

Original Research Article

Serum gastrin level estimation, is it a prognostic indicator in operated carcinoma stomach patients?

Ghosh Soumyodhriti¹, Kumar Vikas², Das Kashinath³, Majumdar Banashree⁴

¹Senior resident, Pediatric Surgery, SMS Medical College, Jaipur

²Senior Resident, Urology, KGMU Lucknow

³Professor, General Surgery, Medical College, Kolkata

⁴Senior Resident, Dermatology, SMS Medical College, Jaipur

***Corresponding author**

Ghosh Soumyodhriti

Email: drsgghosh.surg85@gmail.com

Abstract: In spite of substantial geographic variation, gastric carcinoma still continues to be one of the most common tumours worldwide. Variants of tumour markers have been and are being established for diagnosis of gastric carcinoma. This study attempts to serve as a supplement to those by understanding the clinicopathology and trying to correlate serum gastrin and staging of gastric cancer. A correlation if established might serve to determine feasibility of using serum gastrin in future treatment approaches. The Methods were For the purpose of this study, 30 patients were selected from among those admitted or attending the out patient department of General Surgery, Medical College Hospital, Kolkata. The preoperative serum gastrin level was obtained and correlated with the post operative biopsied staging of the specimen obtained post resection. The Results in The serum gastrin was found to be elevated in all thirty patients. However the correlation established was such that an elevated gastrin was not necessarily associated with an advanced staged disease. In Conclusion the Serum gastrin serves as a marker for diagnosis of gastric cancer. However the level of gastrin does not correlate with the advancement of stages. Higher gastrin level does not correlate to an advanced stage and vice versa.

Keywords: Gastrin, carcinoma stomach, post operative staging

INTRODUCTION

Gastric cancer has long been attempted to be correlated to various etiological factors. There are studies linking different racial, genetic and environmental agents to gastric cancer [1, 2]. In spite of substantial geographic variation, gastric carcinoma still continues to be one of the most common tumours worldwide [1, 3, 4]. Variants of tumour markers have been and are being established for diagnosis of gastric carcinoma [5]. The serum gastrin has been previously studied in association with different conditions including gastrinoma [5, 6, 7]. There is now accumulating evidence that altered local and plasma concentrations of gastrin may play a role during the development of various gastric tumors [8, 9, 10]. In the absence of H pylori infection, marked hypergastrinemia frequently results in the development of gastric enterochromaffin cell-like neuroendocrine tumors and surgery to remove the cause of hypergastrinemia may lead to tumor resolution in this condition. Gastrin and its receptor were shown to be expressed in specimens of

atrophic gastritis, intestinal metaplasia, epithelial dysplasia and the intestinal type of gastric carcinomas [9, 11]. Gastrin seems to be an important growth factor in gastric carcinogenesis.

MATERIALS AND METHODS

Place of work- Department of General Surgery, Medical College Hospital, Kolkata.

For the purpose of this study, 30 patients were selected from among those admitted or attending the out patient department of General Surgery, Medical College Hospital, and Kolkata.

Exclusion criteria

- Patients received chemoradiation.
- Patients with coexistent morbidities.
- Patients unwilling to undergo the necessary investigations.

Period of work- 36 months.

The serum gastrin level was obtained in all patients following a twelve hours fasting period. The patients underwent surgical exploration and the specimen extracted was biopsied. A post operative staging was established based on histopathological, radiological and clinical investigations. Prospective observational study design was used for correlation using standard statistical methods. An attempt was made to correlate the values of serum gastrin with the stage of gastric cancer.

RESULTS

In the present study, Serum gastrin measured in all patients were ubiquitously found to be elevated. We also attempted to establish if the correlation was statistically significant positive correlation with respect to the stages. However, the values clearly establish the

result is not statistically significant. Hence serum gastrin as a marker can be used in patients suffering from carcinoma stomach. The levels are elevated in all patients. However, the rise in serum gastrin cannot be correlated with particular stages of carcinoma stomach. This means that a higher stage of cancer will not necessarily have a higher serum gastrin value than a lower stage malignancy and vice versa. Therefore, a patient presenting with elevated gastrin values due to any cause must be excluded from gastric malignancy. However, the present study is non randomized with limited samples. A randomized sampled study in future will further help to establish the above results conclusively. A number of benign conditions as discussed above also has an elevation in serum gastrin levels. Conditions like gastrinoma can be excluded by severe rise in gastrin. It is therefore clear that a thorough clinical history with other investigations must be applied for a proper differential diagnosis.

