CLINICAL EVALUATION OF TRIPLE AND QUADRUPLE HELICOBACTER PYLORI ERADICATION THERAPY IN PEPTIC ULCER PATIENTS WITH DIFFERENT ABO BLOOD GROUP PHENOTYPES

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ABSTRACT

Objective: This study aimed to examine the pathological changes in gastric mucosa of Helicobacter pylori-infected peptic ulcer patients carrying different ABO phenotypes and to study the response to the 14 days’ standard triple therapy and 10 days’ quadruple therapy in peptic ulcer patients according to their ABO phenotypes.

Methods: Interventional prospective randomized-controlled open-label study was performed on newly diagnosed patients with PUD. The H. pylori-positive patients were allocated into two major study groups in which they are subdivided according to ABO blood group phenotypes: Group 1 received standard H. pylori eradication triple therapy and Group 2 received standard H. pylori eradication quadruple regimen. Patients were monitored after 2 months for successful H. pylori eradication.

Results: Chronic active gastritis was significantly high in patients carrying blood Group O phenotype (81.25%), while the atrophic gastritis and intestinal metaplasia were significantly high in patients carrying blood Group A phenotype (25.00% and 16.67%), respectively. 14 days’ triple therapy showed significantly lower eradication rate in H. pylori-infected peptic ulcer patients carrying blood Group O phenotype (p<0.01), meanwhile higher response was found among patients with blood Group B. 10 days’ quadruple therapy produced a significant high eradication rate in H. pylori-infected patients carrying blood Group O than those with blood Group A (p<0.01), but still both showed lower response compared to that in patients carrying blood Group B and AB phenotypes. Elderly patients showed significantly less healing efficacy than younger patients (p<0.01), and the least healing rate was noticed in female patients after both regimens.

Conclusion: Lower eradication rate in H. pylori-infected was noticed in peptic ulcer patients carrying blood Group O mainly than those with other blood groups and particularly those with duodenal Ulceri. 10 days’ quadruple therapy showed significant higher eradication rate in H. pylori infection and a better ulcer healing efficacy.

Keywords: Peptic ulcer disease, ABO phenotype, Helicobacter pylori eradication therapy.

INTRODUCTION

Peptic ulcer disease (PUD) is still one of the main prevalent unresolved medical problems affecting numerous patients of both genders in a wide range of age worldwide [1]. At least 50% of the population worldwide are infected by Helicobacter pylori [2,3]. Nowadays, there is a decrease in the prevalence and incidence of uncomplicated PUD, largely due to the availability of different protocols for H. pylori eradication and hence declining in the prevalence of infection [4]. Conversely, the up growing use of drugs with adverse gastrointestinal events such as aspirin and other (nonsteroidal anti-inflammatory drugs [NSAIDs]) is becoming another challenge; accordingly, it is possible that peptic ulcer complications such as upper gastrointestinal bleeding or perforation are more prevalent [4]. Much evidence supports that NSAIDs and H. pylori have a synergistic effect in developing PUD. A meta-analysis found that eradication of H. pylori in NSAID-naive users before NSAID initiation was associated with a decline in PUD [5]. Genetically, first-degree relative of people with GU or DU seems to have a three-fold higher risk of ulcer development [6]. There are specific phenotypic features related to PUD patients carrying ABO phenotypes; people with type O blood group are more prone to develop DU than in those with other types, while type A blood group holders are more prone to have GU [7,8]. PUD patients carrying blood type A phenotype are most likely to develop gastric cancer secondary to GU [9]. Those patients are characterized by acid hyposecretion and low serum pepsinogen level [10]. On the other hand, PUD patients carrying blood Group O are prone to have persistent colonization of H. pylori [11] flowing the expression of Lewis antigens (Leb) in gastric mucosa which act as a receptor for bacterial adhesion [12,13], expression of H-antigen on the gastroduodenal cells, acting as a receptor for H. pylori [13-15], the expression of blood group antigen b-binding adhesion (babA) on the outer membrane of H. pylori [16], and cagA-positive virulent strain H. pylori which colonizes in both the corpus and antrum [17,18]. Moreover, patients with blood Group O phenotype stimulate a higher inflammatory responses to H. pylori with higher levels of lymphocyte infiltration in the gastro intestinal mucosa [19] and have low level of Von Willebrand factor (VWF) [20], high frequency of secretor status [19], and high gastric acidity which reduces antibiotic therapy efficacy [21].

