

Research article

Plasma homocysteine, serum vitamin B12 and folic acid status in newly detected schizophrenic patients of eastern India**Neelam Mehta¹, Itishri Jena², Subhashree Ray², Sudeshna Behera², Subrat Kumar Tripathy², Sarthak Ranjan Nayak², Bratati Singh²**¹Department of Pathology, TATA Main hospital, Jamshedpur, 831 001, Jharkhand, India²Department of Biochemistry, IMS & SUM Hospital, Bhubaneswar, 751 003, Odisha, India**(Received: December 2022****Revised: March 2023****Accepted: April 2023)**Corresponding author: **Itishri Jena**. Email: dritishrijena82@gmail.com**ABSTRACT**

Introduction and Aim: Schizophrenia is a disastrous mental disorder that causes chronic disability. Even after many years of scientific research the underlying pathophysiology of this disorder is unclear. Deficiency of vitamin-B12 and folic acid are associated with many mental disorders. Increase in homocysteine increases risk of several disorders including schizophrenia.

Materials and Methods: Plasma homocysteine, serum vitamin B12 and folic acids were measured in 30 newly diagnosed schizophrenic cases and values were compared with 50 age and sex matched controls.

Results: Plasma homocysteine was significantly increased in schizophrenic cases in comparison to controls, vitamin B12 was significantly decreased in cases in comparison to controls. Increase in homocysteine in cases showed a significant negative correlation with vitamin-B12 of cases.

Conclusion: This study proves an association between increase in homocysteine and decrease in vitamin B12 with schizophrenia.

Keywords: Schizophrenia; homocysteine; vitamin B₁₂; folic acid.

INTRODUCTION

Mental disorders contribute to considerable social and economic burden worldwide, both in terms of morbidity and mortality (1). Schizophrenia is a devastating mental disorder that causes chronic disability (2). The disorder is characterized by symptoms like delusions, hallucinations, uncontrolled speech, and behavior along with negative symptoms (3). Many people with schizophrenia have difficulties in their cognitive or thinking ability, such as attention, memory, and problem-solving ability. The disorder affects about 24 million people globally which accounts for 1 case in 300 people (4). According to the survey of mental illnesses done by the Indian State-Level Disease Burden Initiative as part of GBD (Global Burden of Disease) 2017 the prevalence of schizophrenia in India is 0.3% and DALY (disability adjusted life years) loss due to the disease is 9.8% (5).

Schizophrenia is a challenging disorder to the psychiatrist. Even after many years of scientific research the underlying pathophysiology of this multifaceted disorder is unclear. This is known to be a complicated and chronic disorder affecting the brain, that perhaps is caused by multiple gene interactions, which are influenced by environmental factors resulting in aberrant neurodevelopment and/or neurodegeneration (6-8). Approximately 50 years ago it was suggested that some abnormal methylated compounds have affected mental status and behavior, resulting in speculations that some amino acids

linked with methylation pathways may have a role in development of schizophrenia (9,10). Initial supporting data for association of abnormal methylation pathway in the etiopathogenesis of this disorder are from finding that therapy with high per day doses of methionine, resulted in worsening symptoms of schizophrenia (11). There are many other studies supporting alteration of plasma homocysteine level in major psychiatric disorders including schizophrenia (12-15).

Homocysteine is like amino acid cysteine, which is a sulfur containing non-protein amino acid formed during the metabolism of methionine (16,17). Increase in plasma homocysteine is associated with many diseases. Plasma homocysteine level is again dependent upon the vitamin B12 and folic acids as the metabolism of methionine, homocysteine, folic acid, and vitamin B12 are interrelated (18). There are also several other studies suggesting alteration in folic acid and vitamin B12 in schizophrenic patients (19,20).

Taking into consideration all the above facts this study was done to estimate plasma homocysteine, serum vitamin B12 and folic acids level in newly detected schizophrenic cases.

MATERIALS AND METHODS

This study took place in the Biochemistry Department, IMS & SUM Hospital, Bhubaneswar, Odisha, in collaboration with the Department of Psychiatry. The research protocol was approved by

the Ethical Committee of the Institute (IMS SH/IEC/2014/65). It was a hospital based, cross-sectional, case-control study comprising 30 patients and 50 controls. Individuals between 20-60 years of age visiting the Psychiatry Department of IMS and SUM Hospital as outpatients or admitted on an in-patient who were diagnosed with schizophrenia for the 1st time were taken as cases. Age and sex matched healthy individuals visiting the same hospital were taken as controls. Individuals who had history of epilepsy, head injury, altered sensorium, memory deficits, recent high fever, delirium, focal neurological deficits, any type of visual, hearing and/or any sensory deficits, mental retardation, who had undergone ECT in past 6 months, pregnancy or lactation, substance or alcohol abuse, intake of drugs altering serum homocysteine level, vitamin supplements in any form and significant medical illness like diabetes, hypertension, chronic kidney disease, coronary artery disease were excluded from this study. Diagnosis of schizophrenia was made using the International Classification of Diseases- 10, Diagnostic Criteria for Research (ICD-10 DCR) Guidelines.

