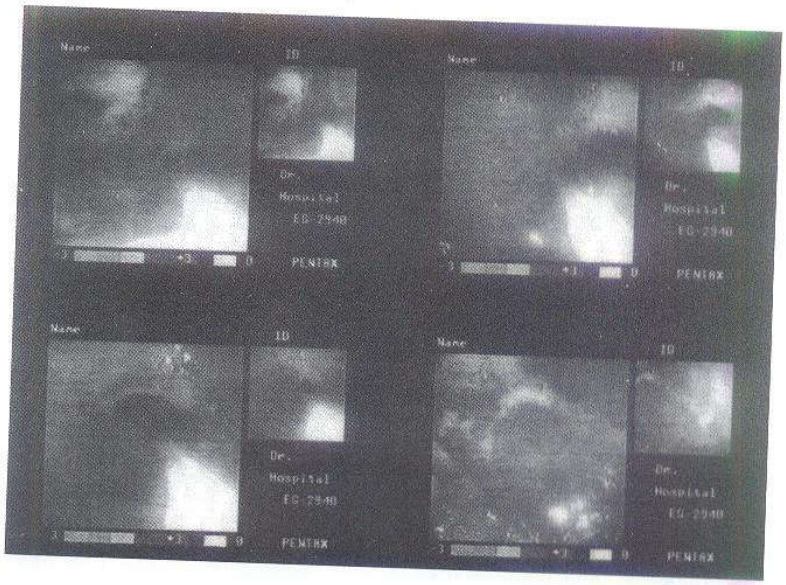

Fig. (1): Biopsy samples obtained from gastric antrum.

All patients with complete ulcer healing confirmed on scheduled endoscopy were then interviewed every 3 months for symptomatology. Maintenance acid-suppression agents were not prescribed during the follow up period. Repeated endoscopic examination was performed whenever patients were symptomatic. All patients were invited for follow up endoscopy at 1 year for ulcer surveillance and determination of H. Pylori status.

RESULTS

From March 1999 to March 2002, 80 patients (66 men and 14 woman), mean age of 49.3 years (SD=16.2) were confirmed to have duodenal ulcer perforation by laparotomy. Sixty-five patients (81%), out of 80 patients were infected with H. Pylori. So this 15 patients were excluded from our study, other 7 patients were excluded for different reasons as 3 cases failed endoscopic examination, 2 patients refused to undergo intraoperative endoscopy, last 2 patients excluded also as long term follow up was not possible for them. Of the remaining 58 patients, 32 were allocated to anti- Helicobacter therapy and 26 to omeprazole alone.

The two groups were evaluated in age, sex, ratio, smoking habit, use of non-steroidal anti-inflammatory drugs, severity of peritoneal contamination and method of repair (Table 1).

Table (1): *Characteristics of patients.*

	Triple therapy N=32	*Omeprazole therapy N=26*
Age (years)	45±13	43±14
Sex:		
• Female	6	5
• Male	26	21
Cigarette smoking:		
• Not smoker or ex-smoker	12	11
• 4-8 packs/week	18	13
• > 8 packs/week	2	2
Dyspepsia >3 months	14	9
Previous ulcer	3	1
Severity of peritonitis:		
• Mild	8	6
• Moderate	21	19
• Sever	3	1
Size of perforation (mm)	4.4±1.5	4.6±1.5
Type of repair:		
• Open method	32	26
NSAIDs intake	13	9

- NSAIDs=Non-steroidal anti-inflammatory drugs
- Previous ulcer signifies a history of peptic ulcer disease confirmed by either barium meal or endoscopy.

As expected, the H. Pylori eradication rate of the anti-Helicobacter treatment group was significantly higher than that of omeprazole alone group (87.5% versus 15%, p<0.001). Four patients in the omeprazole alone group had complete eradication of H. Pylori (Table 2). When case records were reviewed, 3 out of 4 patients had received extra antibiotics, including ampicillin or metranidazole in the early postoperative period (both are effective antibiotics for eradication of H. Pylori).

