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PLASMA HOMOCYSTEINE, FOLATE AND VITAMIN B_{12} LEVELS IN SENILE CATARACT

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ABSTRACT

Elevated plasma Homocysteine level is an independent risk factor for age related (senile) cataract. Certain nutritional deficiencies, in particular Folate, Vitamin B_{12}, Vitamin B_6 relate inversely with Homocysteine level. This study was undertaken to evaluate the plasma level of Vitamin B_{12}, Folate, and Homocysteine of cataract patients and to study the interplay between them. Serum Homocysteine level is significantly increased in cataract patients when compared with control ($p< 0.001$). There was a significant decrease in the level of Folate as compared with control ($p<0.001$). There was a negative correlation between Homocysteine vs. Vitamin B_{12} ($p<0.01$) and Folate ($p<0.01$) in the Cataract patients. Our findings suggest that increased plasma Homocysteine level is associated with decreased plasma levels of Folate and VitaminB_{12} in Cataract patients, which might have a possible role in the root cause of cataract pathogenesis.

KEY WORDS

Homocysteine, Senile cataract, Vitamin B_{12}, Folate.

INTRODUCTION

Cataract may be defined as any light scatter opacity in the lens, not necessarily with any demonstrable effect on vision. Cataract that is significant enough to impair vision is the leading cause of blindness worldwide (1). Senile cataract, which is most common in south India, describes any cataract that occurs after the age of 45 and has no evident cause. Age related cataract is a multifactorial disease in which genetic, environmental, socio-economic and biochemical factors may act synergistically. A number of indicators of poor nutrition have been found to be associated with increased risk of cataract in India (2,3). Elevated Homocysteine (Hcy) levels are seen in various eye diseases such as exfoliation syndrome, glaucoma, and cataract (4,5). It has been proposed that Hcy being a putative oxidant is involved in the pathogenesis of endothelial cell injury and atherosclerotic vascular disease (6,7,8). Vitamin B_{12} (Vit B_{12}) and Folate are involved in the metabolism of Homocysteine in methylating it to Methionine. Vit B_{12} and Folate has strong protective effect against formation of Cataractogenesis (9, 10). So, present study was under taken to assess the Hcy levels in age related cataract in relation to the levels of Vit B_{12} and Folate.

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MATERIALS AND METHODS

Present study was conducted in the Department of Biochemistry, Pondicherry institute of medical sciences, Pondicherry. This study included 40 cataract patients and 20 age matched control subjects. Samples were collected from cataract patients admitted in Ophthalmology ward prior to cataract surgery. Cataract patients were selected based on the vision less than 6/18 and visible opacity in the lens. All these patients were above 50 years of age. They were normotensive and non-diabetic as their blood pressure was normal and random blood glucose was below 140mg%. Similarly controls were non-diabetic and non-hypertensive. Both patients and control subjects were not on vitamin, mineral, any drug or such supplementation.

Random blood samples were collected and non-hemolysed plasma was used for all biochemical parameters. Assays were carried out by using well-established and sensitive methods for Homocysteine, Folate, Vitamin B_{12} by Chemiluminescence (Immulite analyzer) using reagent kits obtained from DPC (11). Protein estimation was done by Biuret method (12), Albumin by BCG method (13) and Random blood glucose by GOD/

POD method (14) in the Dadebehring Autoanalyser. The reagent kits for total protein and albumin were obtained from Biosystems S.A.(Costa Brava 30, Barcelona, Spain) and that for blood glucose estimation was obtained from Reckon Diagnostics P.Ltd (Gorwa,Baroda-390 016,India)

Statistical analysis was done by using student's 't' test for comparison between the groups and correlation was done by Pearson correlation in Microsoft excel and P values < 0.05 were considered as statistically significant.

