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ORIGINAL ARTICLE

Time trends in epidemiology of peptic ulcer disease in India over two decades

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Abstract
Background Epidemiology of peptic ulcer disease (PUD) in India differs from that in the West. It may have undergone a change with recent improvement in hygiene and availability of potent antisecretory and ulcerogenic drugs. We therefore tried to assess time-trends in the frequency of PUD over the past two decades.
Methods Records of patients with uninvestigated dyspepsia and no alarm symptoms who had undergone upper gastrointestinal endoscopy at our institution during the years 1988 (n=2,358), 1992 (n=2,240), 1996 (n=5,261), 2000 (n=7,051), 2004 (n=5,767) and 2008 (n=7,539) were retrospectively reviewed. The frequencies of duodenal and gastric ulcer disease in these groups were compared.
Results Of the 30,216 patients (age:41.7±12.7 years, 34 % females) during the six study periods, 2,360 (7.8 %) had PUD. The frequencies of both duodenal ulcer and gastric ulcer showed a decline from 1988 to 2008, i.e. from 12 % to 2.9 % and 4.5 % to 2.7 %, respectively (p-value <0.001 for trend for each). The decline was more marked for duodenal ulcer, and the ratio of duodenal to gastric ulcer declined from 2.7 in 1988 to 1.1 in 2008.
Conclusions The epidemiology of PUD in India may have changed in the past two decades with the incidence of duodenal ulcer declining more rapidly than that of gastric ulcer.

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Introduction

Peptic ulcer disease (PUD) results from an interplay of environmental, microbial (*Helicobatcter pylori*), pharmacological (non-steroidal anti-inflammatory drugs [NSAIDs]) and genetic factors [1–4]. In western countries, its incidence increased in the early twentieth century but started to decline during the latter part of that century [5]. This decline may have been related to improved hygiene, decrease in prevalence of *H. pylori* infection and the use of potent antisecretory drugs such as histamine-2 receptor antagonists (H_2RA) and proton pump inhibitors (PPI).

Previous studies have shown important differences in the age and sex distribution of PUD and relative proportion of gastric and duodenal ulcer (DU) between the East and the West [6]. It is possible that the epidemiology of PUD in India has changed with time due to improvements in hygiene, changes in lifestyle, and availability and increased use of potent antisecretory drugs as well as ulcerogenic drugs [7].

Our department has generally followed the 'scope and treat' strategy in patients with dyspepsia. In this study, we used the data collected in our department over the past two decades to assess time-trends in epidemiology of PUD.

Methods

Records of all patients who had undergone upper gastrointestinal (UGI) endoscopy at our institution during the years 1988, 1992, 1996, 2000, 2004 and 2008 were screened and patients with dyspepsia but no alarm symptoms were

identified retrospectively. Dyspepsia referred to symptoms of epigastric pain, nausea, bloating, belching, heartburn and acid regurgitation occurring individually or in any combination [8], and uninvestigated dyspepsia referred to such symptoms in a person who had not undergone diagnostic investigations. Alarm symptoms included weight loss, vomiting, dysphagia, abdominal mass, anemia, hematemesis and melena [8]. For patients with multiple endoscopies, only findings from the first examination were included. From the case records, clinical, endoscopic and histology data were extracted and recorded on a structured data sheet. The study was approved by the institutional review board and ethics committee.

As per our department's policy, each endoscopist observes more than 600 UGI endoscopies and performs more than 300 UGI endoscopies under supervision before performing such procedures independently. In the year 1988, fiberoptic endoscopes (Olympus Ltd., Japan) were in use, whereas in 2004 and 2008 only video endoscopes (Olympus) had been used; during the intervening period, both types of endoscopes were used. Sedation was seldom used, except on patient's request. The mucosa in esophagus, stomach, and first and second parts of duodenum was examined systematically. Peptic ulcer was diagnosed when gastric and/or duodenal mucosal break of more than 3 mm with discernible depth was observed [9]. Erosion was diagnosed when there was a break in gastric or duodenal mucosa of <3 mm in diameter which lacked depth [10]. Biopsy was obtained from any growth in esophagus, stomach, duodenum or periampullary region. Biopsies were also obtained from gastric ulcers irrespective of the characteristics of their edges or margins, to exclude malignancy. Deformity of pylorus and/or first part of duodenum was labeled as deformed pyloroduodenal complex [11].

Statistical analysis

Categorical data are presented as proportion and continuous data as mean and standard deviation. Time-trend for continuous variables was assessed using one-way ANOVA with linear degree option in polynomial contrast, and that categorical variables was assessed using chi-square test for trend (linear-by-linear association). Two-tailed p-values of ≤ 0.05 were considered significant. Data were analyzed using Statistical Package for Social Sciences, release 11.0, standard version (SPSS Inc.).

