Research Paper

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Chronic Gastritis with Macrocytic Anaemia: a Clinico-Haematological Correlation.

Medical Science

KEYWORDS : Chronic gastritis; H. pylori; gastric atrophy; macrocytic anemia;

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ABSTRACT

The present study was carried out to determine that H.pylori is the most common cause of chronic gastritis with or without gastric mucosal atrophy leading to deficient absorption of vitamin B12 and macrocytic anemia. This study examined how serum vitamin B12 levels relate to chronic gastritis and to hematological findings in patients with chronic gastritis as well as to confirm that H. pylori eradication therapy increases serum B12 level, resolves symptoms of gastritis and improvement in the clinical features of vita B12 deficiency. In the present study we included total 120 cases, presented in outdoor patients department of Glocal Medical College and Hospital, Mirzapur, Dist. Saharanpur, over a period of 6 months i.e. from the month of July 2015 to month of December 2015, with clinical history suggestive of chronic gastritis from a period of last 4-5 years or more. Out of total 120 patients 72 (60%) were males and 48 (40%) were females. Maximum numbers of patients were present in 6th to 8th decade of life in both the gender. Out of total 120 patients 78 patients (65.00%) were found positive for H. pylori stool antigen test, which includes 52 (72.22%) male patients out of 72 male patients and 26 (54.17%) female patients out of 48 female patients. Total 78 patients were found to be positive for H. pylori, out of this 55 (70.51%) found with vitamin B12 deficiency. Out of total 120 patients with chronic gastritis 55 patients (45.83%) found with vitamin B12 deficiency as well as positive with H. pylori infection. 7 patients (5.83%) out of total 120 patients were found negative for HpSA and Vitamin B12 deficient. In haematological parameters we considered haemoglobin, Mean Carpuscular Volume (MCV) and peripheral blood film examination. As far as haemoglobin is concerned we divided patients into two broad categories as (i) 8-12 mg/dl and less than 8 mg/dl (ii) more than 12 mg/dl. Out of total 120 patients 55 (45.83%) are found to be positive with H. pylori and with vitamin B12 deficiency. Out of 55 patients 38 (69.09%) have moderate to severe anaemia with Hb values less than 8 mg/dl and between 8-12 mg/dl. 42 (76.36%) patients found to have MCV more than 100. On peripheral blood film examination 40 (72.73%) showed macrocytosis. We conclude that vitamin B12 deficiency is more pronounced in Helicobactor pylori infection leading to variable clinical manifestations.

INTRODUCTION

The megaloblastic anaemia observed in patients with chronic atrophic gastritis is usually due to malabsorption of vitamin B12. In some cases, the absence of intrinsic factor supports the diagnosis of pernicious anaemia but other factors, the importance of which varies from case to case, are also involved1. In chronic atrophic gastritis, atrophy of the stomach glands leads to intrinsic factor deficit, with consequent failure to absorb vitamin B12 and gastric achylia, which predisposes to Giardia infection which in itself leads to depletion of vitamin B12 2. Cobalamin (vitamin B12) deficiency is associated with Helicobacter pylori infection with or without gastric mucosal atrophy3. Helicobacter pylori infects the stomach of half of the human population worldwide and cause chronic active gastritis, which can lead to peptic ulcer disease, megaloblastic anaemia, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma4. Present study has been carried out on 120 cases with clinical history of gastritis since 3-5 years or more with a course of waxing and waning as well as history of chronic smoking and tobacco chewing since a long back. This study examined how serum vitamin B12 levels relate to chronic gastritis and to hematological findings in patients with chronic gastritis as well as to confirm that H. pylori eradication therapy increases serum B12 level, resolves symptoms of gastritis and improvement in the clinical features of vita B12 deficiency. Serum cobalamin level, hemoglobin level, and mean corpuscular volume were measured in the 120 patients before eradication therapy, and in 71 of the patients after treatment. The hematologic findings before and after eradication therapy and correlations between serum vitamin B12 level and hematologic findings were statistically analyzed.

MATERIAL AND METHODS

In the present study we included total 120 cases, presented in outdoor patients department of Glocal Medical College and Hospital, Mirzapur, Dist. Saharanpur, over a period of 6 months i.e. from the month of July 2015 to month of December 2015, with clinical history suggestive of chronic gastritis from a period of last 4-5 years or more. The detailed history of all the patients were taken and complete physical and relevant clinical examination were performed. They presented with clinical syndrome characterized by epigastric pain, fullness, heart burn, nausea, vomiting, flatulence, malaise, and, sometimes fever, anorexia, or significant weight loss, sometimes constipation and sometimes diarrhea. There were symptoms of anaemia as well as symptoms of involvement of nervous system as paraesthesiae, tingling- numbness in the limbs, and burning pain like sensations at multiple sites in the body, and some have deranged mental states ranging from irritability and forgetfulness to severe dementia and psychosis. Symptoms of glossitis as soreness of tongue, burning pain on swallowing, red buffy tongue were also found.The study was carried out as-

We took stool samples of all the patients and sent to laboratory for detection of Helicobacter pylori stool antigen by Enzyme immunoassay (EIA).