RESULTS

Table 1 : Plasma levels of Homocysteine, Vitamin B_{12}, Folate, Total Protein, Albumin and Random Blood Glucose in control subjects and Cataract patients

Parameters	Control (n = 20)	Case (n = 40)
Age	56.9 ± 6.82	59.85 ± 10.52
Homocysteine (μmol/L)	5.44 ± 3.20	25.06 ± 8.92**
Vitamin B_{12} (pg/ml)	272.85 ± 91.00	201.8 ± 178.60
Folate (ng/ml)	7.06 ± 2.33	3.42 ± 1.73**
Total Protein (gm/dl)	7.685 ± 0.47	7.69 ± 0.58
Albumin (gm/dl)	4.29 ± 0.39	4.24 ± 0.34
Random blood glucose (mg/dl)	99.3 ± 5.77	89.00± 15.8*

Values are expressed as mean ± SD; **P value < 0.001; *P value < 0.05

Our present study aimed at finding the levels of Hcy, Folate, and Vit B_{12} in senile cataract patients. We selected 40 cataract patients and 20 controls. Table 1 shows comparisons of Hcy, Vit B_{12} and Folate levels in cataract patients with control subjects. Statistically significant increase in the level of Hcy ($p<0.001$) was found in cataract patients as compared to control subjects. Also there was a significantly decrease in the level of Folate ($p<0.001$) and random blood glucose ($p<0.05$) in cataract subjects as compared with controls.

Table 2 reveals the pair wise correlation analysis in cataract patients showed following results. Hcy was negatively correlated with Vit B_{12} ($r = - 0.68$) and Folate ($r = - 0.47$).

Table 2 : Pairwise correlation analysis in cataract patients

Pairwise correlation of parameters	r value
Hcy and Vit B_{12}	-0.68**
Hcy and Folate	-0.47*

**P value < 0.001; *P value < 0.001

DISCUSSION

Homocysteine is derived from the dietary methionine. In normal person Homocysteine is metabolized to Methionine with the help of Folate and Vit B_{12}. It may also be converted to cystathionine by cystathionine -b-synthase. Normal level of Hcy is 5-12 μmol/L. Under certain circumstances Hcy level is increased in blood. Those are 1) Vit B_{12}, Folate deficiency and heterozygous or homozygous trait for Methyl-tetrahydrofolate reductase 2) Heterozygous or homozygous trait for cystathionine -β-synthase activity 3) Renovascular stenosis and volume retention. In our study we found an increased level of Hcy, which correlate with age (15), Folate and Vit B_{12} deficiency (16). It is well known that hyper homocysteinemia produces oxidative stress by generating reactive oxygen species spontaneously (17). Sulfhydryl group of Homocysteine is believed to act catalytically with ferric and cupric ions in a mixed function oxidation system to generate hydrogen peroxide, oxygen radicals (18,19). Superoxide anion, hydrogen peroxide, and hydroxyl radical are produced during auto-oxidation of Homocysteine (20,21). These could promote lipid peroxidation and damage vascular endothelium. Hyperhomocysteinemia is an independent graded risk factor for atherosclerotic disease in coronary, cerebral and peripheral blood vessels (8)

Contemporary hypothesis considers the oxidative stress as a crucial event in age related processes as well as in the age related cataract. Sulfhydryl group of lens protein (Crystallins) is the target of enhanced oxidative stress seen in senile Cataract (22). Recently, it has been shown that post translational modification of lens proteins play crucial role in the formation of age related cataract and also found that oxidized amino acids accumulate in cataractous lenses which are probably due to altered redox balance, thus contribute to lens opaciation (23).

In our study, we found there was a significant decrease in Folate level in cataract patients as compared with controls.Vit B_{12} was also decreased but not statistically significant. This is in accordance with previous study, which reveals low Folate as the strong determinant of Hyperhomocysteinemia in older age (16). In the present study, Hcy level correlates negatively with Vit B_{12} and Folate levels which is in agreement with previous studies proving low Folate, Vit B_{12}, Vit B_6 and older age were all independently associated with elevated Homocysteine (16). Vit B_{12}, Folate supplements has strong protective influence on reducing the prevalence of Cataractogenesis (9).

Accumulating evidences suggest that, prolonged hyperglycemia seen in type 2 diabetes mellitus enhances the glycation of proteins and may be the root cause of cataract formation (24,25). But in our study, random blood glucose

levels of patients were within the reference range and even it showed statistically significant decrease than control group. This suggests that elevated Homocysteine level even in the absence of hyper glycemia or any other virtual metabolic and nutritional disorder as evident by total protein and albumin levels, may play a possible role in the cataract formation. Hyperhomocysteinemia with low Vit B_{12} and Folate levels in older age group can be independent risk factor for Senile Cataract, which might be mediated through oxidative stress. Further studies are needed to unravel the role of oxidative stress arising from elevated Hcy level in older age groups in senile cataract formation.

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