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RESEARCH ARTICLE

PREVALENCE AND CLINICAL PROFILE OF HYPERPLASTIC GASTRIC POLYPS IN NORTH INDIA

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ABSTRACT

Background: The Hyperplastic polyps (HPP) where the most common histopathological type of gastric polyps all over world. This was attributed to its association to the high prevalence of *Helicobacter pylori* (*H. pylori*) globally. Patients with HPP have low but definite chances of future malignancies in polyps and background gastric mucosa. The present study was intended to evaluate the associations and determine the patterns of HPP in our population in Kashmir. **Methods:** The medical record of all patients who had gastric polyps on esophagogastroduodenoscopy in 3 centers in Kashmir from 2011-2018 were reviewed. The data of all patient diagnosed to have HPP on histopathology of gastric polyps were compiled. Their demographic particulars, comprising age, gender, weight, presenting complaints, smoking habit, the anatomic site of polyp and size, Helicobacter pylori infection and the histopathology of the background mucosa were examined and analyzed. **Results***:* Of the 757 patients studied, 480 (63.4%) were male and 277 (36.6%) were female. Mean age was 50 ±14.67 years with the range of 13 to 89 years. Most of the patients where over-weight with mean weight of 68.32±13.474and 25.36% were smokers. Dyspepsia was the most frequent presenting complaint in 468(61.8%) patients. Antrum was commonest anatomic site of HPP (n= 390, 51.5 %) and 549(72.5%) polyps were of size less than 1cm. H. Pylori gastritis was most common type of gastritis in background mucosa (45.7%, n = 346).Apart from HP gastritis, 108(14.2%) had chronic inactive gastropathy (CIG); 40 (5.28%) had reactive gastritis (RG); 37 (4.8%) had intestinal metaplasia (IM); 2 (0.26%) had Portal hypertensive gastropathy (PHTG**). Conclusions.**HPP was more common in males and was associated with smoking in one quarter of patients. Most of the polyps were of size less than 1cm and located in antrum. HP gastritis was most common type of gastritis in HPP.

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INTRODUCTION

The reported prevalence of gastric polyps is rising owing to increased rate of detection, which is direct outcome of more endoscopic examination in clinical practice. The figures are variable however, reflecting significance of local and genetic factors (Peretz *et al*., 2012; Tran-Duy *et al*., 2016; Cao *et al*., 2012). The hyperplastic polyp (HPP) is the second most common gastric polyp after the FGP. The relative prevalence of HPP reported has been variable, with most studies showing it to be much higher in past, ranging from as high as 75% in United States in 1989 (Deppisch, 1989) to just 17% by Carmack *et al* in 2008. Cao *et al*. revealed similar trend, with nearly 50% HPP of all polyps in 2000 while in 2010 accounted for only 20.8% (Cao *et al*., 2016).

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This reduction in numbers to probably due to decrease in the atrophic gastritis and Helicobacter pylori infection (Peretz *et al*., 2012; Cao *et al*., 2012). HPP are usually small sessile or pedunculated polyps less than 2 cm in diameter, most commonly found in the antrum, though they can arise any part of stomach (Nakamura, 1985). Multiple HPP can be found when in areas adjacent to erosions/ulcer or gastroenterostomy sites. On microscopic examination HPP have proliferation of surface foveolar cells lining elongated, tortuous pits, giving a corkscrew appearance and going deep into the lamina propria. HPP may contain all other gastric cell types and can histolpathologically appear similar to hamartomas and inflammatory conditions (Nakamura, 1985). They can be asymptomatic or present with dyspepsia, abdominal pain, anemia, GI bleed due to ulcer or erosion in surface epithelium, or gastric outlet obstruction when they are large and occlude the pylorus. These polyps have little neoplastic potential, less than 1%, and are not considered pre-cancerous lesions but are associated with an increased risk of synchronous cancer

