FREQUENCY OF FOLIC ACID DEFICIENCY IN PATIENTS WITH ISCHEMIC HEART DISEASE

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Author's Contribution

GA:Conducted the study and wrote the article. GH:Helped in review the article. MRUH:Re-arranged data and corrected article.MAD:Tables and figures. JUR and SS were corrections and did the proof reading.

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ABSTRACT

INTRODUCTION:It has been identified over the years of research that folates have definitive importance regarding prevention of Ischemic heart disease. Previously, several studies have shown increased risk of cardiovascular diseases specially endothelial dysfunction in folic acid deficiency. In Pakistani population folic acid deficiency is highly prevalent, which appears to be a major cause of hyperhomocysteinemia.

OBJECTIVE:To determine the mean folic acid levels in patients of ischemic heart disease as compared to normal controls.

METHODS:This case-control study conducted at department of Pathology and Department of Cardiology, Holy Family Hospital, Rawalpindi Medical College, Rawalpindi. Total 120 individuals were included in the study, 60 patients of ischemic heart disease and 60 controls. Data, demographic information and all findings of patients was recorded. Serum samples of 3-5ml for the estimation of folic acid levels were obtained in gel bottle. All samples were processed in pathology laboratory. Data was collected and analyzed using SPSS version 20.

RESULTS:Mean age in both groups cases and controls was 53.85 ± 8.99 and 50.43 ± 9.92 years respectively. Among cases there were 53(88.3%) male and 7(11.7%) females while among controls there were 54(90%) male and 6(10%) females. Folic acid level was measured both in cases and controls. In cases, mean folic acid level was 4.19 ± 2.11 ng/ml and among controls mean folic acid level was 5.05 ± 1.67 ng/ml. Mean folic acid level was high in controls as compared to cases i.e. (P-Value=0.015). In terms of p-value mean folic acid level was statistically different in cases and controls. Among cases low folic acid was noticed in 25(41.7%) cases and among controls low folic acid was noticed in 14 (23.3%). According to the results of this study folic acid level was low in patients of ischemic heart disease. (Cases: 4.19 ± 2.11 ng/ml vs. Controls: 5.05 ± 1.67 ng/ml) (P-value = 0.015)

CONCLUSION:Reduced Folic acid level is linked with cardiovascular diseases and folic acid deficiency was high in patients with IHD.

KEY WORDS:Folic Acid deficiency, Ischemic Heart Disease, Homocysteine.

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INTRODUCTION:

Folic acid (pteroylglutamic acid) is a yellow, crystalline, water soluble substance. Majority of folate compounds are derived from folic acid.[1] Human body is unable to produce folate de novo so dietary intake of the vitamin is necessary to prevent repletion of folic acid. Common sources include dark green leafy vegetables such as spinach, citrus fruits and juices, wheat and other whole grains, and liver.[2]

Different studies have inferred that folic acid reduces homocysteine levels within the blood through biochemical reactions in the human body.[2] Clinical and epidemiological studies results have shown association between total serum homocysteine levels and ischemic heart disease.[3] Folic acid decreases rate of atherosclerosis and helps decreasing the endothelial dysfunction. Both of these are major factors for development of ischemic heart disease.[2]

IHD is the major cause of death for both genders through out the world. It is also a common reason of physical disability, particularly in the rapidly increasing population of older patients.[4] Ischemic heart disease occur secondary to occlusion of coronary arteries which occurs due to progressive atherosclerosis. Recently in Indian study results showed strong association of folic acid deficiency with development of coronary artery disease.[5]In this study folic acid levels were significantly lower (8.40±0.71) in patients of ischemic heart disease as compare to healthy controls (13.04±0.71).

In Pakistani population, folic acid deficiency is highly prevalent, which is secondary to hyperhomocysteinemia.[6] Decreased fresh fruits intake by population and overcooking of food results in deficiency of such micronutrients. Recent local study results showed that folic acid level below 5.5ng/ml results in increased levels of homocysteine. It is considered that folic acid deficiency is one of the major causes for hyperhomocysteinemia in our population.[6]

Prolonged folic acid supplementation improves arterial endothelial functions not only in patients of unstable coronary artery disease with hyperhomocysteinemia but also in healthy cigarette smokers.[7] Therefore, there is a great need to look into the fact that if there exists any association between the patients of ischemic heart disease and folic acid deficiency. If this is really the fact, then clinicians should be advised that simple non toxic, relatively inexpensive folic acid supplementation may potentially decrease the chance of ischemic heart disease.

MATERIALS AND METHODS:

This case-control study was carried out in Department of Pathology and Department of Cardiology, Holy Family Hospital, Rawalpindi from January 2015 till December 2015. Patients were enrolled through non-probability consecutive sampling. Total of 120 patients were included in the study which fulfilled the inclusion criteria. Both groups had 60 patients each. Patients of 25-65 years of ages newly diagnosed as having ischemic heart disease (Cases) were included in group A, while all healthy individuals of same age range and sex attending Medical OPD (Controls) were included in group B. All patients on folic acid or vitamin B12 therapy, pregnant females, patients with known malignancy and those with H/O of megaloblastic anemia were excluded from the study.

Approval was taken from the hospital ethics committee. Informed consent was obtained from every patient. Patients were enrolled in study through non-probability consecutive sampling and patients were divided in two groups i.e. cases and controls. Data, demographic information and all findings of patients were recorded in study proforma. 3-5ml serum samples for estimation of folic acid levels were obtained in gel bottle. All samples were processed in pathology laboratory of RMC and Allied Hospitals within 24 hours of collection. Tests were performed using chemiluminescent Microparticle Immunoassay (CMIA) on "IMMULITE 2000" an automated special chemistry analyzer by SIEMENS. Reports were verified by consultant pathologist.

