

A Quasi Experimental Study of Helicobacter Pylori Eradication in Afghanistan: Comparison of Treatment Preferences for Helicobacter Pylori Eradications, Sequential Therapy Versus Hybrid Therapy

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ABSTRACT

Colonization by *Helicobacter pylori* (*H. pylori*) of the gastric epithelial lining epitomizes a pervasive and clinically consequential infectious etiology. Therapeutic strategies aimed at bacterial eradication inherently hinge on a confluence of determinants-regional antimicrobial resistance spectra, localized clinical algorithms, and pharmaceutical attainability. Best practices in the medical milieu underscore sagacious antibiotic stewardship, predicated on a patient-centric antibiotic historiography prior to therapeutic commencement.

The overarching objective of this study-executed in a quasi-experimental comparative framework at Sheikh Zayed University Teaching Hospital, Khost, Afghanistan-was to discerningly evaluate and contrast two paradigms of treatment: Sequential Therapy and Hybrid Therapy. The subject pool encapsulated a demographically diverse set of individuals, aged 16 to 80, manifesting symptoms of peptic ulcer diseases or gastritis. Those ineligible for inclusion included follow-up patients, immunocompromised subjects, and individuals undergoing oncological interventions.

Employing the Statistical Package for the Social Sciences (SPSS) Version 25 for data stratification, the Hybrid Therapy arm was subjected to an initial seven-day treatment window with amoxicillin (1g, BID) and omeprazole (20mg, BID), succeeded by a seven-day regimen involving clarithromycin (500mg, BID) and metronidazole (400mg, TID). Conversely, the Sequential Therapy cohort received a bifurcated, five-day course of omeprazole and amoxicillin, followed by an additional five-day regimen of omeprazole, metronidazole, and clarithromycin. Outcome variables, inclusive of treatment efficaciousness, regimen completion, and patient adherence, were rigorously evaluated via Chi-Square statistical testing.

Encompassing 145 patients, the study observed a gender dispersion of 156 males (41.1%) to 224 females (58.9%). Per-protocol analysis unveiled a statistically significant eradication rate-86.8% vs 83.0% ($P=0.021$)-tilted in favor of Hybrid Therapy. Both Modified Intention-to-Treat and Intention-to-Treat analyses corroborated this proclivity, registering significant eradication rates of 92.1% versus 67% ($P=0.031$) for Hybrid Therapy.

Conclusively, Hybrid Therapy demonstrated a superior safety and efficacy profile vis-à-vis Sequential Therapy in extirpating *H. pylori*, intimating its plausible preferability for the clinical management of associated peptic ulcer diseases and gastritis.

Keywords- *H. Pylori*, Hybrid treatment, Sequential treatment, Afghanistan.

I. INTRODUCTION

The ubiquity of *Helicobacter pylori* (*H. pylori*) and its established correlation with gastric and peptic

ulcers, gastric carcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma is well-documented in scientific literature. In patients grappling with ulcerative colitis, the prevalence of *H. pylori*

escalates exponentially to a staggering 80-90%, notably in economically underprivileged nations such as Afghanistan (Huang et al., 2017). A myriad of peer-reviewed studies corroborate the assertion that eradicating *H. pylori* can significantly attenuate the recurrence of ulcerative wounds (Talebi, 2014).

H. pylori represents perhaps the most ubiquitous human infection, with epidemiological estimates suggesting a prevalence exceeding half of the global population (Liou et al., 2018). In locales burdened by elevated clarithromycin resistance, a decadal concomitant therapeutic regimen has emerged as a compelling alternative to front-line interventions (Tai et al., 2015).

Traditionally, the mainstream eradication strategy deploys a tripartite pharmacological arsenal consisting of a proton pump inhibitor (PPI), clarithromycin, and either amoxicillin or metronidazole (Graham and Shiotani, 2012). Nevertheless, the suboptimal eradication efficiency of Sequential Treatment regimens has become a burgeoning clinical concern. Contributing variables, including duration, and dosages, are calibrated based on the theoretical robustness of the treatment paradigm (Chey et al., 2017). The enhanced performance of Hybrid Treatment modalities may plausibly be ascribed to extended therapeutic durations, systemic drug dissemination, and the synergistic bacterial cell wall lysis induced by amoxicillin-conditions that augur well for the intracellular bioavailability of macrolides, thereby optimizing clarithromycin efficacy (Chang et al., 2020).