elsewhere in the gastric mucosa, up to 6%, particularly if associated with chronic gastritis (Nakamura, 1985; Abraham, 2001; Daibo, 1987; Bai, 2010; Hattori, 1985; Robbins, 1995; Dore, 2015; Magali Evangelina, 2018; Morais, 2017; Aydin *et al*., 2014; Elhanafi, 2015; Ljubicić, 1999; Bai *et al*., 2010).
HPP has been shown to have strong associated with inflammatory disorders so it is advisable to take biopsy the background flat mucosa in order to determine any etiologic factors and has been described in literature (Hattori, 1985; Almazeedi, 2013). *H pylori* is the one of the common perpetrator, and 80% of HPP will regress with *H pylori* eradication in patients with H. Pylori gastritis (HPG) (Daibo, 1987; Di Giulio, 2015; Ginsberg, 1995). Chronic inactive gastropathy (CIG), reactive gastritis (RG) and intestinal metaplasia (IM) were also seen in patients with gastric polyps (Daibo, 1987). RG is the second most common pathologic diagnosis after HPG (Deppish, 1989; Hnizdil, 2002). RG or chemical gastropathy, as per updated Sydney System, is a reactionary chemical injury to the gastric mucosa secondary to various provocative factors causing constellation of endoscopic and histologic findings (Almazeedi, 2013). The endoscopic findings of RG are mostly nonspecific and can be normal or can exhibit erythema, congestion, edema or erosions. The mucosal changes in RG are usually most prominent in the antrum and pre-pyloric region but involve more proximal part as well (Randall, 1992). The common underlying causes of RG include chronic bile reflux and long-term intake of nonsteroidal anti-inflammatory drugs. Bile reflux usually occurs in patients who have undergone a Billroth II partial gastrectomy; it is also recognized to occur in intact stomachs in individuals with alcohol abuse, cigarette smoking, chronic respiratory disease, or duodenal ulcer, and even in healthy subjects (Nakamura, 1985; Randall, 1992). Foveolar hyperplasia, smooth muscle fibers, vasodilatation and congestion are key histologic parameters for the diagnosis of RG (Tran-Duy 2016; Di Giulio, 2005; Deppish, 1989).

There is difference of opinion whether these polyps should be simply biopsied or resected endoscopically as these have low dysplastic potential. Some authors recommend minimum size of 2cm for polypectomy while others resect all polyps above 5mm size because of the concern that forceps biopsy sampling may miss the dysplastic foci within a HPP (Nakamura, 1985; Robbins, 1995; Boyd, 2014). Surveillance is recommended with a single repeat endoscopy at 1 year, but further surveillance subsequently is not recommended due to lack of evidence and should be an area for future research (Nakamura, 1985). In last 20 years, there has been changes in relative prevalence of different polyps and their clinical profile has also changed but there is only sparse data from our part of world and if the changing trend seen in west holds true to Asian and Indian population has not been studied in large population in recent years. This study was designed to investigate current clinical pattern of HPP in the Asian population especially in Northern India, Kashmir. In addition associations and the relationship with different types chronic gastritis was also evaluated.

MATERIALS AND METHODS

This study was a hospital based retrospective, observational study. Institutional ethics committee cleared the study protocol. The medical record of all patients detected to have gastric polyps on Endoscopicgastrodudenoscopy (EGD) in department of gastroenterology at three centers in Kashmir, India from January 2011 to January 2018, was reviewed. .All consecutive patients with biopsy documented Hyperplastic gastric polyps (HPP) during this period were included in the study. Gastric biopsies graded as per Sydney protocol of these patients taken while removing or taking biopsy of a gastric polyp was also reviewed

Inclusion Criteria: Biopsy proven Hyperplastic gastric polyps

Exclusion Criteria:

- Known malignancies, Chronic diseases (e.g. chronic renal or liver disease, severe respiratory or cardiac disease, connective tissue disorders)
- Pregnancy
- Syndromic gastric polyps with these phenotypes
- Patients whose gastric biopsies were not assessed and properly graded as per the updated Sydney protocol.

