



Prevalence, Clinical Characteristics, and Treatment Response in Patients with Post Cricoid Inlet Patch—A Descriptive Retrospective Study

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Abstract

Objectives The aim of this study was to determine the incidence of post cricoid inlet patch (PC-IP) and to assess the clinical characteristics, pathological features, and treatment response.

Materials and Methods A retrospective cross-sectional study was conducted from April 2016 to April 2021 in the tertiary gastroenterology unit of urban India. All patients with symptoms of globus sensation, chronic cough, heartburn, hoarseness, throat pain, dysphagia, and acid regurgitation after a thorough clinical examination underwent esophagogastroduodenoscopy by experienced endoscopists including biopsy. Sociodemographic data, symptoms and its duration, previous hospital visits, and chronic proton pump inhibitor (PPI) use were noted during the study.

Results Three-thousand two-hundred fifty upper gastrointestinal endoscopies were performed during the study period. The prevalence of PC-IP was 2.7%, comprising 36.3% males and rest females. Mean age was 36.2 ± 17 years. The most common symptom among these patients was globus sensation (81.8%) followed by acid regurgitation (75%), dyspepsia (64.7%), dysphagia (48.8%), throat pain (29.54%), chronic cough (22.72%), hoarseness (22.72%), and others (6.81%). Mean diameter of PC-IP was 1.5 ± 0.5 cm, more than one patch was found in 23.76% of patients. Histopathological examination showed heterotrophic gastric mucosa in 77.27%, out of which 38.23% had oxyntic type, 44.11% had mucoid type, and the rest had mixed cell type. On median follow-up after 20 months, 68.18% of patient had persistent symptoms, 77.27% were PPI responsive, and 22.73% were PPI refractory. On follow-up, 38.63% of patients had a repeat endoscopic procedure and biopsy (20.45%); none showed any changes in size or dysplasia.

Conclusion Prevalence of PC-IP could be higher than the estimated. Careful examination of upper esophagus and use of narrow band imaging will increase the possibility

Keywords

- ▶ argon plasma coagulation
- ▶ Barrett's esophagus
- ▶ gastroesophageal reflux
- ▶ globus sensation
- ▶ heterotopic gastric mucosa
- ▶ NBI endoscopy
- ▶ post cricoid inlet patch

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of identifying IP. Those symptomatic patients need treatment with PPI, sometimes for long term. Ablative therapy with radiofrequency or argon plasma coagulation needs further clarification.

Introduction

Post cricoid inlet patch (PC-IP) is also referred to as esophageal inlet patch, cervical inlet patch, heterotrophic gastric mucosa of esophagus, and gastric inlet patch.

Heterotrophic gastric mucosa occurs most commonly in the post cricoid area; however, they have been reported in duodenum, jejunum, gall bladder, cystic duct, ampulla of Vater, and rectum.¹⁻³

The first clinical description of cervical inlet patch was done by Schmidt in 1805.⁴ PC-IP is well-circumscribed area of gastric mucosa that is salmon pink in color, noted in upper esophagus, commonly located just below the upper esophageal sphincter within 1 to 3 cm. PC-IP varies in size ranging from few millimeter up to 3 cm and are oval, round, or geographically shaped.

Unlike Barrett's esophagus that is a well-established acquired metaplasia of lower end of esophagus due to chronic acid injury, PC-IP has often been described as both congenital remnant of columnar lining of the fetal esophagus or acquired metaplastic transformation as a result of chronic acid injury. Histopathological examinations of PC-IP are classified as oxyntic (glands with parietal cells), mucoid type (glands with mucous cells), or mixed. Occasionally in addition to gastric mucosa, bronchial and pancreatic tissues have been separated in pediatric studies supporting the hypothesis of congenital nature.³

Reported prevalence of PC-IP varies between 4 and 10%.^{5,6}

PC-IP is generally asymptomatic and detected incidentally on upper gastro intestinal endoscopy. However, due to capability of PC-IP to produce acid and mucin, patients present with symptoms of heart burn, globus sensation, dysphagia, chronic cough, acid regurgitation, and throat pain.

