

# Demographic Characteristic of Fundic Gland Polyp and Its Association with Gastritis in Pathology Anatomy Department, Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo Hospital

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## ABSTRACT

**Background:** Fundic gland polyp (FGP) is the most common polyp found in the stomach with the incidence of 47% from all stomach polyps. FGP is more common to be found in female with the ratio of 5:1 and occurs in the average age of 53-year-old. Gastrin is a hormone produced by G cell, which function is to facilitate epithelial cell proliferation. Gastritis is a frequently found digestive tract disturbance. Torbenson et al showed the presence of chronic gastritis in FGP patients. The aim of this study is to observe the demographic characteristics of FGP and to identify the association between number of polyps with morphologic appearances of gastritis in Anatomical Pathology Department, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital in year 2012-2014.

**Method:** This retrospective study was a descriptive analytical study. This study was performed by reviewing the slides of FGP cases and evaluating the severity of gastritis based on visual analog scale from Sydney System (SS).

**Results:** Study of FGP demographic obtained 44 cases with predominantly female aged 30 (68.2%), patients' average age was 55.4 year old with dominant age group in age group 51-60 year old which accounted for 16 (36.4%). This study was performed in 38 cases. The frequency of single polyp was 18 and multiple polyp was 20. Most cases were chronic inflammation which accounted for 21 (55.3%) and mild atrophy 18 (47.4%). Mild intestinal metaplasia was found in 1 case. There was no case of neutrophil infiltration, *H. pylori* infection or dysplasia. Chi-square test revealed that there was no significant association between number of polyps with gastritis.

**Conclusion:** Chi-square test which was performed in this study showed there is no significant association between number of polyps with gastritis.

**Keywords:** fundic gland polyp (FGP), gastritis, gastrin

## ABSTRAK

**Latar belakang:** Fundic gland polyp (FGP) merupakan polip tersering ditemukan pada gaster dengan insidens 47% dari seluruh polip gaster. FGP lebih banyak ditemukan pada wanita dengan rasio 5:1 serta rata-

*rata timbul pada usia 53 tahun. Gastrin adalah hormon yang dihasilkan oleh sel G, salah satu fungsinya dalam memfasilitasi proliferasi sel epitel. Gastritis merupakan gangguan saluran pencernaan yang sering terjadi. Torbenson et al menunjukkan adanya gastritis kronik pada pasien FGP. Tujuan dari penelitian ini untuk melihat karakteristik demografik FGP serta mengetahui hubungan bermakna antara jumlah polip dengan gambaran morfologi gastritis di Departemen Patologi Anatomik, Fakultas Kedokteran, Universitas Indonesia/RS Cipto Mangunkusumo tahun 2012-2014.*

**Metode:** Telaah retrospektif ini merupakan penelitian deskriptif analitik. Penelitian dilakukan dengan pembacaan ulang slide kasus FGP dan menilai berat ringannya gastritis berdasarkan visual analog scale dari Sydney system (SS).

**Hasil:** Telaah demografik FGP didapatkan 44 kasus dengan predominan kelompok wanita 30 (68,2%), usia rata-rata pasien 55,4 tahun dengan kelompok usia dominan pada kelompok usia 51-60 tahun sebesar 16 (36,4%). Penelitian dilakukan terhadap 38 kasus. Jumlah polip single 18 dan multiple 20. Kasus terbanyak inflamasi kronik sedang sebesar 21 (55,3%) dan atrofi ringan 18 (47,4%). Metaplasia intestinal ringan 1. Tidak ditemukan kasus dengan infiltrasi neutrofil, infeksi *H. pylori* maupun displasia. Uji Chi-square menunjukkan tidak terdapat hubungan bermakna antara jumlah polip dengan gastritis.

**Simpulan:** Uji Chi-square yang dilakukan pada penelitian ini menunjukkan tidak terdapat hubungan bermakna antara jumlah polip dengan gastritis.

