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***Prospective Study***

**High rate of *Helicobacter pylori* reinfection in Lithuanian peptic ulcer patients**

JonaitisL *et al. Helicobacter pylori* reinfection in Lithuania

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**Author contributions:** Jonaitis L, Kiudelis G and Kupcinskas L designed and planned the study, carried out the recruitment of the patients, collected all the data, performed all the investigations; Jonaitis L performed statistical analysis; Jonaitis L, Slepavicius P prepared the manuscript; all authors were involved in drafting and revising the manuscript.

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**Data sharing statement:** Technical appendix, statistical code, and dataset available from the corresponding author at laimasj@takas.lt. Participants gave informed consent for data sharing. No additional data are available.

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**Abstract**

**AIM:** To evaluate the frequency of *Helicobacter pylori* (*H.* *pylori*) reinfection in peptic ulcer patients during 9 years after *H. pylori* eradication.

**Methods:** We invited 117 peptic ulcer patients in whom eradication of *H. pylori* was confirmed one year after the eradication treatment by stringent methods (both histology and by rapid urease test were negative). 57 patients were available for the study procedures: 34 (59.6%) males and 23 (40.4%) females. Mean age was 52.3 ± 13.0 years. There were 45 (78.9%) duodenal ulcer and 12 (21.1%) gastric ulcer patients. *H. pylori* was tested by a rapid urease test and histology if endoscopy was performed. If endoscopy was refused the *H. pylori* was tested by C14-urea breath test and serology. *H. pylori* was established, if at least one of the tests was positive.

**Results:** The mean of follow-up duration was 8.9 ± 1.0 years (6 to 12). *H. pylori* has been established in 15 patients: In 2 *H. pylori*-negative patients *H. pylori* had been established during the follow-up period and eradicated. Therefore, we consider that reinfection occurred in 17 patients. If per protocol analysis is performed – reinfection is established in 17 of 57 (29.8%; 95%CI: 19.2-42.2) patients during the follow-up period, The annual rate is 3.36%. If to consider that all non-responders are *H. pylori*-negative, reinfection could be in 14.5% (17/117) patients, the annual rate being 1.63%. The mean age of patients with reinfection was 51.8 ± 14.0 years, without reinfection - 52.5 ± 13.0 years, *P* > 0.05; the mean body mass index of patients with reinfection was 27.2 ± 4.1 kg/m2, without reinfection - 25.7 ± 4.2 kg/m2, *P* > 0.05. There are no differences in the reinfection rates according the location of peptic ulcer, eradication regimen used and smoking status.

**Conclusion:** Reinfection rate of *H. pylori* is relatively high in Lithuania and probably related with the high prevalence of *H. pylori*, what may reflect the differences in the socioeconomic status between Western and Eastern European countries.

**Key words:** *Helicobacter pylori*; Reinfection; Prevalence; Peptic ulcer; Eradication

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**Core tip:** The reinfection rate of *Helicobacter pylori* (*H.* *pylori*) is different in separate areas. In the regions with higher socioeconomic status and lower prevalence of *H.* *pylori* it accounts no more than 1.68% of cases. By contrast, in developing areas the reinfection rate could be much higher. Lithuania, as well as other Eastern and Central European countries, is in the transitional area, where the prevalence of *H.* *pylori* is not such low as in Western regions, but not as high as in the developing countries. According to our study, *H.* *pylori* reinfection rate in Lithuania is relatively high (the annual rate being 3.36%), probably due to the high prevalence of *H.* *pylori*. This could indirectly reflect the differences in the socioeconomic status between Western and Eastern European countries.

