HSJ

Vol.4, Issue. 1

Health Sciences Journal
EISSN: 2959-2259; PISSN:2959-2240

Received: 13 November 2025 | Accepted: 19 December 2025 | Published: 20 December 2025

MDRI

Research Article

A STUDY ON THE ANTIBIOTIC RESISTANCE AND ASSOCIATED RISK FACTORS OF HELICOBACTER PYLORI INFECTION ON POPULATION OF DARYA KHAN DISTRICT BHAKKAR

Faqiaha Wadood[1] | Nazia Bibi[1] | Rifat Bibi[1] | Abdul Manan[1] | Zain Ul Zahidin[1] | Faiqah Ramzan[1] | Ata Ur Rahman[1*] | Muhammad Adeel Razzaq [2] | Muhammad Tariq[1] | Anila Khan[3] | Sana Ullah[1]

[1]Faculty of Veterinary and Animal Sciences, Gomal University D.I. Khan
[2]University of Agriculture, Faisalabad
[3]Institute of Biological Sciences, Gomal University D.I. Khan

Correspondence
Atta Ur Rehman
Email: arehman@ gu.edu.pk

Citation
Wadood F, Bibi N, Manan A, Zahidin ZU, Ramzan F, Rehman AU, Razzaq MA, Tariq M, Khan A, Ullah S, A study on the antibiotic resistance and associated risk factors of helicobacter pylori infection on population of Darya Khan district Bhakkar, Health Sciences Journal, 38-45

ABSTRACT:

Background: Infection with *Helicobacter pylori* is a serious public health issue, especially in underdeveloped nations. A common gastric pathogen linked to several gastrointestinal conditions, such as peptic ulcer disease and dyspepsia, is *Helicobacter pylori*. **Objectives:** The purpose of this study was to find out risk factors and how common *H. pylori* is in patients with dyspepsia at the District Head Quarter (THQ) Hospital in Darya Khan, Punjab, Pakistan. **Methods**: A total of 150 stool samples were taken from patients who had upper stomach pain and heartburn symptoms. Gram staining and biochemical assays, such as catalase, oxidase, and urease tests, were used to establish the presence of *H. pylori* after the samples were cultivated on selective media.
Results: According to the findings, *H. pylori* were found in 10% (15/150) of the stool samples, with females having a greater prevalence (11.3%) than males (8.6%). An examination of the age distribution showed that the greatest number of positive cases occurred in those between the ages of 16 and 29. Incredibly, urban regions had a considerably lower prevalence (8.5%) of *H. pylori* than rural areas (11.5%). According to the data, the most notable risk factor includes poor sanitation which constitutes positive cases, family history, smoking, and unhealthy dieting habits. While amoxicillin and rifampicin exhibited high susceptibility rates of 80% and 86.7%, respectively, antibiotic susceptibility testing revealed resistance rates of 33.3% to metronidazole and clarithromycin. At 20%, moderate levofloxacin and 13.3% tetracycline resistance was observed.
Conclusion: These findings highlight how urgently Pakistan needs to implement comprehensive public health programs and modernize treatment guidelines to properly manage *H. pylori* infections. Given the differences in *H. pylori* incidence between urban and rural populations, it is imperative to continuously monitor resistance patterns and take alternate therapy into consideration.

KEYWORDS: *Helicobacter pylori*, dyspepsia, antibiotic resistance, public health, Risk Factor

1 | INTRODUCTION

Human-to-human transmission of the Gram-negative microaerophilic bacterium *Helicobacter pylori* (*H. pylori*) is the primary cause of peptic ulcer disease, gastric cancer, and chronic gastritis.[1] *H. pylori* is a rod-shaped, motile, Gram-negative, microaerophilic bacterium that can colonize the highly acidic environment of the human stomach. Most *H. pylori* infections are acquired during childhood, with an estimated 30% of young individuals infected or at risk of infection at some point in their lives. The interaction between host immune responses and bacterial virulence factors plays a critical role in the development of *H. pylori*–associated diseases, including gastritis, peptic ulcers, and gastric cancer.[2] Alterations in gastric acid homeostasis and increased acid secretion mediated by changes in G cells, somatostatin-producing D cells, and acid-secreting parietal cells are associated with duodenal ulcer disease and a reduced risk of gastric cancer in infected individuals.[3]

Globally, *H. pylori* infection is estimated to affect nearly 50% of the world's population.[4] However, prevalence varies considerably across geographic regions. In several developed countries, the prevalence of *H. pylori* has declined in parallel with improvements in living conditions and socioeconomic status,[5] whereas high prevalence rates persist in many developing nations.[6] In Japan, the prevalence of *H. pylori* infection was approximately 90% among individuals born before 1950, but declined dramatically to less than 2% among children born after 2000.[7] Understanding the local prevalence of *H. pylori* infection is essential because of its significant public health implications.

