FREQUENCY OF HELICOBACTER PYLORI ANTIBODIES (IgG) IN PATIENTS WITH ISCHEMIC STROKE

Muhammad Shahid Iqbal[1], Adnan Khan[1], Sidra Hamayun[2], Ghulam Farooq[2]

ABSTRACT

Background: Ischemic stroke results from atherosclerosis of cerebral arteries. Atherosclerosis is consequence of the processes of vascular injury, inflammation, and thrombosis; however, the stimulus that triggers the inflammatory response remains unclear. Persistent infectious agent Helicobacter pylori play an important role in atherosclerosis.

Objective: To determine the frequency of H. Pylori antibodies (IgG) among cases of ischemic stroke

Materials and methods: This descriptive cross sectional was done at Department of Neurology, Lady Reading Hospital, Peshawar from 27th August, 2013 to 27th February, 2014, recruiting 145 patients with ischemic stroke presenting within 72 hours of either gender. There serum IgG levels for Helicobacter Pylori antibodies (IgG) was measured,taking titers more than 20 U/ml as positive.All the data was analyzed by SPSS version 16 and results were presented in the form of tables and graphs.

Results: There were 97 (66.90%) males and 48 (33.10%) females with an overall age of 46.58 years ± 9.42SD. Mean ± Standard deviation of H. pylori antibodies level (IgG) was 2.19U/ml ± 7.22SD. The Helicobacter Pylori antibodies (IgG) more than 20U/ml was present in 91 (62.76%) patients with ischemic stroke. Helicobacter Pylori antibodies (IgG) more than 20U/ml were more in males than females(60 (41.38%) vs. 31 (21.38%)) andmaximum in the age group of 51 to 60 years i.e. 30 (20.69%)patients.

Conclusion: Routine screening for H. pylori infection and measure should be taken to manage this risk factor as as large number of patients (62.76%) present with chronic infection of H. pylori and ischemic stroke in our set up.

Key words: Ischemic Stroke; Helicobacter Pylori antibodies; Atherosclerosis.

INTRODUCTION

Stroke is a major health problem worldwide because of its high risks of morbidity and mortality.[1] According to the 2005 WHO report, about 5.7 million deaths are caused by stroke, and over 50 % of cases occurred in Asians.[2,3] Ischemic Stroke accounts for over 50 % of all types of stroke cases, and inflammation and inflammation-related atherosclerosis play a crucial role in stroke progress and prognosis.[4] Exact data about the incidence and prevalence of stroke in Pakistan is lacking but the burden is assumed to be high because of the high prevalence of major risk factor for stroke in our population.[5]

Stroke is defined as a syndrome of rapid onset of cerebral deficit, usually focal, lasting more than 24 hour or leading to death with no cause apparent other than a vascular one.[6] The burden of ischemic stroke is increasing worldwide because of the rise in the major risk factor for ischemic stroke i.e. hypertension, diabetes, obesity, smoking and dyslipidemia.[6] Recently, it has been shown that C-reactive protein level is a stronger predictor of cardiovascular events than low-density lipoprotein cholesterol level.[7] Chronic infection and the subsequent chronic inflammatory processes manifested by elevated levels of plasma fibrinogen, C-reactive protein, interleukin-6, and other cytokines[8] may result in increased coagulation, endothelial dysfunction, plaque instability, and accelerated atherosclerosis. Direct invasion of atherosclerotic plaque or seropositivity for Chlamydia pneumonia[9]or Helicobacter pylori[10] may accelerate the atherosclerotic process. An elevated leukocyte count has been associated with aortic atheroma progression in patients with stroke and transient ischemic attacks.[11]

Helicobacter pylori is a gram-negative spiral bacterium that can cause gastritis, peptic ulcer, and gastric cancer but often remains asymptomatic[12]. Studies show almost 60% to 80% of patients admitted with ischemic stroke are positive for Anti-H.pylori IgG.[13,14] It has been suggested that patients with chronic H.pylori infection are at an increased risk of ischemic stroke.[15,16]

The objective of the study was to find the frequency of Helicobacter pylori among ischemic stroke cases in our setup.