The policy for the evaluation of gastric biopsies in these centers was to fix biopsy sample immediately in formalin solution for 4-8 h at room temperature and were routinely processed for conventional histological assessment. The *H. pylori* organism was identified by hematoxylin and eosin stain or by modified Giemsa stain. In case staining results were negative but infection was suspected on the basis of a histological finding of chronic active gastritis and lymphoid aggregates, a peroxidase conjugated monoclonal anti *H. pylori* immunostaining was carried out. The following data of the participants were compiled and categorized for analysis: age; gender, weight; habit of smoking, presenting complain /indication for EGD, biopsies of background mucosa andHelicobacter pylori infection. Statistical analysis: Statistical analysis was performed using a statistical software program SPSS version 20 (IBM).Continuous variables were expressed as mean and standard deviation (Mean (SD)) and Range. All p values were two-tailed; p value of < 0.05 was considered statistically.

RESULTS

A total of 2350 patients who had polyps on EGD were screened. Of these, 1493 were excluded as per exclusion criteria. (Fig. 1).There were 757 patients with HPP polyps who underwent EGD for different upper gastrointestinal symptoms. Of these patients, 408(63.4%) were male and277 (36.6%) female (Fig. 2).The most common presenting complaint of patients was dyspepsia followed by anemia and others as given in table 1and figure 3. Maximum patients where in 5th decade of their life and ranged from 13 years to 89 years .Figure 4 shows the patients in various age groups. Median weight was 69 kg, range was from 27 to 98 kgs and three quarter of patient were having weight above 60 kgs, figure 5.Overall,192 patients where smokers and 565 where non smokers .Amongst smokers 157 men and 35 where elderly females as shown in Table2. Most polyps were located in Antrum. The distribution of polyps in the stomach is in table 3. Majority of polyps were of smaller size as shown in table 4. There were nine synchronous polyps in these patients, table 5.Histopathology of background gastric mucosa was as shown Tables 5. HPG was most common type of gastritis seen in 45.70% of Hpp patients; 14.26 % of patients had CIG.

DISCUSSION

The present retrospective study was undertaken to assess the demographic characteristics, clinical profile and associations

