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A Prospective Observational Study on Risk Factors Associated with Peptic Ulcer Disease and its Management at a Tertiary Care Teaching Hospital

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ABSTRACT

Approximately 25 million Indians are suffering from peptic ulcer disease at some point in their life time. Duodenal ulcers are 5 to 10 times more common than gastric ulcers. Each year there are 500,000 to 850,000 new cases of peptic ulcer disease seen. It is a chronic disorder causing fatal complications such as haemorrhage, perforation, pyloric obstruction and inter tubular disease. In Hyderabad the staple diet (85%) is rice, and 70% of people use tamarind and spices daily, these agents may lead to ulcers. Hence, the aim of the study is to determine the prevalence of Peptic Ulcer Disease with investigation of various risk factors associated with it and to evaluate the usage of drugs in its management. This study was carried out for a duration of six months at the Gastroenterology department of Osmania General Hospital, Afzalgunj, Hyderabad. The data of 105 patients was collected by using data collection forms and was evaluated to see the prevalence of various risk factors associated with PUD and to assess the treatment. Various risk factors like *H.pylori*, NSAIDs and stress are majorly associated to cause PUD. Triple therapy(PPIs, Amoxicillin and Clarithromycin) is most effective treatment for *H.pylori* positive cases. Amongst different *H.pylori*kits Nexpro kit (Esomeprazole, Amoxicillin, Clarithromycin) is widely used. Monotherapy with PPI was instituted in NSAIDs induced Ulcers and *H.pylori* negative cases for 14 days.

KEYWORDS: *H .pylori*, NSAIDs, Peptic ulcer disease (PUD), Stress,Triple therapy.

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INTRODUCTION

Peptic ulcer disease (PUD) refers to a group of ulcerative disorders of the upper GI tract that require acid and pepsin for their formation.[1] Ulcers that occurs within the stomach and duodenum are often chronic in nature.

Helicobacter pylori infection and the use of non-steroidal anti-inflammatory drugs (NSAIDs) are the most well-known causal factors for PUD. Although the prevalence of PUD caused by *H.pylori* has been decreasing because of eradication therapy, the prevalence of PUD induced by NSAIDs or aspirin is increasing because of the worldwide increase in the aging population.[2]

Risk factors for PUD include: *Helicobacter pylori* infection,Age older than 60 years, Previous peptic ulcer, Previous ulcer-related upper GI complication, Concomitant use of corticosteroid, anticoagulant, antiplatelet drug (clopidogrel), oral bisphosphonates, SSRI's, High-dose NSAIDs., NSAID plus aspirin use, Chronic illness (e.g., cardiovascular disease), Alcohol consumption and Cigarette smoking.[1,3]

Diagnosis of PUD:

Upper Gastro Intestinal (UGI) endoscopy is usually performed to obtain a definitive diagnosis of PUD which is followed up with biopsy that can be examined by histology, Rapid Urease Testing (RUT), brush cytology, or even culture to determine infection with *H.pylori*. The current gold standard to diagnose *H. pylori*infection invasively is a combination of RUT and brush cytology.[4]

General measures for treatment:

- Cigarette smoking, aspirin and NSAIDs should be avoided.
- Alcohol in moderation is not harmful and no special dietary advice is required.
- Reduction of psychological stress,physical stress
- Avoid fasting and maintain optimum gap between meals
- Probiotics, especially strains of lactic acid–producing bacteria such as *Lactobacillus* and *Bifidobacterium*, lactoferrin, and foodstuffs (e.g., cranberry juice, ginger, chilli, oregano, some milk proteins) have been used to supplement *H.pylori*eradication.