Table (2): *Early outcomes.*

	Triple therapy N=36	*Omeprazole therapy N=29*
Patents who underwent initial follow up endoscopy	32 (88.8%)	26 (89.6%)
H.Pylori eradicated	28 (87.5%)	4 (15%), P<0.001
Complete ulcer healing	29 (90.6%)	23 (88.4%)

Initial healing of ulcers was comparable between the two groups (Table 2). There were six non-healing ulcers despite repeated courses of omeprazole, three in the anti-helicobacter group and three in the omeprazole group. Complete ulcer healing was found and documented in 29, 23 patient respectively. Patients with complete ulcer healing were examined by upper endoscopy according to the study protocol (Fig. 2).

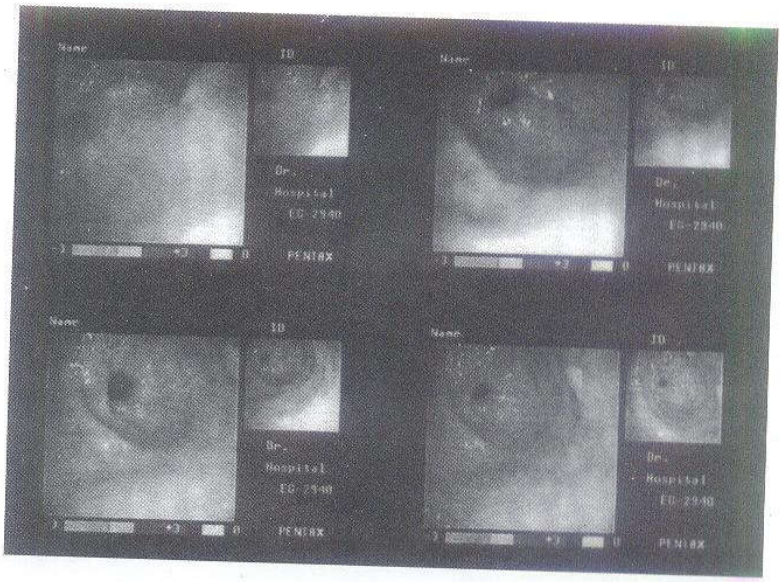

Fig. (2): Follow-up upper endoscopy according to study protocol.

After 1 year, one patient in the anti-helicobacter group and one patient in the omeprazole group were lost to follow-up (Table 3).

Table (3): *Outcomes of patients at 1-year follow-up.*

	Triple therapy	*Omeprazole therapy*
Patients with complete ulcer healing on initial endoscopy	29	23
All ulcer recurrence:	2 (6.2%)	9 (34.6%)
• Duodenal	2	7
• Gastric	0	2
• Gastric +duodenal	0	0
Symptomatic ulcer recurrence:	0 (0%)	6 (26%)
• Pain	-	4
• Bleeding	-	1
• Obstruction	-	1

Two patients in the anti-helicobacter group had ulcer relapse. They were asymptomatic and had recurrent ulcer diagnosed at scheduled 1-year endoscopy six out of 9 patients with ulcer recurrence in the omeprazole alone group; were symptomatic four patients showing severe ulcer pain one with bleeding, and last one with gastric outlet obstruction. The difference in ulcer recurrence between the anti-helicobacter group and the control group was statistically significant (6.2% versus 34.6%, P=0.0001, intention to treat). Ten out of eleven ulcer recurrence were associated with persistent H. Pylori infection; 9 in the omeprazole group and 1 in the anti-helicobacter group.

DISCUSSION

The most perfect surgical treatment for perforated duodenal ulcer has been controversial. Simple repair has been the most commonly performed procedure since its popularization by Graham in 1937 [19]. However, long-term follow up of the patients who underwent simple repair reveals in a high incidence of ulcer relapse [1-4]. In

prospective series by Bornman et al [20], forty-eight of 131 patients (42.5%) had recurrent ulcer disease after simple closure of duodenal perforation over a median follow-up of 42 months. 30% of them required further surgery for intractable symptoms or recurrent ulcer complications. Because of the unsatisfactory results of simple repair, immediate acid- reduction procedures have been strongly advocated

In the 1980, several prospective randomized studies reported significantly fewer ulcer recurrence by adding immediate proximal gastric vagotomy to patch repair of ulcer perforation [8,21-23]. The recent rapid development in laparoscopic surgery has complicated the issue. Since the first successful laparoscopic repair performed by Mouret et al [24] in 1990. Nevertheless, reservations about the use of laparoscopic repair still exist.