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**INTRODUCTION**

It is well established that *Helicobacter pylori* (*H*. *pylori* ) infection is the main cause of chronic gastritis and peptic ulcer disease, and the definite risk factor for gastric cancer[1-4]. Consensuses of different parts of the world strongly recommend eradication of *H.* *pylori* to cure peptic ulcer disease and MALT lymphoma, to decrease risk of gastric cancer[5-7]. *H. pylori* eradication is recommended to alleviate the burden of functional dyspepsia and some other digestive and extragastric pathologies[8-13]. Current treatment modalities allow to eradicate *H.* *pylori* bacterium in up to 90% of cases (less so if there is clarithromycin resistance). Nevertheless, in some cases, recrudescence or reinfection of *H.* *pylori* may occur. Reinfection is considered when *H.* *pylori* is found after confirmed *H.* *pylori* eradication. The confirmation of eradication must be performed not earlier than six months after the eradication treatment. It has been reported, that in highly developed countries reinfection is rare and may account no more than 1.68% of cases[14]. By contrast, in developing areas the reinfection rate could be much higher and had been reported to reach 9.63%[14]. Central and Eastern European countries are the areas of medium to high *H. pylori* prevalence. The reinfection rates could be expected to be in-between these numbers[8-32]. The *H. pylori* related diseases are common in these countries and the *H. pylori* eradication is widely applied treatment option. There are hardly available data from Eastern and Central Europe about the reinfection of *H. pylori*. In the Maastricht consensus, the recommendation to regularly investigate the regional epidemiological status of *H. pylori* has been proposed, assuming that the data of prevalence, eradication rates, resistance to antibacterial and reinfection rates are important[13].

Therefore, we carried out the long term follow-up study to evaluate the frequency of *H. pylori* reinfection in peptic ulcer patients after confirmation of *H. pylori* eradication.

**MATERIALS AND METHODS**

***Patients***

We included peptic ulcer patients from our previous one-year follow-up studies[15,20]. 117 patients, who were *H. pylori*-negative one year after the eradication treatment (therefore, considered to have true eradication), were invited to participate in the study by mail or telephone. Fifty-seven patients responded and were available for the study procedures. Written informed consent from all participants and approval of the Kaunas Regional Biomedical Research Ethics Committee was obtained. During the visits patients were surveyed for the demographic and clinical data. The flow-chart of the study is presented in Figure 1. The previous 1 week eradication regimens of these patients contained omeprazole, amoxicillin and clarithromycin [applied to 33 (58%) patients]; omeprazole, amoxicillin and metronidazole [applied to 12 (21%) patients]; omeprazole, clarithromycin and metronidazole [applied to 12 (21%) patients].

***Diagnosis of Helicobacter pylori***

According to the protocol of previous studies[15,20], the final *H. pylori* status has been determined after 12 mo following eradication therapy by a rapid urease test (RUT) and histology. Patients were considered as *H. pylori*-negative if both tests were negative.

The mean follow-up period was 8.9 ± 1.0 years (6 to 12) after the confirmation of the negative *H. pylori* status. At this time *H. pylori* was tested by RUT and histology if patients agreed to undergo endoscopy. If endoscopy was refused, *H. pylori* was tested by 14C-urea breath test (UBT) “Heliprobe”[18,24-26] and serology (the quantitative test "SureScreen Diagnostics Ltd" which is CE Marked, FDA Approved[17]). *H. pylori*-positivity was established, if at least one of the tests was positive.

Forty three patients were tested by RUT and histology. 14 patients (those who refused endoscopy) were tested by UBT and by additional serology.

***Statistical analysis***

The data were analyzed and compared using χ2 or Student’s *t* test. Values of *P* < 0.05 were considered significant.

**RESULTS**

Fifty seven patients were available for the study procedures. The duration of the follow-up was 8.9 ± 1.0 years (6 to 12 years). The patients’ group consisted of 34 (59.6%) males and 23 (40.4%) females. Mean age was 52.3 ± 13.0 years. There were 45 (78.9%) duodenal ulcer and 12 (21.1%) gastric ulcer patients.

Endoscopy was performed in 43 (75.4%) patients. *H. pylori* has been established in 15 patients, 42 patients were *H. pylori*-negative. In 2 *H. pylori*-negative patients *Helicobacter pylori* had been established by RUT during the follow-up period (both of them had peptic ulcer relapse), and successful eradication treatment had been administered. Therefore, we may count 17 patients that acquired *H. pylori* infection during the follow-up period. They are considered as the *H. pylori* reinfection cases.

If per protocol analysis is considered, reinfection is established in 17 (29.8%; 95%CI: 19.2–42.2) of 57 patients, the annual rate is 3.36%.

If we consider that all non-responders are *H. pylori*-negative (the most optimistic analysis), reinfection rate could be 14.5% (17/117) of patients, the annual rate - 1.63%.