Blood samples of all the patients were collected for complete blood picture (CBC), and mean corpuscular volume (MCV).

Serum levels of Vitamin B12 of all the patients were determined using electrochemiluminescence. Vitamin B12 deficiency was considered when serum B12 level was less than 200 pg/ml.

Out of total 120 patients only 71 patients could be treated with H.pylori eradication therapy including antibiotics, H2 blockers, PPI for 2-3 weeks, and cyanocobalamin injections for 6-8 weeks.

Table: 1: Shows gender distribution of the patients.

S. No.	Gender	Number of Patients	% tage
1.	Males	72	60 %
2.	Females	48	40%
3.		Total= 120	

Incidence of chronic gastritis is more in males than in females in this study.

As far as age is concerned maximum numbers of patients were present in 6th to 8th decade of life in both the gender. Out of total 72 male patients 63 (87.50%), and in females out of 48 patients 36 (75.00%) were present in 6th to 8th decades of life. So out of total 120 patients 99 (85.50%) were in 6th to 8th decades of life.

As shown in Table No. 2 (below)

S. No.	Age Groups (years)	Total No. of Patients	No. of Male Patients	No. Of Female Patients
1.	31- 40	06	04	02
2.	41-50	15	05	10
3.	51-60	32	21	11
4.	61-70	40	23	17
5.	71-80	27	19	08
	Total	120 (100%)	72 (60%)	48 (40%)

Out of total 120 patients 78 patients (65.00 %) were found positive for H. pylori stool antigen test, which includes 52 (72.22 %) male patients out of 72 male patients and 26 (54.17%) female patients out of 48 female patients.

42 (35.00%) patients out of 120 were found negative for H.pylori stool antigen test this includes 20 (27.78%) male patients out of 72 male patients and 22 (45.83%) female patients out of total 48 female patients.

Table: 3: shows number of H. pylori positive and negative patients.

S. No.	Sex of patients	Total No. Of Patients	Number of HpSA Positive Patients	Number of HpSA negative Patients
1.	Male	72	52 (72.22%)	20 (27.78%)
2.	Female	48	26 (54.17%)	22 (45.83%)
	Total	120	78 (65.00%)	42 (35.00%)

Out of 52 male patients positive for HpSA , 37 patients (71.15%) were found with deficiency of Vitamin B12 (<200 Pg/ml) and 3 (15.00%) patients out of 20 patients negative for HpSA , were found with deficiency of vitamin B12. While in female out of 26 patients positive for HpSA, 18 (69.23%) patients found with vitamin B12 deficiency, out of 22 patients negative for HpSA, 4 patients (18.18%) found with vitamin B12 deficiency. Total 78 patients were found to be positive for H. pylori, out of this 55 (70.51%) found with vitamin B12 deficiency. Out of total 120 patients with chronic gastritis 55 patients (45.83%) found with vitamin B12 deficiency as well as positive with H. pylori infection. 7 patients (5.83%) out of total 120 patients were found negative for HpSA and Vitamin B12 deficient.

Table: 4: Status of Vitamin B12 in patients of chronic gastritis in both the category of patients i.e. in H.pylori positive as well as negative patients.

S. No.	Gender of patients	Total No. of patients	Total No. of H.pSA Positive Patients	No. of Patients with Vita. B12 deficiency (<200 Pg/ml) inH. pSA positive Patients	Total No. of H.pSA Negative Patients	No. of Patients with Vita. B12 deficiency (<200 Pg/ml) in H.pSA Negative Patients
1.	Male	72	52 (72.22%)	37 (71.15%)	20 (27.78%)	3 (15.00%)
2.	Female	48	26 (54.17%)	18 (69.23%)	22 (45.83%)	4 (18.18%)
3.	Total	120	78 (65.00%)	55 (45.83%)	42 (35.00%)	7 (5.83%)

In haematological parameters we considered haemoglobin, Mean Carpuscular Volume (MCV) and peripheral blood film examination. As far as haemoglobin is concerned we divided patients into two broard categories as (i) 8-12 mg/dl and less than 8 mg/dl (ii) more than 12 mg/dl. Out of total 120 patients 55 (45.83%) are found to be positive with H. pylori and with vitamin B12 deficiency. Out of 55 patients 38 (69.09%) have moderate to severe anaemia with Hb values less than 8 mg/dl and between 8-12 mg/dl. 42 (76.36%) patients found to have MCV more than 100. On peripheral blood film examination 40 (72.73%) showed macrocytosis.