Our study was designed to determine whether perforated duodenal ulcer is causally related to H. Pylori infection or not. Anti-helicobacter therapy would be a more desirable option than definitive surgery if eradication of the bacterium confers prolonged ulcer remission after simple closure of the perforation.

In our study, patients with perforated duodenal ulcer, H. Pylori infection rates 81%. This figure is much higher than that reported by Reinbach et al [16] but is consistent with that of Metzger et al [5], Sebastian et al [17] and Matsukura et al [18] Ng et al [25], Ng et al [26]. Suggesting as association between H. Pylori infection and duodenal ulcer perforation

Our study showing high consumption rate of NSAIDs 22 out of 58 patients 38% and this cancer with the results other authors as Thompson et al [27], Collier et al [28]. Although perforated peptic ulcers have been related to the use of NSAIDs, our results showing that association was shown mainly in the elderly patients who took these drugs on a long-term basis and this agree with the result of Walt et al [29]. H. Pylori infection, as a risk factor, appears to be more relevant in younger patients, in whom acid-reduction surgery with its attendant complications is most undesirable.

After H. Pylori eradication and without maintenance acid-suppression agents 90 of patients remained ulcer free at 1- year follow up and this results of our study agree with the results of Graham et al [10], Vander et al [11], Ng et al[26].

In this study, there were high prevalence of H. Pylori infection and a few recurrences after eradication. The bacterium is likely to be causally related to the strong ulcer diathesis in patients with duodenal ulcer perforation and this is cancer with the results of Ng et al [26].

Conclusions

There is high prevalence of H. Pylori infection in patients with perforated peptic ulcer. Conventional simple repair is the procedure of choice for duodenal ulcer perforation, H. Pylori status should be determined by either endoscopic biopsy or serology, and bacterium should be eradicated in those who were infected, as an immediate and appropriate H. Pylori eradication therapy for perforated peptic ulcers reduces the relapse rate after simple closure. Response rate to triple eradication protocol was excellent more than omeprazole alone in the hospital setting. Immediate acid reduction surgery is unnecessary unless there are other concurrent ulcer complications, such as obstruction or hemorrhage.

REFERENCES

1. Boey J, Wong J: Perforated duodenal ulcers. World. J. Surg. 1987;11:319.

2. Drury JK, McKay AJ, Hutchison JS, Joffe SN: Natural history of perforated duodenal ulcers treated by suture closure. Lancet.. 1978;2(8093):749-750.

3. Griffin GE, Organ CH: The natural history of the perforated duodenal ulcer treated by suture plication. Ann. Surg. 1976;183:382-385.

4. Sawyers JL, Herrington JL, Mulherin JO, Whitehead WA, Moby B, Marsh J: Acute perforated ulcer. An evaluation of surgical management. Arch. Surg. 1975;110:527-530.

5. Metzger J, Styger S, Sieber C, VonFlue M, Vogelbach P, Harder F: Prevalence of Helicobacter Pylori infection in peptic ulcer perforations. Swiss. Med. Wkly. Feb. 2001;24;131(7-8):99-103.

6. Jordan PH, Thornby J: Perforated duodenal ulcer: Long-term results with omental patch closure and parietal cell vagotomy. Ann. Surg. 1995;221:479-488.

7. Sawyers JL, Herrington JL Jr: Perforated duodenal ulcer managed by proximal gastric vagotomy and suture plication. Ann. Surg. 1977;185:656-660.

8. Hay JM, Lacaine F, Kohlmann G, Fingerhut A: Immediate definitive surgery for perforated duodenal ulcer does not increase operative mortality: a prospective controlled trial. World. J. Surg. 1988;12:705-709.

9. Alamowitch B, Aouad K, Sellam P, Fourmestraux J Gasne P, Bethoux JP, Bouillot JL: Laparoscopic treatment of perforated duodenal ulcer. Gastroenterol. Clin. Boil. Nov. 2000;24(11):1012-7.

