

Therapeutic Guidelines and Antimicrobial Resistance of Helicobacter Pylori in Patients with Peptic Ulcer at Tertiary Care Hospitals of Rawalpindi and Islamabad

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ABSTRACT

Objective: The purpose of this study was to investigate the prevalence of antibiotic resistance among Helicobacter pylori isolates obtained from patients suffering from peptic ulcer disease in Rawalpindi and Islamabad, Pakistan, and to propose a novel anti-H. pylori therapy strategy for use in these locations.

Methodology: A total of 132 H. pylori from the patients suffering with peptic ulcer disease were reported for clinical treatment in institutions in the twin Cities that provide tertiary care. Antibiotics such as ciprofloxacin, clarithromycin, amoxicillin, metronidazole, and tetracycline were tested on the isolates to determine their levels of susceptibility to these drugs. The Epsilon meter test, often known as the E-test, is a quantitative disc diffusion method that is used to determine antibiotic sensitivity. This test was utilised for the purpose of verifying isolates.

Results: The overall rate of resistance among H. pylori was found to be 27.9% for amoxicillin, 38.9% for clarithromycin, and 73.6% for metronidazole. 47 out of 132 isolates exhibited multiple drug resistance, with metronidazole, clarithromycin, and amoxicillin showing the highest frequency of two, three, and four drug resistance patterns. Ciprofloxacin had a low level of tetracycline resistance, ranging from 1.2 to 4%, whereas metronidazole resistance was substantial. In the population of Pakistan, the frequency of H. pylori resistance to metronidazole is quite high, whereas it is moderate in response to clarithromycin and amoxicillin, and low in response to ciprofloxacin and tetracycline. The rates of resistance to clarithromycin and amoxicillin were higher in Rawalpindi than they were in Islamabad. It is imperative, for the sake of the public's health, that Pakistan make an adjustment to its policy regarding antibiotics, one that will permit the use of antibiotic rotation in the treatment of H. pylori.

Keywords: Peptic ulcer, Helicobacter pylori, antibiotic susceptibility.

INTRODUCTION

Helicobacter pylori infection has been linked to a number of diseases, including chronic superficial gastritis, duodenal and stomach ulcers, chronic atrophic gastritis, mucosa-associated lymphoid tissue lymphoma (MALT), non-ulcer dyspepsia, gastric cancer, and coronary artery disease. (1, 2). Eliminating H. pylori infection entirely is the preferred way for treating such infections and inhibiting any bouts of recurrence, as well as being the only method that has been shown to work (3). The most common treatment approaches involve the administration of two antimicrobial medications, such as amoxicillin, clarithromycin, tetracycline, and metronidazole, in addition to a proton pump inhibitor and bismuth salts in a number of combinations, for varying amounts of time, and in a range of dosages (4). There are many different strains of H. pylori, and all of them display antimicrobial agent resistance in vitro (5). This resistance is directly related to the fact that H. pylori cannot be entirely eradicated. In economically disadvantaged nations like Pakistan, eradicating H. pylori requires the adoption of a treatment that combines omeprazole with two antibiotic combinations (6). These antibiotic combinations include metronidazole with clarithromycin or metronidazole in combination with amoxicillin. There have been reports of an increase in the level of resistance shown by H. pylori to the antibiotics metronidazole, clarithromycin, and amoxicillin from hospitals located all over the world (7, 8). Greater levels of resistance are encountered by developing nations than by developed nations (9). The current multicentric study's objectives were to evaluate the evolving profiles of AMR displayed by H. pylori isolates and to suggest appropriate alterations to the country's current protocol for the treatment of H. pylori infections.

METHODOLOGY

In the current investigation, the study was designed for assessment of AMR of H. pylori disease in Rawalpindi and Islamabad. This study design had already been approved by the

appropriate institutional review boards. A total of 132 H. pylori strains were isolated from patients with peptic ulcer disorders who were treated at the gastroenterology departments of the Dr. Akbar Niazi Teaching Hospital in Islamabad and the Holy Family Hospital in Rawalpindi. These patients were seen at the hospitals' respective gastroenterology departments. It was established that not a single one of the people who took part in the research had ever been subjected to endoscopic therapy for anti-H. pylori medication. The body and antrum of the stomach were biopsied in order to get these isolates, which were then identified by morphology and conventional biochemical testing. Using the Disc diffusion assay and the CLSI guidelines, the Resistance to metronidazole, clarithromycin, amoxicillin, ciprofloxacin, and tetracycline was assessed against isolate strains of H. pylori. The growth of the H. pylori isolates was halted in BHI broth for forty-eight hours before it was spread out on Mueller Hinton blood agar plates. This was done so that the McFarland turbidity requirement could be satisfied. The procedure of disc diffusion was carried out in a manner that was in keeping with the CLSI 2019 guidelines (10).

RESULTS

At each of the two centers that took part in the research, 132 different strains of H. pylori were isolated and put through tests to see whether antibiotics were effective against them. The current study included 132 patients, 49 of whom were female and 83 of whom were male. While metronidazole resistance was exceptionally prevalent among the isolates from Islamabad (84.3% at Islamabad and 72.6% at Rawalpindi), it was significantly less prevalent among the isolates from Rawalpindi. Isolates found in Rawalpindi showed significantly greater levels of resistance to amoxicillin (78%) and clarithromycin (93%), respectively (Figure 1). In general, the antibiotics with the highest rates of resistance in Twin Cities include metronidazole (73.6%), clarithromycin (38.9%),

and amoxicillin (27.9%), while ciprofloxacin (1.5%) and tetracycline (1.2%) have the lowest rates of resistance (Figure 3).

