

ORIGINAL ARTICLE

The Efficacy of Levofloxacin-Based Triple Therapy over Standard Clarithromycin-Based Therapy for Eradication of Helicobacter PyloriHaseeb Noor^{1*}, Kazim Abbas Virk², Hyder Wajid Abbasi³, Sana Tahir Virk⁴, Sara Shahid⁵, Muhammad Erfan⁶**ABSTRACT**

Objective: To compare a first-line Clarithromycin-based triple therapy to Levofloxacin-based triple therapy for eradicating H.Pylori.

Study Design: Comparative analysis.

Place and Duration of Study: The study was carried out at the Department of the Gastroenterology of Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, from June 2021 to December 2021.

Methods: A total of 200 patients were enrolled in this comparative study, conducted in the outpatient Department of Gastroenterology. A pretested questionnaire was used to gather the required information; a group was allocated to each patient, and a response was sent to each treatment group after random sampling. The primary outcome was a negative Urea Breath test 4 weeks after completion of treatment.

Results: Out of 200 patients, 58 % (n=116) were males, and 39% (n= 84) were females. The mean age was 40.02 ± 24.4 years. Predominant presenting complaints were Retrosternal burning in 41 % (n=82), and pain and/or discomfort in the upper abdomen 34% (n=68). The response rate in the Clarithromycin based therapy group was 84% (n=84) out of 100 patients, while the response rate was 94% (n= 94) out of 100 in the Levofloxacin-based therapy group.

Conclusion: Levofloxacin-based therapy is superior to Clarithromycin-based therapy in every age group and gender.

Keywords: Clarithromycin, Helicobacter Pylori, Levofloxacin, Peptic Ulcer.

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Introduction

Helicobacter Pylori constitutes a major health problem in terms of it being a causative factor in many stomach and intestine related diseases.¹ Its presence is dependent on factors like geography,

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ethnicity, age and socioeconomic status.² Peptic ulcer disease encompasses a wide spectrum of conditions that has affected 8.09 million of world's population.³ It could either be organic in nature (that is ulcerative) or functional. According to Rome 2 criteria, functional dyspepsia was defined as discomfort centered in the upper abdomen in the absence of other causes ruled out via endoscopy and ultrasound.⁴ Dyspepsia is a complex set of symptoms defying simple categorization. There are many causes of dyspepsia including peptic ulcer due to H. Pylori infection and other causative factors, gastroesophageal reflux disease and gastric cancer. In 60% of the people the results of all the investigations are normal and are designated as having functional dyspepsia.⁴ There is an impregnable connection between this bacteria and dyspepsia.^{5,6} H. Pylori is

closely associated with chronic gastritis, peptic ulcers, Carcinoma stomach and lymphoma and is one of the most prevalent infections in the world.⁷ H. Pylori status can be determined non-invasively by serology, stool for H-Pylori antigen, carbon 13 urea breath test while invasive tests for detection that require an endoscopically obtained biopsy for testing include rapid urease test, culture, histology and pcr.⁸ Pakistan is a developing country in which more than 70% of people have poor living conditions. In a study conducted in Timergara city of Pakistan, 22.1% symptomatic individuals were found to have H. Pylori.⁹ Another study conducted in Peshawar, Pakistan revealed that 45.5% of their patients with the symptoms of dyspepsia had H. Pylori infection.¹⁰ A meta-analysis found 56.6% of patients have H. Pylori in Pakistan.¹¹ This figure is close to other neighboring countries in the region (India 49.5%) (Iran 44.5%).^{1,2} H. Pylori infection can harm the stomach and duodenum in following manner. It can lead to too much or too little acid formation in stomach. In case of too much acid the duodenum can get damaged.¹³ It can also eventually damage the lining of stomach leading to stomach cancer.^{3,4}

Some other disorders associated with H. Pylori are Gastritis: Swelling or irritation (inflammation) of the lining of stomach.¹⁵ Extra Gastrointestinal Diseases like insulin resistance, diabetes mellitus, nonalcoholic fatty liver disease, metabolic syndrome.⁶ Worldwide, there are a lot of regimens available to treat H. Pylori and Clarithromycin remains an important component of these regimens especially in areas with low clarithromycin resistance.⁷ Clarithromycin based triple therapy is extensively used in our region owing to its easy availability and low cost. This has led to high resistance and failure to treat H. Pylori.⁸ Levofloxacin based therapy provides a good alternative to Clarithromycin in areas of high resistance.⁹ This study was done to assess Levofloxacin based therapy performance in our region compared to Clarithromycin based therapy.