The specter of antimicrobial resistance looms large as the etiological fulcrum underlying persistent *H. pylori* infections, post-treatment (Yuan et al., 2013). While Sequential Treatment has been recognized as the current standard of care, it's worth noting that its completion rates hover around 81.25% (Mahachai et al., 2018). Recent empirical inquiries unveil that Hybrid Treatment exhibits superior eradication metrics (89.5% vs. 76.7%) when deployed against peptic ulcer diseases, albeit without reaching a statistical significance threshold (Di Ciaula et al., 2017; Marcus et al., 2016).

II. MATERIAL AND METHODS

In the Division of Internal Medicine at Sheikh Zayed University Teaching Hospital in Khost, Afghanistan, an institutional ethics committee-approved, quasi-experimental comparative study was executed between June 2020 and March 2021, conforming to the ethical guidelines delineated by the same institution. The study focused on the clinical assessment of patients afflicted with peptic ulcer diseases (PUD) and gastritis.

Patient demographic was extensive, capturing ages between 16 to 80 and inclusive of all genders. However, exclusions were made for individuals attending follow-up appointments,

immunocompromised patients, or those undergoing oncological treatments. Statistical rigor was ensured by employing Statistical Package for the Social Sciences (SPSS), version 25, for data analysis.

For the study's purview, two distinct regimens- Hybrid Treatment (HT) and Sequential Treatment (ST)- were compared for efficacy, completion rate, and compliance among *Helicobacter pylori* (*H. pylori*) positive patients. Classification into HT or ST was conducted using the Stratified Nomenclature of Medical Entities (SNOSE) methodology.

Patients in the HT cohort were administered a regimen of amoxicillin (1g bid) and omeprazole (20mg bid) for the initial 7-day phase, succeeded by a combination of omeprazole, clarithromycin (500mg bid), metronidazole (400mg tid), and amoxicillin for the subsequent 7 days. In contrast, the ST group commenced with a 5-day course of omeprazole and amoxicillin, followed by omeprazole, metronidazole, and clarithromycin for the subsequent 5 days. Moreover, all patients with PUD continued with proton pump inhibitors (PPIs) for an additional 5 weeks to facilitate mucosal healing.

A post-treatment follow-up endoscopy was undertaken after a 1.5-month interval to validate wound healing and *H. pylori* eradication. Dual biopsy samples were obtained from the gastric corpus and antrum for urease testing and histological evaluation. The eradication of *H. pylori* was confirmed through a negative urease test or histological evidence. Comparative analysis between the HT and ST therapeutic approaches was performed using the Chi-Square test, again employing SPSS version 25 for statistical validation.

This comprehensive clinical study thus furnishes a comparative evaluation of HT and ST protocols, offering a methodical approach to treating peptic ulcer diseases and gastritis in a tertiary care setting.

III. RESULTS

In a comprehensive analysis delineated in Table 1, a cohort of 145 patients was meticulously scrutinized for conditions related to peptic ulcers and gastritis. The age demographics can be disaggregated as follows: 18 individuals were in the age bracket of 16-20 years; 16 participants, constituting 11.0%, fell within the 21-25 years range. A segment of 8.2% (12 patients) was categorized within the 26-30 years cohort, whereas those in the 31-35 years interval accounted for 5.5% (8 patients). The subsequent age categories revealed 9 patients (6.2%) in the 36-40 years stratum, 11 patients (7.6%) within 41-45 years, and 7 patients (4.8%) in the 46-50 years category. Moreover, 19 patients (13.10%) were aged 51-55 years, followed by 6 patients (4.1%) in the 56-60 years group. For the higher age bands, 14 patients (9.7%) were documented between 61-65 years,

and 18 patients (12.4%) were in the 66-70 years cluster. Only a minuscule 1.2% (4 patients) were aged 71-75 years, and a scant 1.1% (3 patients) fell into the 76-80 years category, as visualized in Figure 1.