Table no.1: oral drug regimens used to eradicate Helicobacter pylori infection [1]

Proton-Pump Inhibitor–Based Three-Drug Regimens			
PPI once or twice daily (14 days)	Clarithromycin 500mg BID (14 days)	Amoxicillin1g BID or Metronidazole 500mg BID (14 days)	
Bismuth-Based Four-Drug Regimens			
PPI (10-14 days) or H_2RAonce or twice daily(4-6 weeks)	Bismuth subsalicylate 525mg QID (10-14 days)	Metronidazole 500mg QID (10-14 days)	Tetracycline 500mg QID (10-14 days)
Sequential Therapy			
PPI once or twice daily on days 1-10 (1-14 days)	Amoxicillin1g BID on days 1-5	Metronidazole 500mg BID on days 6-10	Clarithromycin 500mg BID on days 6-10
Secondary or Rescue Therapy for persistent infectons			
PPI (10-14 days) once or twice daily	Bismuth subsalicylate 525mg QID (10-14 days)	Metronidazole 500mg QID (10-14 days)	Tetracycline 500mg QID (10-14 days)
PPI once or twice daily	Amoxicillin1g BID	Levofloxacin 250mg BD	

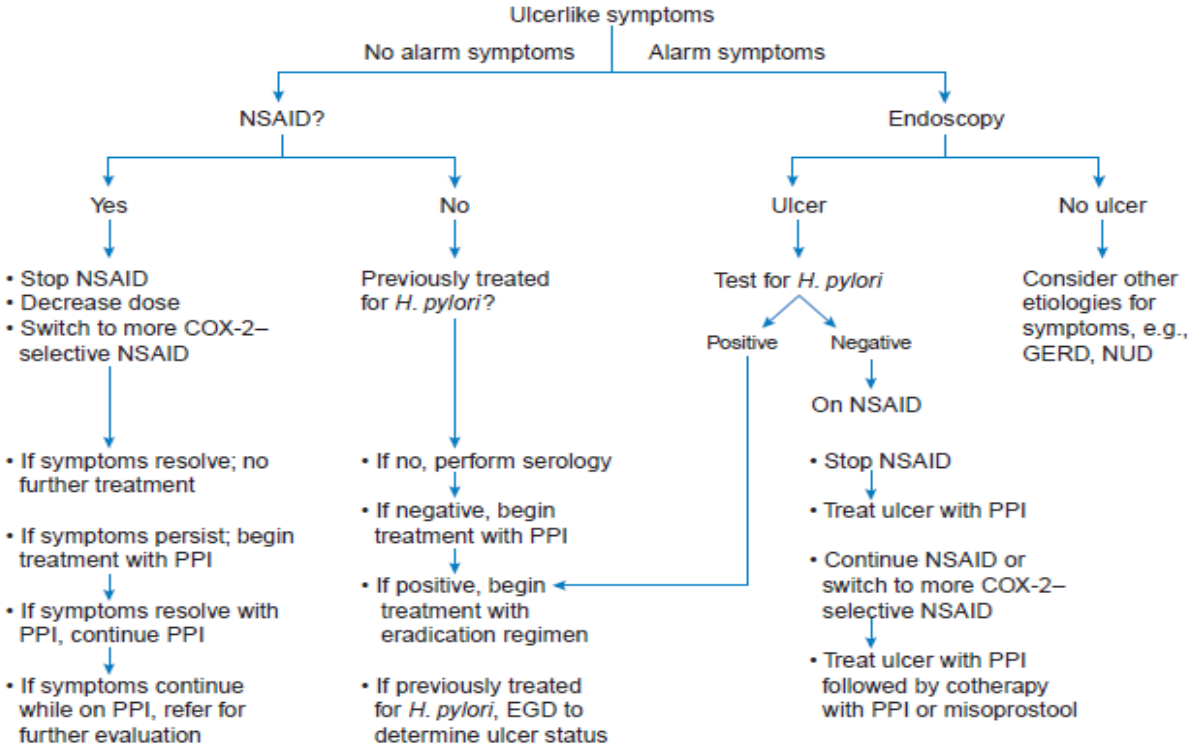


Figure no.1 management of PUD[3]

Complications: It is a chronic disorder producing life threatening complications such as haemorrhage, perforation, penetration, pyloric obstruction and inter-tubular disease.[5]

From clinical experience and retrospective hospital based surveys, it has been suspected that peptic ulcer is widespread in India, common among the population of South India than North India and the clinical behaviour of peptic ulcer in India is different from that in the West. In Hyderabad the staple diet 85% is rice, and 70% of people use tamarind and spices daily. These agents may cause ulcers. Hence, a study of risk factors and management of PUD is required.[6]

Study represents various risk factors of peptic ulcer disease (PUD), their complication and their management. We aimed to create awareness among people about the risk factors, its avoidance, and minimization, as in all age groups, a fast paced lifestyle, high level of stress, irregular eating habits, insufficient intake of fibre and water and lack of daily exercise contributes to prevalence of PUD.

