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Assessment of Homocysteine level in H.pylori infected Sudanese Patients

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Abstract

The body turns back homocysteine into methionine with the help of vitamin B12. H.pylori induced -gastritis impairs folate and vitamin B12 absorption leading to B12 deficiency. Consequently homocysteine level will increase because this reaction cannot take place. The study aimed to assess the homocysteine level in H.pylori infected patients and H.pylori non-infected controls, to correlate the level of homocysteine with the duration of infection. A case control study was conducted in Khartoum state, Sudan. Thirty patients with H.pylori infection were recruited; 7 cases were treated. Age and sex matched 30 apparently healthy subjects with no H.pylori infection were enrolled as controls. The presence of H.pylori infection was diagnosed clinically and confirmed by stool antigen test. Plasma homocysteine level was measured using Biosystem reagents (homocysteine enzymatic cycling) and fully automated Biosystem device (A15). Homocysteine was increased in 21 (70%) out of 30 H.pylori infected cases. There was a significant difference in homocysteine level (P-value: 0.018) between cases and controls; with a mean of 17.6, 14.5 µmol/L ; respectively. Moreover, there was a significant association between H.pylori infection and Homocysteinemia (P-value was < 0.0002). However there was no significant difference in homocysteine level (P-value: 0.23) between treated and un-treated cases; with a mean of 17.1, 19.3 µmol/L ; respectively. In a linear regression analysis; there was a moderate positive correlation between plasma homocysteine level and durations of H.pylori infection (6-12 ,>12 months); with correlation co-efficient; R : 0.5; (p =0.004 , p=0.0001;) respectively. The plasma homocysteine level increases in H.pylori infection. There is a positive correlation between Homocysteine level and the duration of H.pylori infection.

Keywords: *Homocysteine, H.pylori, gastric atrophy, gastritis etc.*

Introduction

H. pylori is a gram-negative bacterium with perfect adaptation to the acidic environment of the stomach and high affinity to gastric epithelial cells (1). It is a bacterium that occurs worldwide with a prevalence specially it is common in developing countries. H. pylori infection causes peptic ulcer, gastritis, dyspeptic symptomatology, low-grade mucosa-associated lymphoid tissue lymphoma and gastric adenocarcinoma. The association between H. pylori infection and gastric disease has been well established (2,3). In fact it has been classified as a type 1 carcinogen by the World Health Organization. Additionally recent studies showed that there is a significant association between the H. pylori and extragastric disease such as iron deficiency (4) anemia, hepatocellular (5) carcinoma and asthma (6). Methionine is an essential amino acid obtained from protein in the diet. Some methionine is turned into homocysteine. The body turns much of this homocysteine back into methionine with the help of vitamin B12. If someone is B12-deficient, homocysteine levels will increase because this reaction cannot take place. Keeping homocysteine at levels associated with lower rates of disease requires both adequate B12 and folic acid status.

Low vitamin B6 status can also cause elevated homocysteine in some people (7). Normal serum homocysteine levels are from 2.2 to 13.2 µmol/l. (8) Levels of homocysteine in typical Western populations are about 12 µmol/l (9). Elevated homocysteine levels may be due to genetic defects of enzymes in methionine metabolism. However, the majority of cases of hyperhomocysteinemia are attributed to low levels of vitamin B12 and/or folic acid, which are co-factors of the most important enzymes of the methionine metabolic pathway (10).

Recently, several studies have suggested an epidemiological association between Helicobacter pylori infection and atherosclerotic-related diseases (11, 12). H. pylori infection is the main cause of chronic active gastritis (12). An intriguing hypothesis postulates that the gastric damage induced by H. pylori infection may affect

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atherosclerotic processes via increased serum homocysteine levels (13). Long-lasting infection may lead to atrophic gastritis (14, 15) which may in turn impair folate and vitamin B12 absorption owing to diminished acid secretion, lower ascorbic acid levels in gastric juice and reduced secretion of intrinsic factor (16). Factors that increase the plasma concentration of homocytseine include deficiency of folate, pyridoxine and failures in absorption of vitamin B12, systemic disorders such as (renal failure , liver failure, hypothyroidism, malignancies and transplantation), pharmacological and toxic factors such as excessive consumption of coffee and/or alcohol, smoking, oral administration of methionine (17). Thus, present study aimed to assess and compare the level of homocystein in H.pylori infected and non—infected subjects, to correlate its level with the duration of H.pylori infection.

Material and method

A case control study design was carried out in Asia Hospital-Omdurman, Khartoum state, Sudan. Sixty subjects were recruited, 30 were H.pylori infected patients (15 males and 15 females); their ages range was 20-50 years. Age and sex matched controls group were 30 apparently healthy subjects with no H.pylori infections. Diagnoses of H.pylori infection was made clinically and by serology. Patient Known to have renal failure, liver failure, hypothyroidism, malignancies, diabetic patients and transplantation, smoker, and alcoholic were excluded. Ethical clearance was taken from Al-Neelain University Review board- ethical committee. All enrolled subjects informed about the objectives and procedures of the study after signing to join to the study. Stool specimen was collected from each patient and control for detection of H.pylori using stool antigen test (Biocreditkits). EDTA anticoagulated venous blood sample (5 ml) was collected also for measurement of homocysteine using Biosystem reagents (homocysteine enzymatic cycling) and fully automated Biosystem device (A15).