OBJECTIVE

The objective of the study was to determine the

[1] Department of Neurology, Govt Lady Reading Hospital, Peshawar.
[2] Department of Medicine, Hayatabad Medical Complex, Peshawar.

Address for correspondence:
Dr. Muhammad Shahid Iqbal
Senior Registrar, Neurology Unit, Rehman Medical Institute, Peshawar, KPK.
E-mail: exkmcite@gmail.com

frequency of H. Pylori antibodies (IgG) among cases of ischemic stroke.

MATERIAL AND METHODS

This cross sectional study was carried out at Department of neurology, Lady Reading Hospital, Peshawar from 27th August, 2013 to 27th February, 2014, recruiting 145 Patients of either gender presenting within 72 hours of acute ischemic stroke.Exclusion criteria adopted was; Patients with transient ischemic attacks and hemorrhagic stroke. Patients with history of peptic ulcer disease, using proton pump inhibitors were also excluded.

After approval from hospital ethical committee,all patients meeting the inclusion criteria were included in the study through outpatient department (OPD) and emergency and were admitted if required in the neurology ward for further evaluation. The ischemic stroke was defined as a syndrome of rapid onset of cerebral deficit, usually focal, lasting more than 24 hour or leading to death with no cause apparent other than a vascular one confirmed on computed tomography (CT) scan or magnetic resonance imaging (MRI) and presenting to our unit within 72 hours. Anti-H. PyloriIgGwere defined as the antibodies which show chronicity of infection and were measured by ELISA (EIA WELL, REF K5HPG kit, Roma, Italia) on confirmed cases of ischemic stroke. Values higher than 20 U/ml were considered reactive. Sensitivity and the specificity of the method is 95.8 and 96.2%, respectively.[11]

The inclusion and exclusion criteria werestrictly followed to control confounder bias in study results. The purpose and benefits and risks of the study was explained to all patients' relatives and they were assured that the study is done purely for data publication and research purpose, and if agreed upon an informed written consent was obtained from all patients.

All patients were subjected to detailed history and physical examination and routine investigations were carried out in all patients. 2cc of venous blood was taken from all patients, under strict aseptic technique and was sent to the laboratory on the same day to measure serum IgG levels. Titers more than 20 U/ml were regarded as positive. Other specific necessary investigations were carried out accordingly like CT scan and/or MRI brain to confirm ischemic stroke. Doppler ultrasound of both carotid arteries was carried out to look for atherosclerosis. The type of treatment was according to medical ethics, beneficial and non harmful to the patients.

All the above mentioned information including name, age, gender and address was recorded in the study Performa. A strict exclusion criterion wasfollowed to control confounders and bias in study results.

All the data was analyzed in SPSS version 16. Mean ± standard deviation were calculated for continuous variables like age of the patient and Anti-H.pyloriIgG levels. Frequencies and percentages were calculated for categorical variables like gender and Anti-H.pyloriIgG antibodies above 20U/ml. All results were presented in the form of tables and graphs. Anti-H.pyloriIgGabove 20U/ml was stratified among age and gender to see effect modifiers.

RESULTS

The total number of patients presenting with ischemic stroke was 145 comprising of 97 (66.90%) males and 48 (33.10%) females. Maximum patients were from the age group of 60 years and above i.e. 61 (42.07%)followed by 54 (37.24%) from the age group of 50-60 years. Patients from the age group 40-50 were 30 (20.69%). The mean age of males and females were 59.81 ± 8.93 and 59.12 ± 10.43 respectively with an overall age of 59.58 ± 9.42.