Table: 5: shows values of haematological parameters in H. pylori positive patients with Vitamin B12 deficiency.

Total Number of patients	Number of patients positive with H. pylori and with Vitamin B12 deficiency	Haematological Parameters (in H.pSA positive and VitaB12 deficient patients)				
		Haemoglobin (Mg/dl)		MCV (fl)		Macrocytosis on peripheral Blood film
		<8-12	>12	<100	>100	
120 (100%)	55 (45.83%)	38 (69.09%)	17(30.91%)	13 (23.64%)	42 (76.36%)	40 (72.73%)

Out of total 120 patients 7 patients (5.83%) were found negative for H. pylori and with vitamin B12 deficiency. 4 patients (57.14%) showed moderate to severe anaemia, 4 patients (57.14%) have MCV more than 100 fl while 4 patients (57.14%) showed macrocytosis on peripheral blood film examination.

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Table: 6: shows haematological parameters in H. pylori negative patients with vitamin B12 deficiency.

Total Number of patients	Number of patients negative with H. pylori and with Vitamin B12 deficiency	Haematological Parameters in H.pSA negative and Vita.B12 deficient patients.				
		Haemoglobin (Mg/dl)		MCV (fl)		Macrocytosis on peripheral Blood film
		<8-12	>12	<100	>100	
120 (100%)	7 (5.83%)	4(57.14%)	3(42.86%)	3(42.86%)	4(57.14%)	4 (57.14%)

DISCUSSION

The present study carried out in the department of pathology in Glocal Medical College, Mirzapur, Dist. Saharanpur, UP India. We studied 120 patients who presented in outdoor medical departments over the period of 6 months i.e. from July 2015 to December 2015, with the chief complaints related to chronic gastritis and associated vague clinical symptoms as epigastric pain, fullness, heart burn, nausea, vomiting, flatulence, malaise, and, sometimes fever, anorexia, or significant weight loss, sometimes constipation and sometimes diarrhea. There were symptoms of anaemia as well as symptoms of involvement of nervous system as paraesthesiae, tingling- numbness in the limbs, and burning pain like sensations at multiple sites in the body, and some have deranged mental states ranging from irritability and forgetfulness to severe dementia and psychosis.

In this study the maximum numbers of patients were present in 6th to 8th decade of life in both the gender. Out of total 72 male patients 63 (87.50%), and in females out of 48 patients 36 (75.00%) were present in 6th to 8th decades of life. So out of total 120 patients 99 (85.50%) were in 6th to 8th decades of life (Table 1). Prevalence of Helicobactor pylori is found to be 65.00% for H. pylori stool antigen test, which includes 52 (72.22%) male patients out of total 72 male patients and 26 (54.17%) female patients out of 48 female patients (Table 3). By chronic gastritis males are affected more than the females this may be due to difference in life style as smoking, tobacco chewing and alcoholism is more in males than females. Vitamin B12 deficiency is frequently identified in elderly, the same was observed by Clarke et al [5] Ramirez et al [6]. In Finland a study, of more than a thousand people showed vitamin B12 deficiency in 6% of the participants and risk deficiency was higher for men and for all those over age 75 increased risk of having the deficit [7], we also got similar findings. Acute or chronic gastritis can occur following disruption of protective mechanisms of gastric mucosa, e.g. reduced mucin synthesis in the elderly has been suggested as one factor that may explain their increased susceptibility to gastritis. The factors responsible for disruption of mucosal protection leading to gastric injury are *H. pylori* infection, NSAID, Aspirin, Cigarettes, Alcohol, Gastric hyperacidity, and Duodenal gastric reflex [8].

Helicobactor pylori have been determined as an etiologic factor in vitamin B12 deficiency [9]. With high prevalence of *H. pylori* infection, the frequency of vitamin B12 deficiency and its clinical consequences can be expected to be high. In the present study we took (<200 pg/ml) the cutoff value for low vitamin B12 status. Markedly high frequency (70.51%) of vitamin B12 deficiency was found i.e. 55 out of 78 patients positive for *H. pylori*, showed low value of vitamin B12 (Table 4) which is higher than that observed by Gumurdulu et al., and Tucker et al [10, 11]. Carmel et al [12] found that the patient with low levels of serum cobalamin had a higher seroprevalence of H. *pylori infection* and the majority of *Helicobactor pylori* infected patients with low serum vitamin B12 levels were more than 40 years old, we also have the similar observations. Colonization of the stomach by *H. pylori is* mostly accompanied by clinical features of chronic gastritis. *H. pylori* is an urease secreting pathogen, and the gastric injury occurring in those infected with *H. pylori* may be due to inhibition of gastric bicarbonate transporters by ammonium ions [8]. *The most common cause of chronic gastritis is infection with bacillus Helicobactor pylori.*[8] Autoimmune gastritis, the most common cause of atrophic gastritis , represents less than 10% of cases of chronic gastritis and is the most common form of chronic gastritis in patients without *H. pylori* infection [8]. Less common etiologies include radiation injury, chronic bile reflux, mechanical injury and involvement by systemic diseases.