As delineated in Table 2 and Figure 2, gender distribution within the 145-patient cohort revealed that 156 individuals (41.1%) identified as male, while 224 (58.9%) were female.

Pertaining to the efficacy of *Helicobacter pylori* eradication in peptic ulcer patients, a comparative analysis was conducted between two treatment modalities: Standard Treatment (ST) and High-dose Treatment (HT). By employing the Per Protocol (PP)

analysis, it was ascertained that the eradication rate of *H. pylori* was 83.0% with ST as compared to 86.8% with HT, yielding a p-value of 0.021. In addition, a Modified Intention-to-Treat (mITT) analysis revealed an eradication rate with a p-value of 0.031, whereas a full Intention-to-Treat (ITT) analysis recorded rates of 67% versus 92.1%. These results are comprehensively explicated in Tables 3 and 4, as well as Figure 3.

Statistical intricacies further unveil that 112 cells (or 86.2% of the total) manifested an expected count of less than 5, with the lowest anticipated count reaching 0.41, bolstering the robustness of the undertaken analyses.

Table 1. Age distribution of patients

Age	Frequency	Percent
16-20 YEARS	18	12.4
21-25 YEARS	16	11.0
26-30 YEARS	12	8.2
31-35 YEARS	8	5.5
36-40 YEARS	9	9.7
41-45 YEARS	11	6.2
46-50 YEARS	7	4.8
51-55 YEARS	19	13.1
56-60 YEARS	6	4.1
61-65 YEARS	14	9.7
66-70 YEARS	18	12.4
71-75 YEARS	4	1.2
76-80 YEARS	3	1.1
Total	145	100.0