The Helicobacter Pylori antibodies (IgG) more than 20U/ml was present in 91 (62.76%) patients with ischemic stroke while 54 (37.24%) patients were having less than 20U/ml.(Graph No. 1)

Mean ± Standard deviation of H. pylori antibodies level (IgG) in males and females were 22.19U/ml ± 7.24SD and 22.18U/ml ± 7.28SD respectively with an overall mean level of 22.19U/ml ± 7.22SD. (Table No. 1)

According to Gender distribution, Helicobacter Pylori antibodies (IgG) more than 20U/ml was present

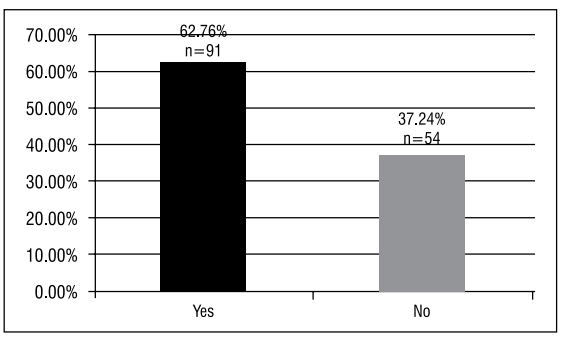

Figure. 1 Frequency of Helicobacter Pylori Antibodies (Igg) in Patients with Ischemic Stroke

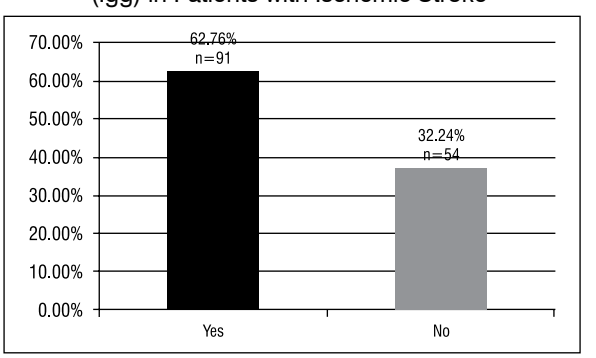

Figure. 2 Frequency of Helicobacter Pylori Antibodies (Igg) > 20 U/Ml In Patients With Ischemic Stroke

Table no. 1 Mean ± standard deviation of h. Pylori antibodies level (igg) in patients with ischemic stroke

Gender	Mean ± Std. Deviation
Male	22.19 ± 7.24
Female	22.18 ± 7.28
Total	22.19 ± 7.22

Table No. 2 Age Distribution of Frequency of Helicobacter Pylori Antibodies (Igg) > 20 20u/Ml In Patients With Ischemic Stroke

Age groups (Years)	H. pylori IgG	
	Yes	No
41 – 50	8 (5.52%)	22 (15.17%)
51 - 60	33 (22.76%)	21 (14.48%)
61 and above	50 (34.48%)	11 (.59%)

in 60 (41.38%) males and 31 (21.38%) females. (Graph No. 2)

According to age wise distribution, presence of Helicobacter Pylori antibodies (IgG) more than 20U/ml was maximum in the age group of 60years and above i.e. 50 (34.48%)patients followed by 33 (22.76%) patients in the age group of 51-60 years. (Table no. 4)

DISCUSSION

The relationship of infection, inflammation, and atherosclerosis has been subjected to intensive investigation in recent years. Potential mechanisms whereby chronic infections may play a role in atherogenesis are myriad. Chronic Helicobacter pylori infection is known to increase the pH level of the gastric juice and to decrease ascorbic acid levels, both of which will lead to a reduced folate absorption. Low folate hampers the methionine synthase reaction. This leads to an increased concentration of homocysteine in the blood, resulting in damage of endothelial cells. Inflammatory markers are independent predictors of cardiovascular and cerebrovascular events.[16]

In our study, the Helicobacter Pylori antibodies (IgG) were present in 62.76% patients with ischemic stroke while. Helicobacter Pylori antibodies (IgG) were more in ischemic stroke male patients (41.38%) than females (21.38%). The maximum affected age group was 60 years and above. Compared to local study, we have less frequency of H. pylori antibodies detection in ischemic stroke patients. In a local study by Shaikh MA et al [13] found that H.pylori antibodies (IgG) were present in 121 (80.7%) cases among which males were 99 (66%) and females were (14.7%).

