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Research Paper

HYPERHOMOCYSTEINEMIA: A RISK FACTOR FOR CORONARY ARTERY DISEASE.

Medical Science

KEYWORDS : Secretor, Non Secretor, Childhood Asthma, Blood Group

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ABSTRACT

Background : The aim of the study is to evaluate the relationship of childhood asthma with ABO secretor.

Objectives: To assess risk factors associated with childhood asthma with special reference to ABO secretor

Methods: 150 Cases and 150 Controls were studied. Simple agglutination method was used to find out the secretor status of the subjects.

Results: The odds of being a non secretor is almost 4 times higher among child asthmatic patients than normal children. Odds ratio being 3.838 (which is greater than 2.0) proves that being a non secretor may be considered as potential risk factor of childhood asthma.

Conclusions: Being a Non Secretor may be considered as a potential risk factor of Childhood Asthma.

Cardiovascular Disease is the world's number one killing disease. About 30% of annual worldwide deaths are cause by this disease. Up to 80% of all heart attacks occur in people with normal cholesterol In 25% of adults, the first sign of heart disease is sudden death from a myocardial infarction.

Homocystiene is a sulfur containing non essential amino acid. It is not found in diet and so obtained by conversion of dietary methionine in the body. In the last decade, increasing recognition that approx. 1/3rd of patients Coronary Artery Disease lack conventional risk factors.

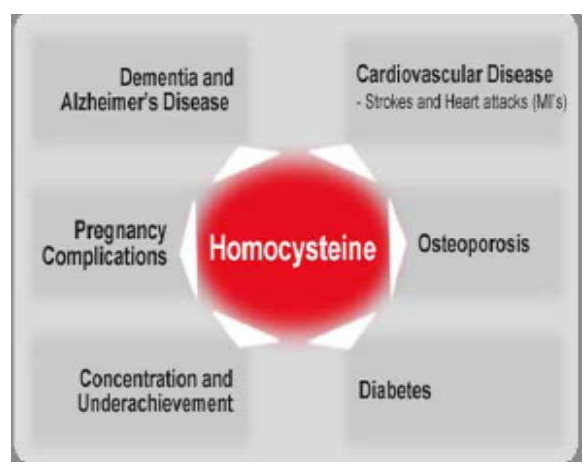
This has led to search for additional new risk factors that may predispose the individual to coronary artery disease. Dr Kilmer McCully, a researcher who graduated from Harvard Medical School in the mid-1960s and came up with the hypothesis that moderate elevations of homocysteine could lead to heart attacks and strokes. It was the time that the cholesterol-heart-attack theory was gaining tremendous momentum and Mc Cully's hypothesis clearly challenged its future. He found himself moved down to the basement, funding for his research dried up and he was eventually asked to leave Harvard. Prevalence of hyperhomocysteinemia is not insignificant: general population: 5 - 10% elderly population: 30 - 40% , pts with vascular disease: 20 - 40%.

Table 1: Summary of main findings of the observational studies of homocysteine and risk of coronary heart disease, by year of publication

Year of Publication	Author	No. of CHD cases	Main findings for CHD risk
1976	Wicken	25	First identified association of tHcy with CHD
1991	Clarke	60	tHcy association with CHD identified as being independent of other risk factors
1995	Boushey	2458	5 µmol/L lower tHcy →**60%** lower CHD risk in retrospective studies
1999	Danesh and Lewington	3740	5 µmol/L lower tHcy →**30%** lower CHD risk in retrospective studies
2002	Homocysteine Studies Collaboration	5073	25% lower usual tHcy →**10%** lower CHD risk in prospective studies

Methionine which is derived from meat, eggs, milk, cheese, white flour, canned foods and highly processed foods is metabolised by methyl transferase enzyme to Homocysteine. The enzyme requires vitamin B12 and folic acid as co factors for its action. The Homocysteine formed is inturn converted to cysteine by enzyme cystathionine synthase which requires vitamin B6 as cofactor. There is an abnormal increase in homocysteine level in case of nutritional deficiencies, drugs, life style habits and diseases like Alzheimer's disease, diabetes etc.

Experiments on arteries of both animals and humans with an elevated level of homocysteine showed that homocysteine level in blood is an independent risk factor for atherosclerotic vascular disease affecting the coronary (arteries supplying the heart), cerebral (arteries supplying the brain) and peripheral arteries (supplying the rest of the body). High levels of homcysteine, or a high "H Score," predicts the risk of more than 100 diseases and medical conditions



Homocysteine changes the Low Density Lipoprotein (LDL) cholesterol in the body into what is called oxidized LDL It changes coagulation factor levels so as to encourage blood clot formation It causes the smooth muscle cells that support the arterial wall to multiply-part of the atherogenic process. It causes platelets to aggregate-part of the clotting process. The net result is a threefold increase in heart attack risk. If cholesterol and a high-fat diet are the key culprits in heart disease, why haven't we seen more of a reduction in our number-one disease killer over these past several decades?