In China, *H. pylori* infection is associated with approximately 9.2% of cancer diagnoses and 9.8% of cancer-related deaths, with gastric cancer being the most common outcome. Reported prevalence ranges from 41.5% to 72.3%, depending on socioeconomic conditions and hygiene practices. A decline in prevalence from 60.5% to 52.2% has been observed before and after the year 2000. Nevertheless, the true national prevalence of *H. pylori* infection in China remains inadequately defined, potentially limiting the effectiveness of gastric cancer prevention and eradication programs.[8] *H. pylori* is typically acquired during childhood, and its global prevalence has shown a gradual decline over the past two decades. In North America, approximately 50% of the population is infected, with risk factors including male gender, limited access to healthcare, and inadequate household water supply. Among asymptomatic children, the prevalence is lower (14.2%); however, infection rates remain high in Africa (~70%), where they are associated with poor sanitation, poverty, high birth order, unsafe drinking water, and farming-related exposures. Across Asia, risk factors vary widely and include low income and education levels, rural residence, overcrowding, smoking, alcohol consumption, and dietary habits. In Europe, the prevalence among children is approximately 25%, with the highest reported rate in Portugal (66.2% at 13 years of age). Identified risk factors include rural living conditions, poor hygiene, low parental education, and unemployment. Further research is required to better explain these regional disparities.[9] The aim of the present study was to determine the prevalence of *H. pylori* infection among patients presenting with dyspepsia at the Tehsil Headquarter (THQ) Hospital in Darya Khan, Punjab, Pakistan, and to identify the major risk factors associated with its occurrence.

2 | MATERIAL AND METHODS

2.1 | Study Area

The study was conducted at the Department of Microbiology, Gomal University Dera Ismail Khan, Khyber Pakhtunkhwa. Samples were collected from patients visiting Tehsil Head Quarter (THQ) Hospital Darya Khan. The Darya Khan is the district of Bhakkar, Punjab, Pakistan.

2.2 | Study Design, Sample Size and Setting

This study presents a cross-sectional (Descriptive) study conducted on patients who visited the THQ Hospital Darya Khan District Bhakkar. A total of 150 samples collected from clinical specimens of various patients were included in the study. All the participants belong to general population of Darya Khan District Bhakkar in Punjab (Pakistan).