Methods

The study was carried out at the Department of the Gastroenterology of Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan from 6th June 2021 to 6th December 2021 after taking approval from the institutional review committee held on 10th

April 2021 vide letter no: PIMS-ERB-006. Total 200 patients were included in this study. After taking an explained and written consent from the patients, the patients were enrolled in study. History was taken in detail and thorough examination was performed. After clinical suspicion, diagnostic test Urea Breath Test was performed. In case of positive result, we allocated patients into two groups by randomization each with 100 patients. Group A was given Amoxicillin 1000 mg, Clarithromycin 500 mg and rabeprazole 20 mg, all twice daily for 10 days. Group B was given Amoxicillin 1000 mg twice daily, Levofloxacin 500 mg once daily and rabeprazole 20 mg, twice daily for 10 days. All patients were informed about all possible side effects of drugs and advised to stop all drugs if they appear with follow-up in Gastroenterology OPD. Brand name of drugs were kept same in all patients. Patient were counselled not to use any additional drug during eradication tenure. Moreover, patients were requested to refrain from using any treatment following completion of treatment duration so as not to interfere with resetting via Urea Breath test. After completion of 4 weeks, Urea Breath test was repeated and outcome was noted.

Statistical Analysis

The data was analyzed by SPSS software version 17. Calculations were done for all variables like age, gender and efficacy. Frequency and percentage were presented for gender and efficacy. Mean and standard deviations were calculated for the patients' ages, being a continuous variable. The results are shown in terms of tables. Effect modifiers were controlled by stratification. Post-stratification chi-square test was applied. *P* value <0.05 was taken as significant.

Results

The mean age of patients was 40.02 ±24.4 yrs. Ranging from 18 to 65 years. Most (67.5%) were younger than 50. Male gender was predominant, with a 58% proportion compared to females who were 42% in the current study. (Table 1).

In our study almost 51% of the patients presented from Islamabad and its surroundings. Only 11 (5.5%) patients presented from Khyber Pakhtoon Khwa 61 (30.5%) from Rawalpindi and its surroundings. The family income of patients was < Rs. 10000/= in 73

Table 1 : Baseline Characteristics of study patients (n=200)

Age (years)		
Mean +-SD	40.02+-24.4	
Range (Min-Max)	18-65	
Age categories (years)	Frequency (n)	Percentage (%)
18-20	05	2.5
21-20	31	15.5
31-40	42	21
41-50	57	28.5
51-60	48	24
>61	17	8.5
Gender		
Male	116	58
Female	84	42

(36.5%) cases, while the majority, 127 (63.5%) of the study patients, had income more than PKR. 10000 per month. Most of the patients 81 (40.5%) were enrolled from the inpatient department, while 119 (59.5%) came from the outpatient department. (Table 2). The presenting complaints of patients were retrosternal burning in 82 (41%) cases, bloating in 29 (14.5%) cases, pain and/or discomfort in the upper

abdomen in 68 (34%) and water brash was present in 21 (10.5%) of the study cases. (Table 3). In our study, we divided the study patients in two groups, each with 100 patients. Overall response rate was 94% in Levofloxacin based therapy group while 84 % in Clarithromycin based group. (Table 4). We found out that in Group A (Clarithromycin-based therapy) 59 (88%) male patients responded.

Table 2: Socioeconomic characteristics and mode of presentation (n=200)

Variables	Frequency (n)	Percentage (%)
Place of Residence		
Islamabad	102	51
Khyber Pakhtoon Khwah	11	5.5
Rawalpindi	61	30.5
Murree	26	13
Family Income		
<Rs 10000	73	36.5
>Rs 10000	127	63.5
Mode of Presentation		
Outpatient	119	59.5
Inpatient	81	40.5

Table 3: Presenting complaints in the study Patients (n=200)

Symptoms	Frequency (n)	Percentage (%)
Pain or discomfort in upper abdomen	68	34
Retrosternal burning	82	41
Bloating	29	14.5
Water Brash	21	10.5

to Clarithromycin based therapy while 08 (12%) male patients had no response to it. In Group B, (Levofloxacin based treatment), we found out that 47 (95.9%) male patients responded to Levofloxacin based therapy while 02 (4.1%) male patients had no response to this therapy. In females, we found out that in Group A (Clarithromycin-based therapy), 25