Triple therapy has been the accepted standard therapy for H. pylori eradication since 1990s [22]; however, it may not be the most effective first-line treatment in certain regions due to increasing antimicrobial resistance. There is controversy over the most effective duration of treatment for this regimen [23]. Evidence suggests that therapy is more successful if extended to >7 days [24,25], and many experts recommend 10–14 days treatment [26]. The initial H. pylori eradication rate of this regimen was around 80–90% and has progressively declined below 70-80%, in the last few years [27]. H. pylori resistance rates to antibiotics vary in different countries and even in different regions of the same country. Choice of treatment can be modified according to antibiotic resistance rates of H. pylori since the ideal therapeutic regimen for H. pylori infection should achieve an eradication rate.
of ≥80% [28]. In some countries, triple therapy with a proton-pump inhibitor, amoxicillin, and clarithromycin is still the best option, and on the other hand, countries with clarithromycin resistance >20%, bismuth-containing quadruple therapy, non-bismuth sequential, or concomitant therapies may be the preferred option [29]. Studies had revealed higher prevalence of $H. pylori$ positive than $H. pylori$ negative among Iraqi population, and in dyspeptic patients, $H. pylori$ prevalence was approximately 74–77% [30,31]. Moreover, most cases of DU were prevalent in peptic ulcer patients carrying blood Group O, while GU and gastric carcinoma were prevalent in blood Group A carriers [32,33]. Strong association was found among Iraqi population as well [34]. Taken together all the previous findings, this study is the first attempt to the best knowledge (though in a small scale) to examine the histopathological picture of $H. pylori$-infected peptic ulcer patients carrying different ABO blood group phenotypes, and also to evaluate the response of 14 days standard $H. pylori$ eradication triple therapy, and 10 days standard $H. pylori$ eradication quadruple therapy in peptic ulcer patients according to their ABO blood groups.

MATERIALS AND METHODS

Patients

This interventional prospective randomized-controlled open-label study was performed on newly diagnosed patients with PUD (male and female), who attended the endoscopy unit. Patients were enrolled if they showed positive endoscopic examination of PUD. Demographic data were collected through direct interview with the patient before endoscopy. A total of 201 patients whom fit the endoscopic criteria of PUD, 47 patients were $H. pylori$ negative according to the histology and stool antigen test or urea breath test (UBT) (which is used to specify the presence of $H. pylori$), and 154 patients showed evidence of positive $H. pylori$ test whom were included in this study. Four patients were lost (one patient from blood Group O, one patient from Group B, and two patients from blood Group A) during follow-up, so only 150 included throughout the study.

Study intervention

The $H. pylori$-positive patients were allocated into two major study groups, in which they are subdivided according to ABO blood group phenotypes: Group 1 includes 84 patients received standard $H. pylori$ eradication triple therapy ($clarithromycin$ [500 mg] capsules, amoxicillin [1g] capsules, and esomeprazole [20 mg] capsules all given twice daily) for 14 days’ duration [29] and Group 2 includes 66 patients received standard $H. pylori$ eradication quadruple regimen ($pylera®$ containing 140 mg bismuth subcitrate potassium, 125 mg metronidazole, and 125 mg tetracycline hydrochloride [Aptalis Pharma, Canada]). In the 10-day quadruple regimen, the three-in-one capsules were taken 4 times daily (after meals and at bedtime) and swallowed whole with 250 mL of water. Moreover, esomeprazole capsule [20 mg] was taken with pylera® capsules after morning and evening meals. Patients were monitored by reendoscopic examination after 2 months at the end of treatment.

Methods

Three biopsies were taken from the antral part of the stomach of each patient for histopathological examination during the endoscopic investigation because $H. pylori$ was not evenly distributed throughout the gastric mucosa [35]. ABO phenotypes and Rh factor evaluations were carried out by standard hemagglutination assays [36]. $H. pylori$ positivity was assessed through $H. pylori$ antigen rapid test device (feces) [37] or UBT [38]. Successful $H. pylori$ eradication was represented as a negative stool antigen test and improved clinical symptoms.

Statistical analysis

Data were analyzed using the Statistical Analysis System 2012 Version 9.1. Chi-square test was used to compare between parameters among different patients groups [39]. Analysis of $H. pylori$ eradication efficacy was assessed through "per-protocol" analysis basis. Values with $p<0.05$ were considered to be statistically significant.