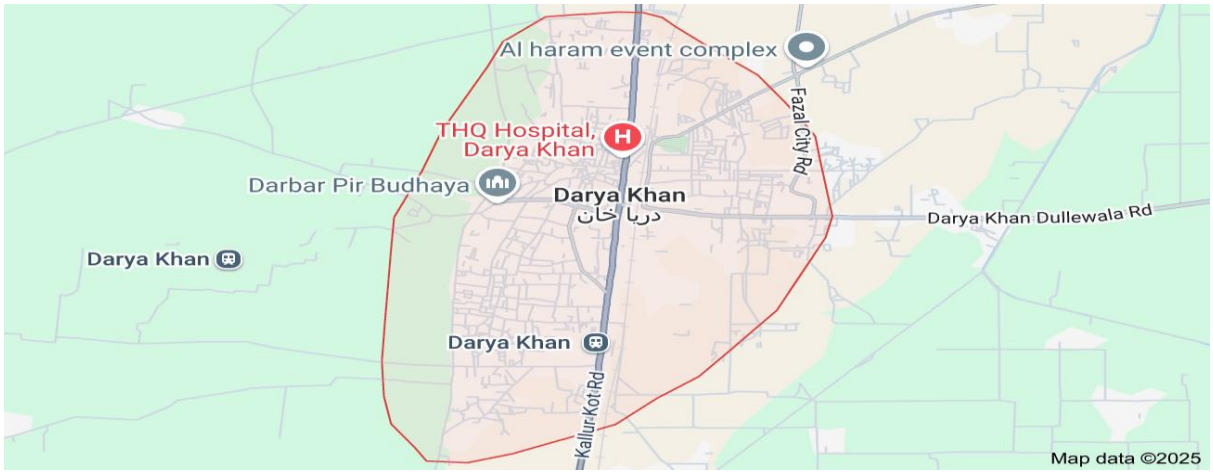

Figure 1 Map showing area of the study participants

Health Sciences Journal
EISSN: 2959-2259; PISSN:2959-2240

2.3 | Sample Collection

A total of 150 stool samples were collected from dyspeptic patients visiting Darya khan (THQ). The requirements for inclusion included a history of heartburn and upper abdominal pain that needed to be defined histologically. A suitable form was created for sample collection, which included the patient's name, age, gender, and condition. Stool samples from participants were collected following a specific protocol to ensure sample integrity and accuracy. A dry, clean container covered with plastic wrap was used to prevent contamination. Each sample was labelled with the participant's name, the time, and the date of collection. Within 24 hours, the samples were taken to a microbiology lab for additional analysis after being preserved at 4°C. The study gathered random stool samples from 150 gastric patients (M 70, F 80) between the end of 2023 and the summer of 2024. The age range of the participants was 3 to 55. The samples gathered were split up into three age groups: 30 patients between the ages of 3 and 15, 59 patients between the ages of 16 and 29, and 61 patients between the ages of 30 and 55.

2.4 | Isolation of Bacterial Strains

Stool samples were collected and a loopful was streaked onto selective Columbia blood agar to isolate H. pylori. The inoculated plates were incubated in a humidified anaerobic environment at 37°C for 72 hours and monitored daily for the appearance of golden-pigmented colonies, resulting from tetrazolium chloride reduction. Plates showing no growth after seven days were considered culture negative. Suspected colonies were further examined using Gram staining to assess morphology and Gram reaction, followed by biochemical characterization including catalase, oxidase, and urease tests. The catalase test was performed by adding hydrogen peroxide to a bacterial smear and observing bubble formation, while the oxidase test involved rubbing colonies onto oxidase test strips to detect cytochrome c oxidase activity, indicated by a purple color change. The urease test was carried out using urea agar with phenol red, where a color change from yellow to pink confirmed urea hydrolysis. All three biochemical tests were used collectively to confirm H. pylori identification. Antibiotic susceptibility of confirmed isolates was assessed using the Epsilometer (E-test) method on Mueller-Hinton agar supplemented with 10% defibrinated sheep blood. E-test strips for amoxicillin, tetracycline, metronidazole, clarithromycin, rifampicin, and levofloxacin were applied, and plates were incubated under microaerobic conditions at 37°C for 72 hours. Minimal inhibitory concentrations were determined at the point of ellipse intersection on the strip, adjusted to the nearest twofold dilution, and interpreted according to CLSI guidelines as susceptible, intermediate, or resistant.

3 | RESULTS AND DISCUSSION

Age and Gender Wise Distribution
A total of 150 stool specimens obtained from different patients were observed with antibiotic susceptibility and biofilm formation in Darya khan THQ hospital. Age distribution among 150 patients was analyzed as 30(20%) belong to 3 to 15years of age and 59(39.0%) belong 16 to 29 years of age However, 61 (40.7%) of the 150-stool sample were from 30-55years of age. According to reports, gender was known a total of 70(46.7%) men and 80(53.3%) women. Out of 150 samples, only 68(45.3%) sample in rural areas, whereas 82(54.6%) in urban

Table 1 Result indicating Frequency and Percentage of Helicobacter pylori Isolated

Variable	Response	Frequency	Percentage%
TOTAL	150	150	100.0
	3-15	30	20.0
Age (years)	16-29	59	39.0
	30-55	61	40.7
	Male	70	46.7
Gender	Female	80	53.3
	Urban	82	54.6
Area of residence	Rural	68	45.3