In majority of patients, symptoms are mild but chronic and persistent affecting patient's quality of life significantly. Hence, there is a need for therapeutic intervention in these patients to improve symptoms and quality of life.

In symptomatic patients, if the histopathology detected parietal cells in the biopsy specimen, acid suppression with proton pump inhibitors (PPIs) improves symptoms.⁷ However, response to PPI was rather unsatisfactory in some studies.⁸

No prospective, controlled trial conducted in this regard to clarify the use of PPI in long term to control symptoms.

Argon plasma coagulation is now considered an effective treatment in eradicating the ectopic tissue. Klare et al demonstrated significant improvement in scores of symptoms/global assessment in patients in argon plasma coagulation group with good long-term efficacy (76%).⁹

Rarely PC-IP can also be associated with complications such as stricture, ulcers, bleeding, tracheoesophageal fistula, esophageal perforation, and carcinomas.^{10,11}

Inclusion and Exclusion Criteria

Inclusion Criteria

1. Age equal to more than 12 years.
2. All patients presenting to gastro clinic with symptoms of globus sensation, chronic cough, heartburn, hoarseness, throat pain, dysphagia, and acid regurgitation for more than 4 weeks were included in the study after informed consent.

Exclusion Criteria

1. Age less than 12 years.
2. Patients with psychiatric illness, severe systemic disease.
3. Patients undergoing endoscopy for bleeding was excluded from the study.

Globus sensation was identified by standard definition as persistent or intermittent non painful sensation of a lump or a foreign body in the throat for more than 3 months.¹²

Materials and Methods

A retrospective cross-sectional study was conducted from April 2016 to April 2021 in the tertiary gastroenterology unit of urban India. All patients with symptoms of globus sensation, chronic cough, heartburn, hoarseness, throat pain, dysphagia, and acid regurgitation after a thorough clinical examination underwent esophagogastroduodenoscopy by experienced endoscopists. Sociodemographic data, symptoms and its duration, previous hospital visits, and chronic PPI use were noted during the study.

Endoscopic Procedure

In all cases, informed written consent was taken. After an overnight fasting, patients included in the study underwent a routine esophagogastroduodenoscopy with high-definition white light video endoscopy with narrow band imaging (NBI) features (Olympus Videoendoscope GIF-170 and 180 series - Olympus Medical Systems India Pvt. Ltd., India). Endoscopy was performed in left lateral position after topical xylocaine spray and conscious sedation using midazolam.

The endoscope was introduced and careful examination of esophagus, stomach, and duodenum up to second part was performed. Upon removing the endoscope slowly, detailed re-examination of upper esophagus was carried out. If PC-IP was suspected, the endoscope was reintroduced in NBI mode for detailed morphological study.

PC-IP was identified as one or more circumscribed flat salmon colored lesion with well-defined margins. Size of the PC-IP was estimated by comparing the affected area with the diameter of open biopsy forceps. When more than one lesion

was present, the size of largest patch was noted as shown in ►Fig. 1.

Minimum of two biopsies were obtained from the suspicious area and sent for histopathological examination by the same pathology service. Histopathological examination (HPE) were classified into oxyntic type, mucoid type or mixed as shown in ►Fig. 2A and B.

Most of these patients had a follow-up period of 5 years. During follow-up, symptom resolution and responses to PPI were noted. A section of patients with persistent symptoms, poor quality of life, unresponsive to PPI, and continued need for PPI were subjected to a repeat endoscopic examination to reassess for interval change in size of the PC-IP and a repeat biopsy if indicated.

Statistical Analysis

Convenience sampling and consecutive patient selection were employed. The chi-squared test or Fisher's exact test was used for the correlations and risk was calculated with odds ratio with 95% confidence interval.

Statistical significance was set at a *p*-value of less than 0.05.