Results

This study showed that level of homocysteine was increased in 21 (70%) out of 30 H.pylori infected cases. There was as significant differences in homocysteine level (P-value: 0.018) between cases and controls; with a mean of 17.6, 14.5 µmol/L ; respectively(Table 1). Moreover, there was a significant association between H.pylori infection and Homocysteinemia (P-value was < 0.0002). However there was no significant difference in homocysteine level (P-value: 0.23) between treated (7 cases) and un-treated cases; with a mean of 17.1, 19.3 µmol/L ; respectively, (Table 2).

In a linear regression analysis; there was a moderate positive correlation between plasma homocysteine level and durations of H.pylori infection (6-12 ,>12 months); with correlation co-efficient; R : 0.5; (p =0.004 , p=0.0001;) respectively (Table 3).

Table 1: Comparison of Homocysteine levels (µmol/L) in cases and controls

Group	N	Mean	SD	T-test P. value
H.pylori +ve Cases	30	17.6	23.1	0.018*
H.pylori –ve Controls	30	14.5	6.8	

Table 2: Comparison of Homocysteine levels (µmol/L) in treated and untreated cases

Group	N	Mean	SD	T-test P. value
Untreated Cases	23	19.3	20.3	0.23*
treated Cases	7	17.1	28.4	

Table 3: Hompcysteine level (µmol/L) at different durations of H. pylori infection

Duration of Infection/month	Mean	SD	P. value
Control	14.51	2.6	
< 6	15.36	5.1	0.59
6-12	20.10	3.0	0.004
>12	21.00	0.0	0.0001

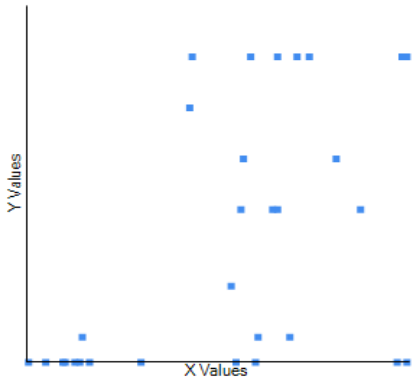

Figure 1: Correlation between Homocysteine levels (X) and duration of H.pylori infection (Y)

Discussion

The present study revealed an increase in plasma homocysteine levels in H.pylori infected cases as compared to H.pylori non-infected controls, analysis of these data showed that plasma homocysteine levels was significantly different between cases and controls, majority of H.pylori infected cases showed abnormal high homocysteine level (70%).

The study findings also revealed a significant association of H. pylori infection with hyperhomocysteinaemia, this could be due to impaired folate and vitamin B12 absorption that are caused by long lasting H.pylori infection which leads to atrophic gastritis; especially that most of the study patients were suffered from H.pylori infection for long period of time. A study was done by Tamura *et al*, who measured plasma homocysteine, vitamin B12 and folate in 57 patients who underwent diagnostic coronary arteriography and positive for H.pylori infection suggested that H.pylori induced chronic atrophic gastritis decreases plasma

vitamin B12 and folic acid levels, thereby increasing homocysteine levels (18).

Another study, done by Harun, *et al* in 2007, estimated the plasma folate and homocysteine level in 43 patients with angiographically proven slow coronary flow and presence of H.pylori was defined as 14 C urea breast test and suggested that elevated levels of plasma homocysteine, possibly caused by H. pylori infection and/or a possible disturbance in its metabolism may play a role in the pathogenesis of SCF (19).

The analysis results of this study showed a moderate positive correlation between plasma homocysteine level and durations of H.pylori infection, the mean plasma homocysteine level was ascendingly increased when duration of infection increased compared with control group.

The mean of plasma homocysteine levels significantly increased with duration of infection from 6 to 12 and duration of >12 compared with a duration of < 6 months; this indicates that increase in duration of H.pylori infection can cause increase in plasma homocysteine level in these patients.

In comparison result of plasma homocysteine level (µmol/L) between treated and untreated H.pylori infected cases; the level of plasma homocysteine was slightly increased in untreated group compared to treated ones but the result was insignificant. A study done by Birol Ozer, Ender Serin *et al*, in 2005 among 73 dyspeptic H.pylori-positive patients reported that the eradication of H pylori decreases serum homocysteine even in patients who do not exhibit gastric mucosal atrophy. It ppears that the level of homocysteine in serum related to complex interaction among serum vitamin B 12 ,serum folate and erythrocyte folate level (20). The result of our study may be contributed to the smalls ample size and that the number of treated patients was very low (only 7 cases) compared with the number of untreated patients, also an infected cases who were underwent a treatment for H.pylori were not completely eradicated from infection. A possible other cause might these patients were re-infected with this bacterium.

The major limitations of the present study are the small sample size, the need to define and consider the gastric damage caused by long lasting H.pylori infection, and measuring levels of serum vitamin B12 and folate .

Conclusion

The plasma level of homocysteine was increased in H.pylori infected patients as compared to non-infected normal controls. There was a positive correlation between Homocysteine level and the duration of H.pylori infection.

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