Reactive Gastropathy is Associated with Inflammatory Conditions Throughout the Gastrointestinal Tract

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Background

Reactive gastropathy is a histopathologic term widely understood by gastroenterologists as an indication of gastric damage associated with either bile reflux or chronic NSAID use. The epidemiology of reactive gastropathy and its relationship with other conditions of the gastrointestinal tract associated with NSAID use have not been evaluated.



Figure 1. Antral mucosa with reactive gastropathy: "corkscrewlike" foveolar hyperplasia, mucin depleted epithelium, and bundles of hyperplastic smooth muscle arranged perpendicular to the surface.

Purpose

We tested the hypothesis that if reactive gastropathy shares a common etiologic factor with these conditions, the analysis of a large cohort would unveil associations. A secondary aim was to determine the relative prevalence of reactive gastropathy in different areas of the US.

Study Setting

This study was conducted at the Miraca Research Institute, part of Miraca Life Sciences, a specialized gastrointestinal laboratory that receives specimens from gastroenterologists operating in private outpatient endoscopy and surgery centers across the U.S. All demographic, histopathologic, endoscopic, and clinical information is stored in a searchable SQL database.



To identify the records for eligible patients, we extracted data for subjects who had at least one gastric biopsy submitted to Miraca Diagnostics between 1/2008 and 12/2011.

Patients with a history or a diagnosis of upper gastrointestinal cancer or surgery were excluded; when an individual had multiple encounters, only the first one was included in this analysis. We collected all patients whose gastric biopsies carried the histopathologic diagnosis of either "reactive" or "chemical gastropathy."

Controls were patients in whom all gastric biopsies were diagnosed as normal.

To evaluate for possible pathologic associations we also extracted the diagnoses of *H. pylori* infection, intestinal metaplasia, duodenal lymphocytosis, peptic duodenitis, active ileitis, lymphocytic colitis, collagenous colitis, and focal active colitis. Patients with a diagnosis or known history of inflammatory bowel disease were excluded from the analyses for active ileitis and focal active colitis.

To determine whether reactive gastropathy was commonly associated with certain clinical presentations, we also evaluated patients for a history of epigastric or abdominal pain, dyspepsia, anemia, gastroesophageal reflux disease (GERD), and diarrhea.



Patients and Controls



Figure 2. Prevalence of reactive gastropathy (solid lines) and of H. pylori-gastritis (dotted lines) in males and females for each decade of life.

Results

Gastritis type	Total	(%)	Females	(%)	Males	(%)	OR	(95% CI)	Mean Age
Total	504,011	(100)	312,005	(61.9)	192,006	(38.1)			55.9
Normal gastric mucosa	82,012	(16.3)	47,269	(57.6)	34,743	(42.4)	1.00		51.9
Reactive gastropathy	78,745	(15.6)	51,792	(65.7)	26,953	(34.2)	1.41	(1.38 - 1.44)	59.4
H. pylori-gastritis	51,857	(10.3)	30,454	(58.7)	21,403	(41.3)	1.05	(1.02 - 1.07)	55.8
H. pylori-negative gastritis	17,310	(3.4)	10,546	(60.9)	6,764	(39.1)	1.15	(1.11 - 1.19)	57.2
Chronic inactive gastritis	29,843	(5.9)	18,836	(63.1)	11,007	(36.9)	1.26	(1.22 - 1.29)	57.1
Atrophic gastritis	2,565	(0.5)	1,690	(65.8)	875	(34.1)	1.42	(1.31 - 1.54)	68.1
Intestinal metaplasia	17,514	(3.5)	10,255	(58.6)	7,259	(41.4)	1.04	(1.00 - 1.07)	63.4

Table 1 – Stratification of patient population by gastritis type, gender, and age. Odds ratios (OR) are age-adjusted; values of more than 1 indicate a greater probability that the condition occurs in women. CI: Confidence Interval; SD: Standard Deviation.