The mean age of patients with reinfection was 51.8 ± 14.0 years, without reinfection - 52.5 ± 13.0 years, *P* > 0.05; the mean body mass index of patients with reinfection was 27.2 ± 4.1 kg/m2, without reinfection - 25.7 ± 4.2 kg/m2, *P* > 0.05. The comparison of some characteristics of patients with and without reinfection is presented in Table 1.

**DISCUSSION**

The reinfection rate of *Helicobacter pylori* could be mostly dependent on the prevalence of *Helicobacter pylori* in the certain region. It could be considered as an indirect indicator of the socioeconomic status of the investigated regions. Yan *et al*[14] analyzed correlation between *Helicobacter pylori* recurrence rate and socioeconomic development (as represented by Human Development Index (HDI)), using data from 77 studies, which were considered reliable. Countries with very high HDI had a mean annual rate of 1.68%, which was significantly lower than that of high HDI countries at 6.05%, medium HDI countries at 7.04%, and low HDI countries at 9.63% (global annual rate being 2.82%)[14]. Lithuania is placed in the very high HDI category.

The studies indicate low socioeconomic status as one of the major risk factors for high prevalence of *H. pylori* infection[16,23]. Eastern and Central European countries are in the transitional area, where the prevalence of *H. pylori* is not such low as in Western regions, but not as high as in the developing countries[27]. There are no large epidemiological studies on the prevalence of *H. pylori* in this region, but there are data on the prevalence of *H. pylori* in some specific settings of patients. The prevalence of *H. pylori* in middle aged outpatient setting is 69%[21]. The prevalence of *H. pylori* in 22-year-old medical students established by serology is 30.4% and has decreased substantially during last 17 years[22].

In our study, considering per protocol analysis, *H. pylori* reinfection is established in 29.8% (95%CI: 19.2–42.2) (17/57) of patients during our 9 years follow-up, the annual rate being 3.36%. For the sake of interest we calculated the reinfection rates in case if all non-responders could be *H. pylori*-negatives: in this case reinfection could be found in 14.5% (17/117) of patients, the annual rate being 1.63%. In reality, the reinfection rate is probably in-between these numbers (1.63%-3.36%). It could be considered as a relatively high *H. pylori* reinfection rate. This may indicate that in Lithuania the decrease of the prevalence of *H. pylori* infection[21,22] is not as fast as it was supposed, probably due to not too quick development of the socioeconomic state of the country. Or we may speculate that the rate of *H. pylori* prevalence is decreasing much slower than the speed of socioeconomic development. It is quite logical to believe that the similar results could be found in the neighboring countries.

The advantage of our study is that we established true reinfection, as all our patients were *H. pylori*-negative after one-year after eradication regimen. We would like to stress that our study is the first, which reports on the reinfection rates of adult peptic ulcer patients from Central and Eastern Europe. In contrast to many South European countries, where the prevalence of antimicrobial drug resistance is significant, the rate of *H. pylori* susceptibility to the standard antibiotics in Lithuania remains high[19]. Therefore, high reinfection rate could be the most important issue in the management of *H. pylori* infection in the country.

We also have recognized some drawbacks. The low number of responses (57 out of 117 patients) to follow-up investigations allows us to speculate with most pessimistic and most optimistic numbers, not being able to have as exact as possible rates of *H. pylori* reinfection. Besides, we had not had the epidemiological data of our patients, thus we could not look for the reasons of reinfection. Our investigated demographic and clinical characteristics were not predictive for the reinfection.

In conclusion, the reinfection rate of *H. pylori* in the cohort of peptic ulcer patients in Lithuania is relatively high, and this may be related to the relatively high prevalence of *H. pylori* infection, suggesting that the socioeconomic differences between Western and Eastern European countries are probably still remarkable.

**COMMENTS**

***Background***

It is strongly recommended to eradicate *Helicobacter pylori* (*H. pylori*) in order to cure peptic ulcer disease and MALT lymphoma, to decrease risk of gastric cancer and to alleviate the burden of functional dyspepsia and some other digestive and extragastric pathologies. At present the eradication of *H. pylori* could be achieved in up to 90% of cases. Nevertheless the recrudescence or reinfection may occur over time.