MATERIALS AND METHODS:

The study was conducted in the department of Gastro-enterology, Osmania General Hospital, Hyderabad, India for a period of 6 months, from October 2017 to march 2018. It is a prospective observational study conducted in a total of 105 patients fulfilling the selection criteria.

Inclusion criteria: Patients of age > 18 years, either sex, both in patients and out patients diagnosed of PUD and on treatment, and both complicated and uncomplicated cases.

Exclusion criteria: Patients refusing to be a part of the study, pregnant and lactating mothers, those with other gastric complications other than PUD.

Patients satisfying inclusion criteria were enrolled, Informed consent was obtained from the subjects after explaining the purpose of the study.

Approval has been taken from Institutional Ethics Committee (IEC). Data is noted in a pre-designed data collection form and analyzed.

Data collection form includes patients demographic data, other details of patient, addictions, complaints, investigations and past, recent and current medications.

Data is collected in the designed form, from case notes, patient and attender. Data is analyzed for prevalence of risk factors associated with peptic ulcer disease and evaluation of treatment.

STATISTICAL ANALYSIS:

Standard descriptive statistics were applied to the data collected. The summary of categorical data was presented in terms of counts (n) and percentages (%).

Odds ratio, confidence interval and level of significance were used to measure the strength of association between the risk factors and occurrence of peptic ulcer disease.

RESULTS:

The study involved sample of 105 patients who were suffering from Peptic Ulcer Disease. According to Distribution of Data based on In-patients and Out-patients, it was found that 73.3% were Out Patients and 26.6% were In Patients which includes both Male and Female Patients. Epigastric pain was most common symptom which accounts for 67%, followed by nausea and vomiting, burning in epigastria region, bloating, fullness, acid reflux, weight loss

Table no.2: distribution of patients based on age

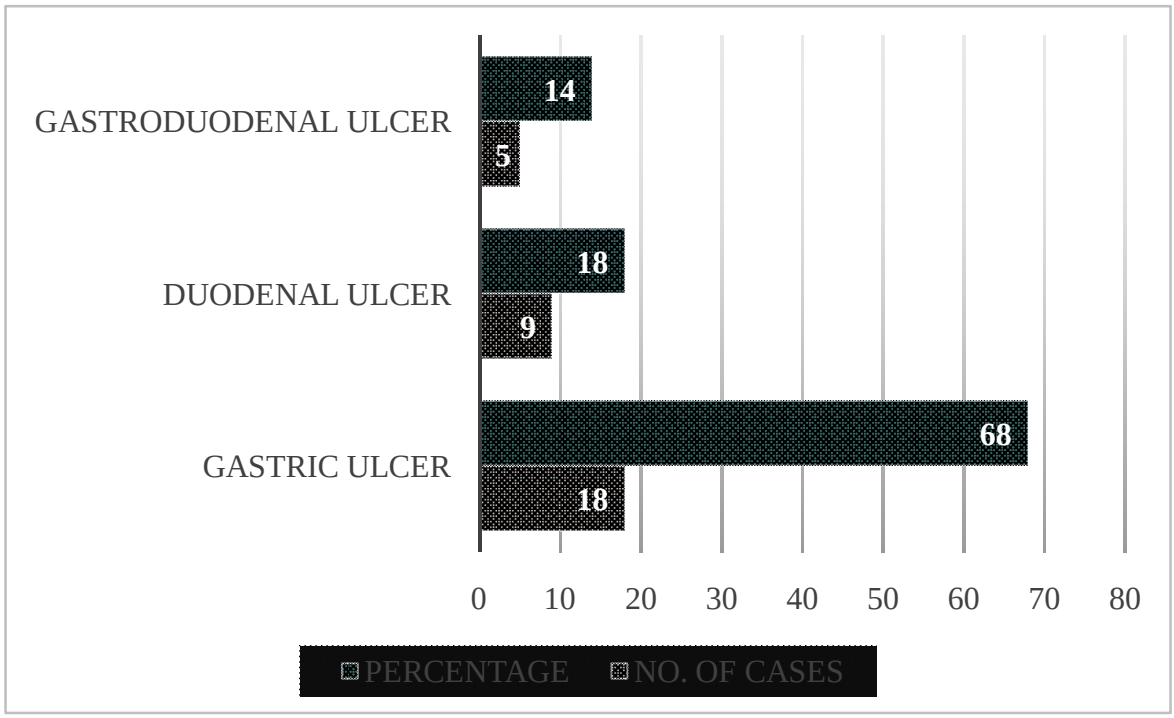
Age groups	No. of males (57)	No. of females (48)	Total no. of patients (105)	Percentage
18-27	07	08	15	13%
28-37	13	23	36	30%
38-47	13	11	24	25%
48-57	07	04	11	13%
58-67	08	05	13	13%
68-77	02	01	03	02%
>77	02	01	03	04%