RESULTS AND DISCUSSION

Histopathological changes observed in gastric antral mucosa in $H. pylori$-positive peptic ulcer disease patients according to ABO phenotypes

Biopsy sections were then examined by two experienced histopathologists for any pathological changes in gastric mucosa and presence of spiral bacteria in the superficial mucous layer or along the luminal surface of the gastric epithelial cells as a positive test.

The histopathological changes seen in gastric antral mucosa in $H. pylori$-positive patients according to ABO phenotypes (Table 1) were intestinal metaplasia (IM), atrophic gastritis (AG) and chronic active gastritis (CAG). The CAG was significantly high in patients carrying blood Group O phenotype (81.25%), while the AG and IM were significantly high in patients carrying blood Group A phenotype (25.00% and 16.67%), respectively.

The present study demonstrated that CAG was more prevalent in $H. pylori$-infected peptic ulcer patients carrying blood Group O. This finding was consistent with that reported by Mattos et al. who suggested an association between the blood Group O phenotype and peptic ulcer and CAG in Brazilian patients [40]. The previous study demonstrated a significant association between cagA-positive $H. pylori$ strain, and the development of peptic ulcer observed among Taiwanese patients carrying blood Group O [41]. Furthermore, other studies revealed that high rates of infection by cagA-positive $H. pylori$ strain were in patients belonging to the blood Group O phenotypes [6,42]. Moreover, infection with cagA-positive $H. pylori$ strains induces a marked inflammatory response, with a great density of polymorphonuclear cells in the gastric mucosa and high levels of serum TNFα and gastrin, which were seen as markers of inflammation in $H. pylori$ infection, when compared with the cagA-negative strains [43,44]. In Brazilian population, an association between cagA and severe inflammation was noticed in patients with DU and gastric carcinoma [45,46]. The findings of the current study showed that AG and IM were more prevalent in patients carrying blood Group A than other blood group phenotypes in $H. pylori$-positive patients. This result was in consistent with that reported elevated risk of gastric atrophy and IM in blood Group A phenotype [16,47,48]. CagA is the most investigated $H. pylori$ virulence factor, which showed a significant correlation with atrophic lesions, gastric cancer, and

| Table 1: Histopathological changes observed in gastric antral mucosa in $H. pylori$-positive peptic ulcer patients according to ABO phenotypes |
|--------------------------------|---|---|---|
| ABO phenotypes | Patients (number) | $n$ (%) | CAG | AG | IM |
| A | 24 | 14 (58.3) | 6 (25.0) | 4 (16.7) |
| O | 32 | 26 (81.3) | 4 (12.5) | 2 (6.3) |
| B | 16 | 11 (68.8) | 3 (18.8) | 2 (12.5) |
| AB | 12 | 9 (75.0) | 2 (16.7) | 1 (8.3) |
| Chi-square value - $\chi^2$ | - | 8.692** | 4.688* | 4.711* |

Data presented as $n$: Number and percentage (%). CAG: Chronic active gastritis, AG: Atrophic gastritis, IM: Intestinal metaplasia, *$p<0.05$ significant different, **$p<0.01$ highly significant. $H. pylori$: Helicobacter pylori
gastritis [49]. Previous studies have demonstrated a significant relationship between infection with $CagA$-positive strain of $H. pylori$ and blood Group A in peptic ulcer patients and the risk of gastric malignancy [32,42]. $H. pylori$ strains are associated with an increased risk of gastric adenocarcinoma [50]. In the gastric epithelium, the ABO blood group antigens and their related carbohydrate structures, such as the Leb antigens, are one of the major functional receptors for $H. pylori$ [40]. The observed association between ABO blood groups and risk of $H. pylori$-induced gastric cancer can thus be explained by differential binding of the bacterium to the blood group antigens. In particular, on the bacterial side, the binding is mediated by the outer-membrane protein babA, encoded by the gene babA2 [40]. The binding between babA and Leb antigen is important not only for $H. pylori$ to adhere to the stomach surface but also to anchor the bacterial secretion system (T4SS) to the host cell surface so that bacterial factors, including the $CagA$ protein, can be effectively injected into the host cell cytosol. This interaction plays an important role in potentiating T4SS-mediated secretion, resulting in inflammation and IM [47,51], although we cannot address how specifically blood group type A affects $H. pylori$ attachment to gastric epithelial cells. Animal experiments revealed that babA could stimulate the inflammatory cells to release more IL-8, CCL5 pro-inflammatory cytokines, and precancer-related factors (CDX2 and MUC2) [51]. Since inflammatory response to $H. pylori$ infection plays an important role in cellular proliferation and gastric mucosal damage, the upregulation of pro-inflammatory cytokines in people with chronic gastritis may be an important clinical implication in gastric carcinogenesis. The presence of babA 2 is correlated with the presence of $cagA$ and vacA s1; strains positive for the three genes carries the highest risk of gastric cancer [50]. Another possible explanation for the increased incidence of gastric cancer in blood Group A patients is that those patients were more susceptible to pernicious anemia and is more prone to gastric cancer compared with non-A blood group patients [15,52]. In addition to that, a clinical study has demonstrated that altered gastric secretary function may be related to the ABO blood group, and patients with blood Group A were characterized by acid hyposcretion [53].