***Research frontiers***

In the Maastricht consensus, the recommendation to regularly investigate the regional epidemiological status of *H. pylori* has been proposed, assuming that the data of prevalence, eradication rates, resistance to antibacterial and reinfection rates are important. The reinfection of *H. pylori* has been reported to be not so infrequent finding, especially in the areas of high prevalence of *H. pylori*. More studies are necessary to establish the rate of reinfection in different parts of the world. Factors which may attribute to the occurrence of *H. pylori* reinfection have to be elucidated.

***Innovations and breakthroughs***

There are hardly available data from Eastern and Central Europe about the reinfection of *H. pylori*. This article presents the long term follow-up study, which evaluates the frequency of *H. pylori* reinfection in Lithuanian peptic ulcer patients after confirmation of *H. pylori* eradication. These are probably the first data from Eastren-Central European region regarding the reinfection of *H. pylori* in peptic ulcer patients.

***Applications***

The results of the study add important scientific information on the *H. pylori* reinfection rates in the Central and Eastern Europe. This is important knowledge reflecting the current Maastricht consensus. It also encourages us to rethink the present epidemiological situation regarding the prevalence of *H. pylori* in Lithuania and whole region. The reinfection rate of *H. pylori* in the cohort of peptic ulcer patients in Lithuania may be related to the relatively high prevalence of *H. pylori* infection in this region, suggesting that the socioeconomic differences between Western and Eastern European countries are probably still remarkable.

***Terminology***

Reinfection of *H. pylori* is considered when a new strain of *H. pylori* is found after confirmed eradication. The confirmation of eradication must be performed not earlier than six months after the eradication treatment. Recrudescence of *H. pylori* is considered as a recurrence of the previuos infection by the same *H. pylori* strain.

***Peer-review***

The subject of the present manuscript is interesting and important, as there are not many studies on the annual rate of *H. pylori* reinfection in this geographic area. However, some additions and clarifications should be performed to improve the manuscript

**REFERENCES**

1 **Cover TL**, Blaser MJ. Helicobacter pylori in health and disease. *Gastroenterology* 2009; **136**: 1863-1873 [PMID: 19457415 DOI: 10.1053/j.gastro.2009.01.073]

2 **Fuccio L**, Zagari RM, Eusebi LH, Laterza L, Cennamo V, Ceroni L, Grilli D, Bazzoli F. Meta-analysis: can Helicobacter pylori eradication treatment reduce the risk for gastric cancer? *Ann Intern Med* 2009; **151**: 121-128 [PMID: 19620164]

3 **Hopkins RJ**, Girardi LS, Turney EA. Relationship between Helicobacter pylori eradication and reduced duodenal and gastric ulcer recurrence: a review. *Gastroenterology* 1996; **110**: 1244-1252 [PMID: 8613015]

4 **McColl KE**. Clinical practice. Helicobacter pylori infection. *N Engl J Med* 2010; **362**: 1597-1604 [PMID: 20427808]

5 **Malfertheiner P**, Megraud F, O'Morain CA, Atherton J, Axon AT, Bazzoli F, Gensini GF, Gisbert JP, Graham DY, Rokkas T, El-Omar EM, Kuipers EJ. Management of Helicobacter pylori infection--the Maastricht IV/ Florence Consensus Report. *Gut* 2012; **61**: 646-664 [PMID: 22491499]

6 **Chey WD**, Wong BC. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *Am J Gastroenterol* 2007; **102**: 1808-1825 [PMID: 17608775]

7 **Fock KM**, Katelaris P, Sugano K, Ang TL, Hunt R, Talley NJ, Lam SK, Xiao SD, Tan HJ, Wu CY, Jung HC, Hoang BH, Kachintorn U, Goh KL, Chiba T, Rani AA. Second Asia-Pacific Consensus Guidelines for Helicobacter pylori infection. *J Gastroenterol Hepatol* 2009; **24**: 1587-1600 [PMID: 19788600]

8 **Raghunath A**, Hungin AP, Wooff D, Childs S. Prevalence of Helicobacter pylori in patients with gastro-oesophageal reflux disease: systematic review. *BMJ* 2003; **326**: 737 [PMID: 12676842 DOI: 10.1136/bmj.326.7392.737]

9 **Laine L**, Sugg J. Effect of Helicobacter pylori eradication on development of erosive esophagitis and gastroesophageal reflux disease symptoms: a post hoc analysis of eight double blind prospective studies. *Am J Gastroenterol* 2002; **97**: 2992-2997 [PMID: 12492181]

