Level of Gastrin Serum and Ulcer Size on Gastric Ulcer Correlated to *Helicobacter pylori* Infection

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ABSTRACT

***Background**: Previously has been defined that peptic ulcer has strongly correlated to Helicobacter pylori (H. pylori) infection. But it hasn't determined about correlation of gastrin serum level to the ulcer severity on H. pylori infection. The aims of this study were to find the percentage of H. pylori infection on peptic ulcer cases and its correlation to the gastrin serum level.*

***Method**: This is analytic cross sectional study in 50 patients with gastric ulcer who came to Adam Malik hospital from February to October 2007. The correlation between gastrin serum level and the size of ulcer with positive and negative Urea breath test (UBT) group was analyzed by unpaired student t-test. The correlation between gastrin serum level and ulcer size were investigated with Pearson correlation test and linier regression.*

***Result**: Fifty eligible patients, 33 (66%) had positive UBT and 17 (34%) were negative. There were statistically significant difference on gastrin serum level in positive UBT and negative respectively (p = 0.017). There were also significant difference between mean of ulcer size in positive UBT and negative respectively (p = 0.025). There were correlation between gastrin serum level and ulcer size (r = 0.315; p = 0.026). It can predict the increasing ulcer size in 0.012 mm every 1 pg/mL of gastrin serum elevated.*

***Conclusion**: Patients with positive UBT has greater ulcer size and higher gastrin level as compared to the negative group. There were positive correlation between gastrin serum level to the size of ulcer in peptic ulcer patients and increase of ulcer size followed with elevated of gastrin serum level.*

***Keywords:** Helicobacter pylori infection, gastrin serum level, ulcer size*

INTRODUCTION

Peptic ulcer induces many problems in million individual in United States with great impact of the cost and suffering. One year frequency of peptic ulcer in US was 1.8% or 4.5 million people and there were various incidents in many countries in the world. A major causative factor (60% of gastric and up to 90% of duodenal) ulcer is chronic inflammation due to *Helicobacter pylori* (*H. pylori*) that colonizes in antral mucosa. Gastrin stimulates the production of gastric acid by parietal cells, and in *H. pylori* colonization responses that increase gastrin, the increase in acid can contribute to the erosion of the mucosa and therefore ulcer formation.

The other aggressive factors that worsen the condition were nonsteroidal anti-inflammatory drugs (NSAIDs) user, smoking, steroid drugs, alcohol, bile acid reflux and stress could increase the risk of ulcer as well. However, on the other hand a few protective factors can improve this condition such as gastric mucous, liquid secretion, bicarbonate, mucosal vascular flow, prostaglandin and mucosal regeneration. If imbalance condition was happened between each factors, this condition will be change by mucosal break or ulcer.[1,2,3] The prevalence of peptic ulcer is almost similar in man and woman group likely each 11-14% and 8-11%. Where as disturbance of immune system such as burning, central nerve

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trauma and surgery have the main role in stress ulcer formation.[3,4,5,6]

H. pylori which accumulated in the antrum consequently caused antrum predominant gastritis which could destroy D cell. D cell produced somatostatin that play a role in the inhibition of gastrin hormone product by G cell. As the result of destroyed D cell, somatostatin production decreased and the production of gastrin will increased. Elevated of gastrin hormone stimulates the parietal cell to produce more gastric acid. The increased secretion of gastric acid will go into the duodenum which induce duodenitis and duodenal ulcer.[7] There is only 20-25% of endoscopic abnormality for patients with epigastric pain, nausea, vomiting, anorexia in endoscopic investigation. Diagnosis of ulcer can be confirmed by double contrast radiography procedure, however endoscopy remain more sensitive mainly to detect the small ulcer or less than 0.5 cm, taking the specimen as sample biopsy, to find out malignancy or *H. pylori* present through campylobacter like organism (CLO) test as well.[8,9] The aims of this study were to find the percentage of *H. pylori* infection on peptic ulcer cases and its correlation to the gastrin serum level.