Health Sciences Journal
EISSN: 2959-2259; PISSN:2959-2240

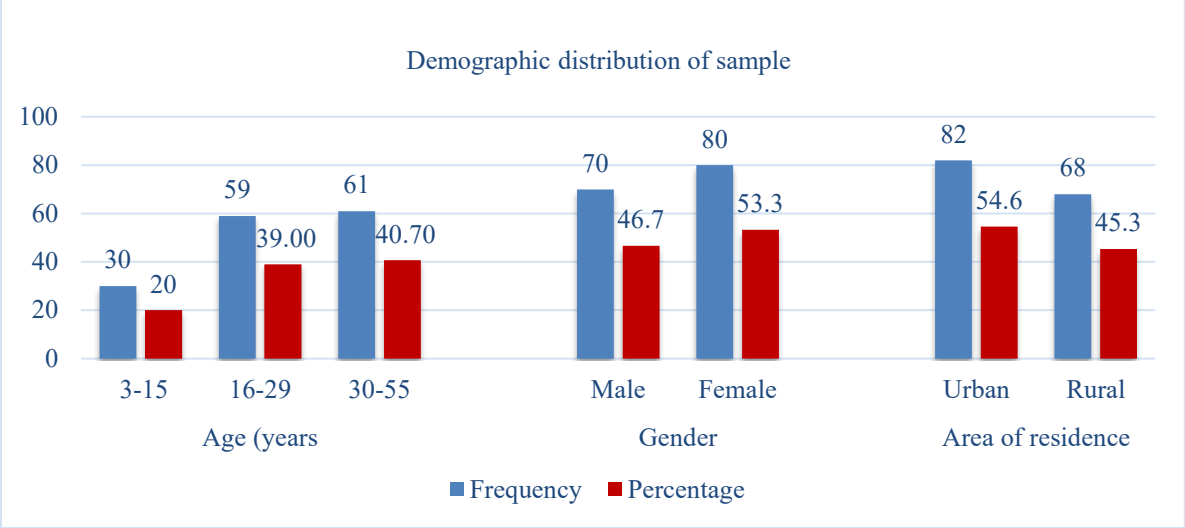

Figure 2 Demographic distribution of sample

3.1 | Distribution of *Helicobacter pylori* positive and negative Cases by the Specified Risk Factors

H. pylori was detected in 10% (15/150) of stool samples. Compared to positive sample of men 6(8.6%), women 9(11.3%) had a higher prevalence. Those between the ages of 16 and 29 had the greatest number of positive cases. The prevalence of *H. pylori* growth was much lower in urban regions 7(8.5%) than in rural areas 8(11.8%) positive samples).

Table 2 Helicobacter pylori cases by specified risk factors

Participant	Category	Positive (% age)	Negative (% age)	P-value
Age (years)	3-15	5 (16.7)	25 (83.3)	3.19
	16-29	6 (10.2)	53 (89.8)	
	30-55	4 (6.6)	57 (93.4)	
Gender	Male	6 (8.6)	64 (91.4)	0.786
	Female	9 (11.3)	71 (88.8)	
Area of residence	Urban	7 (8.5)	75 (91.5)	0.590
	Rural	8 (11.8)	60 (88.2)	
Smoking	Smokers	4 (11.4)	31 (88.6)	0.75
	Non-Smokers	11 (9.6)	104 (90.4)	
Poor Sanitation	Poor Sanitation	11 (18)	50 (82)	0.01
	Good Sanitation	4 (4.5)	85 (95.5)	
Family History	Having family history	10 (16.4)	51 (83.6)	0.05
	No family history	5 (5.6)	84 (94.4)	
Dietary Habits	Healthy food eaters	3 (4.2)	68 (95.8)	0.03
	Junk feeders	12 (15.2)	67 (84.8)	
Poor Dental Hygiene	Poor Dental Hygiene	7 (12.5)	49(87.5)	0.575
	Good Dental Hygiene	8 (8.5)	86 (91.5)	
Contaminated Food/Water	Contaminated	13 (19.7)	53 (80.3)	0.01
	Non-Contaminated	2 (2.4)	82 (97.6)	
Raw or Undercook Meat	Consumers	9 (13.8)	56 (86.2)	0.183
	Non-Consumers	6 (7.1)	79 (92.9)	
Health workers	Health worker	6 (18.2)	27 (81.8)	0.99
	Non worker	9 (7.7)	108 (92.3)	

Table 2 give information on the distribution of *Helicobacter pylori*-positive cases by the specified risk factors, such as smoking, poorness of sanitation, family anamnesis, and special eating habits. According to the data, the most notable risk factor includes poor sanitation which constitutes positive cases, family history, smoking, and unhealthy dieting habits. Antibiotic Susceptibility Testing. Out of the 15 *H. pylori*-positive isolates, resistance patterns were determined using the Epsilometer (E-test) method.