10. Graham DY, Lew GM, Klein PD et al: Effect of treatment of Helicobacter Pylori infection on the long-term recurrence of gastric or duodenal ulcer: a randomized, controlled study. Ann. Intern. Med. 1992;116:705-708.

11. Vander Hulst RW, Rauws EA, Koycu B et al: Prevention of ulcer recurrence after eradication of Helicobacter Pylori: a prospective long-term follow-up study. Gastroenterol. 1997;113:1082-1086.

12. Hosking SW, Ling TK, Chung SC et al: Duodenal ulcer healing by eradication of Helicobacter Pylori without anti-acid treatment: a randomized controlled trial. Lancet. 1994;343:508-510.

13. Sung JJ, Leung WK, Suen R et al: One-week antibiotics versus maintenance acid suppression therapy for Helicobacter Pylori-associated peptic ulcer bleeding. Dig. Dis. Sci. 1997;42:2524-2528.

14. Helicobacter Pylori in peptic ulcer disease. NIH Consensus Statement. 1994;12:1-23.

15. The European Helicobacter Pylori Study Group. Current European concepts in management of Helicobacter Pylori infection. The Maastricht Consensus report. Gut. 1997;41:8-13.

16. Reinbach DH, Cruickshank G, McColl KE: Acute perforated duodenal ulcer is not associated with Helicobacter Pylori infection. Gut. 1993;34:1344-1347.

17. Sebastian M, Chandran VP, Elashaal YI, Sim AJ: Helicobacter Pylori infection in perforated peptic ulcer disease. Br. J. Surg. 1995;82:360-362.

18. Matsukura N, Onda M, Tokunaga A et al: Role of Helicobacter Pylori infection in perforation of peptic ulcers. An age and gender-matched case-control study. J. Clin. Gastroenterol. 1997;25:S235-S239.

19. Graham RR: The treatment of perforated duodenal ulcers. Surg. Gynecol. Obstet. 1937; 64:235.

20. Bornman PC, Theodorou NA, Jeffery PC et al: Simple closure of perforated duodenal ulcer: a prospective evaluation of a conservative management policy. Br. J. Surg. 1990; 77:73-75.

21. Boney J, Branicki FJ, Alagartnam TT et al: Proximal gastric vagotomy - the preferred operation for perforations in acute duodenal ulcer. Ann. Surg. 1988;208:169-174.

22. Christiansen J, Anderson OB, Bonnesen T, Baekgaard N: Perforated duodenal ulcer managed by simple closure versus closure and proximal gastric vagotomy. Br. J. Surg. 1987;74:286-287.

23. Ceneviva R, de Castro, Silva Jr O, Castelfranchi PL, Modnea JLP, Santos RF: Simple closure with or without proximal gastric vagotomy for perforated duodenal ulcer. Br. J. Surg. 1986;73:427-430.

24. Mouret P, Francois Y, Vignal J, Barth X, Lombard-Platet R: Laparoscopic treatment of perforated peptic ulcer. Br. J. Surg. 1990;77:1006.

25. Ng EK, Chung SC, Sung JJ et al: High prevalence of Helicobacter Pylori infection in duodenal ulcer perforation not caused by non-steroidal anti-inflammatory drugs. Br. J. Surg. 1996;83:1779-1781.

26. Ng EK, Lam YH, Sung JY et al: Eradication of Helicobacter Pylori prevents recurrence of ulcer after simple closure of duodenal ulcer perforation. Ann. Surg. 2000; Vol. 231, No. 2, 153-158.

27. Thompson MR: Indomethacin and perforated duodenal ulcer. Br. Med. J. 1980;280:448.

28. Collier DSTJ, Pain JA: Non-steroidal anti-inflammatory drugs and peptic ulcer perforation. Gut. 1985;26:359-363.

29. Walt R, Katchinski B, Logan R, Ashley J, Longman MJS: Rising frequency of peptic ulcer perforation in elderly people in the United Kingdom. Lancet. 1986;1:489-492.