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Analysing the level of Pepsinogen-I and Pepsinogen- II in patients with Gastric Dysplasia and Malignancy

Dr. Anup Bahadur Jain[1], Dr. Shailendra Singh Thakur[2], Dr. Aksharaditya Shukla[2], Dr. Suneel Kumar Jaiswal[2,*], Dr. Rakesh Mehar[2] and Dr. Chhaya Dhangar[2]

[1] District Hospital Mandsaur, Indore.
[2] Department of Pathology, MGMMC Indore.
* Correspondence: suneel9013@gmail.com

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Abstract: Gastric cancer, ranking as the fourth most prevalent cancer and the second leading cause of cancer-related deaths worldwide, poses a significant public health challenge with approximately 800,000 new cases and 650,000 deaths annually, with 60% of cases occurring in developing countries. Regions with the highest incidence rates, exceeding 40/100,000 in males, are Eastern Asia, the Andean regions of South America, and Eastern Europe. Incidence rates are notably higher among socio-economically disadvantaged groups and in developing countries. The aim of this study was to analyze the levels and ratios of pepsinogen-I and pepsinogen-II in gastric dysplasia and malignancy. Conducted at the Pathology Department of MGM Medical College and Maharaja Yashwantrao Hospital in Indore, Madhya Pradesh, the prospective study spanned one year from May 2020 to April 2021 and included a total of 30 cases diagnosed with gastric dysplasia and malignancy through endoscopy and histopathology. The results revealed a significant decrease in serum mean PG-I level and PG I/II ratio in patients with gastric cancer (P=0.00). Moreover, both the mean serum PG-I level and PG I/II ratio were lower in patients with gastric cancer compared to those with dysplastic lesions.

Keywords: Gastric cancer; Pepsinogen; Dysplasia; Malignancy; Serum levels.

1. Introduction

Gastric cancer is a significant global health concern, ranking as the fourth most common cancer and the second leading cause of cancer-related deaths worldwide. Each year, approximately 800,000 new cases of gastric cancer and 650,000 related deaths are reported, with 60% of them occurring in developing countries [1,2]. High incidence rates of gastric cancer, exceeding 40 cases per 100,000 males, are observed in Eastern Asia, the Andean regions of South America, and Eastern Europe. Conversely, lower incidence rates are found among blacks, lower socio-economic groups, and in developing nations [3]. In high-risk areas, intestinal type adenocarcinoma is more prevalent, whereas low-risk areas have a relatively higher incidence of diffuse type gastric cancer [4]. However, incidence rates have shown a decline over the past few decades in most parts of the world [5]. Notably, there has been an increase in the occurrence of diffuse type gastric cancer while sporadic intestinal types have decreased [6,7]. The male-to-female ratio of gastric cancer is approximately 2:1, indicating a higher incidence among males [8]. Certain dietary factors have been associated with an increased risk of gastric cancer, such as the consumption of broiled and charbroiled animal meats, salt-preserved foods, and smoked foods. Conversely, diets rich in fiber, fresh vegetables, and fruits have shown an inverse association with gastric cancer risk [9,10].

Helicobacter pylori (H. pylori), a Gram-negative bacterium, has been classified as a class I carcinogen for gastric cancer development by the World Health Organization since 1994 [11]. The risk of developing gastric cancer is particularly strong when the infecting strain of H. pylori is CagA-positive. These findings highlight the importance of understanding the role of H. pylori infection in gastric cancer pathogenesis and the potential for targeted interventions to reduce the burden of this disease.

In conclusion, gastric cancer poses a significant global health burden, with high incidence rates and mortality rates, especially in developing countries. The distribution of gastric cancer varies across different

regions, with distinct patterns observed between high-risk and low-risk areas. Various factors, including dietary habits, gender, and the presence of H. pylori infection, contribute to the development and progression of gastric cancer. Improved understanding of these factors is crucial for the implementation of effective prevention and control strategies to reduce the impact of gastric cancer on individuals and populations worldwide.

1.1. Precancerious Lesions

Gastric atrophy is recognized as the initial significant step in the development of intestinal type gastric carcinoma [12]. Chronic atrophic gastritis often coexists with intestinal metaplasia, further indicating the progression towards gastric carcinoma [13,14]. The prevalence of intestinal metaplasia is significantly higher in individuals infected with H. pylori (43%) compared to H. pylori-negative subjects (6.2%) [15]. Proximal gastric cancer has been associated with a worse prognosis compared to cancers located in the mid or distal portion of the stomach [16]. Furthermore, gastric cancer is less commonly observed in individuals with blood group O, while blood group A is frequently associated with the disease [17].

The most crucial factor determining survival in gastric cancer is the stage at diagnosis. Hence, efforts have been made to develop effective screening methods that can detect gastric cancer at an early stage, thereby reducing mortality rates [18]. The sequential events leading to gastric cancer development involve a progression from normal mucosa to chronic active gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia, and ultimately carcinoma in situ [18].