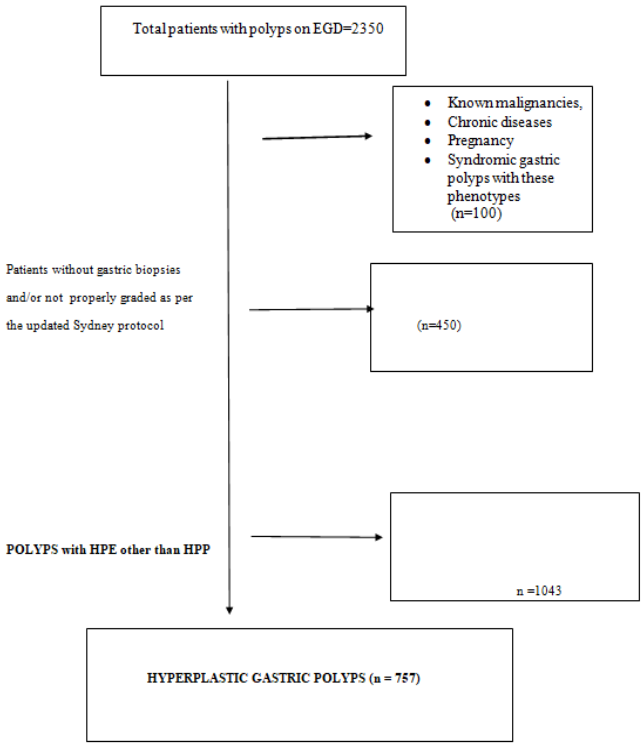


Fig 1.Flow chart to present study protocol, n= number of patients

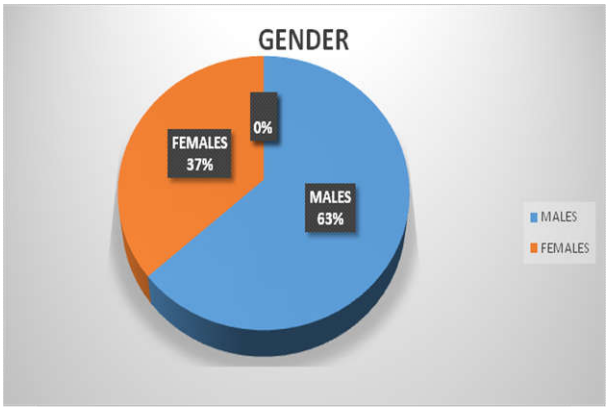
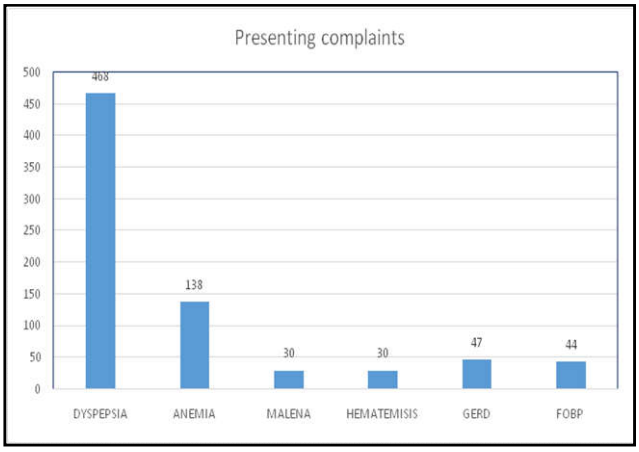


Figure 2.



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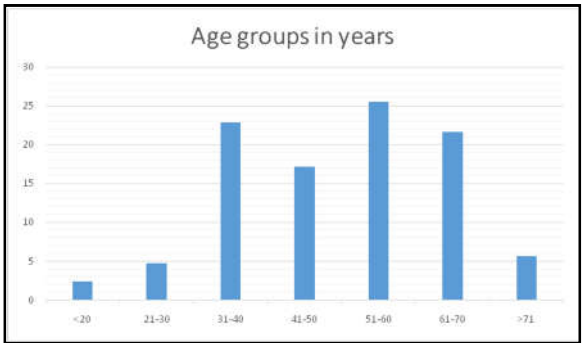

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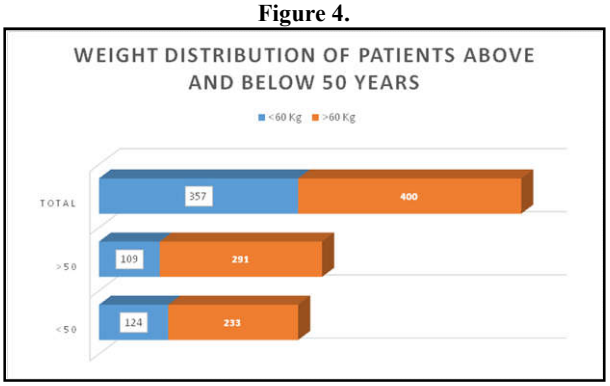

Figure 5

Table 1. Presenting complaints

	Frequency	%
ANEMIA	138	18.2
DYSPEPSIA	468	61.8
FOBP	44	5.8
GERD	47	6.2
HEMATEMESIS	30	4.0
MALENA	30	4.0

Table 2.

	SMOKER(n)		
	NO	YES	TOTAL
FEMALES	242	35	277
MALES	323	157	480
TOTAL	565	192	757

Table 3.

LOCATION OF POLYP		
Location	n	%
ANTRUM	390	51.5
CORPUS	130	17.2
FUNDUS/CARDIA	227	30.0
PYLORIS	10	1.3
Total	757	100.0

Table 4.

Polyp Size equal to greater than 1cm		
	n	%
NO	549	72.5
YES	208	27.5

Table 5.

SYNCHRONOUS_POLYP	
HPE	n
AC	1
AP	1
FGP	3
NET	2
XANTHOMA	2

Table 6. Biopsy Findings of Gastric mucosa

Biopsy finding	(n,%)
CIG	108(14.26)
HPG	346(45.70)
IM	37 (4.88)
PHTG	2(0.264)
RG	40 (5.28)
NORMAL	224 (29.59)
TOTAL	757 (100)

of patients with Hyperplastic gastric polyps over a period of seven years. During this study period, total of 757 patients with histopathological diagnosis of HPP were enrolled. The median age of presentation was 52 years with the range of 13 years to 89 years. Fifty three percent of our patients were above 50 years of age and one third were in their 3rd and fourth decade of life while only 7% were below thirty years of age. Similar observations have been made elsewhere in Asian and Western Literature with most patients in older age group though there are reports of HPP even in neonates (Nakamura, 1985; Abraham, 2001; Morais *et al*., 2007). Magali Evangelina *et al* (Magali Evangelina, 2018) found the median age of patients with gastric polyps in their series was 58 years. Elhanafi S *et al* (Elhanafi, 2015) found that, per unit increase in age increased the odds of hyperplastic polyp type by 3% as compared to fundic gland polyps.