The main objective of the study was to find out possible association between hyper homocysteinemia and coronary artery disease. Researchers conclude that homocysteine is up to 40 times more predictive than cholesterol in assessing cardiovascular disease risk. Many studies concluded that the risk of arteriosclerotic vascular disease does in fact increase with the homocysteine

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level, regardless of whether cholesterol is normal or elevated. The lack of epidemiological data in our population regarding homocyteine prompted us to undertake this study of defining their association to CAD.

Materials and Methods.
After getting approval from the institutional ethical committee the data for the study has been collected from the inpatients who fulfill the inclusion and exclusion criteria in the department of medicine, L.G. Hospital who were proved as cases of Coronary Artery Disease. It was a Case Control study of 60 people with 30 cases and 30 controls.

Data was collected by patient evaluation which was done by detailed history taking and clinical examination through a structured proforma specially designed for this study.

Inclusion criteria:- All cases of CAD- this includes all patients both sexes estabilished cases of CAD, who give history of myocardial infarction and their echocardiography shows motion wall abnormalities.

Exclusion Criteria:-
- Patients < 18 years
- Patients with renal transplant
- Patients on haemodialysis
- Patients on drugs such as methotrexate, theophylline and niacin.

Controls:-
Sex and age matched controls from general population without any evidence of CAD.

Homocysteine is measured using a simple blood test. It can be measured at any time of day. No special preparations were used during the study for measurement of Homocysteine levels. The Serum sample was separated within 1 hr after blood collection as Homocysteine levels increase ~10% for every hour the serum/plasma is not separated from the RBCs at room temperature which was kept in mind and protocol was maintained throughout the duration of the study.

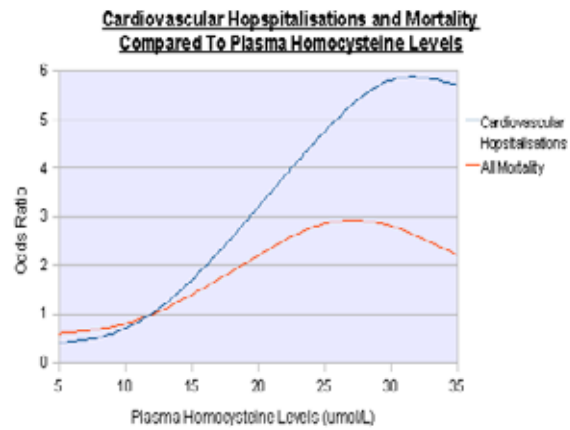
Observation and Discussion
Homocysteine Level 14 +/- 2 micromol/L is considered as normal range.

Table 1. Level of homocystiene in patients with proven Coro nary Artery Disease and Controls without any disease.

Homocysteine level/group	Case	Control	Total
High	22	12	34
Normal	8	18	26
Total			

Odds ratio >4 suggestive of strong association between hyper homocysteinemia and CAD. Homocysteine levels were found to be elevated in the patients of coronary artery disease and there was statistically significant difference in plasma homocysteine levels in cases as compared to controls. Still this association need further verification in large prospective case control study.

Studies in the past have shown that 1/3rd cases of CAD show low prevelance of conventional risk factors such as:-
- Hypertension
- Dyslipidemia
- Sedentary life style
- Diabetes mellitus
- Smoking



The mechanism by which homocyteine exerts its cardiovascular disease effects are now being elucidated. The working hypothesis is that elevated homocysteine levels:-

- Promote oxidant injury to the vascular endothelium – elevated homocysteine levels release extracellular superoxide dismutase from endothelial wall, causing a higher likelihood of atherosclerotic changes to the blood vessel.
- Impairs endothelium dependant relaxation- Hyperhomocysteinemia decreases bioavailability of nitric oxide thus decreasing endothelial vasodilator function.

Homocystiene levels are also increased in other medical conditions of importance like:-
- Raised homocysteine levels are seen in sufferers of chronic fatigue syndrome [CFS]
- Homocysteine accelerates the aging process by shortening telomeres.
- RA patients are 20-30% more likely to have higher homocysteine levels than the normal population.
- In traditionally-treated dialysis patients, 91% of HD and 67% of PD patients have elevated Hcy levels.

Homocysteine should be measured:
- in patients with a history of atherothrombotic vessel diseases
- in elderly subjects
- In adipose subjects
- in vegetarians
- in post-menopausal women
- in renal patients
- in diabetics
- in early pregnancy

The lower the homocysteine level, the lower the risk of developing coronary artery disease and suffering fatal heart attacks and strokes . Homocysteine level is the best single indicator of whether you are going to live a long and healthy life, or die young. A high homocysteine level is a greater risk factor for many health problems Without any doubt, the demand for plasma homocysteine testing will increase in the coming months and years, perhaps explosively.

Risk factor treatment of cardiovascular disease is an accepted clinical practice. Treatment is inexpensive and unobtrusive under medical supervision

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