In our study we did not studied the significance of association of H pylori infection and ischemic stroke, though in the literature its association has been studied with different significance,however, it is still unsolved issue.Masoud SA et al[17] in their study found that seropositivity for H. pylori (IgG or IgA) was 72.5% with significantly high mean of serum IgG levels in stroke group ($P < 0.005$).PreuschMR et al,[18] has found that CagAseropositivity was more common in patients (60.0%) than in control subjects (43.2%; odds ratio, 1.97; 95% CI, 1.33 to 2.91; $P<0.001$). Park MH et al,[19] found that H. pylori seropositivity was more common in the stroke patients than in the controls (80.0% vs. 60.0%, $P=0.001$). Moreover, H. pylori seropositivity was more common in the stroke subtype of large artery disease (87.7%, $P<0.001$).while Yang X, et al[20] in a case-control study indicated that Helicobacter pylori/IgG-positive rate in the patient group was higher than that in the healthy control group, but the difference was not statistically significant [67.3% versus 61.8%; odds ratio (OR) = 1.272; $P = 0.336$]. According to Wasay M[21] Patients with H Pylori gastritis were more likely to die or have cardiac and or neurological event as compared to Non H pylori gastritis (OR 1.23, 95% CI 0.89-1.67) but this relationship was not significant after adjusting for cardiovascular risk factors (AOR 0.85, 95% CI 0.45- 1.31).

We performed the study in a community setting with patients of various socioeconomic classes. Participants' compliance was good and statistical analyses were straightforward, and missing data analysis was not required. Our study has mlimitations. In our study, we attempted to detect the H. pylori infection by measuring IgG antibodies which show chronicity of infection by ELISAon confirmed cases of ischemic stroke and values higher than 20 U/ml were considered reactive. Thus, although preclinical atherosclerosis may have been present, it is highly unlikely that it is an important confounding variable in explaining the observed frequency of ischemic stroke. The gold standard for detection of chronic H. pylori infection is invasive assessment of gastric mucosa by histopathological study. Because the number of participants was large (n=145) and the patients did not have a clinical indication for an invasive study due to exclusion criteria adopted, we did not consider it justified or ethical to perform invasive assessment of gastric mucosal biopsy. The number of participants in the time-interval groups was small, and thus, our findings should be interpreted with caution. Another limitation of our study is the period of follow up. There is no data to suggest time lag between H Pylori infection and development of atherosclerosis. We believed that the findings of this study were interesting and could be used to identify persons at high risk of IS and, subsequently, for prevention of its incidence.

This was a pilot study and further research is required to elaborate the association between H. pylori infection and ischemic stroke.

CONCLUSION

From the results of my study it has been concluded that; Patients presenting within 72 hours of acute ischemic stroke must be investigated for chronic H. pylori infection as large number of patients (62.76%) present with chronic infection of H. pylori and ischemic stroke in our set up.

From the results of this study we recommend routine screening for H. pylori infection and measure should be taken to manage this risk factor to reduce the mortality and morbidity associated with ischemic stroke. Also the patients who are diagnosed as having H.pylori infection should be screened for cerebral atherosclerosis.