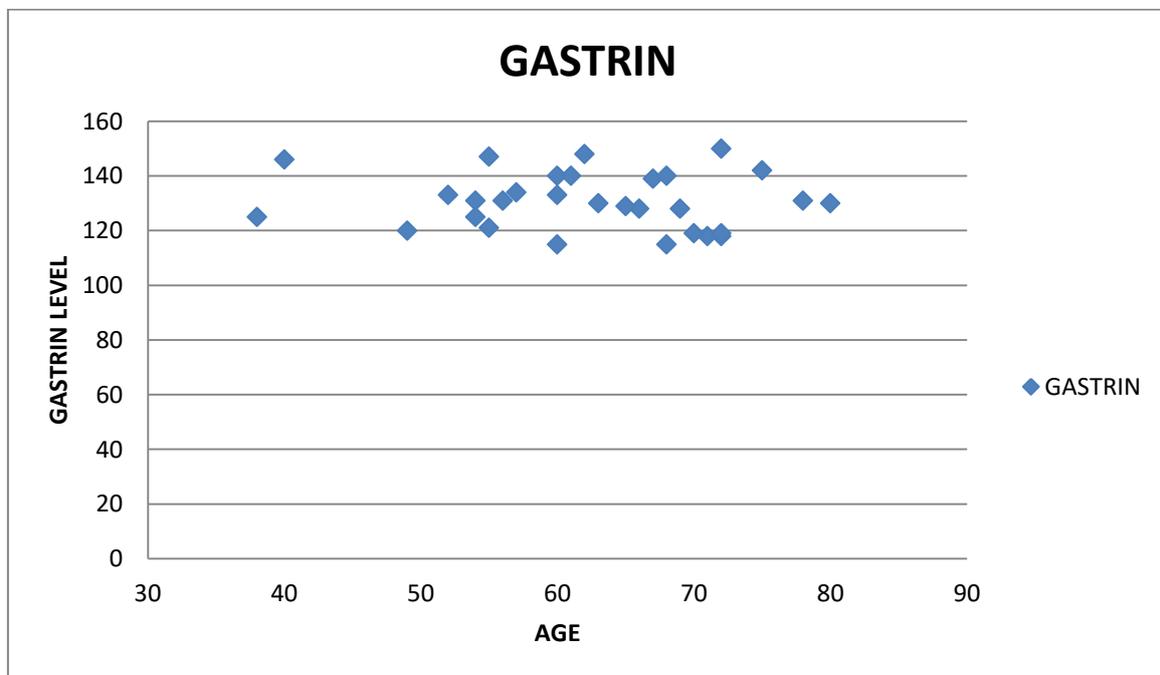


Fig-1: Co-relation between serum gastrin level and age

DISCUSSION

The presence of a hormone that stimulated gastric acid secretion in the pyloric mucosa was first demonstrated in 1906 [1, 3, 9, 10]. Gastrin was subsequently shown to be secreted from neuroendocrine G cells which are principally located in the antrum of the stomach. The gastrin gene is located on the long arm of chromosome 17 and encodes a 101 amino acid polypeptide, progastrin [12, 13, 14]. This gene product is subjected to a series of post translational modifications which result in the synthesis of a number of biologically active peptides, including gastrin [4, 5, 15]. In addition to regulating acid secretion, the gastric antral hormone gastrin regulates several important

cellular processes in the gastric epithelium including proliferation, apoptosis, migration, invasion, tissue remodelling and angiogenesis [3, 4, 5, 6]. Elevated serum concentrations of this hormone are caused by many conditions, particularly hypochlorhydria (as a result of autoimmune or Helicobacter pylori (H pylori)-induced chronic atrophic gastritis or acid suppressing drugs) and gastrin producing tumors (gastrinomas). There is now accumulating evidence that altered local and plasma concentrations of gastrin may play a role during the development of various gastric tumors. In the absence of H pylori infection, marked hypergastrinemia frequently results in the development of gastric enterochromaffin cell-like neuroendocrine tumors and