Histopathologic Diagr

Patients with esophagea

Normal esophagus

Eosinophilic esophagitis

Lymphocytic esophagitis

Reflux esophagitis

Barrett's metaplasia, No c

Barrett's metaplasia, Dys

Patients with duodena

Normal duodenum

Peptic duodenitis

Intestinal lymphocytosis

Patients with ileal biops

Normal ileum

Active ileitis*

Patients with colon biop

Normal colon

Lymphocytic colitis

Collagenous colitis

Focal active colitis* Ischemic colitis

Table 2 – Association of reactive gastropathy with selected conditions of the digestive tract. An odds ratio (OR) greater than 1 indicates that the condition is more likely to occur in patients with reactive gastropathy than in those with a normal gastric mucosa. *Patients with a history or diagnosis of inflammatory bowel disease were excluded from these analyses. CI : Confidence Interval.

nosis by Organ	RG	%	Normal Stomach	%	OR	(95% CI)
al biopsies (n = 69,101)	31,346		37,755			
	10,187	32.5	15,264	40.4	0.71	(0.69 - 0.73)
	521	1.7	1,189	3.1	0.52	(0.47 - 0.58)
S	35	0.11	20	0.05	2.11	(1.22 - 3.65)
	11,766	37.5	12,061	31.9	1.28	(1.24 - 1.32)
dysplasia	2,932	9.4	2,942	7.8	1.22	(1.16 - 1.29)
plasia	166	0.5	137	0.4	1.46	(1.17 - 1.83)
biopsies (n = 55,453)	23,313		32,140			
	18,531	79.5	27,121	84.4	0.76	(0.72 - 0.79)
	2,516	10.8	2,624	8.2	1.36	(1.28 - 1.44)
	706	3.0	781	2.4	1.25	(1.13 - 1.39)
sies (n = 55,453)	1,431		3,065			
	1,003	70.1	2,520	82.2	0.51	(0.44 - 0.59)
	127	8.9	151	4.9	1.88	(1.47 - 2.40)
osies (n = 4,496)	10,653		15,970			
	2,404	22.6	5,080	31.8	0.62	(0.59 - 0.66)
	90	0.8	121	0.8	1.12	(0.85 - 1.47)
	87	0.8	87	0.5	1.50	(1.12 - 2.03)
	284	2.7	274	1.7	1.57	(1.33 - 1.86)
	44	0.4	49	0.3	1.35	(0.90 - 2.03)





Region	Reactive gastropathy	H. pylori-gastritis
Northeast	22.3%	13.4%
New England	23.5%	7.3%
Middle Atlantic	22.2%	14.2%
Midwest	22.4%	7.9%
East North Central	22.3%	8.4%
West North Central	22.5%	6.7%
South	20.3%	10.2%
South Atlantic	20.3%	10.0%
East South Central	21.4%	8.5%
West South Central	20.0%	10.9%
West	19.8%	9.6%
Mountain	19.7%	9.1%
Pacific	19.9%	10.4%
Grand Total	20.9%	10.5%

Table 3 – Percentage of patients with reactive gastropathy and *H. pylori*-gastritis in different US census regions. The prevalence of reactive gastropathy shows much less variability than that of *H. pylori* infection.

Study Highlights

- This is the largest study to date to examine reactive gastropathy in the United States.
- Reactive gastropathy is the most common histopathologic change of the gastric mucosa in US outpatients who have gastric biopsies.
- The prevalence of reactive gastropathy is characterized by a clear age-dependent rise, it is significantly higher in women, and shows no associations with geographic residence within the United States.
- The associations of reactive gastropathy with other histopathologic changes of the gastrointestinal tract support the contention that NSAID use and bile reflux may contribute to its occurrence.

References

- 1. Dixon MF, O'Connor HJ, Axon AT, et al. Reflux gastritis: distinct histopathological entity? J Clin Pathol 1986;39:524-530.
- 2. Genta RM. Differential diagnosis of reactive gastropathy. *Semin Diagn Pathol* 2005;22:273-283.
- 3. El-Zimaity HM, Genta RM, Graham DY. Histological features do not define NSAID-induced gastritis. *Hum Pathol* 1996;27:1348-1354.

(SD)
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