1.2 (0.0-2.8)	
	2024	2/115	1.7 (0.0-4.5)	

CI: Confidence interval.

Table 4 Antibiotic resistances of *Helicobacter pylori* treatment-naïve patients across different regions in Taiwan

	Region	Patient number	Proportion, % (95%CI)	P value (χ^2 test for linear trend)
Amoxicillin	South	11/818	1.3 (0.6-2.2)	0.606
	North	5/501	1.0 (0.2-1.9)	
	East	2/89	2.2 (0.0-5.8)	
Clarithromycin	South	144/818	17.6 (15.0-12.2)	0.360
	North	88/501	17.6 (14.2-20.9)	
	East	21/89	23.6 (14.6-32.6)	
Metronidazole	South	248/818	30.3 (27.2-33.5)	0.784
	North	160/501	31.9 (27.8-36.0)	
	East	29/89	32.6 (22.7-42.5)	
Tetracycline	South	8/818	1.0 (0.3-1.7)	0.080
	North	1/501	0.2 (0.0-0.6)	
	East	2/89	2.2 (0.0-5.8)	
Levofloxacin	South	253/818	30.9 (27.8-34.1)	0.044
	North	133/501	26.5 (22.7-30.4)	
	East	18/89	20.2 (11.7-28.7)	

CI: Confidence interval.

bismuth quadruple therapy can overcome single-agent resistance, the appearance of tetracycline-metronidazole dual resistance could compromise even this regimen. Although increasing metronidazole doses can overcome resistance, the rising dual resistance observed in our survey imply that if tetracycline-metronidazole dual resistance increased, even these quadruple regimens could encounter treatment failure. This also indicates that empiric therapy must be chosen carefully, and may increasingly require culture-based susceptibility guidance.

Furthermore, we found that no significant regional differences in resistance rates except for levofloxacin, which only used in second line therapy of *H. pylori* eradication. This result likely reflects Taiwan's centralized health system and antibiotic stewardship. Since the National Health Insurance provides universal coverage and follows national guidelines, prescribing behaviors are relatively consistent from north to south to east. These factors probably contribute to the lack of regional differences of resistance. In turn, this suggests that our data on antibiotic resistance are broadly representative of the country, without major local outliers. Levofloxacin resistance in *H. pylori* appears to be linked to community fluoroquinolone use. A multinational study reported significantly higher resistance rates in regions with higher outpatient fluoroquinolone consumption[23]. The higher resistance in southern Taiwan may reflect regional prescribing habits contributing to increased selection pressure. In contrast, lower resistance in eastern Taiwan may be attributed to its more rural setting and lower antibiotic exposure. These findings suggest regional variations in levofloxacin resistance are likely driven by local antibiotic use rather than inherent biological differences.

Our study has several limitations. Firstly, by virtue of its retrospective design, causality cannot be established. The isolates were obtained at medical centers and may not fully represent community clinics, causing potential selection bias. Second, we did not include molecular analyses, so we cannot specify the genetic basis of observed resistance or track clonal spread of resistant strains. Third, we are lacking data of clinical outcomes linking to antibiotic resistance, so we cannot measure how these resistance trends impacted eradication rate. Finally, although our consortium includes multiple hospitals, coverage may still be incomplete (for example, eastern regions were under-represented), potentially missing local pockets of resistance.

CONCLUSION

In summary, our 2019-2024 data reveal both stability and change in Taiwan's *H. pylori* resistance pattern. Primary antibiotic resistance to tetracycline in *H. pylori* has increased in Taiwan from 2019 to 2024, while resistance to metronidazole have decreased during the same period. Additionally, the dual resistance to clarithromycin plus tetracycline and metronidazole plus tetracycline both increased significantly. These changes carry major clinical implications: It threatens the efficacy of bismuth-based quadruple therapy and limit the treatment options. Furthermore, no significant regional differences in resistance frequencies except for levofloxacin were detected. Therefore, continuous nationwide surveillance is warranted to guide eradication strategies.