Gender based analysis revealed that we had 63.4% males and 36.6% females in our study population. Although female preponderance has been reported by authors all over world (Abraham, 2001; Murakami, 2001; Yao, 2002), but some have found incidence more in males (Morais *et al*., 2007).A female-to-male ratio of 3:1 was observed by Magali Evangelina *et al*. (2018) for the presence of gastric polyps, and this difference was sustained for the fundic gland and hyperplastic subtypes of polyps. Our figures seem to be contradictory to most past observations .This may be due to the fact that, we had screened more males than females because of various reasons. Firstly, women are usually hesitant for routine endoscopic examination. Moreover, they are investigated less for anemia, which is one of the common reason for endoscopies, presuming it to be secondary to menstrual loss or loss during pregnancies. To determine actual prevalence and male –female ratios in our population, we need to have homogenous study populations without such confounding factors. Most of the HPP are asymptomatic and when symptomatic present with dyspepsia, heartburn, abdominal pain, anemia , GI bleed or rarely with gastric outlet obstruction when large (Nakamura, 1985; Morais, 2007).

Since we had not done endoscopies in asymptomatic patients all our patients had presenting complaints. Dyspepsia followed by anemia were main symptoms of presentation in 61.8% and 18.2% respectively. Other symptoms such as GI bleed, gastroesophageal reflux disease (GERD)and, fecal occult blood positive**(**FOBP) were present in about 1/5th of cases. The smoking habit has been seen to increases the risk for benign epithelial gastric polyps in patients with atrophic body gastritis (Almazeedi, 2013). Of all patients with HPP I/4th were smokers, with around 32.7 % of men and 12.6% of women smokers When smoking habit was analyzed as per the type of gastritis, around 30% of Reactive Gastritis patients happened to be smokers as against all other types having around 24 to 27 % smokers as seen in past (Nakamura,1985; Randall, 1992; Fu-Wei, 2018).

Since data about height of patients was not available so we couldn't calculate BMI but most of the patients had weight on higher side. Median weight was 68.3 kgs and 72.8% patients above 50 years, that excluded children and young adults, were having weight above 60 kg. This will need further studies. Although higher prevalence of gastric polyps detected in patients with an increased body weight was not confirmed by the multivariate analysis in previous studies. This is consistent with studies carried out in patients undergoing bariatric surgery where the incidence of gastric polyps found in these patients was not increased compared to the general population [Almazeedi, 2013; Raghavendra, 2012]. The HPP may be located anywhere in the gastric mucosa. In our study, they were more frequent in the antrum ,in 51.5% followed by body of stomach ,in 17.2%. Our observations confirmed previous reports (Morais, 2007; Aydin, 2014; Deppish, 1989; Randall, 1992). We didn't find any focus of carcinoma in our series on histological examination like some authors in past (Dore, 2015) .HPP are not considered to be pre-cancerous owing to their low risk of harboring carcinoma or transforming in to malignant lesion. The risk of focal adenocarcinoma within HPP as per previous reports is less than 1% mostly (Morais, 2007), but infrequently more than 1 %(8) and can go upto 6% in the surrounding mucosa (Cao, 2012; Nakamura, 1985; Deppisch, 1989; Nakamura, 1985; Morais, 2007; Muehldorfer, 2002; Martínez, 2011). DAIBO *et al*. (2002) suggested these polyps can develop dysplastic foci followed by the carcinoma once they grow into large polyps. This author also suggested that HPP could have malignant transformation, though this was rare. This progression into malignant lesion is not well understood yet and insufficient studies have examined its histogenesis (Cao, 2012; Abraham, 2001; Di Giulio, 2005; Hattori, 1985; Robbins, 1995; Morais, 2007; Ginsberg *et al*., 1995; Fernández-Martos, 2011).