Results

A total of 30,216 patients with dyspepsia had been seen during the six one-year periods studied. Their mean age was 41.7 (SD 12.7) years and 10,270 (34 %) were female. PUD had been found in 2,360 (7.8 %) patients; this included 1,578 (5.2 %) patients with DU, 710 (2.3 %) with gastric ulcer and 72 (0.2 %) with both DU and GU. Esophagitis was seen in 980 (3.2 %) patients and upper gastrointestinal malignancy in 484 (1.6 %) patients. Table 1 shows the number and age and sex distribution of patients with PUD and gastrointestinal malignancy during the individual years. The mean age of dyspeptic patients increased over time ($p<0.001$ for trend). Compared with DU, GU occurred at an older age (46.9 [13.2] years vs. 41.9 [12.7] years, $p<0.001$).

Table 2 shows the time trends of proportion of patients undergoing endoscopy who had DU, GU and DU/GU ratio. The frequency of GU declined from 4.5 % in 1988 to 2.7 % in 2008 ($p<0.001$ for trend), with a nadir of 1.4 % in between during the year 2000 (Fig. 1). DU showed a steady decline in frequency (Fig. 1) from 12 % in 1988 to 2.9 % in 2008, ($p<0.001$ for trend). The mean age of patients with DU increased during the study period, while that of patients with GU remained unchanged.

On comparing the first (1988) and the last time periods (2008), the decline in GU was 1.67-fold and that in DU was 4.1-fold. The DU/GU ratio therefore declined significantly from 2.7 in 1988 to 1.1 in 2008 (p-value <0.001 for trend).

Discussion

Dyspepsia affects 10 % to 40 % of general population [12]. It is prevalent globally and significantly impairs quality of life [13]. The term 'dyspepsia' has included a variable combination of symptoms such as epigastric pain, bloating,

Table 1 Annual number of patients diagnosed with peptic ulcer disease and gastrointestinal malignancy among patients with dyspepsia undergoing upper gastrointestinal endoscopy in different years

Characteristic	1988 (n=2,358)	1992 (n=2,240)	1996 (n=5,261)	2000 (n=7,051)	2004 (n=5,767)	2008 (n=7,539)
Age (years)	40.4 (12.6)	40 (12.9)	41.9 (12.8)	42.5 (13)	40.7 (11.9)	42.3 (12.8)
Female sex (number [%])	629 (26.7 %)	671 (30.0 %)	1,838 (34.9 %	2,345 (33.3 %)	2,080 (36.1 %)	2,707 (35.9 %)
Peptic ulcer (number [%])	399 (16.9 %)	306 (13.7 %)	504 (9.6 %)	369 (5.2 %)	341 (5.9 %)	441 (5.9 %)
Gastrointestinal malignant lesions (number [%])	52 (2.2 %)	41 (1.8 %)	119 (2.3 %)	122 (1.7 %)	66 (1.1 %)	84 (1.1 %)

Table 2 Time-trend of gastric and duodenal ulcers over time

Disease	Characteristic	1988 (*n*=2,358)	1992 (*n*=2,240)	1996 (*n*=5,261)	2000 (*n*=7,051)	2004 (*n*=5,767)	2008 (*n*=7,539)	*p*-value for trend
Gastric ulcer	Number of patients[a]	106 (4.5 %)	56 (2.5 %)	128 (2.4 %)	102 (1.4 %)	115 (2 %)	203 (2.7 %)	<0.001
	Age (years) (mean [SD])	46.8 (13.9)	46.3 (13.7)	48.8 (14.6)	47 (12.7)	45.3 (11.5)	46.8 (12.8)	ns
	Sex (% female)	21.7	23.6	35.2	20.6	33	26.6	ns
Duodenal ulcer	Number of patients[a]	284 (12 %)	248 (11.1 %)	364 (6.9 %)	252 (3.6 %)	210 (3.6 %)	220 (2.9 %)	<0.001
	Age (years) (mean [SD])	40.5 (11.9)	39.9 (12.9)	42.8 (12.7)	43.9 (13)	40.2 (11.8)	44 (13.2)	0.003
	Sex (% female)	10.2	10.9	21.9	15.5	15.7	22.7	<0.001
Duodenal ulcer to gastric ulcer ratio		2.7	4.4	2.8	2.5	1.8	1.1	<0.001

[a] Data in parenthesis show percent values (as proportion of those undergoing upper gastrointestinal endoscopy for unexplained dyspepsia with no alarm symptoms)

belching, nausea, early satiety, heartburn and regurgitation [8]. Several studies have assessed the causes of uninvestigated dyspepsia; however lack of a uniform definition of dyspepsia has made comparisons between these difficult [8]. For instance, the ROME II committee excludes predominant reflux symptoms from the definition of dyspepsia, where are the Canadian Dyspepsia Working Group does not make this distinction [8, 14]. Our study was based on retrospective data that had been collected well before these definitions were formulated and thus included patients with a broader definition of dyspepsia.