One study indicated that the immune reaction to tumors in individuals with blood Group A was reduced compared with the non-A blood group patients [54]. Some research has shown that the structure of certain tumor antigens is similar to the structure of antigens of ABO blood group system. Smith et al. (1992) presented the Forssmann antigen that, predominantly in stomach and colon tumors, is almost structurally identical to the A antigen determinant [55]. Therefore, the blood Group A carrier may have diminished tumor immune response due to reduced ability to recognize and attack tumor cells that express the antigen structurally similar to the ABO antigen [56].

Thomsen–Friedenreich antigen (TF) is the core disaccharide structure of ABO blood Group (H) substance. It has been postulated that TF has a role in adhesion and metastasis through tumor–endothelial cell interactions, which is the key role in cancer metastasis [57]. Many Gram-negative organisms carry TF antigen, and due to antigenic similarity of TF to A antigen, blood Group A individuals have the least aggressive humoral immune response against the TF than Group O individuals, so it might be readily confused by the immune system of blood Group A individuals [11], and hence, blood Group O is less susceptible to cancer or have less aggressive disease.

VWF serves as an adhesive link between platelets and the endothelium. Several reports have demonstrated increased VWF antigen levels in the plasma of patients with ovarian, bladder, and colon cancers, with increased VWF antigen correlating with more metastasis and poor prognosis [58]. Non-O blood groups are having the highest VWF concentrations and the Group O secretors are having the lowest concentration of VWF: Antigen and VIII: Antigen [59].

All these findings, collectively, may lead to the hypothesis that these tumors have more chance to thrive in A blood group patients and be more aggressive than in O blood group patients.

Demographic data and disease characteristics of patients with $H. pylori$-positive peptic ulcer disease

Several studies demonstrated a higher prevalence of $H. pylori$ positive than $H. pylori$ negative in peptic ulcer and dyspeptic patients [60-62]. Furthermore, the probability of $H. pylori$-positive individuals to have any lesion in the gastric mucosa was found to be 10 folds greater than $H. pylori$-negative individuals [59]. Studies conducted in Iraq had demonstrated higher prevalence $H. pylori$ positive than $H. pylori$ negative among population and dyspeptic patients approximately (74-77%) [57,63]. Furthermore, similar finding was found in peptic ulcer patients enrolled in this study, where 75% of them showed positive $H. pylori$ infection. Furthermore, previous studies presented variations of $H. pylori$ infection among blood donors in different regions in the same place and in different countries [64].

Basic characteristics of the PUD patients in both groups involved in the study are presented in Table 2.

In the present study, the mean age of the peptic ulcer patients infected with $H. pylori$ ranges between 35 and 39 years which was similar that reported previously [65], though a bit older in other studies (46-50 years) [2]. The percentages for $H. pylori$-positive patients were higher among male patients as noticed previously when male gender showed a marginal predominance [66]. Moreover, the percentage of $H. pylori$-positive patients presented with DUs was higher than GU patients in the present study, with epigastric pain as a major complaint as reported by many others [48,67,68]. Higher incidence of $H. pylori$ infection was within blood Group O phenotype patients with Rh positivity compared to other blood groups [69,70]. Many other studies showed higher frequency of DU among patients with blood Group O with significantly higher $H. pylori$ positivity [47,52], including Iraqi population [70].