(75%) female patients responded, while 08 (25%) female patients had no response. In Group-B, (Levofloxacin based therapy), we found out that 47 (92%) female patients responded to Levofloxacin based therapy while 04 (08%) female patients had no response. (Table 5). In our study we found out that the response rate in

Table 4: Overall Response Rates in two Groups (n=200)

Name of Therapy	Number of Patients Responded (n)	Percentage of Response (%)
Clarithromycin Based Therapy Group A (n=100)	84	84
Levofloxacin Based Therapy Group B (n=100)	94	94

Group A (Clarithromycin based therapy) was 60%, while in Group B, the response rate was 40% in patients aged 18-20 years. The response rate in Group A (Clarithromycin based therapy) was 54% while in Group B the response rate was 32% in patients having age 21-30 years (0.001). The response rate in Group A was 40%, while in Group-B, the response rate was 54.8% in patients having age 31-40 years (0.001); the response rate in Group A (Clarithromycin-based therapy) was 66.6%, while in

Group B the response rate was 22.8% in patients having age 41-50 years (0.001). The response rate in Group A was 18%, while in Group B, the response rate was 72% in patients aged 51-60 years (0.001). The response rate in Group A was 23% while in Group B the response rate was 71% in patients having age more than 60 years (0.001). (Table 6).

Discussion

Helicobacter pylori was discovered by Dr Barry Marshall and Dr. Robin Warren.¹⁰ H. Pylori infection is

Table 5: Stratification according to Gender (n=200)

Gender	Clarithromycin-based Therapy n (%)	Levofloxacin Based Therapy n (%)	P value
Male (n=116)	Yes 59 (88)	Yes 47 (95.9)	0.001
	No 8 (12)	No 2 (4.1)	
Female (n=84)	Yes 25 (75)	Yes 47 (92)	0.001
	No 08 (25)	No 04 (8)	

Table 6: Stratification according to Age (n= 200)

Age Categories (years)	Clarithromycin-based Therapy n (%)	Levofloxacin-based Therapy n (%)	P-value
18-20 (n =5)	Yes 3 (60)	Yes 2 (40)	0.001
	No 0 (0)	No 0 (0)	
21-30 (n =31)	Yes 17 (54)	Yes 10 (32.3)	0.001
	No 4 (13)	No 0 (0)	
31-40 (n =42)	Yes 17 (40)	Yes 23 (54.8)	0.001
	No 2 (5)	No 0 (0)	
41-50 (n =57)	Yes 34 (62.6)	Yes 13 (22.8)	0.001
	No 7 (5.2)	No 3 (5.2)	
51-60 (n =48)	Yes 9 (18)	Yes 34 (72)	0.001
	No 3 (6.2)	No 2 (4.3)	
>61 (n =17)	Yes 4 (23.5)	Yes 10 (71.5)	0.001
	No 0 (0)	No 3 (3.1)	

nowadays recognized as one or the most common infections having a wide spectrum of implications from epigastric discomfort and halitosis to cancer.¹⁰⁻¹¹ Its prevalence is highest in Africa (79.1%), Latin America and the Caribbean (63.4%), and Asia

(54.7%).¹¹ In Pakistan, its prevalence is around 56-60%.¹² Compared to our findings, previous studies report variable rates. In a study conducted in Saudi Arabia, 62% infection cure rate was reported in

Clarithromycin-based therapy, while in Group B (Levofloxacin based therapy) cure rate was 74.5%.¹³ In another study conducted in Iran, 66.3% of the cure was reported to be in Clarithromycin-based therapy while in Group B (Levofloxacin based therapy) cure rate was 75.2%.¹⁴ In yet another study of Myanmar, a 47.5% cure rate was reported in Clarithromycin - based therapy while in Group B (Levofloxacin based therapy), the cure rate was 50.8%.¹⁵

The average presenting age of our study patients was 40.0 ± 24.4 years ranging from 18 to 65 years. There is a slight variation in the presenting age between different geographical regions. In our study male gender was predominant with 58% proportion and ratio of 1.5: 1. The presenting complaints in our study patients were retrosternal burning (41%), bloating (14.5%), pain/discomfort upper abdomen (34%) and water brush was present in 10.5% cases. Compared to our findings another study conducted in Sudan mentioned that the main symptoms were either Nausea (25.5%) or Gastric Pain (24.5%).¹⁶