Majority (72.5%) of polyps were less than 1cm in size and in Synchronous polyps were seen in only 9 patients. Most of these polyps are under 1cm but can have larger size (Di Giulio, 2015). Background mucosal biopsies taken as per Sydney protocol reviewed. Maximum number of the patients had H. Pylori related gastritis (HPG) with figures of 45.7%.Though it was most common type of gastritis in our patients as has been reported in literature, but the figures were lower than theearlier reports. This could be explained by lower threshold for H.pylori infection testing and treatment by clinicians in our part of world and overall decrease in H.Pylori infection because of better standards of living and improved sanitary. Other types of gastritis found in these patients were CIG was seen in 14.3%, RG in 5.3%, IM in 4.9%,P HTN in 0.3% and normal in 29.6%. Elhanafi *et al*. (2015) found in the unadjustedanalysis, age, *H. pylori* status and portal hypertension were seen to be associated with hyperplastic polyps. After adjusting for all othercauses, *H. pylori* status and portal hypertensivegastropathy were the only remained significant factorsin the final adjusted model. Positive *H. pylori* statushas 5.3 times higher odds to have hyperplastic polypscompared with negative *H. pylori* status. Patients with portal hypertensive gastropathy are 6.4 times more likely to have hyperplastic polyps after adjusting for *H. pylori*. However, in our series we had only 0.3% cases of portal gastropathy because we had excluded patients with known portal hypertention This a strong association between hyperplastic polyps, chronic gastritis and *H. pylori* infection supports what was reported in other studies (Ljubicić *et al*., 1999; Dirschmid, 2006).

It has been reported that HPP in portal hypertensive patients are pathologically different from the classic hyperplastic polyps seen in nonportal hypertensive patients with uncertain malignant potential [Lam, 2011; Boyd, 2014; Amarapurkar, 2013; Boyd, 2014; Amarapurkar, 2013; Abraham, 2002; Sanna, 1991 Lee, 2013]. These polyps should be managed conservatively rather than by polypectomies due to higher chances of bleed associated thrombocytopenia and coagulopathy (Lam, 2011; Boyd, 2014). Carmack *et al* in their study found Hyperplastic polyps, reported to be associated with *H. pylori* gastritis and atrophy, were associated with intestinal metaplasia (OR 2.0, 95 % CI: 1.68 – 2.38), but negatively associated withcurrent *H. pylori* infection (OR 0.47, 95 % CI: 0.37 – 0.60). It isconsistent with the notion that long-standing forms of *H. pylori* inducedatrophic gastritis, particularly when extensive intestinalmetaplasia is present, tend to lose the active infection (Carmack, 2009). There have been some disagreement in results from various studies due to the different designs and study population with different race and genetics. This study had a positive point of having large sample size and being conducted in department of gastroenterology in a tertiary Centre using only EGD to diagnose polyps, thus less chance of missing polyps and decreases clinical heterogeneity. This study suffered from number of disadvantages. Firstly, it entails patients who were referred to us from various parts of the valley of Kashmir and therefore cannot be truly representative of population at large. Secondly, this study being retrospective study had limited observational data available and no scope of evaluating things in more detail. Nevertheless, the data collected offers insight into overall clinical profile and demographic features of patients with HPP in our population.

Summary and Conclusion

In present retrospective study; clinical presentation and demographic profile of patients with HPP and their background gastric mucosa was reviewed. The following conclusions were drawn:

- These polyps were seen most commonly in their 5th to 6th decade of life.
- Dyspepsia was dominant clinical feature.
- HPG is most common gastritis associated with HPP
- Smoking and increased weight seems to increase the risk of HPP

Recommendation

- Take multiple biopsies of the flat uninvolved mucosa surrounding the polyp because of the risk of adenocarcinoma in the surrounding nonpolypoid tissue is greater than in the polyp itself.
- Remove polyps greater than 1 cm by polypectomy as biopsies can miss dysplastic focus.

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