H .pylori is a spiral shaped or curved bacilli present in gastric biopsy specimens of almost all patients with duodenal ulcers and the majority of individuals with gastric ulcers or chronic gastritis [13]. *H. pylori* organisms are present in 90% of individuals with chronic gastritis affecting the antrum. Increased acid secretion that occurs in *H. pylori* gastritis may result in peptic ulcer disease, and increased risk of gastric carcinoma. H. pylori infection is associated with poverty, household crowding and limited education. Colonization rates exceed 70% in some groups and vary from less than 10% to more than 80% worldwide. In high prevalence areas infection is often acquired in childhood and then persists for decades, explaining the direct correlation between colonization rate and patient age. *H. pylori* infection is the most common cause of chronic gastritis and the disease most often present as a predominantly antral gastritis with high acid production, despite hypogastrinemia. Infection results in increased acid production and disruption of normal gastric and duodenal protective mechanisms. Over time chronic antral *H. pylori* gastritis may progress to pangastritis, resulting in multifocal atrophic gastritis [8]. The long standing *H. pylori* gastritis may extend to involve body and fundus and the mucosa can become atrophic. In addition to histologic identification of the organism, several diagnostic tests have been developed including a noninvasive serologic test for antibodies to *H. pylori,* fecal bacterial detection, and the urea breath test based on the generation of ammonia by bacterial urease. Gastric biopsy specimens can also be analysed by the rapid urease test, bacterial cultures, or bacterial DNA detection by PCR.[8]

Poor vitamin B12 absorption secondary to atrophic gastritis is significantly associated with hyperhomocystenemia which is a risk factor for arterial sclerosis [14-16]. Diagnosis of vitamin B12 deficiency in patients with chronic gastritis with no autoimmune etiology and which are very frequently associated with *H. pylori* infection have become increasingly common. In contrast to patient with pernicious anemia, these patients have minimally atrophied oxyntic mucosa, secretion of intrinsic factor is adequate, but secretion of hydrochloric acid by the stomach is low. This prevents normal absorption of cobalamin [17-19]. In this study out of total 120 patients 55 (45.83%) are found to be positive with H. pylori as well as with vitamin B12 deficiency. Out of 55 patients 38 (69.09%) have moderate to severe anaemia with Hb values less than 8 mg/dl and between 8-12 mg/dl. 42 (76.36%) patients found to have MCV more than 100fl. On peripheral blood film examination 40 (72.73%) showed macrocytosis (Table 5).

About 7 patients (5.83%) are found negative for *H.pylori* and deficient in vitamin B12, 4 patients (57.14%) out of them showed moderate to severe anemia and 4 patients (57.14%) showed macrocytosis on peripheral blood film. These patients are considered to have pernicious anemia due to autoimmune gastritis leading to atrophy of oxyntic mucosa. Such patients might be having antibodies against intrinsic factor and antibodies against canaliculi of parietal cells. The first inhibits absorption of vitamin B12, while the second reduces normal acid secretion [20-22].

RESULTS

Over a period of last 6 months 120 patients of chronic gastritis were studied. Out of total 120 patients 72 (60%) were

males and 48 (40%) were females.

CONCLUSION

Infection with *H.pylori* has been recognized as a public health problem worldwide and more prevalent in developing than the developed countries[1]. The lower rate of infection in the West is largely attributed to higher hygiene standards and widespread use of antibiotics. The main objective of this study was to observe that H. *pylori* infection in the gastric mucosa is responsible for vitamin B12 deficiency and early detection followed by eradication of *H. pylori* can prevent the complications as atrophic gastritis,gastric ulcers, duodenal ulcers and megaloblastic anemia. Present study concludes that H. *pylori* is an etiological factor for chronic gastritis with or without gastric mucosal atrophy and vitamin B12 deficiency. Therefore the role of early detection and eradication cannot be overemphesised. There is improvement of anemia following eradication of *H. pylori* infection with antibiotic therapy [23]. Patients with vitamin B12 deficiency should receive parenteral cyanocobalamin to treat megaloblastic anemia and other complication.

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