REFERENCES

1. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. Lancet 2011;377:1693-702.
2. Li N, He Z, Xu J, Liu F, Deng S, Zhang H. Association of PDE4D and IL-1 gene polymorphism with ischemic stroke in a Han Chinese population. Brain Res Bull 2010;81:38–42.
3. Gunarathne A, Patel JV, Gammon B, Gill PS, Hughes EA, Lip GY. Ischemic stroke in South Asians: a review of the epidemiology, pathophysiology, and ethnicity related clinical features. Stroke 2009;40:415–23.
4. Martin CO, Rymer MM Hemorrhagic stroke: aneurismal subarachnoid hemorrhage. Mo Med 2011;108:124–7.
5. Khealani BA, Hameed B, Mapari UU. Stroke in Pakistan. J Pak Med Assoc 2008 ;58:400-3.
6. Clarke CRA. Neurological diseases. In: Kumar P, Clark M, editors. Clinical medicine. 7th ed. New Delhi: Saunders Elsevier; 2009.p.1126.
7. [Ionita CC1, Siddiqui AH, Levy EI, Hopkins LN, Snyder KV, Gibbons KJ. Acute ischemic stroke and infections. J Stroke Cerebrovasc Dis 2011 Jan-Feb;20(1):1-9.
8. Emsley HC, Hopkins SJ. Acute ischaemic stroke and infection: recent and emerging concepts. Lancet Neurol 2008;7:341-53.
9. Alamowitch S, Labreuche J, Touboul PJ, et al. Chlamydiapneumoniaeseropositivity in etiological subtypes of brain infarction and carotid atherosclerosis: A case-control study. J NeurolNeurosurg Psychiatry 2008;79:147-51.
10. Senmaru T, Fukui M, Tanaka M, Kuroda M, Yamazaki M, Oda Y, Naito Y, et al. Atrophic gastritis is associated with coronary artery disease.J ClinBiochemNutr 2012 Jul;51(1):39-41.
11. Worthmann H, Tryc AB, Deb M, Goldbecker A, Ma YT, Tountopoulou A, et al. Linking infection and inflammation in acute ischemic stroke. Ann N Y AcadSci 2010 Oct;1207:116-22.
12. Rožanković PB, Huzjan AL, Cupić H, Benčić IJ, Bašić S, Demarin V. Influence of CagA-positive Helicobacter pylori strains on atherosclerotic carotid disease. J Neurol2011 ;258:753-61.
13. Muzaffar AS, Manzoor AL, Muhammad RR, Roohi B, Zafarullah, M. Saleem R. Frequency of Helicobacter pylori in ischemic stroke. J LiaquatUni Med Health Sci 2011;10:153-6.
14. De Bastiani R, Gabrielli M, Ubaldi E, Benedetto E, Sanna G, Cottone C, et al. High prevalence of CagA positive H pylori strains in ischemic stroke: a primary care multicenter study. Helicobacter 2008;13:274-7.
15. Wang ZW, Li Y, Huang LY, Guan QK, Xu da W, Zhou WK. Helicobacter pylori infection contributes to high risk of ischemic stroke: evidence from meta analysis. J Neurol 2012;259:2527-37.
16. Corrado E, Novo S. Role of inflammation and infection in vascular disease.ActaChirBelg 2005 Nov-Dec;105(6):567-79.
17. Masoud SA, Arami MA, Kucheki E. Association between infection with Helicobacter pylori and cerebral noncardioembolic ischemic stroke.Neurol India. 2005 Sep;53(3):303-6.
18. Preusch MR, Grau AJ, Buggle F, Lichy C, Bartel J, Black C, Rudi J. Association between cerebral ischemia and cytotoxinassociated gene-A-bearing strains of Helicobacter pylori. Stroke 2004;35:1800-4.
19. Park MH, Min JY, Koh SB, Kim BJ, Park MK, Park KW, et al. Helicobacter pylori infection and the CD14 C(-260)T gene polymorphism in ischemic stroke. Thromb Res 2006;118(6):671-7.
20. Yang X, Gao Y, Zhao X, Tang Y, Su Y. Chronic Helicobacter pylori infection and ischemic stroke subtypes. Neurol Res. 2011 Jun;33(5):467-72.
21. Wasay M, Jafri W, Khealani B, Azam I, HussainiA.. Helicobacter Pylori gastritis and risk of ischaemic stroke. JPMA 2008;58:368.