In our study overall response rate was 84% in Clarithromycin based therapy group and 94 % in Levofloxacin based therapy group. Higher eradication rates were achieved in Levofloxacin group (Group B) which is consistent with a study in Egypt that were done to ascertain same outcome.²⁷ Ahmadi B also achieved above 90 % eradication rates in H. Pylori patients treated with Levofloxacin based therapy as compared to Clarithromycin based therapy where the results were suboptimal.¹⁷

Interestingly our study showed that female patients had higher rates of treatment failure (25% vs 12%) in Clarithromycin based group (Group A). This is consistent with study performed by Chang Y W which showed that female gender was independently associated with treatment failure of Clarithromycin based treatment for H. Pylori.¹⁸

Age-wise categorization of response rates showed that young adults (21-30yrs) showed highest rate of treatment failure in Clarithromycin based therapy group. This is consistent with a study in Hong Kong conducted over 15 years that evaluated clarithromycin failure in different age groups and called for early treatment of H. Pylori in the younger population.¹⁹

Standard triple therapy for eradicating H. Pylori

consists of a Proton pump inhibitor, amoxicillin, and Clarithromycin. Clarithromycin resistance is the major cause treatment failure.^{19,20} Collective data from 20 studies showed a success rate of 88% in Clarithromycin sensitive strains.^{21,22} Therefore, clarithromycin failure in a population is a big factor.⁷ A Review showed that Clarithromycin resistance varies in different regions, and its affects efficacy of Standard Amoxicillin-based standard therapy in eradicating H. Pylori. Hence, it is still acceptable to advise a Clarithromycin based treatment in areas with Clarithromycin non response of < 10%. However, in many other countries where Clarithromycin resistance is high Levofloxacin-based therapy is one of the regimens used. Moreover, regardless of clarithromycin resistance rates, it is shown that standard therapy's maximum efficiency in curing H. Pylori is up to 64.66 % in patients who have been exposed to COVID -19.²³ This is especially important in current times due to the massive exposure of population to Covid-19. In another study in which patients underwent endoscopy, biopsy and got tested for H. pylori, those who tested positive were divided into two groups and It was observed that Levofloxacin based therapy was more efficacious (89% cure rate) as compared to one with Clarithromycin (67% cure rate).²⁴ In yet another multicenter study carried out, they divided their patients into three groups. All groups received treatment for seven days. The patients in group A received amoxicillin standard triple therapy; the patients in group B received Levofloxacin based triple therapy; and the patients in group C received Levofloxacin, Clarithromycin and esomeprazole. Treatment of this stomach bug was successful in 136/150 (90.6%) of the patients in group C, in 127/150 (84.7%) of the patients in group B and in 118/150 (78.6%) of the patients in group A.²⁵ These findings demonstrate the need for new therapies in populations in which there is resistance to Clarithromycin and possibly testing before starting regimes containing this drug.²⁶

In Pakistan, Clarithromycin resistance is very high.^{27,28} Factors responsible could be clinical misuse and easy availability.^{29,30} Keeping this in mind the current research was planned to evaluate an alternative efficacious therapy. By treating this infection with

the help of an efficacious drug regime, we can improve the quality of life as well as reduce the risk of gastric carcinoma in these patients.

Conclusion

Clarithromycin-based triple therapy achieves suboptimal response in areas with high resistance. In Pakistan, Levofloxacin-based triple therapy provides a good alternative option in terms of availability, ease of use and a good side effect profile albeit at the cost of increased financial burden. More studies are needed to study the resistance of Clarithromycin and its comparison to Levofloxacin in eradicating H. Pylori.