**Kata kunci:** fundic gland polyp (FGP), gastritis, gastrin

## INTRODUCTION

The stomach is an important organ in the body, which functions as food storage and digestion, and also protects the body from bacteria and produces hormone. Chemical, hormonal, and bacterial exposure may cause lesions in the stomach, ranging from inflammation, polyps, to neoplasm. The most common polyps found in the stomach is the fundic gland polyp (FGP), hyperplastic polyp, and adenoma.<sup>1-3</sup> FGP is the most frequent polyp found in the stomach with the incidence rate of approximately 47% from all stomach polyps and most commonly occur in female compared to male with the ratio of 5:1. The highest prevalence was middle-aged group with the average age of 53 year old.<sup>4,5</sup> As for FGP cases documented in Cipto Mangunkusumo Hospital from January 2012 to December 2014 were 44 cases.

Definition of FGP is non-neoplastic polyp, single or multiple, that originates from gastric oxyntic mucosa, contains hyperplastic inner part of gland, irregular, and with cystic dilatation, layered by parietal, chief, and mucous neck cells accompanied with the increased smooth muscle in the lamina propria.<sup>2,3,6,7</sup> Clinically, FGP is classified into 2, which are:

syndromic and sporadic, where syndromic FGP is associated with familial adenomatous polyposis syndrome (FAP), Gartners syndrome, Peutz-Jeghers syndrome, Cowdens syndrome and Juvenile polyposis, while sporadic FGP is known to be associated with

atrophic gastritis, Zollinger-Ellison syndrome and the use of proton pump inhibitors (PPI). Young-aged FGP patients with multiple number of polyps (>10) must be suspected for syndromic FGP although morphologically, syndromic and sporadic FGP give similar appearance.<sup>3,8,9</sup>

There is a difference in the etiology of syndromic FGP and sporadic FGP; syndromic FGP, as has been widely known, is caused by the presence of second somatic hit in adenomatous polyposis coli (APC) gene, while the cause of sporadic FGP remains unknown. Torbenson et al in their study found the presence of mutation in the exone of 3 gene  $\beta$ -catenin.<sup>7</sup> Gastrin is a hormone produced by G cell which is found in the gastric antrum that plays role in the regulation of stimulation of gastric acid secretion, facilitates epithelial cell proliferation, tissue recovery, and angiogenesis.<sup>10</sup> Increased level of gastrin can be triggered by the presence of Zollinger Ellison syndrome, kidney failure, vagotomy, hyperplasia of antral G cell, retained antrum syndrome, gastric outlet obstructions, H2-blockers, PPI, *Helicobacter pylori* (*H. pylori*) infection and atrophic gastritis.<sup>10,11</sup> Gastritis is one of the most frequent digestive tract disturbance. Generally, definition of gastritis is a condition where inflammation occurs in the gastric mucosa as an inflammatory response to injury.<sup>12,13</sup> Study conducted by Torbenson et al revealed the presence of chronic gastritis in FGP patients.<sup>7</sup> Sydney system (SS) is a chronic gastritis classification system which has been introduced since year 1990, where identification of gastritis is based on etiology, topography,



and morphology.<sup>14</sup> Reporting gastritis according to this system includes the presence of chronic inflammation (lymphocyte and plasma cells), infiltration of neutrophil cells (PMN), gland atrophy, intestinal metaplasia, and *H. pylori* infection.<sup>13,15</sup> Objectives of this study were to observe the demographic characteristics of FGP and to identify the significant association between the number of polyps with morphologic appearances of gastritis in Anatomical Pathology Department, Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo Hospital.

## METHOD

This retrospective study was a descriptive analytical study. Samples were obtained from secondary data (forms and slides) retrieved from the medical records of histopathology laboratory in the Anatomical Pathology Department, Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo Hospital dated between January 2012 to December 2014 (3 years period). Case identification was performed using topographic code which were C16 (Gaster) and morphologic code H759 (FGP) and H534 (gastritis). Further, investigation and collection were performed on the examination result forms and histopathologic slides from all identified cases. Form documentations included age, sex, and number of polyps.