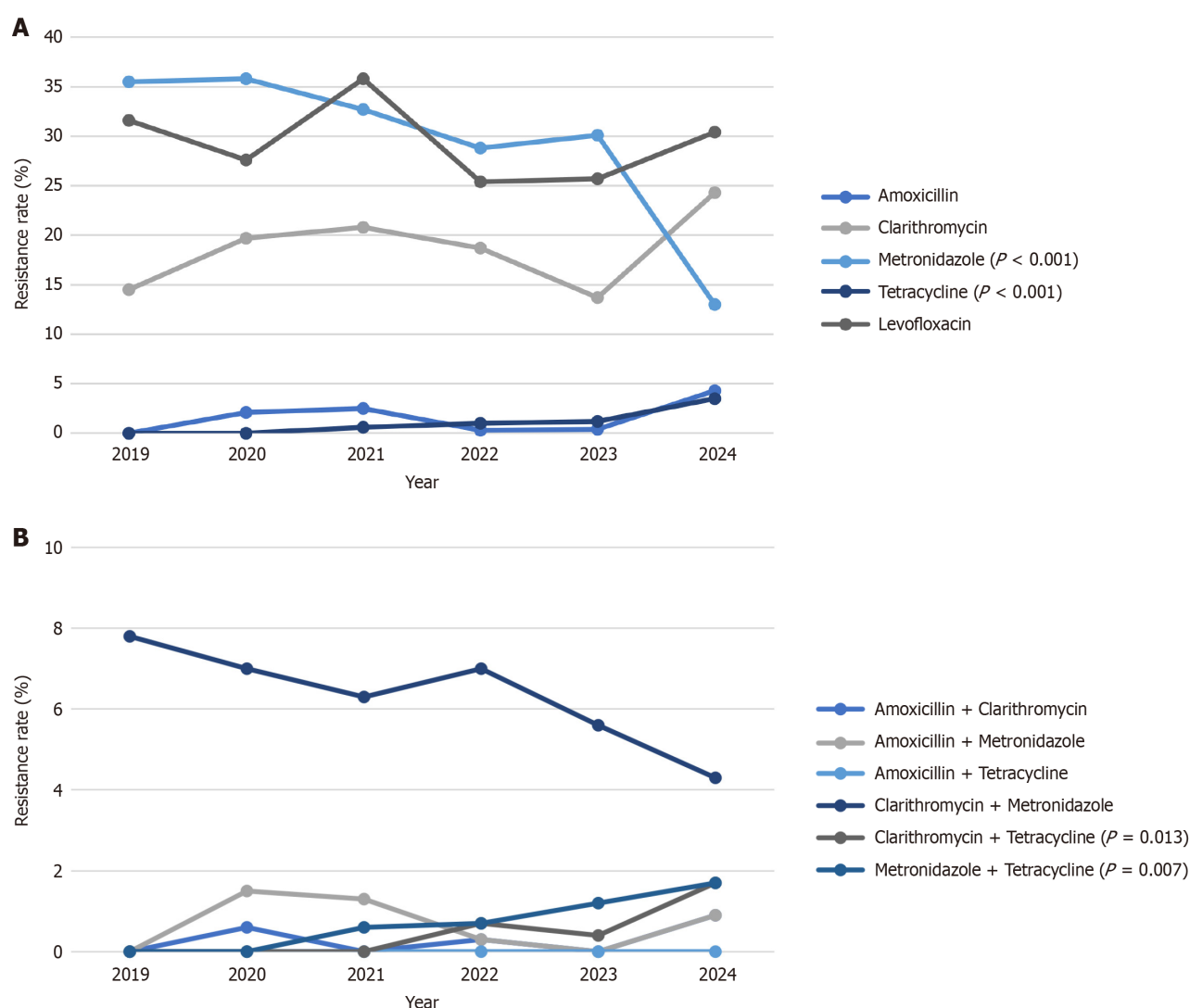


Figure 1 Sequential changes of antibiotic resistances and dual resistances of *Helicobacter pylori* in Taiwan from 2019 to 2024 among treatment naive patients. A: Illustrated sequential changes of antibiotic resistances to amoxicillin, clarithromycin, metronidazole, tetracycline, and levofloxacin. There was a statistically significant decreasing trend in metronidazole resistance; and a significant increasing trend in tetracycline resistance ($P < 0.05$ means significant change in linear trend); B: Illustrated sequential changes of antibiotic dual resistances. The dual resistance to clarithromycin plus tetracycline and metronidazole plus tetracycline both increased significantly from 0% to 1.7% during the study period ($P < 0.05$ means significant change in linear trend).

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FOOTNOTES

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