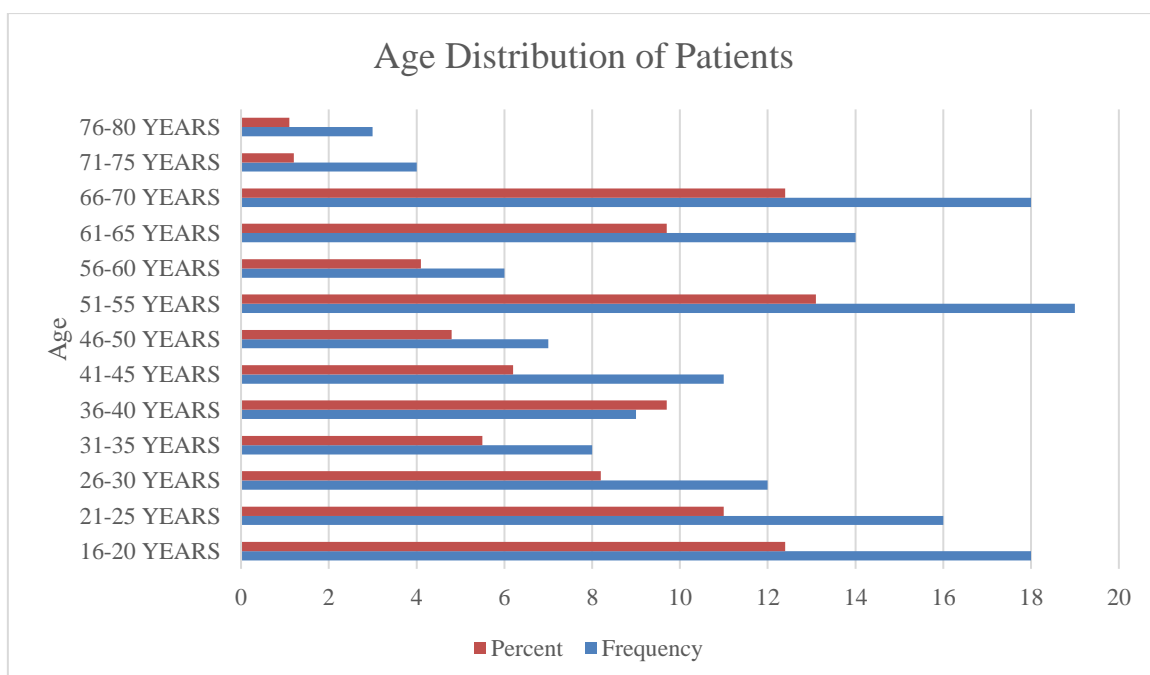


Figure 1. Age Distribution of patients

Table 2: Gender distribution of Peptic ulcer Patients

Gender	Frequency	Percent
MALE	86	59.3
FEMALE	59	40.6
Total	145	100.0

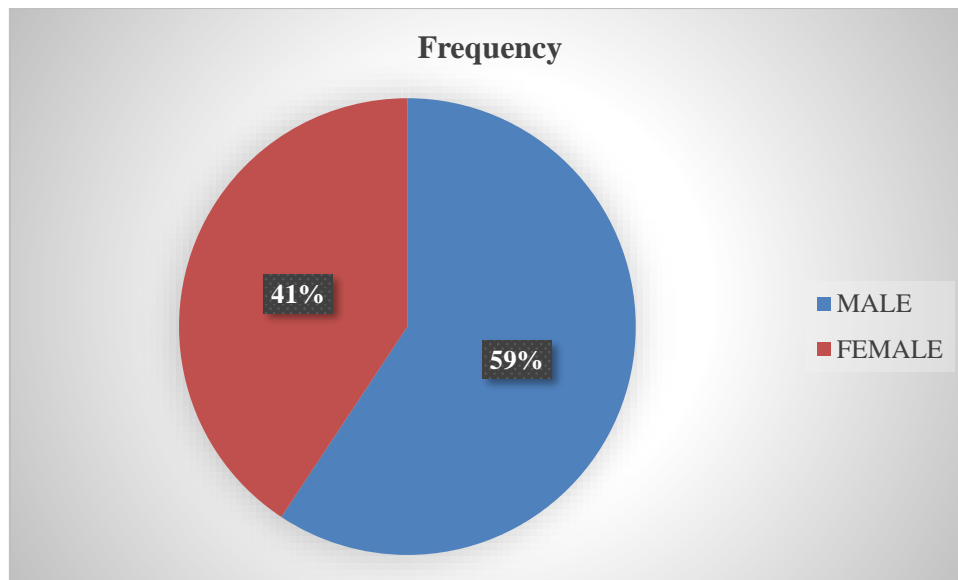


Figure 2: Gender Distribution

Table 3. Comparing the helicobacter pylori eradication rates with the sequential therapy and hybrid therapy

Type of Analysis	Sequential Treatment	Hybrid Treatment	<i>P value Chi squares</i>
Per Protocol	83.0[54 /65]	86.2[69/80]	0.021
Modified Intention To Treat	72.3[47 /65]	89.8[71/79]	0.031
Intention To Treat	67.6[45 /65]	92.1[70/76]	0.005

