Helicobacter pylori infection, effect on gastric histology and clinical outcome

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H*elicobacter pylori (H. pylori)* cause chronic gastritis characterized by neutrophil and mononuclear cell infiltration and play an important role in the pathogenesis of peptic ulcer disease (PUD) and gastric cancer. The long-term infection leads to the development of atrophy and intestinal metaplasia (IM), which are histological changes that predisposes to the progression of the disease to gastric cancer. The geographical distribution and the genetic variability of *H. pylori* were found to have great impact on the severity of gastric histology and the disease outcome. *Helicobacter pylori* reside naturally in the non-acid secreting area of the stomach, the antrum, but it can also be found in the acid-secreting area of the body.[1] Research on these issues are still lacking in Libya. In this study, the severity of the histological changes that occur at different gastric sites in *H. pylori* infected patients were correlated with PUD.

Forty-five patients admitted to the endoscopy unit at the 7th April Teaching Hospital in Benghazi, Libya were enrolled, consisting of 25 females and 20 males with an age range of 25-90 years (average 57). Biopsies were obtained from each patient one from the antral site and one from the body site of the stomach. Each biopsy was fixed in 10% formalin and sections were stained with hematoxylin and eosin, methylene blue and periodic acid shift stains. Histological scores were adopted according to the updated Sydney system[2] (0: absence, 1: mild, 2: moderate, 3: marked). Data were analyzed using chi-square and Fisher exact tests. Statistical significance was set as p values of <0.05. Of the 45 patients, 20 (44%) had duodenal ulcers (DU), 3 (7%) with gastric ulcers and 22 (49%) with gastritis *Helicobacter pylori* was prevalent in 36 (80%) patients of which 20 (100%) with DU, 3 (100%) with gastric ulcer and 13 (58%) with gastritis were infected with the bacterium (**Table 1**). Examination of histological sections showed the presence of *H. pylori* in 36 of the antral biopsies and in 30 of the body biopsies. *Helicobacter pylori* density was higher in the antral site than in the body site. The histological changes seen in the antral sections (such as, neutrophil infiltration of the lamina propria and the glands and the increase in the number of lymphocytes and plasma cells) were on average of mild scores. The average score for neutrophil infiltration was significantly higher in patients with DU and gastric ulcer than those with gastritis. Similar changes but at a lesser grade were seen in the body sections. Two patients with DU had atrophy and one with IM. Both conditions were of mild histological score. The prevalence of *H. pylori* infection in this study was 80% among all patients. The association of *H. pylori* infections with gastritis and peptic ulceration is well documented. The critical role of *H. pylori* in PUD have been established and the prevalence of infection was found to be of 90-95% that reaches up to 99% in patients with DU and 60-80% in patients with gastric ulcers. In this study, we have found that all patients with DU and those with gastric ulcers were *H. pylori* positive. This was statistically significant when compared to gastritis patients, which further substantiate the correlation of *H. pylori* with PUD. It has been shown that patients with DU have more severe chronic and acute inflammation and epithelial cell degeneration in the gastric antrum than in the gastric body.[3] These parameters together with *H. pylori* density were significantly higher in the antrum of patients with DU than in patients with gastric ulcer or no ulcer. Neutrophil and mononuclear cell infiltration in the antrum, but not in the body, was correlated with the intensity of colonization. The presence of *H. pylori* in chronic gastritis sections when correlated with cellular infiltration showed that 75% neutrophil infiltration and 67% mononuclear cell infiltration in *H. pylori* positive sections compared to 33% neutrophil infiltration and 14% mononuclear cell infiltration in the absence of H. pylori.[4] It was suggested that *H. pylori* infection plays an important role in the pathogenesis of chronic gastritis. Such cellular infiltration together with *H. pylori* density was also the characteristic feature of chronic active gastritis in our histological sections. The characterization of such histological findings provides a better understanding of the pathogenesis and possibly the progression of the disease. Atrophy and IM

Table 1 - Prevalence of *Helicobacter pylori* and the average scores of gastric histology according to the disease.

Disease	N	*H. pylori*		Antrum*		Body*	
		n	(%)	N	M	N	M
Gastritis	22	13	(58)	0.73	1.29	0.50	1.11
Duodenal ulcer	20	20	(100)	1.55	1.64	1.31	1.28
Gastric ulcer	3	3	(100)	1.23	1.49	1.02	1.19

* - average score, N - neutrophil, M - mononuclear cells, *H. pylori - Helicobacter pylori*.

consistently begin in the antrum and IM is common in chronic gastritis and increases in prevalence with disease duration. Earlier reports indicated the detection of atrophy and IM in DU patients and in some gastritis patients.[5] In this study, mild scores of such conditions might be reflected on the low incidence of gastric cancer cases in Libya. According to the world health organization (WHO) report, the annual rate in Libya is very low compared to those reported for Asian countries such as Japan (0.083% versus 57.65%). This fact demonstrates that geographic distribution and possibly genetic variability (as shown in our recent report were Turkish *H. pylori* strains were genetically similar to Western but not to Asian strains)[6] are important factors in the disease outcome. From this study, we conclude that *H. pylori* density at different gastric sites affects the severity of the gastric histology and the disease outcome. The mild histological scores and the few precancerous lesions detected might be correlated with the genotype of *H. pylori* strains in the Libyan patients examined. Further investigation in this regard is required.

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Fludarabine as a second-line treatment of advanced stage chronic lymphocytic leukemia

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Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in adults in the Western countries, accounting for approximately 25-30% of all leukemias. The traditional management of patients with CLL is chlorambucil with or without corticosteroids. They are in general safe, given on an out patients basis and significantly cheaper than purine nucleoside analogues. Chlorambucil alone or in combination with corticosteroids is associated with a complete and partial response rate of 30-70% in previously untreated patients.[1] Furthermore, until last year no effective alternative agents for the management of patients with CLL who were resistant to alkylating agents and corticosteroids. Fludarabine is indicated for the treatment of patients with B-cell CLL who have not responded to, or whose disease has progressed during or after treatment with alkylating agent-containing regimen. Response and survival after treatment with fludarabine in advanced CLL are strongly correlated with disease stage and degree of previous chemotherapeutic regimen. Resistance of disease to alkylating agents is also significant correlated to outcome. Fludarabine induces higher response rates with a substantial number of complete remissions, but no improvement in overall survival has been observed.[2]

In this report, from 2 center followed from May 1997 to September 2002, the clinical response rate and duration, toxicity and survival of 36 patients with 32 months follow-up of treatment with fludarabine in refractory CLL has been evaluated. The diagnosis was made according to physical examination and morphologic and immuno-phenotypic features of peripherally blood and bone marrow. Diagnostic criteria consisted of lymphocytosis with an absolute lymphocytes greater than 5.000/µl on at least 2 previous occasions one month apart and had more than 30% lymphocytes in the bone marrow. All of patients had surface marker analysis providing evidence of a monoclonal B-cell proliferation. The disease in each patient was assigned according to the Rai staging system at the time of fludarabine treatment.[3] Patients were included only if they had failed to respond or had relapsed during or after previous treatment with at least one therapeutic regimen containing an