Table no.3: statistical analysis for various risk factors

S.No	Risk Factors	Odds Ratio	Confidence Interval	Significance Level
		Independent factors		
1	NSAIDS	1.9167	1.1797-3.1141	0.0086
2	*H.pylori*	0.5217	0.3211-0.8477	0.0086
3	Stress	0.7797	0.4868-1.2486	0.3003
4	Age >60 years	0.1932	0.1076-0.3469	<0.0001
5	Smoking	0.2500	0.1443-0.4331	<0.0001
6	Alcoholism	0.2500	0.1443-0.4331	<0.0001
		Dependent factors		
7	Tea or coffee intake	0.2500	0.1443-0.4331	<0.0001
8	Spicy food	0.8750	0.5473-1.3989	0.5770
9	Tobacco chewer	0.1413	0.0745-0.2682	<0.0001
10	Betel leaves	0.0396	0.0141-0.1115	<0.0001

Table no.4:distribution based on location and number of ulcers

Location	No. of cases	Percentage
Gastric	74	70.4%
Single	47	63.5%
Multiple	14	18.9%
Duodenal	19	18.09%
Single	11	57.8%
Multiple	08	42.2%
Both	12	11.4%
Single	03	25%
Multiple	09	75%



Graph no.1: Rapid Urease Test Findings

Rapid Urease Testwas performed to evaluate *H.pylori* infection. 32 cases were found to be positive. Out of which 68% were gastric ulcers, 18% were duodenal ulcers and 14% were gastroduodenal ulcers.

Table no.5: distribution of types of proton pump inhibitors used

Types of PPI	No. of cases	Percentage
Pantoprazole	49	46.6%
Esomeprazole	33	31.4%
Rabeprazole	19	18%
Lansoprazole	04	3.8%

Table no.6: drug therapy given to peptic ulcer disease patients

Therapy	Gastric ulcer	Duodenal ulcer	Both	Total	Percentage
Monotherapy	24	02	01	27	25.7%
Triple therapy	17	10	05	32	30.4%
PPI+Ulcerprotectiive agent(UPA)	09	02	04	15	14.2%
PPI+Domperidone	09	-	01	10	9.5%
PPI+ Antacids	06	01	01	08	7.6%
PPI+Domperidone+UPA	05	-	-	05	4.7%
PPI+Anticholinergic+Domperidone	01	01	-	02	1.9%
PPI+H_2Receptor Blocker	01	01	-	02	1.9%
PPI+Antibiotic	01	01	-	02	1.9%
PPI+Prokinetic	01	01	-	02	1.9%

The most widely used drug therapy is triple therapy, which is prescribed in the form of Pantocid kit (Pantoprazole, Amoxicillin, Clarithromycin) orNexpro kit (Esomeprazole, Amoxicillin, Clarithromycin).The next most widely used drug therapy is Monotherapy (Pamtoprazole, Esomeprazole, Lansoprazole, and Rabiprazole)

Other therapies, include PPI plus ulcer protective agents(suralfate), PPI plus domperidone, PPI plus antacids (aluminium hydroxide, magnesium carbonate), PPI plus domperidone plus UPA, PPI plus anticholinergic(metoclopromide) plus domperidone, PPI plus H2 receptor blocker(Ranitidine) , PPI plus antibiotic, PPI plus prokinetic.