surgery to remove the cause of hypergastrinemia may lead to tumor resolution in this condition. Gastrin and its receptor were shown to be expressed in specimens of atrophic gastritis, intestinal metaplasia, epithelial dysplasia and the intestinal type of gastric carcinomas [16, 17]. Gastrin seems to be an important growth factor in gastric carcinogenesis. The development of gastric and other malignancies of the gastrointestinal (GI) tract requires a multistep process involving genetic mutations combined with environmental cofactors, whereby normal epithelial cells undergo metaplastic and dysplastic transformation, followed by proliferation and eventual histological progression to neoplasia. The polypeptide hormone gastrin is still considered the most potent substance known to stimulate gastric acid secretion [3, 5, 11, 12, 18]. However, another biological property attributed to gastrin is its trophic effect on GI mucosa. There is now accumulating evidence that altered local and plasma concentrations of gastrin may play a role during the development of various gastric tumors [19, 20]. In the absence of *H. pylori* infection, marked hypergastrinemia frequently results in the development of gastric enterochromaffin cell-like neuroendocrine tumors and surgery to remove the cause of hypergastrinemia may lead to tumor resolution in this condition. In animal models such as transgenic INS-GAS mice, hypergastrinemia has also been shown to act as a cofactor with *Helicobacter* infection during gastric adenocarcinoma development [14]. Similar studies carried out in human models showed gastrin and its receptor to be expressed in specimens of atrophic gastritis, intestinal metaplasia, epithelial dysplasia and the intestinal type of gastric carcinomas [14, 21, 22]. Gastrin seems to be an important growth factor in gastric carcinogenesis. Studies have also shown that all gastric carcinoma cell lines express gastrin-gastrin receptors (GR). Thirty-one of 48 (65%) gastric tumors expressed GR, and its expression was prominent in elevated-type tumor with an intestinal histologic feature.

The present study establishes serum gastrin as a marker for carcinoma stomach. An elevated gastrin mandates exclusion of gastric cancer. However, elevations in serum gastrin may not indicate advancement in the staging of the patients. A larger randomised study, will better establish the positive correlation between serum gastrin and staging of gastric cancer.

REFERENCES

1. Konturek PC, Konturek SJ, Bielanski W, Karczewska E, Pierzchalski P, Duda A, *et al.*; Role of gastrin in gastric cancerogenesis in *Helicobacter pylori* infected humans. *Journal of physiology and pharmacology: an official journal of the Polish Physiological Society.* 1999; 50(5):857-73.
2. Westerveld BD, Pals G, Lamers CB, Defize J, Pronk JC, Frants RR, *et al.*; Clinical significance of pepsinogen A isozymogens, serum pepsinogen A and C levels, and serum gastrin levels. *Cancer.* 1987; 59(5):952-8.
3. Varis K, Kekki M, Härkönen M, Sipponen P, Samloff IM; Serum pepsinogen I and serum gastrin in the screening of atrophic pangastritis with high risk of gastric cancer. *Scandinavian Journal of Gastroenterology.* 1991; 26(sup186):117-23.
4. Leung WK, Wu MS, Kakugawa Y, Kim JJ, Yeoh KG, Goh KL, *et al.*; Screening for gastric cancer in Asia: current evidence and practice. *The lancet oncology.* 2008; 9(3):279-87.
5. Konturek SJ, Starzynska T, Konturek PC, Karczewska E, Marlicz K, Lawniczak M, *et al.*; *Helicobacter pylori* and CagA status, serum gastrin, interleukin-8 and gastric acid secretion in gastric cancer. *Scandinavian journal of gastroenterology.* 2002; 37(8):891-8.
6. Takashima M, Furuta T, Hanai H, Sugimura H, Kaneko E; Effects of *Helicobacter pylori* infection on gastric acid secretion and serum gastrin levels in Mongolian gerbils. *Gut.* 2001; 48(6):765-73.
7. Katelaris PH, Seow F, Lin BP, Napoli J, Ngu MC, Jones DB; Effect of age, *Helicobacter pylori* infection, and gastritis with atrophy on serum gastrin and gastric acid secretion in healthy men. *Gut.* 1993; 34(8):1032-7.
8. Kuipers EJ, Pena AS, Festen HP, Meuwissen SG, Uytendaele AM, Roosendaal R *et al.*; Long-term sequelae of *Helicobacter pylori* gastritis. *The Lancet.* 1995; 345(8964):1525-8.
9. Miyaji M, Ogoshi K, Tajima T, Mitomi T; Association between serum gastrin levels, gastric acid secretion and age in early gastric cancer. *Tumor biology.* 1997; 18(5):311-20.
10. Haruma K, Yoshihara M, Sumii K, Tari A, Watanabe C, Kodoi A, *et al.*; Gastric acid secretion, serum pepsinogen I, and serum gastrin in Japanese with gastric hyperplastic polyps or polypoid-type early gastric carcinoma. *Scandinavian journal of gastroenterology.* 1993; 28(7):633-7.
11. Konturek PC, Konturek SJ, Sulekova Z, Meixner H, Bielanski W, Starzynska T, *et al.*; Expression of hepatocyte growth factor, transforming growth factor alpha, apoptosis related proteins Bax and Bcl-2, and gastrin in human gastric cancer. *Alimentary pharmacology & therapeutics.* 2001; 15(7):989-99.
12. Haj-sheykholeslami A, Rakhshani N, Amirzargar A, Rafiee R, Shahidi SM, Nikbin B, *et al.*; Serum pepsinogen I, pepsinogen II, and gastrin 17 in relatives of gastric cancer patients: comparative study with type and severity of gastritis. *Clinical Gastroenterology and Hepatology.* 2008; 6(2):174-9.