10 **Schwizer W**, Thumshirn M, Dent J, Guldenschuh I, Menne D, Cathomas G, Fried M. Helicobacter pylori and symptomatic relapse of gastro-oesophageal reflux disease: a randomised controlled trial. *Lancet* 2001; **357**: 1738-1742 [PMID: 11403809]

11 **Manes G**, Mosca S, Laccetti M, Lioniello M, Balzano A. Helicobacter pylori infection, pattern of gastritis, and symptoms in erosive and nonerosive gastroesophageal reflux disease. *Scand J Gastroenterol* 1999; **34**: 658-662 [PMID: 10466875]

12 **Malfertheiner P**, MOssner J, Fischbach W, Layer P, Leodolter A, Stolte M, Demleitner K, Fuchs W. Helicobacter pylori eradication is beneficial in the treatment of functional dyspepsia. *Aliment Pharmacol Ther* 2003; **18**: 615-625 [PMID: 12969088]

13 **Bruley Des Varannes S**, Fléjou JF, Colin R, Zaïm M, Meunier A, Bidaut-Mazel C. There are some benefits for eradicating Helicobacter pylori in patients with non-ulcer dyspepsia. *Aliment Pharmacol Ther* 2001; **15**: 1177-1185 [PMID: 11472320]

14 **Yan TL**, Hu QD, Zhang Q, Li YM, Liang TB. National rates of Helicobacter pylori recurrence are significantly and inversely correlated with human development index. *Aliment Pharmacol Ther* 2013; **37**: 963-968 [PMID: 23550618]

15 **Kupcinskas L**, Jonaitis L, Kiudelis G. A 1 year follow-up study of the consequences of Helicobacter pylori eradication in duodenal ulcer patients: unchanged frequency of erosive oesophagitis and decreased prevalence of non-erosive gastro-oesophageal reflux disease. *Eur J Gastroenterol Hepatol* 2004; **16**: 369-374 [PMID: 15028968]

16 **Calvet X**, Ramírez Lázaro MJ, Lehours P, Mégraud F. Diagnosis and epidemiology of Helicobacter pylori infection. *Helicobacter* 2013; **18 Suppl 1**: 5-11 [PMID: 24011238]

17 Available from: URL: https: //www.surescreen.com/diagnostics/picture.php?prodid=*H. pylori*T

18 **Jonaitis LV**, Kiudelis G, Kupcinskas L. Evaluation of a novel 14C-urea breath test "Heliprobe" in diagnosis of Helicobacter pylori infection. *Medicina (Kaunas)* 2007; **43**: 32-35 [PMID: 17297281]

19 **Kupcinskas L**, Rasmussen L, Jonaitis L, Kiudelis G, Jørgensen M, Urbonaviciene N, Tamosiunas V, Kupcinskas J, Miciuleviciene J, Kadusevicius E, Berg D, Andersen LP. Evolution of Helicobacter pylori susceptibility to antibiotics during a 10-year period in Lithuania. *APMIS* 2013; **121**: 431-436 [PMID: 23078193]

20 **Jonaitis L**, Kiudelis G, Kupcinskas L. Gastroesophageal reflux disease after Helicobacter pylori eradication in gastric ulcer patients: a one-year follow-up study. *Medicina (Kaunas)* 2008; **44**: 211-215 [PMID: 18413988]

21 **Jonaitis L**, Kiudelis G, Kupcinskas L, Kupcinskas J. Prevalence of Helicobacter pylori among outpatient middle-aged patients in Lithuania and its relation to dyspeptic symptoms. *Helicobacter* 2013; **18**: 104

22 **Jonaitis L**, Kiudelis G, Kupcinskas L. Prevalence of Helicobacter pylori among medical students in Lithuania decreased during last 17 years. *Helicobacter* 2012; **17**: 88

23 **Silva FM**, Navarro-Rodriguez T, Barbuti RC, Mattar R, Hashimoto CL, Eisig JN. Helicobacter pylori reinfection in Brazilian patients with peptic ulcer disease: a 5-year follow-up. *Helicobacter* 2010; **15**: 46-52 [PMID: 20302589 DOI: 10.1111/j.1523-5378.2009.00734]