A total of 32 *H.pylori*positive cases were detected, out of which 14 cases were given Pantocid kit, 18 cases were given Nexpro kit.

Table no.7: treatment efficacy

	No. of cases	Percentage
Cured	97	92%
Recurrent	08	8%

Table no.8: complications of peptic ulcer disease

Type of complication	No. of cases (n=105)
Perforation	0
Bleeding	10
Gastric outlet obstruction	0

DISCUSSION:

We have performed a prospective observational study in Gastroenterology Department, to assess risk factors associated with PUD and its management.

In present study, a total of 105 patients were observed of which Male population was predominant with 57 cases (54%) than female population with 48 cases (46%), which were in accordance with Mirzaei, et al.(2015), Najm, et al.(2011).[7,8] It was seen that people of age group 28-37 were more effected with disease (30%).This may be due to the reason that, people in this age develop habits like smoking, alcoholism, eating spicy and junk foods and also have work related stress. Out patients(77%) were predominant than In patients(28%).

In present study NSAIDs, *H.pylori* and stress were found to be the most powerful independent risk factors for PUD, which is in accordance with Perez, et al. (2014)[9]. Other independent risk factors include, age (above 60yrs), smoking and alcoholism. Dependent factors were tea or coffee intake, spicy food intake, chewing of betel nut andbetel leaves, amongst which tea intake and spicy food intake were more powerful.

About (26%) NSAIDs use cases were reported. Statistical analysis showed an odds ratio of 1.9167.NSAIDs use has a strong association with ulcer formation and hence the major risk factor in this population and these findings were similar with Salih,et al.(2007).[10]*H.pylori* was the next independent risk factor (30%) followed by smoking (20%). Alcoholism was reported in 20% of patients. Alcohol intake induces duodenal ulcers. Age >60 yrs is an independent risk factor contributing to 16% of patients.

Most prominent symptoms were epigastric pain which accounts for 66% followed by burning in epigastric region, acid reflux, nausea, vomiting, early satiety, bloating, fullness, loss of appetite, weight loss. These findings were in accordance with Rai RR,et al.(2017).[11]

According to endoscopic findings Gastric ulcer were predominant (70%) than duodenal ulcer (19%) and gastroduodenal (11%). These findings were in accordance with Jayaram, et al. (2014)[2], Gisbert, et al. (2003)[12], Sonnenberg, et al. (2010)[13] , and Feldman, et al. (2013)[14]

The diagnosis of PUD was made on basis of endoscopy and the definitive diagnosis for determination of *H.pylori* infection was based on RUT and biopsy. It was noted that these tests were done only in small percentage of patients and empirical treatment was started which is in consistent with Gisbert, et al. (2003).[12]

RUT test was performed in 32 cases, and from those which were *H.pylori* positive, 18 cases (68%) were gastric ulcer, 9 (18%) were duodenal ulcer and 5 (14%) were both. For patients with risk factors for uncomplicated PUD, it is important to take preventive measures to reduce the likelihood of ulcer development. According to recommendations of Maastricht III Consensus Report(2007), the rapid urease test can detect the presence of *H.pylori*, within one hour with a satisfactory accuracy (>90%). False negative results can occur in patients taking antisecretory drugs.[15]

Maastricht III Consensus Report (2007) suggested that patients who are receiving long term aspirin and have an ulcer disease and a history of significant bleeding should be tested for *H.pylori* infection and, if positive, be given eradication therapy. Patients receiving long term PPI treatment for prevention of NSAID ulcers should be tested for *H.pylori* to reduce the PPI-*H.pylori* interaction leading to accelerated loss of specialised glands and atropic gastritis.[15]In our study 10 cases of UGI bleeding were observed.