Wilcoxon test was used for comparison of symptoms before and after PPI therapy.

Ethics committee approval was taken before the start of study.

Result

In the study period from April 2016 till April 2021, 3,250 number of upper gastrointestinal endoscopies was per-

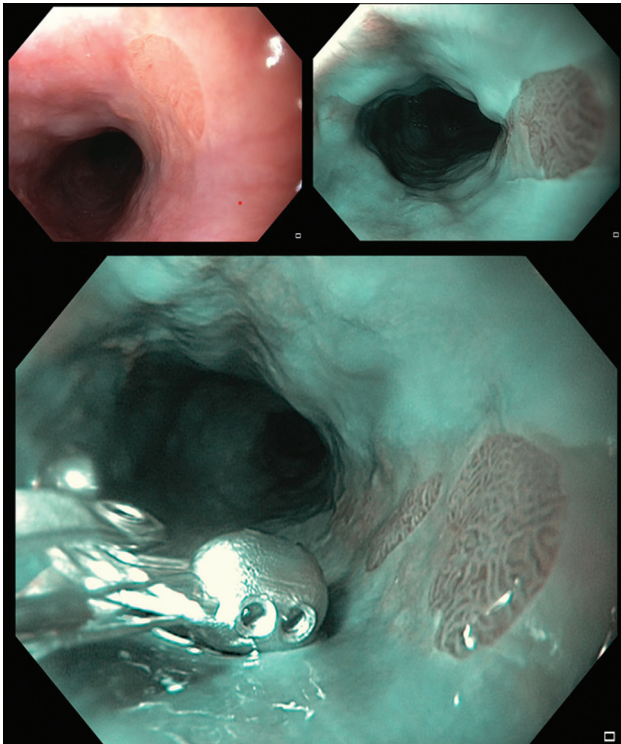


Fig. 1 Post cricoid inlet patch on white light endoscopy and on narrow band imaging.

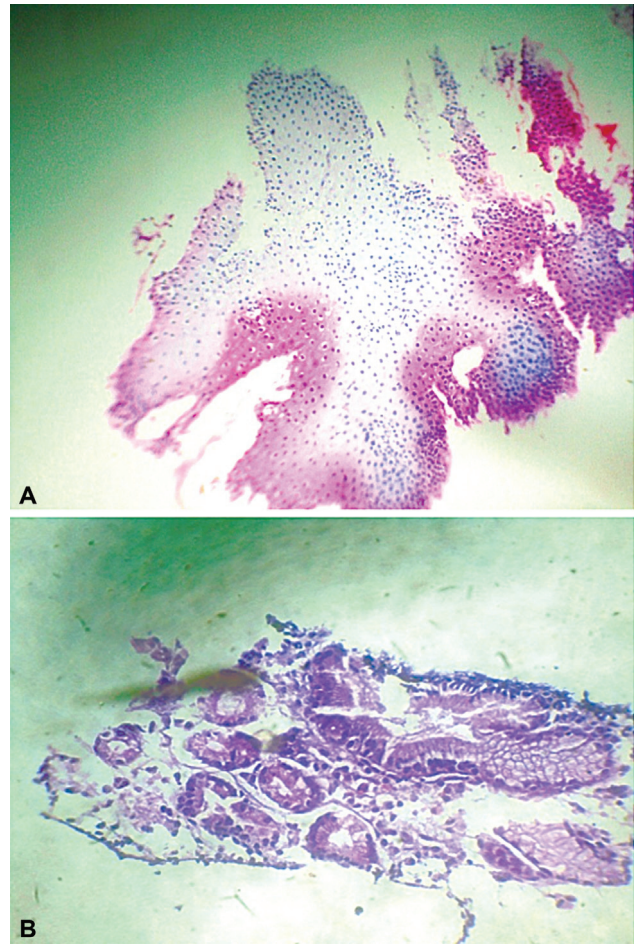


Fig. 2 (A) Histopathology specimen of post cricoid (PC) inlet patch showing gastric type mucosa with parietal cells adjacent to normal esophageal mucosa. (B) Histopathology specimen of PC inlet patch showing mucoid-type mucosa as there are no oxyntic (acid-secreting parietal cell) glands.

formed. The prevalence of PC-IP was noted in 88 (2.7%) of patients of whom males comprised of 36.3% ($n = 32$) and rest were females. Mean age was determined as 36.2 ± 17 (range: 30–70 years).