Data was entered and analyzed using SPSS version 20. Descriptive statistics were calculated for both qualitative and quantitative variables. For qualitative variables, like gender and folic acid deficiency, frequency and percentage were calculated. For quantitative variables, like age and folic acid levels; mean and standard deviation was calculated. Independent sample t- test was used to compare folic acid deficiency in two groups. A p-value of <0.05 was considered to be statistically significant.

RESULTS:

Overall mean age of all 120 cases and controls was 52.14±9.58 years. Age range was 28-70 years. Mean age of cases and controls was 53.85±8.99 and 50.43±9.92 years respectively. Minimum and maximum age among cases was 28 and 70 years while in controls minimum and maximum age was 28 and 65 years respectively.

Table-1: Descriptive statistics for folic acid level in cases & controls

		Cases	Controls	Total
Folic Acid Level	**N**	60	60	120
	Mean	4.19	5.05	4.62
	SD	2.11	1.67	1.94
	Minimum	1.59	1.72	1.72
	Maximum	11.40	7.90	11.40
*Folic Acid	**Low**	25(41.7%)	14(23.3%)	39(32.5%)
	Normal	35(58.3%)	46(76.7%)	81(67.5%)
Total		**60**	**60**	**120**

t-Test =--2.464
p-value = 0.015 (Significant: p-value<0.05)
*Chi-Square test= 4.569
*P-value= 0.032 (Significant: p-value<0.05)

Among cases there were 53(88.3%) male and 7(11.7%) females while among controls there were 54(90%) male and 6(10%) females. Overall male were dominating in cases and controls. Among cases mean CKMB level was 211.63 ± 128.96. Minimum and maximum CKMB level was 20 and 570. Among cases 87% patients Trop-T test was positive while among the remaining 13% Trop-T was negative. ECG findings showed that 77% cases had ST elevation myocardial infarction (STEMI) and the remaining 23% cases had Non ST elevated myocardial infarction (NSTEMI) or unstable angina.

Folic acid level was assessed both in cases and controls. In cases, mean folic acid level was 4.19±2.11 and among controls mean folic acid level was 5.05±1.67.In terms of p-value, mean folic acid level was statistically different in cases and controls. Mean folic acid level was low in cases as compared to controls.i.e. (p-value=0.015) Among cases low folic acid was detected in 25(41.7%) cases while the remaining 35(58.3%) cases had normal folic acid. While among controls low folic acid was detected in 14(23.3%) controls while the remaining 46(76.7%) controls had normal folic acid level. Among cases, folic acid deficiency was high as compared to that of controls. i.e. (p-value=0.032).

DISCUSSION:

Low folic acid levels leads to increased homocysteine levels which leads to atherosclerosis, thromboembolism and Ischemic heart disease. The study performed in UK showed that reduced level of folic acid might be contributing to twice as many Ischemic Heart Disease (IHD) deaths.

Lower concentrations of folate and vitamin B12 in Great Britain's Asians revealed that deficiencies of B-complex vitamins in daily nutrition might be leading to increasing rates of IHD. It is indicating that there is an epidemic of cardiovascular diseases in urban South Asians and it has also been believed that prevention for ischemic heart disease and folic acid deficiency may be started at in early age. [8, 9]

Pakistan is included in South Asian region and have extremely rising trends of Ischemic heart disease. According to official estimates, Cardiovascular Disease (CVD) leads to more than 100,000 deaths annually.[4] Present study was done to determine the plasma/serum levels of folate in healthy Pakistani adults similar to other studies conducted before.[10-12] Several studies have pointed out a link between decreased folic acid and vascular disease independent of the conventional factors.[13-17] In many Western and European populations, it has been concluded by many researchers that homocysteine decreases as folate levels increase. [18-26]

Hangyuan Guo in his study determined the effect of therapy of folic acid on homocysteine level and arterial endothelial function and he observed the concentrations of folic acid and Vitamin B12 were significantly lower in patients with cardiovascular morbidity(p-value<0.05) (7.0±2.5 vs. 5.1±2.0). Many risk factors for coronary artery disease including male sex, elder population, smoking, diabetes mellitus, hypertension and hypercholesterolemia were linked to the high homocysteine levels and reduced folic acid concentration.[27]

Previous studies showed that folic acid replacement is beneficial in decreasing plasma homocysteine level and thereby improving arterial endothelial function in IHD patients with high risk.[28-30] The first prospective randomized placebo-controlled intervention study proposed that coronary arterial endothelial function gets better after treatment with folic acid and cobalamin. Folic acid considerably improves endothelial function in otherwise healthy cigarette smokers and during pregnancy.

Folic acid supplementation may down-regulate these inflammatory responses secondary to increased homocysteine levels. Moreover, there may be a tendency to turn around the coagulation process and coronary oxidative stress.[31-34]

High total homocysteine levels on admission robustly forecast the cardiac events in acute coronary syndromes. It is also possible that folic acid itself may have direct antioxidant effects on the endothelium and thereby leads to an improvement in endothelial function.

According to the results of a large meta-analysis

of more than 90 genetic and prospective studies recommended that increase intake of folic acid would diminish the risk of ischemic heart disease by 16%, deep vein thrombosis by 25%, and stroke by 24%. [34]

The data that is available world wide strongly recommend an advantage of folate supplementation in decreasing cardiovascular risk. Many observational studies established an association between folate levels and morbidity due to cardiovascular disease.

CONCLUSION:

High frequency of folic acid deficiency was observed in patients with ischemic heart disease so it is important to take serious consideration regarding micronutrient supplementation in cardiac patients to minimize the risk of ischemic heart disease and its related events in our community.

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