METHOD

This study enrolled 50 gastric ulcer patients by endoscopic examination observed the size, amount and location of ulcer to record. Basic characteristics of the patients such as complete blood count, AST/ALT, blood glucose, gastrin serum level and urea breath test (UBT) at the same time were examined. All of this laboratory examinations and UBT were conducted in Prodia laboratory. The UBT has been proved to be a very accurate diagnostic method and it is even used as the gold standard in some studies, with accuracy (sensitivity and specificity) above 95%. The standard test uses 75 gram of ^{13}C urea and citric acid as the test meal, with a sample collection before and 30 minutes after ^{13}C urea ingestion.[10] The gastrin serum level examination was checked in fasting patients and was done as soon as possible at the end of the endoscopic procedure. The patients should be free from proton pump inhibitor (PPI), antibiotic or H_2 blocker administered at least two weeks before the study.

Statistic analysis using unpaired t-test was applied to compare between the ulcer size, gastrin serum level and the positivity of urea breath test (UBT) result. Pearson correlation test and linier regression were applied to determine the correlation between gastrin serum level and the ulcer size in each patient regardless of the UBT test.

RESULTS

There were 50 patients diagnosed with gastric ulcer which consisted of 31 male and 19 female with mean age 20-70 years old. The main complain were various such as epigastric pain, nausea, vomiting, anorexia and bloated. There were 50 gastric ulcer patients from 446 patients who underwent endoscopic investigation. Antrum and prepyloric area were the most common location of ulcer, but there is no ulcer found in the corpus and fundus area. The size and amount of the ulcer were various, in case of more than one ulcer diameter were calculated by amount of each diameter.

There is no abnormality in complete blood count, liver function test, blood glucose and platelet count detected. The UBT result showed that 33 (66%) cases were positive and 17 (34%) cases were negative.

Table 1. The mean differences between gastrin hormone on UBT positive and negative

UBT	n	Average rate of gastrin		p
		X	SD	
Positive	33	100.4	± 97.27	0.017
Negative	17	54.91	± 7.23	

Table 2. The average differences size of ulcer on UBT positive and negative

UBT	n	Average size of ulcer		p
		X	SD	
Positive	33	6.97	± 3.67	0.025

Table 1 showed the significant difference of the gastrin serum level on both group. On table 2 showed the significant differences by statistics in size of ulcer and UBT positivity.

Pearson correlation test result positive correlation ($p = 0.02$) between the rate of serum gastrin level with the size of ulcer although its correlation is weak ($r = 0.315$) (figure 1). This correlation was examined with linear regression test in order to see the positive

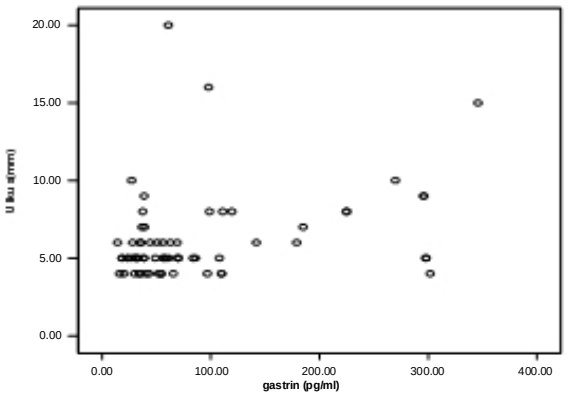

Figure 1. Spreading diagram of the correlation between gastrin rate and ulcer size

correlation between ulcer size and serum gastrin level. With the equality of linear regression y = a + bx, it is found that result of ulcer size is equal with y = 5.346 + 0.012 serum gastrin level (pg/mL). It means that every 1 pg/mL serum gastrin level rising will be followed 0.012 mm ulcer size enlargement.