Therapy was chosen based on regional bacterial resistance patterns, local recommendation, and drug availability, which were in accordance with Fashner, et al. (2013).[16]

In the present study we found that the most widely used PPI is Pantoprazole (46.6%) as compared to Esomeprazole (31%), Lansoprazole (4%), Rabeprazole (18%).

Our findings showed that, the most widely used drug therapy is triple therapy which accounts for 30.4% followed by monotherapy which is 25.7% and other therapies includes PPI +ulcer

protective agents, PPI+domperidone, PPI+antacids, PPI+domperidone+UPA, PPI +anticholinergic+domperidone, PPI +H2 receptor blocker, PPI +antibiotic, PPI +prokinetic

Monotherapy with PPI for 2 weeks was most common in patients with uncomplicated PUD and combination of antibiotics with PPI (triple therapy) was given to *H.pylori* positive cases. The most widely prescribed *H.pylori* kit was nexpro kit (esomeprazole, amoxicillin, clarithromycin) as compared to pantocid kit (pantoprazole, amoxicillin, clarithromycin) this was in contrast with Nagraj, et al. (2014).Eradication therapy was given for 2 weeks and after that maintenance therapy with PPIs was given for 4 weeks. Maastricht III Consensus Report(2007)[15] formulated that standard triple therapy composed of PPI, clarithromycin and amoxicillin/or metronidazole is more successful if extended to more than seven days. Increased resistance to antibiotics used in the PPI triple therapy needs to be considered in the selection of treatment. Recently sequential treatment consisting of five days of a PPI plus amoxicillin followed by five additional days of a PPI plus clarithromycin plus tinidazole has been shown to be better than the combination of a PPI plus amoxicillin and clarithromycin for seven days and deserves further evaluation in different regions. Bismuth based quadruple therapy is a preferred option as second choice treatment if not previously used. However the participants highlighted the fact that bismuth is not currently available in many countries.

It was observed in our study that 81% cases were cured and 19% were recurrent. Studies indicate that eradication of infection not only heals peptic ulcers, but also reduces the ulcer recurrence rate. Maintenance therapy should be continued with PPI use following *H. pylori* eradication in all patients to prevent ulcer recurrence or complications. According to Lee SW et al. (2010) Standard dose PPI treatment should be prescribed for 4 weeks in patients with duodenal ulcers and for 8 weeks in patients with gastric ulcers.[17]

The strength of our study is occurrence of various dependent and independent factors in Indian population. The present study has some limitations. Firstly, RUT was not performed in all patients due to unavailability, insensitivity and unaffordability. Secondly, there is a possibility that some patients were unaware that they were taking NSAIDs or its consequences on the development of PUD.

CONCLUSION:

The present study is focused on risk factors associated with peptic ulcer disease and its management. The disease is more prevalent in males (54%) than in females (46%). The age group 28-37 (30%) is more prone to develop PUD.Based upon odds ratio, *H.pylori*, NSAIDs, smoking, age, alcohol, tea or coffee intake, tobacco and betel leaves intake have significant strength of association

with the occurrence of peptic ulcer disease at significance level of less than 0.05. Other less significant factors were stress and spicy food.

Most common type of peptic ulcer disease observed was gastric ulcer which accounts for 70% of total peptic ulcer disease cases, followed by duodenal ulcer which accounts for 19% and gastro duodenal ulcer 11%.Triple therapy is most effective treatment for *H.pylori* positive cases which includes use of PPIs, Amoxicillin and Clarithromycin as Pantocid and Nexpro kits. Monotherapy with PPI was instituted in NSAIDs induced Ulcers and *H.pylori* negative cases for 14 days. Widely used PPI is Pantoprazole. Apart from triple and monotherapy it was observed that other combination treatments were given, which includes the use of Ulcer Protective Agents, antacids, H2 receptor blockers (Ranitidine) and prokinetics.Eradication of *H.pylori*is highly recommended in all perceived patients, NSAIDs used should be closely monitored and stress should be managed. Out of 105 cases, 97(92 %) cases were cured.

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