The gastric mucosa produces two distinct types of pepsinogen: Pepsinogen I (PGA), synthesized by chief and mucous neck cells in the fundic glands, and Pepsinogen II (PGC), secreted by these cells as well as by the cells in the pyloric glands and Brunner's glands [19]. Pepsinogen II serves as a valuable marker for the diagnosis of gastritis, as it differentiates between individuals with gastritis and those with normal mucosa. The level of PGII remains constant in H. pylori infection affecting the fundic gland mucosa. Serum pepsinogen (SPG) serves as a marker for assessing the functional and morphological status of the gastric mucosa, including atrophic changes, inflammation, H. pylori infection, atrophic gastritis, and intestinal metaplasia. Normal values for Pepsinogen I range from 30-160 μg/L, while Pepsinogen II ranges from 3-15 μg/L. The normal ratio of serum Pepsinogen I to Pepsinogen II is 3-20 (Ratio). The present study aims to define appropriate cutoff points for serum PG I and PG I/II ratio to utilize this test as a screening tool for the diagnosis of gastric carcinoma.

In summary, understanding the progression of gastric cancer from atrophy to intestinal metaplasia and beyond is crucial for early detection and intervention. Additionally, the characterization of pepsinogens as diagnostic markers offers promise in the screening and diagnosis of gastric carcinoma. These advancements contribute to the potential reduction in mortality rates associated with this devastating disease.

2. Materials and Methods

This prospective study was conducted in the Pathology Department of MGM Medical College, Maharaja Yashwantrao Hospital in Indore (M.P.) over a one-year duration from May 2020 to April 2021. A total of 30 cases diagnosed with gastric dysplasia and malignancy based on endoscopy and histopathology were included. Serum pepsinogen (PG) levels were measured using the PG I and II DRG kit, manufactured by DRG Diagnostics and commercially available.

3. Results

Among the 30 cases included in the study, 3 cases were diagnosed as dysplasia or benign (10

Of the 30 cases, 10 were classified as poorly differentiated carcinoma, 17 as moderately differentiated carcinoma, and 3 as benign or showing dysplasia.

Our study revealed a decrease in serum PG I levels and PG I/II ratio in patients with gastric dysplasia and malignancy.

The distribution of lesions is presented in Table 1, and the number of cases categorized by sex is shown in Table 2. The histological groups in the study patients are illustrated in Figure 1. Table 3 displays the levels of pepsinogen I, II, and the PGI/PGII ratio in gastric dysplasia and cancer patients. Additionally, Table 4 presents the mean level of pepsinogen I and the PGI/PGII ratio in gastric carcinoma and dysplastic lesions among the

Table 1. Distribution of lesions

Nature of lesion	Number of cases	Percentage
Dysplastic lesion	3	10 %
Malignant	27	90%
Total	30	100%

Table 2. Sex wise number Of cases

Sex	No Of Cases	%
Male	18	60 %
Female	12	40%
Total	30	100%

study cases. Our results demonstrated that the mean value of serum PG I level and PG I/II ratio decreased significantly in patients with gastric malignancy compared to those with dysplastic or benign lesions.

Moreover, a correlation between the number of cases, mean value of PGI/PGII, standard deviation, and p-value is shown in Table 5. The serum mean PG II/PGII ratio was found to be lower in patients with poorly differentiated adenocarcinoma compared to moderately differentiated adenocarcinoma and lower than those with dysplastic lesions, showing statistical significance (p=0.00).

The study also includes visual representations of gastric signet ring cell carcinoma (Figure 2), moderately differentiated adenocarcinoma of the stomach (Figure 3), and poorly differentiated adenocarcinoma of the stomach (Figure 4).

4. Discussion

The mortality of gastric cancer continues to be within the leading standing of all cancers. The 5-year survival rate of gastric cancer is low, and identification and an improved management of risk factors appear to be the most effective means of prevention. Screening for early detection of gastric precancerous lesion is helpful in diagnosis and treatment of gastric cancer. In our study 30 patients with gastric cancer were studied in which the mean age is 52.0 years. similar results were obtained in the study done by Xiao-mei Zhang et all with mean age of > 50 years. [20].

Our results showed that serum mean PG I level and PG I/II ratio decreased in patients with gastric cancer, it is statistical significance is observed (P=0.00). However, mean serum PG I level and PG I/II ratio in patients with gastric cancer were lower than those with dysplastic lesion, Our studied agreement with the previous studied Wasan A. Bakir et.all , Xiao-mei Zhang et.all, Liang He et. all ,Abdol Rahim Masjedizadeh et.all [20,21].