REFERENCES

1. Haq I, Muhammad A, Fazli Zahir MK, Anwar F, Akhtar MS, Ullah F. Serological and Epidemiology study of Helicobacter pylori infection among Dyspeptic patients in District Peshawar Pakistan. *Advanced Biomedical Research*. 2020; 11: 81-5. doi: 10.15515/abr.0976-4585.11.3.8185
2. Kharel S, Bist A, Shrestha S, Homagain S. Helicobacter pylori healthy South Asians. *JGH Open*. 2020; 4: 1037-46. doi: 10.1002/jgh3.12426
3. Maleki I, Mohammadpour M, Zarrinpour N, Khabazi M, Mohammadpour RA. Prevalence of Helicobacter pylori infection in Sari Northern Iran; A population based study. *Gastroenterology and Hepatology from Bed to Bench*. 2019; 12:31-7.
4. McColl KEL, El-Omar E, Gillen D. Helicobacter pylori gastritis and gastric physiology. *Gastroenterology clinics of North America*. 2000; 29: 687-703. doi: 10.1016/S0889-8553(05)70138-2
5. Wang YK, Li C, Zhou YM, Zeng L, Li YY, Huang SL, et al. Histopathological Features of Helicobacter pylori Infection in Gastric Mucosa. *Journal of Inflammation Research*. 2022; 15: 6231-43. doi: .10.2147/JIR.S383075
6. Cho J, Prashar A, Jones NL, Moss SF. Helicobacter pylori Infection. *Gastroenterology Clinics of North America*. 2021; 50: 261-82. doi: 10.1016/j.gtc.2021.02.001
7. Pellicano R, Ianiro G, Fagoonee S, Settanni CR, Gasbarrini A. Extragastric diseases and Helicobacter pylori. *Helicobacter*. 2020; 25: e12741. doi.org/10.1111/hel.12741
8. Suzuki S, Kusano C, Horii T, Ichijima R, Ikehara H. The ideal Helicobacter pylori treatment for the present and the future. *Digestion*. 2022; 103: 62-8. doi: 10.1159/000519413
9. Khurshid MB, Ahmed S, Javed S, Javed MA, Faizan M, Bangash H, et al. Therapeutic Guidelines and Antimicrobial Resistance of Helicobacter Pylori in Patients with Peptic Ulcer at Tertiary Care Hospitals of Rawalpindi and Islamabad. *Pakistan Journal of Medical & Health Sciences*. 2022; 16: 672-4. doi: 10.53350/pjmhs22168672
10. Arj A, Mollaei M, Razavizadeh M, Moraveji A. The comparison of levofloxacin-and clarithromycin-based bismuth quadruple therapy regimens in Helicobacter pylori eradication. *Journal of Research in Pharmacy Practice*. 2020; 9: 101-5. doi: 10.4103/jrpp.JRPP_19_86
11. McNicholl AG, O'Morain CA, Megraud F, Gisbert JP, As Scientific Committee of the Hp-Eureg on Behalf of the National Coordinators. Protocol of the European registry on the management of Helicobacter pylori infection (Hp-EuReg). *Helicobacter*. 2019; 24: e12630. doi: 10.1111/hel.12630
12. Werdmuller BF, Van Der Putton TB, Balk TG, Lamers CB, Loffeld RJ. Clinical presentation of Helicobacter pylori-positive and negative functional dyspepsia. *Journal of Gastroenterology and Hepatology*. 2000; 15: 498-502. doi: 10.1046/j.1440-1746.2000.02080.x.
13. Mehmood K, Awan AA, Muhammad N, Hasan F, Nadir A. Helicobacter Pylori prevalence and histopathological findings in dyspeptic patients. *Journal of Ayub Medical College Abbottabad*. 2014; 26: 182-5.
14. Azab ET, Thabit AK, McKee S, Al-Qiraiqiri A. Levofloxacin versus Clarithromycin for Helicobacter pylori eradication: are 14 day regimens better than 10 day regimens?. *Gut Pathogens*. 2022; 14: 24. doi: 10.1186/S13099-022-00502-3
15. Keikha M, Askari P, Ghazinivi K, Karbalaee M. Levofloxacin-based therapy as an efficient alternative for eradicate Helicobacter pylori infection in Iran: a systematic review and meta-analysis. *Journal of Global Antibiotic Resistance*. 2022; 29: 420-9. doi: 10.1016/j.jgar.2021.10.019
16. Aung WP, Aye TT, Aye KS, Kyaw AMM. Levofloxacin-based Helicobacter pylori eradication in chronic dyspepsia. *Gastrohep*. 2021; 3: 394-400. doi: 10.1002/ygh2.478
17. Abbas M, Sharif FA, Osman SM, Osman AM, El Sanousi SM, Magzoub M, et al. Prevalence and associated symptoms of Helicobacter pylori infection among schoolchildren in Kassala State, East of Sudan. *Interdisciplinary perspectives on infectious diseases*. 2018; 2018: 4325752. doi: 10.1155/2018/4325752
18. Elantouny NG, Abo Bakr AA, EL-Sokkary RH, Elshahat YE. Levofloxacin versus clarithromycin-based therapy for eradication of Helicobacter pylori infection: A comparative study. *Zagazig University Medical Journal*. 2019; 25: 500-7.