Ulcer healing efficacy of standard triple and quadruple $H. pylori$ eradication therapy in peptic ulcer patients according to ABO phenotypes

Per-protocol analysis was performed to compare eradication efficacy for all patients with different blood groups who finished the course of treatment. The healing efficacy in Group 1 patients on triple therapy regimens according to ABO phenotypes is as follows: 58.33% in peptic ulcer patients carrying blood Group A, 50% in patients carrying blood Group O, 75% in patients carrying blood Group B, and 66.67% in patients carrying blood Group AB, as shown in Table 3, with overall healing efficacy of 59.52%. Statistically, high significant difference in the healing efficacy was found among ABO phenotypes after treatment course (p<0.01). Patients with blood Group O presented with the least healing efficacy than patients with blood Groups A, B, and AB phenotypes. On the other hand, the per-protocol analysis in Group 2 patients who finished the course of treatment showed statistically high significant difference among ABO phenotypes. The increase in the ulcer healing efficacy with quadruple therapy was noticed mainly in patients carrying blood Group O phenotype (p<0.01) compared to $H. pylori$ eradication triple therapy.

Individuals with blood Group O were found to be more susceptible to peptic ulcer disease for decades without known cause until the relationship between Lewis b antigens and the attachment of $H. pylori$ to gastric mucosa was observed [71]. As mentioned previously, the gastric mucosa of blood Group O person is more prone to the attachment of $H. pylori$ because they had more receptors and $Le^a$ antigens mediated the attachment of $H. pylori$ to the mucosa [16]. Taken together all the previous evidence which may allow interpreting the low response of blood Group O patients to $H. pylori$ eradication triple therapy.

The Maasricht III consensus meeting has accepted a bismuth-based quadruple regimen as an alternative first-line therapy and has been generally used as the optimal second-line therapy after proton pump inhibitor (PPI) clarithromycin-amoxicillin failure, to be the recommended “rescue” regimen in several guidelines [72,73]. Previous studies reported a success rate of >90% for bismuth-
Table 2: Demographic data and disease characteristics of patients with H. pylori-positive PUD

| Variables                  | Group 1 n=84 | Group 2 n=66 |
|----------------------------|-------------|-------------|
| Age (years)                | 39.1±1.8   | 35.2±2.09   |
| Range (years)              | (15–77)    | (16–60)    |
| Gender                     |            |            |
| Female                     | 30 (35.7)  | 30 (45.5)  |
| Male                       | 54 (64.3)  | 36 (54.6)  |
| ABO phenotypes             |            |            |
| A                         | 24 (28.6)  | 18 (27.3)  |
| O                         | 32 (38.1)  | 26 (39.4)  |
| B                         | 16 (19.0)  | 16 (24.2)  |
| AB                        | 12 (14.3)  | 06 (9.1)   |
| Rh factor                  |            |            |
| Positive                   | 81 (96.4)  | 64 (97.0)  |
| Negative                   | 3 (3.6)    | 2 (03.0)   |
| Type of ulcer              |            |            |
| DU                         | 53 (63.1)  | 41 (62.1)  |
| Gastric ulcer              | 31 (36.9)  | 29 (37.9)  |
| Family history of PUD      |            |            |
| Yes                        | 26 (31.0)  | 17 (25.8)  |
| No                         | 58 (69.0)  | 52 (78.8)  |
| BMI (Kg/m²)                | 25.8±2.2   | 27.5±2.9   |

Data presented as mean±SE; (n) number of patients, and (%) percentage. PUD: Peptic ulcer disease, BMI: Body mass index, SE: Standard error, H. pylori: Helicobacter pylori, DU: Duodenal ulcer

Table 3: Ulcer healing efficacy of standard triple and quadruple H. pylori eradication therapy in peptic ulcer patients according to ABO phenotypes after 2 months

| ABO phenotype | Study groups | Group 1 Healing efficacy n (%) | Group 2 Healing efficacy n (%) |
|---------------|--------------|-------------------------------|-------------------------------|
|               |              | Group 1 Healing efficacy n (%) | Group 2 Healing efficacy n (%) |
| A             | 14/24(58.3)  | 14/18(77.8)                   |
| O             | 16/32(50.0)  | 24/26(92.3)                   |
| B             | 12/16(75.0)  | 16/16(100.0)                  |
| AB            | 08/12(66.7)  | 06/06(100.0)                  |
| Total         | 50/84(59.5)  | 60/66(91.0)                   |     |
| Chi-square (χ²) | 8.637**     | 8.946**                      |