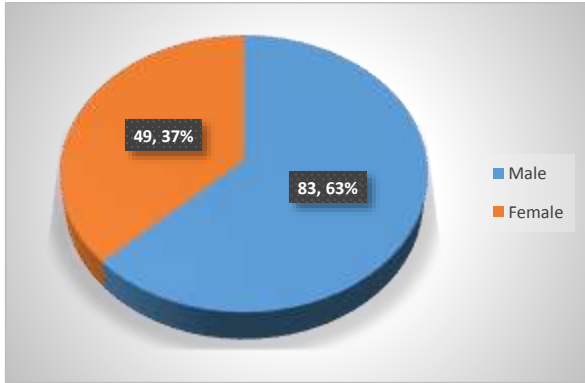


Figure 1: Gender wise distribution of patients with peptic ulcer

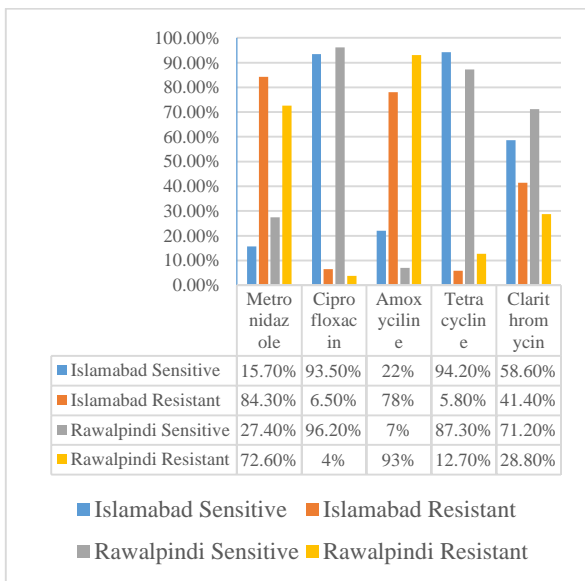


Figure 2: Antimicrobial Susceptibility Profile of Isolates with geographical distribution

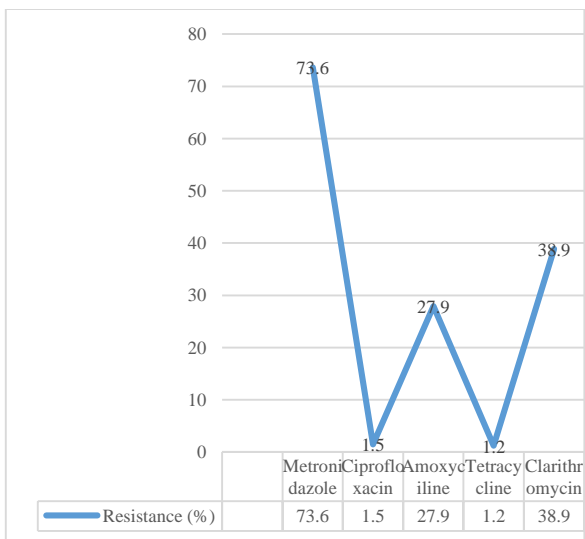


Figure 3: Overall Resistance profile of H. pylori in clinical isolates

DISCUSSION

The process of extracting H. pylori from clinical samples is just as meticulous as the testing process used to determine whether or not it is resistant to antibiotics. It is common knowledge that the concentrations necessary to overcome H. pylori resistance are 2 milligrams per liter for clarithromycin and 8 milligrams per liter for metronidazole (11, 12). Chavez et al. came up with the idea that there is an intermediate category of H. pylori strains that can be suppressed by metronidazole at 8 mg/L (13). In the current inquiry, the data collected from the participating centers served as the basis for the analysis, which employed comparable breakpoints of 4 milligrams/L for tetracycline and 2 milligrams/L for ciprofloxacin (11). There is a significant disparity between the rates of primary metronidazole resistance of H. pylori in developed (6-49%) and developing (77-95%) countries. This disparity can be attributed to the extensive use of nitroimidazoles in the treatment of parasite illnesses in developing nations (14). The extensive use of nitroimidazoles may accelerate the onset of drug resistance as well as pathogenicity in pathogens. This study discovered a significant proportion of metronidazole resistance, which is suggestive of primary resistance, despite the fact that it did not enrol patients who had a history of receiving particular H. pylori therapy.

There have been reports of regional variations in metronidazole resistance and growing clarithromycin resistance in H. pylori isolates from Japan (15), the Germany (16), and Brazil. These findings are comparable to the ones that were found in our investigation. According to the findings of research conducted by Kato et al., the rate of metronidazole resistance in the Kyoto region of Japan is substantially greater than in the Sapporo region (8.1%) (17). According to the findings of their analysis, the percentage of people who exhibited resistance to clarithromycin between the years 1996 and 1999 looked to have increased from 9.1 to 18.7%. According to reports, the frequency of primary H. pylori clarithromycin resistance varied from 15% to 18% worldwide (18). On the other hand, it was discovered that fifty percent of the H. pylori isolates in Peru were resistant to clarithromycin (19).

Recommendations: According to the findings of the current research, it is recommended that a metacentric clinical trial using the most recent international H. pylori treatment regimens be carried out. The findings call attention to the necessity for regional and national monitoring studies on the H. pylori resistance profiles, and they also propose antibiotic rotation in the treatment of H. pylori in Pakistan. In order to complete the H. pylori treatment protocol in Twin Cities, an immediate switch to metronidazole is required. Before that time comes, it is possible that susceptibility testing performed prior to the beginning of medicine, particularly when metronidazole is prescribed, could be beneficial to the efficacy of the therapy.

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