In western countries, incidence of PUD increased till 1960s; this was accompanied by a preponderance of DU over GU, and a higher disease range among males than in females [5, 6]. El-Serag et al. showed a decline in PUD in USA from 1975 to 1995 [15]. A subsequent study by Manuel et al. from 1996 to 2005 showed a stable trend in PUD [16]. The ratio of DU to GU in the West has varied from 4:1 to 1:1 in 1980s [6, 12, 17].

In contrast, reports from Australia and Asian countries in 1980s and 1990s showed a high DU:GU ratio. This ratio was 5.4:1 in Australia (1981), 5:1 in Pakistan (1976–89), and 32:1 (1979), 17.1:1 (1989, Kashmir, general population) and 5:1 (1991, Chandigarh) in studies from India [18–22]. In addition, the overall frequency of PUD among dyspeptic patients has also shown a decline in some Asian countries including India [23–25]. A study from southern India showed a decline in both DU and GU between 1989 and 2004 with DU:GU ratio of around 2.5:1 during 2001 to 2004. Interestingly, recent reports from Korea have shown an increase in GU and a decline in DU over time [26, 27]. Significant observations in our study were (i) a reduction in the overall frequency of PUD, (ii) a decline in the frequency of each of its components, namely DU and GU, and (iii) a decline in the DU:GU ratio, over a 20-year period. This changing pattern observed in our study is reminiscent of the trend in PUD in the West three decades ago [5].

Causative factors for PUD include *H. pylori* infection, smoking, NSAID intake, dietary factors and genetic influences [1, 5, 28, 29]. The improving socioeconomic conditions in developing countries, widespread availability of gastric acid suppressants and cyclooxygenase 2-selective NSAIDs may explain the falling incidence of PUD. Improved living conditions, socioeconomic status and better hygiene may have led to a reduction in prevalence of *H. pylori* infection; this may explain the declining frequency of PUD as well as an increasing age of patients with this disease due to a birth-cohort effect [30, 31]. Furthermore, introduction of *H. pylori* therapy may have also played a role. Treatment with PPI is associated with a high healing rate for PUD; however following treatment with these drugs alone, the ulcer relapse rate remains high [32]. This relapse rate decreased dramatically after the introduction of *H.*

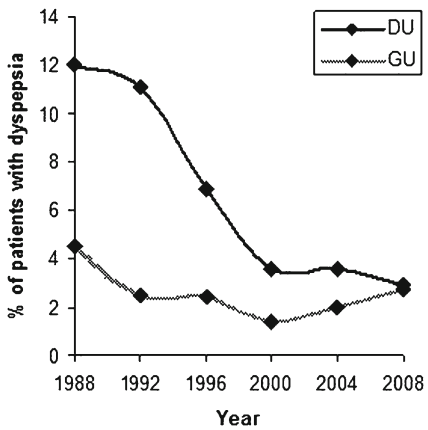

Fig. 1 Frequency of duodenal and gastric ulcer in dyspeptic patients from 1988 to 2008

pylori eradication therapy [33]. We are unable to comment on the frequency of *H. pylori* infection since regular testing for this infection was not done in the initial years. Availability of potent gastric acid suppressants (PPI/H_2RA), increased awareness of benefits of unsaturated fat and fibers in diet (proposed to protect against peptic ulcer) and ill effects of smoking may also have contributed to changing trends in PUD [34–36].

Our study shows a more marked fall in DU higher than in GU. A study from Italy on risk factors for PU in 4,943 inpatients showed that PPI (protective) and NSAID (harmful) use were associated with DU but not with GU [37]. This suggests that there are differences in the pathogenesis of GU and DU, or that factors other than *H. pylori* and gastric acid may be responsible for GU.

Our study is limited by its retrospective design. During the study period, the increase in number of patients attending our department was two times more than the rise in total number of patients seen in our hospital. Hence it is possible that the profile of patients changed with time, with people accessing our department or undergoing endoscopy for less serious symptoms in later years. Further, the change in number or the proportion of patients undergoing endoscopy was not always in tune with the overall number of patients seen in the gastroenterology department. Thus it is possible that the threshold for doing endoscopy or proportion of patients with dyspepsia attending over department changed over the study period. Though our hospital has served as a referral center for patients mainly from eastern and southern India for many years, the possibility of a change in the drainage population and referral pattern over the study period can also not be excluded. Improvements in endoscopes over the past many years may have also improved our ability to detect lesions; however, this factor cannot explain our findings since this would have led to an apparent increase in the frequency of ulcer disease.

In conclusion, the epidemiology of peptic ulcer disease in India seems to have changed during the past two decades. The changes include a reduction in the frequency of both GU and DU, with a more marked decline in the former.

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