Inclusion criteria in demographic characteristic included all cases of FGP which were the results of diagnosis through histopathologic examination, while the inclusion criteria of the study were all FGP cases which had non-polyp gastric mucosa. Any cases which had no non-polyp gastric mucosa became the exclusion criteria of the sample in this study. Evaluation of gastritis was completed by identifying the severity of chronic inflammation, neutrophil (PMN) infiltration, gland atrophy, intestinal metaplasia, and *H. pylori* infection based on visual analog scale from SS. The evaluation was conducted by 2 researchers, who were the writer and the supervisor, and discussion was performed if discrepancy was found.

Data analysis was performed using SPSS for Windows (Version 23) by means of Chi-square test to identify the significant correlation between the number of polyps with chronic inflammation and gland atrophy.

## RESULTS

Based on the medical record data in Anatomical Pathology, Faculty of Medicine, Univeritas Indonesia/Cipto Mangunkusumo Hospital within the period of

year 2012-2014, there were 44 cases diagnosed as FGP through histopathologic examination, in which 7 cases was found in 2012, 4 cases were found in 2013, and most cases were found in 2014 which were 33 cases. The incidence rate of FGP in 3 years is presented in Figure 2. The demographic data of FGP patients found 14 cases in male (31.8%) and 30 cases in female (68.2%). The number of single and multiple polyps were 24 cases (54.5%) and 20 cases (45.5%), respectively. Distribution of age in FGP patients ranged between 9 year old to 88 year old with the average age of 55.4 year old, with dominant age group of 51-60 year old, which accounted for 16 cases (34.2%) (Table 1).

Number of cases excluded in this study was 6 cases; therefore 38 cases were included in the study. From all cases in this study, we found single polyps in 18 cases and multiple in 20 cases. Re-evaluation of morphologic appearance of gastritis obtained most cases were moderate chronic inflammation which were 21 cases (55.3%) and mild atrophy in 18 cases (47.4%). Mild intestinal metaplasia was found only in 1 case. No case of neutrophil infiltration or *H. pylori* infection was found (Table 2). Dysplasia was not found in all cases.

Study analysis was conducted in 38 cases of FGP using Chi-square test to identify the association between number of polyps with gland atrophy (Table 3).

**Table 1. Demographic data of FGP patients in Anatomical Pathology Department FMUI/CMGH in the year 2012-2014 period.**

Characteristic	n (%)
Sex	
Male	14 (31.8)
Female	30 (68.2)
Age (year old)	
0-10	1 (2.3)
11-20	0 (0)
21-30	1 (2.3)
31-40	1 (2.3)
41-50	12 (27.2)
51-60	16 (36.4)
61-70	8 (18.2)
71-80	4 (9)
81-90	1 (2.3)
Number of polyps	
Single	24 (54.5)
Multiple	20 (45.5)

**Table 2. Results of re-evaluation of gastritis**

Characteristic	n (%)
Chronic inflammation	
Normal	0 (0)
Mild	10 (26.3)
Moderate	21 (55.3)
Severe	7 (18.4)
Neutrophil infiltration (PMN)	
Normal/not found	38 (100)
Mild	0 (0)
Moderate	0 (0)
Severe	0 (0)
Gland atrophy	
Normal/not found	7 (18.4)
Mild	18 (47.4)
Moderate	12 (31.6)
Severe	1 (2.6)



Characteristic	n (%)
metaplasia	
Normal/not found	37 (97.4)
Mild	1 (2.6)
Moderate	0 (0)
Severe	0 (0)
<i>H. pylori</i>	
Normal/not found	38 (100)
Mild	0 (0)
Moderate	0 (0)
Severe	0 (0)

**Table 3. Results of Chi-square test between number of polyps and chronic inflammation and gland atrophy**

	Number of polyps		P
	Single	Multiple	
Chronic inflammation			
Mild	4	6	0.784
Moderate	11	10	
Severe	3	4	
Gland atrophy			
Normal/not found	2	5	0.332
Mild	11	7	
Moderate	5	7	
Severe	0	1	

## DISCUSSION

Nan-Nan Fan et al in their study conducted in Chinese population where FGP was mostly found in female compared to male with the ratio of 1.39:1 and average age of 53.9 year old.<sup>16</sup> Identification of FGP in young-aged patients necessitates the suspicion of a FAP and was found in 8 year old child.<sup>16,17</sup> Similarly, several previous studies mentioned that female has higher prevalence compared to male with the ratio of 5:1.<sup>4,5</sup>