►Table 1 shows the demographic characteristics, symptoms of PC-IP, comorbidities, habits, and drug use. The most common symptoms encountered among these patients were globus sensation (81.8%) followed by acid regurgitation (75%), dyspepsia (64.7%), dysphagia (48.8%), throat pain (29.54%), chronic cough (22.72%), hoarseness (22.72%), and others (6.81%).

Normal endoscopic findings except PC-IP were noted in 36.36% ($n = 32$) of patients as shown in ►Table 2. Other associated endoscopic findings included Barrett's esophagus in 2.27% ($n = 2$), hiatus hernia in 36.36% ($n = 32$), esophagitis in 31.81% ($n = 28$), erosive gastroduodenitis in 10.22% ($n = 9$), gastroduodenal ulcers in 6.81% ($n = 6$), and positive rapid urease test in 40.9% ($n = 36$).

Identification of PC-IP was done based on its salmon-colored appearance with distinct margins in upper esophagus, confirmed on NBI. Mean diameter of PC-IP was 1.5 ± 0.5 cm; more than one patch was found in 23.76% ($n = 27$) of patients.

Table 1 Demographic characteristics and prevalence of IP symptoms

1	Age (years)	36.2 ± 17 years
2	Male/female	36.3/63.6% (32/56)
3	Prevalence	2.70%
4	Symptoms	
	a. Globus sensation	72 (81.81%)
	b. Dysphagia	43 (48.86%)
	c. Acid regurgitation	66 (75%)
	d. Throat pain	26 (29.54%)
	e. Hoarseness	20 (22.72%)
	f. Chronic cough	20 (22.72%)
	g. Dyspepsia	57 (64.71%)
	h. others	6 (6.8%)
5	Normal weight	46 (52.2%)
6	Over weight	30 (34.09%)
7	Obesity	12 (13.63%)
8	Smoking	27 (30.68%)
9	Alcohol use	36 (40.9%)
10	Hypertension	32 (36.36%)
11	Type 2 DM	26 (29.54%)
12	Thyroid disease	12 (13.63%)
13	Rheumatological issues	2 (2.27%)
14	Cardio illness	14 (15.9%)
15	Antiplatelet agents	12 (13.63%)
16	NSAIDs	4 (4.54%)
17	PPI use for > 3 months	49 (55.68%)

Abbreviations: DM, diabetes mellitus; IP inlet patch; NSAIDs, nonsteroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

Biopsy as reported by pathologist showed heterotrophic gastric mucosa in 77.27% ($n = 68$) followed by chronic inflammatory changes in 15.9 ($n = 14$) and normal esophageal mucosa in 6.8% ($n = 6$). There was no case of dysplasia or carcinoma in any of the samples.

Among all samples with heterotrophic gastric mucosa, 38.23 ($n = 26$)% had oxyntic type, 44.11% had mucoid type, and the rest had mixed 17.64% cell type as shown in ►Table 3.

On initial presentation, no reports of complications of IP such as bleeding, stricture, and malignancy found in our study. On median follow-up after 20 months (range: 6–30 months), 68.18% of patient had persistent symptoms, 77.27% were PPI responsive, and 22.73% were PPI refractory. On follow-up, 38.63 ($n = 34$) of patients had a repeat endoscopic procedure, none had a noticeable increase in size of the IP, nor did we encounter any complications like ulcer, bleeding, or stricture in any patient. Repeat biopsy was done in 20.45% ($n = 18$) of patients; none showed any changes of dysplasia. *Helicobacter pylori* infection/colonization was not seen our study.