Table 3 Result indicating percentage of antibiotics susceptibility against *H. pylori*

Antibiotics	Susceptible (%)	Intermediate (%)	Resistant (%)
Amoxicillin (AMX)	12 (80%)	2 (13.3%)	1 (6.7%)
Tetracycline (TET)	10 (66.7%)	3 (20%)	2 (13.3%)
Metronidazole (MET)	6 (40%)	4 (26.7%)	5 (33.3%)
Clarithromycin (CLA)	7 (46.7%)	3 (20%)	5 (33.3%)
Rifampicin (RIF)	13 (86.7%)	2 (13.3%)	0 (0%)
Levofloxacin (LEV)	9 (60%)	3 (20%)	3 (20%)

Table 3 shows the Significant resistance rates of 33.3% to metronidazole and clarithromycin, indicate a reduction in the effectiveness of first-line therapies. Amoxicillin and Rifampicin are attractive therapy options due to their high susceptibility rates (80% and 86.7%, respectively). Levofloxacin: 20% moderate resistance, but still available for specialized treatments.

Table 4 Comparison of all antibiotics

Antibiotic	Amoxicillin (12)	Tetracycline (10)	Metronidazole (6)	Clarithromycin (7)	Rifampicin (13)	Levofloxacin (9)	Significant Comparisons (P<0.05)
Amoxicillin	-	0.464	0.016	0.03	0.625	0.224	Metronidazole, Clarithromycin
Tetracycline	0.464	-	0.09	0.145	0.224	0.625	Metronidazole
Metronidazole	0.016	0.09	-	0.807	0.004	0.224	Amoxicillin, Tetracycline, Rifampicin
Clarithromycin	0.03	0.145	0.807	-	0.009	0.33	Amoxicillin, Rifampicin
Rifampicin	0.625	0.224	0.004	0.009	-	0.09	Metronidazole, Clarithromycin, Levofloxacin
Levofloxacin	0.224	0.625	0.224	0.33	0.09	-	Rifampicin

The comparison of H. pylori susceptibility across six antibiotics indicates variable patterns of effectiveness. Amoxicillin showed significant differences in susceptibility when compared with metronidazole and clarithromycin, while tetracycline was significantly different only from metronidazole. Metronidazole demonstrated significant differences with amoxicillin, tetracycline, and rifampicin, and clarithromycin showed significant differences with amoxicillin and rifampicin. Rifampicin had significant differences with metronidazole, clarithromycin, and levofloxacin, whereas levofloxacin differed significantly only from rifampicin. Overall, these results suggest that metronidazole, clarithromycin, and rifampicin exhibit distinct resistance patterns compared to the other antibiotics, highlighting the importance of targeted therapy based on susceptibility testing.

4 | DISCUSSION

Helicobacter pylori was found in 10% (15/150) of stool samples, suggesting a moderate prevalence in the study population of Darya Khan District, Bhakkar.[10] This is consistent with global estimates, which show that *H. pylori* infection rates vary widely by region and are strongly influenced by socioeconomic conditions and sanitation standards.[10] Those between the ages of 30 and 50 years had the highest number of positive cases. This pattern is consistent with epidemiological evidence indicating that *H. pylori* infection is typically acquired in early childhood and persists into adulthood.[11]

Antibiotic resistance represents a major challenge in the treatment of *Helicobacter pylori* infection. Six antibiotics were evaluated for susceptibility, intermediate resistance, and resistance rates using the Epsilometer (E-test) method. Two antibiotics showed high resistance rates (33.3%), indicating declining effectiveness of conventional first-line therapies. This resistance pattern aligns with global trends showing increasing resistance to clarithromycin and metronidazole due to their widespread use in treating other infections.[12]

The most recommended triple or quadruple treatment regimens for *H. pylori* include omeprazole, clarithromycin, and amoxicillin. Additional antimicrobials such as rifabutin, levofloxacin, metronidazole, and tetracycline are also used. However, infection with clarithromycin-resistant strains is a major risk factor for treatment failure. When resistance to key antimicrobials is present, successful eradication becomes difficult. As a result, *H. pylori* treatment is often initiated empirically.[13]

High susceptibility rates (80% and 86.7%) indicate that some treatment options remain effective. Previous studies have shown that resistance to amoxicillin remains relatively low, likely due to its mechanism of action and the limited number of resistance-conferring mutations in *H. pylori*.[14] Moderate resistance rates (20%) suggest continued usefulness, particularly in tailored treatment strategies. However, increasing fluoroquinolone resistance—attributed to widespread use—necessitates cautious application.[15] Given resistance rates exceeding 30% for metronidazole, levofloxacin, and clarithromycin, empirical therapy without knowledge of local resistance patterns is inappropriate. Resistance to amoxicillin, rifabutin, and tetracycline remains low. Due to limited available data and significant heterogeneity across studies, continuous surveillance with systematic data collection has become essential for effective *H. pylori* management.[16]