Data presented as number (n) and percentage (%); **(p<0.01) high significant. H. pylori: Helicobacter pylori

Both duodenal ulcer (DU) and gastric ulcer in Group 1 patients showed the least ulcer healing efficacy in blood Group O carriers compared with other blood groups (p<0.01) after 2 months of H. pylori eradication triple regimen, Table 4. Nevertheless, up ceiling healing efficacy was noticed in all patients in Group 2 after 10 days’ quadruple regimens, mainly in blood Groups O patients with DU than with GU (p<0.01).

Nomatched studies to the best of our knowledge that could interpret this result, however, the high percentage of healing efficacy in patients with DU compared to gastric ulcer in the offended blood Group O is due to higher antral density of colonization by H. pylori as previously mentioned by Yung-Chih et al. revealed where high antral density of H. pylori was associated with a significant reduction in the eradication rate after anti-H. pylori treatment [83]. In addition, patients with blood Group O have high gastric acidity [10,33], and high gastric acidity was associated with reduced antibiotic therapy efficacy [84-86], which targeted by the complex actions of bismuth compound in the quadruple regimen.

Ulcer healing efficacy of standard triple and quadruple H. pylori eradication therapy in peptic ulcer patients according to age groups in different ABO phenotype

There is declining in ulcer healing efficacy in both study group patients with most of ABO phenotypes with older age, Table 5, particularly those treated with conventional triple H. pylori eradication therapy. These results were agreement with that of Hussein et al. who presented better H. pylori eradication rates in younger age group [30], and the eradication failure occurs in older age [42]. This is probably due to bad compliance in elderly patients, naive NSAID users, and H. pylori resistance to antibiotics [87].

Uncer healing efficacy of standard triple and quadruple H. pylori eradication therapy in peptic ulcer patients according to gender in different ABO phenotype

The small scale of this study did not show clear results in respect to the type of gender responding to the H. pylori eradication therapy, and hence, the overall results showed the least response in female gender carrying blood Group O phenotype (Table 6). A very high resistance rates toward metronidazole have been reported, particularly in female patients in developing countries [88], which may be more likely due to the prior treatment with metronidazole for gynecological diseases [89].

In a summary, many bacterial and host factors are contributes to failure of H. pylori eradication particularly in patients carrying blood Group O phenotype as mentioned earlier leading to aggressive colonization in the gastric antrum, and in turn, this may potentially produce an extensive, non-invasive inflammatory and oxidative stress reaction in the gastric mucosa leading to epithelial injury in H. pylori infection [90]. Accordingly, further studying other anti-ulcer protocols or alternative perspectives of a combination of standard anti-ulcer drugs with adjuvant herbal medicines is warranted to optimize eradication rate and prevent relapse particularly in those blood group phenotype [91].

CONCLUSION

This study is an attempt (though at a smaller scale) to evaluate the response of Iraqi group of peptic ulcer patients with different ABO phenotypes to the conventional triple and quadruple H. pylori eradication therapy. Lower eradication rate in H. pylori infected was noticed in peptic ulcer patients carrying blood Group O mainly than those with other blood groups and particularly those with DU. 10 days’ quadruple therapy showed significant higher eradication rate in H. pylori infection and a better ulcer healing efficacy.

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Table 4: Ulcer healing efficacy of standard triple and quadruple H. pylori eradication therapy in peptic ulcer patients according to location of ulcer in different ABO phenotype after 2 months

| ABO phenotype | Study groups | Group 1 healing efficacy n (%) | Group 2 healing efficacy n (%) |
|--------------|-------------|--------------------------------|--------------------------------|
|              | DU          | GU                             | DU                             | GU                             |
| A            | 06/10 (60.0)| 08/14 (57.1)                  | 06/07 (85.7)                   | 8/11 (72.7)                    |
| O            | 13/26 (50.0)| 03/06 (50.0)                  | 19/20 (95.0)                   | 05/06 (83.3)                   |
| B            | 08/11 (75.0)| 04/05 (80.0)                  | 10/10 (100.0)                  | 06/06 (100.0)                  |
| B            | 04/06 (66.7)| 04/06 (66.7)                  | 04/04 (100.0)                  | 02/02 (100.0)                  |
| Total        | 31/53 (58.5)| 19/31 (61.3)                  | 39/41 (95.1)                   | 21/25 (84.0)                   |