13. Webb PM, Hengels KJ, Møller H, Newell DG, Palli D, Elder JB, *et al.*; David Forman For The Eurogast Study Group. The epidemiology of low serum pepsinogen A levels and an international association with gastric cancer rates. *Gastroenterology*. 1994; 107(5):1335-44.
14. Song DH, Rana B, Wolfe JR, Crimmins G, Choi C, Albanese C, Wang TC, Pestell RG, Wolfe MM. Gastrin-induced gastric adenocarcinoma growth is mediated through cyclin D1. *American Journal of Physiology-Gastrointestinal and Liver Physiology*. 2003; 285(1):G217-22.
15. Thorburn CM, Friedman GD, Dickinson CJ, Vogelman JH, Orentreich N, Parsonnet J; Gastrin and colorectal cancer: a prospective study. *Gastroenterology*. 1998; 115(2):275-80.
16. Hamashima C, Shibuya D, Yamazaki H, Inoue K, Fukao A, Saito H, *et al.*; The Japanese guidelines for gastric cancer screening. *Japanese Journal of Clinical Oncology*. 2008; 38(4):259-67.
17. Sipponen P, Marshall BJ; Gastritis and gastric cancer: Western countries. *Gastroenterology Clinics of North America*. 2000; 29(3):579-92.
18. Raijman I, Strother SV, Donegan WL; Gastric cancer after gastric bypass for obesity: case report. *Journal of clinical gastroenterology*. 1991; 13(2):191-7.
19. Walsh JH, Grossman MI; Gastrin. *New England Journal of Medicine*. 1975; 292(26):1377-84.
20. Watson S, Durrant L, Morris D; Gastrin: growth enhancing effects on human gastric and colonic tumour cells. *British journal of cancer*. 1989; 59(4):554.
21. Hansen S, Vollset SE, Derakhshan MH, Fyfe V, Melby KK, Aase S, *et al.*; Two distinct aetiologies of cardia cancer; evidence from premorbid serological markers of gastric atrophy and *Helicobacter pylori* status. *Gut*. 2007; 56(7):918-25.
22. Sipponen P, Valle J, Varis K, Kekki M, Ihamäki T, Siurala M; Fasting levels of serum gastrin in different functional and morphologic states of the antrofundal mucosa: an analysis of 860 subjects. *Scandinavian journal of gastroenterology*. 1990; 25(5):513-9.