Over a 15-year period, the most common resistance pattern among treatment-failure cases (secondary resistance) was observed against metronidazole (69.5%), followed by clarithromycin (38.5%), tetracycline (8%), and amoxicillin. These findings are consistent with broader antimicrobial surveillance data. In newly diagnosed patients, initial resistance rates were lower, with metronidazole at 38.1% and clarithromycin at 10.5%, approximately half the rates seen in patients with treatment failure.[17]

Yangzhou, located in Jiangsu Province, China, continues to report high gastric cancer incidence (44.05 per 100,000 population in 2013), with *H. pylori* infection recognized as the primary risk factor. Long-term cohort studies from Taiwan demonstrate that eradication of *H. pylori* significantly reduces gastric cancer incidence and mortality. However, high infection prevalence and increasing antibiotic resistance remain major barriers to effective treatment, with eradication failure observed in a substantial proportion of patients. These findings highlight the urgent need for localized resistance profiling.[18]

Antibiotic resistance is a global public health concern affecting numerous bacterial pathogens. Due to rising clarithromycin resistance, the World Health Organization classified *H. pylori* as a high-priority pathogen in 2017. Recent studies indicate persistently high resistance rates to clarithromycin and levofloxacin over the past eight years, particularly in southern Europe, while culture-based resistance monitoring remains limited (<10%).[19]
In the present study, *H. pylori* prevalence differed markedly between urban and rural populations, with 20% of positive cases from urban areas and 80% from rural settings. National data suggest that over 58% of Pakistan's population is infected with *H. pylori*, many of whom remain asymptomatic.[20] Factors such as healthcare access, hygiene practices, and water sanitation likely contribute to this disparity. Rural populations face higher infection risks due to poor living conditions and increased household transmission.[21]

Urban populations may also be at significant risk due to environmental and lifestyle factors. Molecular studies in Pakistan have identified point mutations in the 23S rRNA gene associated with clarithromycin resistance in *H. pylori* isolates, complicating treatment strategies and underscoring the importance of routine susceptibility testing.[22] High metronidazole resistance rates have been reported, reaching 73.6% in some studies.[23] This level of resistance compromises the effectiveness of standard treatment regimens. Amoxicillin resistance has been reported at 27.9%, raising concerns about its continued reliability despite lower resistance compared to clarithromycin and metronidazole.[23]
The increasing antimicrobial resistance in *Helicobacter pylori* necessitates a reassessment of current treatment protocols in Pakistan. Empirical therapy is no longer universally effective, and culture-guided susceptibility testing should be considered to optimize antibiotic selection. Public health interventions must target both urban and rural populations due to the high prevalence observed in both settings.

5 | CONCLUSION

In conclusion, new data highlight how urgently Pakistan needs to implement comprehensive public health initiatives and updated treatment protocols to effectively manage *Helicobacter pylori* infection. The findings highlight the importance of continuous surveillance of *Helicobacter pylori* resistance patterns. Given the increasing resistance to

Health Sciences Journal
EISSN: 2959-2259; PISSN:2959-2240

metronidazole and clarithromycin, alternative therapies such as amoxicillin and rifampicin should be considered. Additionally, addressing disparities in *H. pylori* prevalence between urban and rural areas through improved sanitation and targeted public health interventions remains crucial. In addition to all these information risk factors associated with *Helicobacter pylori* infection briefly describe the epidemiological aspect of disease in the human population of Darya Khan District Bhakkar.

6 | LIMITATIONS

This study was limited by a relatively small sample size and its single-center design, which may restrict generalizability to the wider population of Bhakkar District. Additionally, molecular characterization of resistance mechanisms and long-term follow-up of treatment outcomes were not performed, potentially limiting insights into resistance dynamics

Conflict of Interest statement: All authors declare no conflict of interest
Data Availability Statement: Data was available from the primary author and will be provided on special request
Authors' Contribution: All authors equally contributed to writing, reviewing and finalizing the draft
Funding: Not Applicable
Informed consent: Not Applicable
Ethical Approval: Not Applicable
Acknowledgement: We would like to express profound gratitude to each participant who shown their consent and cooperation for their data of this study.

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