24 **Pathak CM**, Kaur B, Khanduja KL. 14C-urea breath test is safe for pediatric patients. *Nucl Med Commun* 2010; **31**: 830-835 [PMID: 20864821 DOI: 10.1097/MNM.0b013e32833c3647]

25 **Bentur Y**, Matsui D, Koren G. Safety of 14C-UBT for diagnosis of Helicobacter pylori infection in pregnancy. *Can Fam Physician* 2009; **55**: 479-480 [PMID: 19439698]

26 **Ozdemir E**, Karabacak NI, Degertekin B, Cirak M, Dursun A, Engin D, Unal S, Unlü M. Could the simplified (14)C urea breath test be a new standard in noninvasive diagnosis of Helicobacter pylori infection? *Ann Nucl Med* 2008; **22**: 611-616 [PMID: 18756364 DOI: 10.1007/s12149-008-0168-6]

27 **Oona M**, Rägo T, Maaroos IH. Long-term recurrence rate after treatment of Helicobacter pylori infection in children and adolescents in Estonia. *Scand J Gastroenterol* 2004; **39**: 1186-1191 [PMID: 15742994 DOI: 10.1080/00365520410003461]

28 **McMahon BJ**, Bruce MG, Hennessy TW, Bruden DL, Sacco F, Peters H, Hurlburt DA, Morris JM, Reasonover AL, Dailide G, Berg DE, Parkinson AJ. Reinfection after successful eradication of Helicobacter pylori: a 2-year prospective study in Alaska Natives. *Aliment Pharmacol Ther* 2006; **23**: 1215-1223 [PMID: 16611283 DOI: 10.1111/j.1365-2036.2006.02880]

29 **Kim SY**, Hyun JJ, Jung SW, Koo JS, Yim HJ, Lee SW. Helicobacter pylori recurrence after first- and second-line eradication therapy in Korea: the problem of recrudescence or reinfection. *Helicobacter* 2014; **19**: 202-206 [PMID: 24612156 DOI: 10.1111/hel.12117]

30 **Kim MS**, Kim N, Kim SE, Jo HJ, Shin CM, Lee SH, Park YS, Hwang JH, Kim JW, Jeong SH, Lee DH, Kim JM, Jung HC. Long-term follow-up Helicobacter pylori reinfection rate and its associated factors in Korea. *Helicobacter* 2013; **18**: 135-142 [PMID: 23066652 DOI: 10.1111/hel.12018]

31 **Ryu KH**, Yi SY, Na YJ, Baik SJ, Yoon SJ, Jung HS, Song HJ. Reinfection rate and endoscopic changes after successful eradication of Helicobacter pylori. *World J Gastroenterol* 2010; **16**: 251-255 [PMID: 20066746 DOI: 10.3748/wjg.v16.i2.251]

32 **Zhang YY**, Xia HH, Zhuang ZH, Zhong J. Review article: 'true' re-infection of Helicobacter pylori after successful eradication--worldwide annual rates, risk factors and clinical implications. *Aliment Pharmacol Ther* 2009; **29**: 145-160 [PMID: 18945250 DOI: 10.1111/j.1365-2036.2008.03873]

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 117 *H. pylori*-negative patients 1 year after eradication

In 2 patients HP diagnosed and eradication regimen administered

Nine-year follow-up period

 57 patients available

 42 *H. pylori*-negative patients 15 *H. pylori*-positive patients

**Figure 1 The flow-chart of the follow-up.** *H. pylori*: *Helicobacter pylori.*

**Table 1 Characteristics of patients with and without *Helicobacter pylori* reinfection *n* (%)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Reinfection (*n* = 17)** | **No reinfection (*n* = 40)** | ***P* value** |
| Male gender | 12 (70.6) | 22 (55) | > 0.05 |
| Smokers | 7 (41.2) | 19 (47.5) | > 0.05 |
| Duodenal ulcer | 13 (76.5) | 32 (80) | > 0.05 |
| Primary eradication regimen - 7 d triple therapy:1. Omeprazole, clarithromycin,

amoxicillin1. Omeprazole, metronidazole,

amoxicillin(3) Omeprazole, clarithromycin, metronidazole | 9 (52.9)4 (33.3)4 (33.3) | 24 (60)8 (20)8 (20) | > 0.05> 0.05> 0.05 |