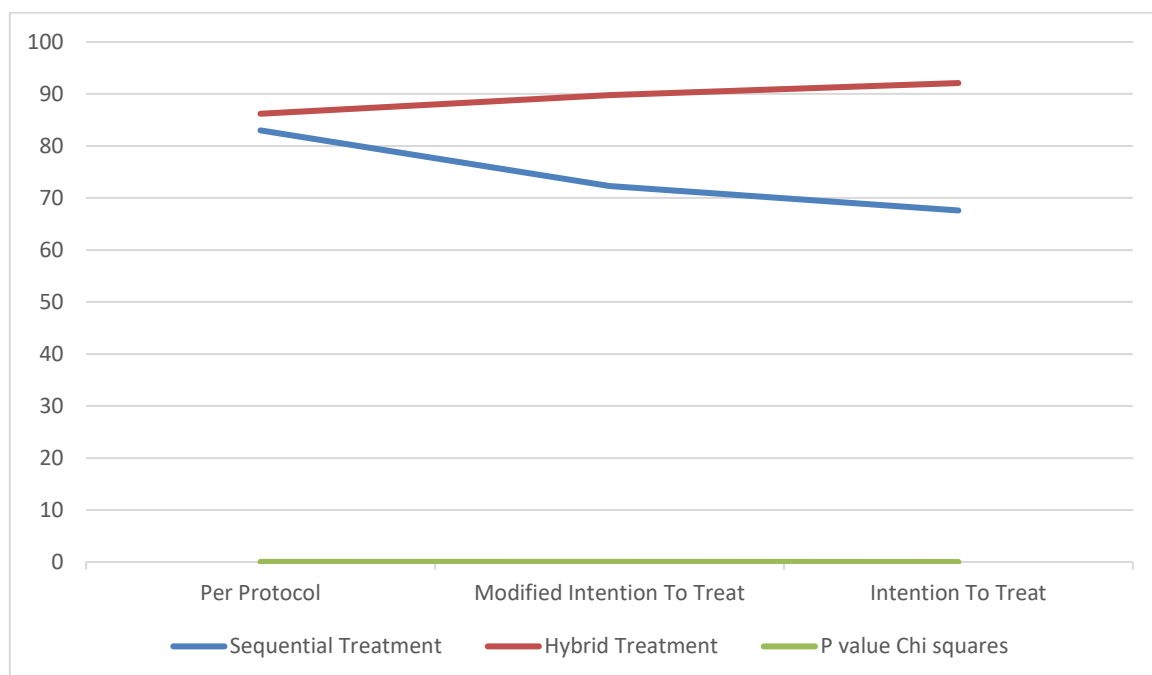


Figure 3: Hybrid treatment show less complications as compared to sequentialtreatment, i.e 3:9.

Table 4. Showed significant results.

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1603.020 ^a	108	.000
Likelihood Ratio	1155.418	108	.000
Linear-by-Linear Association	271.344	1	.000
N of Valid Cases	380		

IV. DISCUSSION

In emerging economies such as Afghanistan, healthcare economics become especially critical, given the onus of medical expenditures falls predominantly on the individual, with universal healthcare coverage remaining largely inaccessible (Jung et al., 2021). Within this context, our current investigation scrutinizes the cost-efficacy of Helicobacter pylori eradication through either Hybrid Therapy or Sequential Treatment modalities (Yang et al., 2021).

Our financial evaluation unveils a pivotal role for treatment cost in shaping the scalability and adoption of Hybrid Therapy. Notably, an elongated therapeutic window-14 days for Hybrid Treatment compared to a 10-day course for Sequential Treatment-precipitates an incremental financial burden (Mohsina et al., 2016). While the Hybrid regimen achieves superior eradication efficiencies, this amplified cost metric warrants consideration when advocating for its universal implementation (Vlăduț et al., 2020).

Further granularity in our data reveals that Hybrid Treatment is particularly advantageous in contexts where dual antibiotic resistance to clarithromycin and metronidazole exists. Despite this, the attrition rate in the Hybrid cohort is relatively elevated, attributable to the protracted treatment period and the sustained administration of amoxicillin in a low-dose continuum. The latter results in an attrition rate ranging from 0% to 1.6% compared to other antibiotics still under therapeutic consideration. This is consonant with findings from Lin Hay et al., where neither treatment approach demonstrated resistance as a significant variable contributing to therapy termination (Lin et al., 2015).

Toward the assessment of adverse drug reactions, our findings resonate with extant literature, typifying gastrointestinal discomforts like diarrhea as the most prevalent sequela in both treatment cohorts. Parallel investigations, particularly from Korean studies, highlight additional complications such as bitter taste and epigastric discomfort. Crucially, however, our comparative analysis divulged no statistically significant variation in the incidence of side effects between Hybrid and Sequential Treatments (Di Ciaula et al., 2017).

Thus, while Hybrid Therapy demonstrates higher eradication rates, the fiscal implications and potential for increased treatment attrition contribute

nuanced complexities to its broader adoption, especially in economically constrained environments.

V. CONCLUSION

In summary, our analysis compellingly elucidates that hybrid therapy stands as a paramount modality in the eradication of Helicobacter pylori, substantially outperforming sequential treatment approaches in terms of efficacy. This accentuates the pivotal role that hybrid therapy could potentially play in revolutionizing current gastroenterological paradigms, offering a higher likelihood of complete microbial obliteration. Thus, clinicians and healthcare providers might consider prioritizing hybrid therapeutic regimes as the gold standard for H. pylori elimination to optimize patient outcomes.

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