5. Conclusion

The results showed that low PG I level and low PG I/II ratio were valuable serologic markers for predicting gastric cancer, especially low PGI/II ratio was an effective parameter for screening individuals

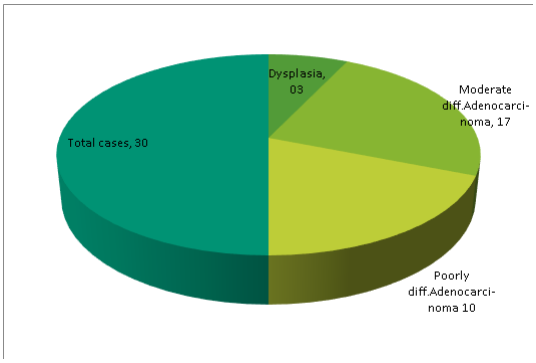

Figure 1. Histological group in study patients

Table 3. Levels of pepsinogen I, II and the PGI/PGII ratio in gastric dysplasia and cancer patients

Serial no.	Pepsinogen-I μG/L	Pepsinogen-II μG/L	PGI/PGII Ratio
1	46.5	18.8	2.4
2	45.6	17.2	2.6
3	45.8	17.8	2.5
4	48.6	17.8	2.7
5	42.8	16.4	2.6
6	47.6	19.6	2.4
7	48.6	19.8	2.4
8	49.5	18.7	2.6
9	58.4	20.4	2.8
10	54.5	18.7	2.9
11	46.8	18.4	2.5
12	52.4	18.7	2.8
13	71.5	20	3.5
14	49.6	19.9	2.4
15	50.1	16.8	2.9
16	52.8	18.4	2.8
17	50.2	18.6	2.6
18	58.8	20.4	2.8
19	54.4	19.8	2.7
20	51.5	21.4	2.4
21	72.6	22.4	3.2
22	48.5	19.8	2.4
23	55.8	18.8	2.9
24	72.8	21.5	3.3
25	50.6	20.5	2.4
26	63.3	22.4	2.8
27	44.1	18.4	2.3
28	55.5	20.5	2.7
29	42.4	19.5	2.1
30	48.7	17.5	2.7

Table 4. Mean level of pepsinogen-I and PGI/PGII ratio gastric carcinoma and dysplastic lesion in study cases

Nature of Lesion	No. of Cases	PGI μg/L	PGI/PGII Ratio
Dysplasia Or Benign	3	72.2	3.3
Gastric Carcinoma	27	50.5	2.5

Table 5. Correlation between number of cases, mean value PGI/PGII and Sd and P-value

PGI/PGII Ratio	Number of Cases	Mean Value PGI/PGII Ratio	Sd	P-value
Dysplastic Lesion	3	3.33	0.15	0
Moderately Differentiated Adenocarcinoma (Adenocarcinoma-II)	17	2.71	0.14	
Poorly Differentiated Adenocarcinoma (Adenocarcinoma-III)	10	2.39	0.12	
Total	30	2.67	0.3	

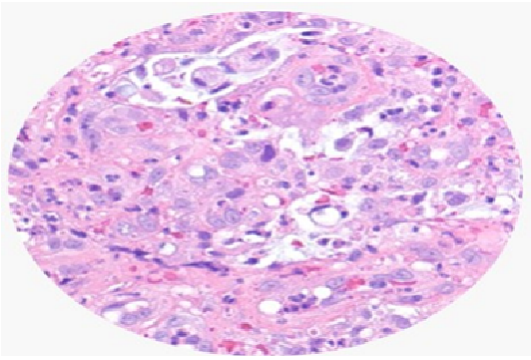

Figure 2. Gastric signet ring cell carcinoma

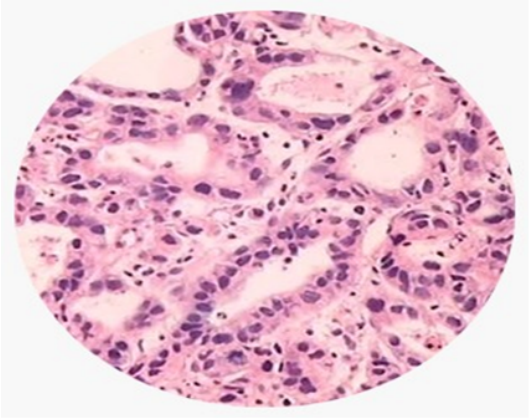

Figure 3. Moderately differentiated adenocarcinoma of stomach

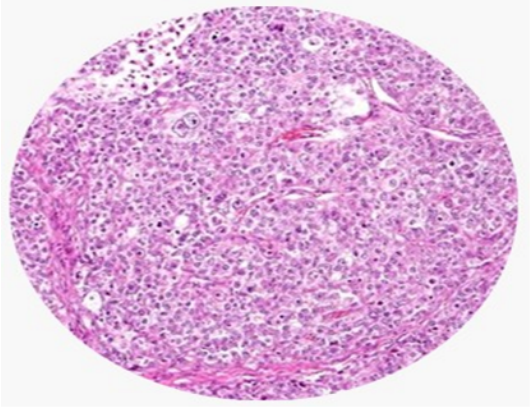

Figure 4. Poorly differentiated adenocarcinoma of stomach

at high risk of early gastric cancer. Combined use of serum PG I level and PG I/II ratio may help the predict and early diagnosis of gastric cancer

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