Chi-square ($\chi^2$) = 7.613**, 9.482**, 5.028**, 8.944**

Data presented as number (n) and percentage (%); **(p<0.01) high significant. H. pylori: Helicobacter pylori

Table 5: Ulcer healing efficacy of standard triple and quadruple H. pylori eradication therapy in peptic ulcer patients according to age groups in different ABO phenotype after 2 months

| Variables | Healing efficacy in ABO phenotype, n (%) |
|-----------|----------------------------------------|
|           | A                                      | O                                      | B                                      | AB                                     |
| Group 1   |                                        |                                        |                                        |                                        |
| Age (years) |                                        |                                        |                                        |                                        |
| <20       | 2/2 (100.0)                           | 3/4 (75.0)                             | 1/1 (100.0)                            | 2/2 (100.0)                            |
| 20–40     | 4/6 (66.7)                           | 9/15 (60.0)                            | 5/6 (83.3)                             | 4/5 (80.0)                             |
| >61       | 5/10 (50.0)                           | 2/5 (40.0)                             | 3/4 (75.0)                             | 1/2 (50.0)                             |
| Chi-square ($\chi^2$) | 9.053**                             | 11.247**                              | 11.043**                              | 10.617**                              |
| Group 2   |                                        |                                        |                                        |                                        |
| Age (years) |                                        |                                        |                                        |                                        |
| <20       | 2/2 (100.0)                           | 2/2 (100.0)                            | 2/2 (100.0)                            | 1/1 (100.0)                            |
| 21–40     | 8/10 (80.0)                           | 10/12 (83.3)                           | 6/6 (88.3)                             | 3/3 (100.0)                            |
| >61       | 4/6 (66.7)                           | 8/8 (100.0)                            | 8/8 (100.0)                            | 2/2 (100.0)                            |
| Chi-square ($\chi^2$) | 9.427**                             | 6.93**                                | 0.00 NS                                | 0.00 NS                                |

Data presented as number (n) and percentage (%); **(p<0.01) high significant. NS: Non-significant. H. pylori: Helicobacter pylori

Table 6: Ulcer healing efficacy of standard triple and quadruple H. pylori eradication therapy in peptic ulcer patients according to gender in different ABO phenotype after 2 months

| Variables | Healing efficacy in ABO phenotype, n (%) |
|-----------|----------------------------------------|
|           | A                                      | O                                      | B                                      | AB                                     |
| Gender    |                                        |                                        |                                        |                                        |
| Group 1   |                                        |                                        |                                        |                                        |
| Male      | 9/16 (56.3)                           | 11/20 (55.0)                           | 7/10 (70.0)                            | 5/8 (62.5)                             |
| Female    | 5/8 (62.5)                            | 5/12 (41.7)                            | 5/6 (83.3)                             | 3/4 (75.0)                             |
| Chi-Square ($\chi^2$) | 0.770 NS                              | 0.465 NS                               | 0.51 NS                                | 0.665 NS                               |
| Group 2   |                                        |                                        |                                        |                                        |
| Male      | 8/10 (80.0)                           | 12/12 (100.0)                          | 10/10 (100.0)                          | 4/4 (100.0)                            |
| Female    | 6/8 (75.0)                            | 12/14 (85.7)                           | 6/6 (100.0)                            | 2/2 (100.0)                            |
| Chi-Square ($\chi^2$) | 1.492 NS                              | 6.155**                               | 0.00 NS                                | 0.00 NS                                |

Data presented as number (n) and percentage (%); **(p<0.01) high significant. NS: Non-significant. H. pylori: Helicobacter pylori

AUTHORS’ CONTRIBUTION

The search idea study design was prepared by the corresponding author, and the methods were processed by pharmacist Rana Hussein Kutaif with assistance of Consultant Gastroenterologist Dr. Akram Ajeel Najeeb whom contributes in patients’ selection according to study criteria. Finally, statistical analysis, editing, and formatting were prepared by Dr. Yassir Mustafa Kanal.

CONFLICTS OF INTEREST

The author reported no conflicts of interest, and no funding was received on this work.

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