- doi: 10.21608/zumj.2019.8141.10510
19. Ahmadi B, Hajmohammadi M, Saeed Pour A, Zaherara M, Shafieepour S, Ghazizadeh Ahsaei H. Evaluation of Levofloxacin-containing Regime in Comparison with Clarithromycin-containing Regime in Eradicating *Helicobacter pylori* Infection in Kerman. *Journal of Kerman University of Medical Sciences*. 2022; 29: 123-33. doi: 10.22062/jkmu.2022.91889
 20. Chang YW, Ko WJ, Oh CH, Park YM, Oh SJ, Moon JR, et al. Clarithromycin resistance and female gender affect *Helicobacter pylori* eradication failure in chronic gastritis. *The Korean journal of internal medicine*. 2019; 34:1022-9. doi: 10.3904/kjim.2018.054
 21. Jiang F, Guo CG, Cheung KS, Li B, Law SY, Leung WK. Age of eradication and failure rates of clarithromycin-containing triple therapy for *Helicobacter pylori*: A 15-year population-based study. *Helicobacter*. 2022; 27: e12893. doi:10.1111/hel.12893
 22. Nestegard O, Moayeri B, Halvorsen FA, Tonnesen T, Sorbye SW, Paulssen E. *Helicobacter pylori* resistance to antibiotics before and after treatment: Incidence of eradication failure. *PLOS One*. 2022; 17: e0265322. doi: 10.1371/journal.pone.0265322
 23. Chuah SK, Tsay FW, Hsu PI, Wu DC. A new look at anti-*Helicobacter pylori* therapy. *World Journal of Gastroenterology*. 2011; 17: 3971-5. doi: 10.3748/wjg.v17.i35.3971
 24. Kamal A, Ghazy RM, Sherief D, Ismail A, Ellakany WI. *Helicobacter pylori* eradication rates using Clarithromycin and levofloxacin-based regimens in patients with previous COVID-19 treatment: a randomized clinical trial. *BMC Infectious Diseases*. 2023; 23: 1-8. doi: 10.1186/s12879-023-07993-8
 25. Dib J Jr, Alvarez B, Mendez L, Cruz ME. Efficacy of PPI, Levofloxacin and amoxicillin in the eradication of *Helicobacter pylori* compared to conventional triple therapy at a Venezuelan hospital. *Arab Journal of Gastroenterology*. 2013; 14: 123-5. doi: 10.1016/j.ajg.2013.09.001
 26. Assem M, El Azab G, Rasheed MA, Abdelfatah M, Shastery M. Efficacy and safety of Levofloxacin, Clarithromycin and Esomeprazole as first line triple therapy for *Helicobacter pylori* eradication in Middle East. Prospective, randomized, blind, comparative, multicenter study. *European Journal of Internal Medicine*. 2010; 21: 310-4. doi: 10.1016/j.ejim.2010.05.011
 27. Kocsmar E, Buzas GM, Szites I, Kocsmar I, Kramer Z, Szijarto A. Primary and secondary clarithromycin resistance in *Helicobacter pylori* and mathematical modeling of the role of macrolides. *Nature Communications*. 2021; 12: 2255. doi:10.1038/s41467-021-22557-7
 28. Anis S, Farooqi SR, Niaz SK. Characterization of domain V mutations in clinical isolates of *Helicobacter pylori* in Pakistan and their effect on Clarithromycin MIC. *Infection and Drug Resistance*. 2021; 14: 3393-403. doi: 10.2147/IDR.S306878
 29. Bilal H, Khan MN, Rehman T, Hameed MF, Yang X. Antibiotic resistance in Pakistan: a systematic review of past decade. *BMC infectious diseases*. 2021; 21: 1-9. doi: 10.1186/s12879-021-05906-1
 30. Chokshi A, Sifri Z, Cennimo D, Horng H. Global contributors to antibiotic resistance. *Journal of global infectious diseases*. 2019; 11: 36-42. doi:10.4103/jgid.jgid_110_18

Authors Contribution

HN: Idea conception
KAV: Study designing
HWA: Data collection
STV: Data analysis, results and interpretation
SS: Manuscript writing and proof reading
ME: Idea conception, manuscript writing and proof reading