DISCUSSION

Previously, we considered that the acid factor is a very important factor in the pathogenesis of peptic ulcer. The parietal cell is producing hydrochloric acid (HCl) in gaster and the chief cell is producing pepsinogen. HCl and pepsins as an aggressive factor, may irritated and cause defect on the mucosal barrier. Damage of the mucosal and other defensive factors such as mucus, bicarbonate, mucosal blood flow and prostaglandin quickly occurs. Warren and Marshall found a new pathogen microbe called *Helicobacter pylori* in 1983. Since then the experts made a new postulated term "no *Helicobacter pylori* no ulcer".[1,3]

H. pylori produces urease which breaks the urea into ammonia as toxic nature on mucosal cells. Protease and phospholipids which also produced by this organism subsequently reduce the mucus secretion, make derangement of the lipid layer, reduce the mucosal immunity and consequently cause the necrosis and then cause the ulcer formation. Gastric gland (known as oxintic gland) make up 70-80% of the total gastric gland, are responsible for secreting mucus, pepsinogen, HCl and intrinsic factor. Pyloric gland at distal gastric area which secret mucus, histamin and gastrin make up only 15% of the total gland. Pyloric gland consisted of entero chromaffin like cells (ECL), G Cell and D Cell respectively produce histamin, gastrin and somatostatin. The role of somatostatin in reducing parietal cell secretion via SS2 receptor was contrasts by gastrin and histamin wich are stimulates HCl secretion by parietal cell. In case of hypoacidity such as atrophic gastritis, gastric carcinoma or gastric outlet obstruction (GOO) or gastric hypersecretion due to glandular hyperplasia such as G cell hyperplasia, gastrinoma and Zollinger Ellison Syndrome the level of gastrin was absolutely prominent.[7,9,11,12]

H. pylori infection influences the D Cell in reducing the G cell gastrin hormone production, and then increases the gastrin serum level. The normal value of gastrin serum level without any damage or disturbance of gastro-intestinal tract is 0–200 pg/mL.[11] On the other hand in duodenal ulcer many studies found a lower, normal, or higher rate of gastrin hormone level, so that pathogenesis or the role of gastrin in this disorder remain unclear.[8,9,11] On this study we found an increasing rate of gastrin hormone level and size of ulcer in UBT positive group as compared to negative group with significantly differences by statistics.

The accumulation of food in the lumen of gaster stimulates G cell in producing gastrin hormone and subsequently this result stimulates the acid secretion of parietal cell. An over production of gastrin hormone could accelerate the activity of parietal cell in producing HCl and causing mucosal break or ulcer. On the other hand the *H. pylori* infection can cause alkalization by producing urease which stimulates the gastrin hormone secretion as a respond to the alkali nature in gastric lumen.[11,12] Gastric parietal cell will be activated by serum gastrin hormone level to produce hydrogen ion in order to maintain acidity of gastric acid. In addition, the gastrin hormone plays a role as a tropic factor on parietal cell hyperplasia. It is well-known that hyperacidity of gastric fluid is a risk factor for gastric and duodenal ulcer.[8,11]

The most common location of gastric ulcer in this study was at the antrum and prepyloric area which 66% of those ulcers due to *H. pylori* infection. The size of ulcer among *H. pylori* infection or UBT positive patients were greater than negative group (p = 0.025) and serum gastrin level in *H. pylori* infection or UBT positive patients were higher than negative group (p = 0.017). According to the statistic analysis, it was shown that the gastrin hormone elevation was followed by a greater ulcer size regardless of *H. pylori* infection (r = 0.315). It seems that the stimulation of gastrin hormone subsequently induce greater or enlargement of ulcer size. It has been reported that a close relationship between recurrent peptic ulcer and high gastrin hormone level.[7,9,11]

In this study there we found that there was a weak relationship between the serum gastrin level and size ulcer. In this fifty cases the gastrin serum level were within normal limit (0-200 pg/mL). The limitations of this study was firstly, that the cases and ulcer numbers were small and *H. pylori* infection was more dominant in the duodenal ulcer than in the gastric ulcer. Secondly, we considered that *H. pylori* was only positive from the UBT examination, these criteria could decrease the sensitivity of the *H. pylori* detection.

CONCLUSION

We found an increasing *H. pylori* infection in this study. *H. pylori* infection induces the gastrin hormone hypersecretion and ulcer size enlargement. Hypergastrinemia increased the severity of ulcer size regardless of *H. pylori* infection.

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