Clinically, syndromic FGP is marked by the presence of abundant amount of polyps which may reach hundreds, with the diameter of < 5 mm with the base of the polyp forming a sessile shape or multiple known as sporadic fundic gland polyposis, where it has been proven that it is not included in FAP and mutation of  $\beta$  catenin gene is present. It has been shown that cases of sporadic FGP with single polyp was more frequent compared to syndromic FGP.<sup>3,7,8</sup> Limited information given by clinicians regarding history of family illness, number of polyps, history or previous illness, and therapy which had been administered cause difficulty for the writer to differentiate types of FGP.

The rationale of our thoughts to correlate between FGP and gastritis was the study performed by Di Giulio et al which stated that in patients with atrophic body gastritis (ABG), 5% of them would develop into benign epithelial gastric polyps (BEGP). ABG is a condition marked by the presence of atrophy of oxyntic mucosa which leads to the decreased secretion of acid (hypo/achlorhidria); this condition automatically will cause negative feedback to increase gastrin

level (hypergastrinemia) which increase the risk for neoplasm in the stomach.<sup>18</sup>

Gastrin is a gastrointestinal hormone which stimulate secretion of gastric acid and plays role in cell proliferation. Gastrin mechanism in cell proliferation has not been known precisely; it is suspected that gastrin stimulates secretion of Reg protein produced by endocrine cells in gastric mucosa which plays role as a growth factor of gastric epithelial cells. Gastrin serum level is also an important marker in evaluating inflammation condition in the stomach. To demonstrate the presence of gastrin in the mucosa, immunohistochemistry examination is needed as performed by Takamura et al who used gastrin immunohistochemistry to identify the expression of gastrin in stomach mucosa particularly in foveola epithelial cells and parietal cells.<sup>19</sup>

Torbenson et al who stated that the presence of scarce inflammatory cells, smooth muscle, and oedema in the lamina propria in sporadic sporadic fundic gland polyposis; similar to those found in single sporadic FGP without the presence of *H. pylori* infection or even intestinal metaplasia.<sup>7</sup> Statistical Chi-square test performed in this study showed there is no significant association between number of polyps with gastritis. Ljubicic et al in their study on hyperplastic polyp, FGP and adenoma stated that hyperplastic polyp was the most frequent polyp and was associated with active chronic gastritis and *H. pylori* infection, adenoma is associated with chronic atrophy gastritis and intestinal metaplasia, while FGP was reported to be very rare.<sup>20</sup> The correlation between FGP and *H. pylori* infection until now is still debatable.<sup>9</sup> Nan-Nan Fan et al reported that there were *H. pylori* infection in 82 cases from 2047 FGP cases (4%).<sup>16</sup>

Dysplasia is usually found in 40% of FAP patients and is found only 1% in sporadic FGP patients. Follow-up is performed if the presence of dysplasia is found to identify the possibility of a FAP. The incidence of stomach cancer increases in patients with FAP and FGP. Sporadic FGP may regress spontaneously and is a benign lesion which is not at risk from developing into malignancy.<sup>17,21,22</sup>

## CONCLUSION

Information from clinicians regarding history of family illness, number of polyps, history of previous illness, and medications which were administered to the patient is important to be documented for the purpose of identification of the risk factors of FGP and its differentiation as syndromic or sporadic FGP. In this

study, after Chi-square test has been performed, we found no significant association between the number of polyps with gastritis. Further study may be conducted using immunohistochemistry staining of gastrin to identify the pattern of gastrin-producing cells in the stomach.

## ACKNOWLEDGEMENT

I would like to say thank you to dr. Ening Krisnuhoni, MS, Sp.PA(K) for her time and supervision during this retrospective study. I also extend my gratitude to the medical record division, histopathology laboratory, and also to all Anatomical Pathology Resident fellows for their support and suggestions. Hopefully, this retrospective study will be beneficial for us to develop the knowledge, particularly in the field of anatomical pathology.

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