Table 2 Endoscopic findings in patients with IP

1	Normal except IP	36.36%
2	Barrett's esophagus	2.27%
3	Esophagitis	31.81%
4	Erosive gastroduodenitis	10.22%
5	Gastroduodenal ulcers	6.81%
6	Positive rapid urease test	40.9%
7	Hiatus hernia	36.36%

Abbreviation: IP, inlet patch.

Table 3 Histopathological findings

Heterotrophic gastric mucosa	
Oxyntic type	38.23%
Mucoid type	44.11%
Mixed type	17.64%
Chronic inflammatory changes	15.9%
Normal esophageal mucosa	6.81%
<i>Helicobacter pylori</i> detection on HPE	0%

Discussion

After the first description of heterotrophic gastric mucosa in the year 1806, several studies have been published describing the clinical profile and a few on therapeutic interventions. Our study was an attempt to study the clinical profile of patients presenting with gastroesophageal reflux disease/upper gastrointestinal symptoms and endoscopic confirmation of inlet patch along with biopsy.

In our study, the prevalence of heterotrophic gastric mucosa was 2.70%. Prevalence in other studies was between 0.1 and 10%.^{13,14} Out of the 88 patients with PC-IP, 32 (36.3%) were male and 56 (63.6%) were females. This result was consistent with previous studies reporting higher prevalence among females. Mean age in our study was 36.2 ± 17 years. The mean age and prevalence varied between different studies depending upon the geography and population studied. The real prevalence could be much higher than what is published as a result of underestimation, faster withdrawal time, small lesions, and nonavailability of NBI-enhanced endoscopes.

Clinical manifestations of PC-IP range from being asymptomatic to complications of gastroesophageal reflux including stricture and malignancy. In our study, acid regurgitation (75%) followed by globus sensation (72.81%) was the most common symptom followed by the others described in our results.

Globus sensation was highly associated with gastroesophageal reflux than with PC-IP in a study conducted by Hori et al^{15,16} in Japan.

The much-debated association of PC-IP with Barrett's esophagus and gastroduodenal lesions secondary to *H. pylori* infection has been inconclusive across multiple studies.¹⁷ In our study, we found Barrett's esophagus in 2.27%,

gastroduodenitis in 10.22%, and gastroduodenal ulcers in 6.81%. Overall, 40.9% of the patients were positive for *H. pylori* rapid urease test. This could be due to higher prevalence of *H. pylori* infection in Indian population. All patients positive for urease test were treated as per standard guidelines. However, it was impossible to draw any conclusions, if any symptom improvement were due to *H. pylori* eradication or the PPIs that is included in the anti-*H. pylori* treatment.

Contrary to the findings of oxyntic mucosa cell type being more common histology detected, our study showed mucoid type was higher than oxyntic type (44.11 vs. 38.23%). Satellite lesions were noted in 23.76% ($n=27$) of the patients in our study. These findings were in accordance with the literature.

Though majority of our patients were PPI responsive (77.27%), they were found to be PPI dependent on follow-up. It was interesting to note that 22.73% of patients who were refractory to standard dose of PPI were managed with higher dose PPI and addition of histamine-2 receptor antagonist or tricarboxylic acid cycle to their treatment.

No consensus guidelines were available on surveillance of PC-IP due to the low incidence and lack of information on its natural history and its prognosis. However, attention should be given to unusual findings and malignancy detected on histopathology.

Treatment of complications of PC-IP including stricture and malignancy is managed as per standard existing guidelines.

Conclusion

Prevalence of PC-IP could be higher than the estimated. Careful examination of upper esophagus and use of NBI will increase the possibility of identifying IP. Those symptomatic patients need treatment with PPI, sometimes on long term basis. Ablative therapy with radiofrequency or argon plasma coagulation of PC-IP needs further clarification preferably with randomized controlled prospective studies.

Conflict of Interest

None declared.

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