Informed consents were taken from all participants before enrolling them into this study. Venous blood was withdrawn from all after overnight fasting. EDTA plasma sample was used for homocysteine and serum was used for folic acid and vitamin B12 estimation. Estimation of plasma homocysteine was done using Cobas integra 400 plus, using the principle of enzymatic assay, where as estimation of

serum folic acid and vitamin B12 were done by Cobas e-411 using the principle of direct competitive chemiluminescence immunoassay in both.

Data were analyzed using SPSS version 22.0. Variables are expressed as mean $\pm$ SD. Student's unpaired t-test was used to analyze differences between two variables and relationships between the variables were analyzed through Pearson's correlation coefficient. $P < 0.05$ was taken to be statistically significant.

RESULTS

30 newly diagnosed schizophrenic cases and 50 age and sex matched healthy controls were included in the study. Table 1 shows the comparison between plasma homocysteine (HCY), serum vitamin B12 (vit-B12) and folic acids (FA) between cases and controls. There is a statistically significant (p -value < 0.001) increase in plasma homocysteine in schizophrenic cases in comparison to control, whereas there is a statistically significant (p -value < 0.001) decrease in serum vitamin B12 in schizophrenic cases in comparison to control. There is no statistically significant difference between folic acid between cases and controls. Table 2 shows the correlation of serum vitamin B12 and folic acid with plasma homocysteine. There is a significant negative correlation between serum vitamin B12 and plasma homocysteine (r -value -0.20, p -value 0.04), whereas correlation between serum folic acid and plasma homocysteine acid is not significant.

Table 1: Biochemical parameters in the studied groups

Parameters	Cases n= 30	Controls n=50	p-Value
Plasma Homocysteine (μ mol/L)	15.48 $\pm$ 2.71	9.09 $\pm$ 0.83	<0.001
Serum Vitamin B12 (pg /ml)	256.56 $\pm$ 97.41	686.04 $\pm$ 105.99	<0.001
Serum Folic Acid (ng/ml)	8.26 $\pm$ 1.22	7.93 $\pm$ 0.84	NS

NS: Not significant (p -value > 0.05)

Table 2: Correlation of homocysteine with vitamin B12 and folic acid

Parameters	Homocysteine	
	r-Value	p-Value
Vitamin B12	- 0.20	0.04*
Folic Acid	- 0.47	NS

* p -value < 0.05 , NS: Not significant (p -value > 0.05)

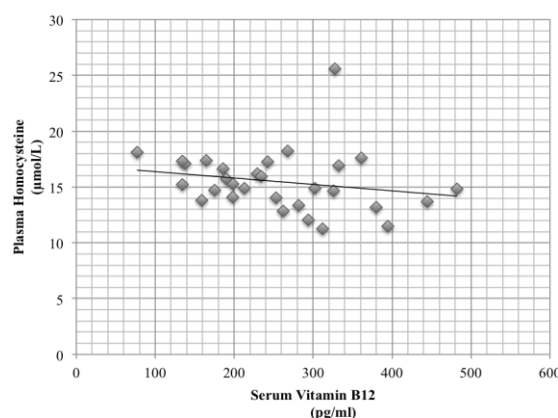


Fig. 1: Correlation of plasma homocysteine with serum vitamin B12 in cases (r -value -0.20, p -value 0.04).

DISCUSSION

Folic acid and vitamin B12 deficiencies are linked to neuropsychiatric symptoms like neuropathy, myeloneuropathy and impaired cognitive functions. Vitamin B12, in the form of methyl-cobalamin acts as cofactor for methionine synthase. This enzyme catalyzes the reaction of formation of methionine from homocysteine, where N⁵-methyl-tetrahydrofolate acts as donor of methyl group. The metabolism of folic acid, vitamin B12 and methionine are interrelated, abnormal metabolism or deficiency of one may lead to alteration of all other parameters (18-20).

Our study demonstrated an increase in plasma homocysteine in schizophrenia patients which is also statistically significant. This finding is like the findings of Taweel *et al.*, (2), Tomioka *et al* (19). Blood homocysteine level is dependent on transmethylation and trans-sulfuration associated with methionine and cysteine metabolism. Several factors like genetics, diet, lifestyle, and many drugs increase blood homocysteine. Hyperhomocysteinemia increases the risk of neurovascular disorders, epilepsy, migraine, dementia, and developmental disorders. The underlying mechanism behind this may be due to inflammation with release of several cytokines, oxidative stress, endoplasmic reticulum stress, DNA damage and protein homocysteinylation. Hyperhomocysteinemia induced inflammation may also play role in damaging blood brain barrier and possible neurotoxicity (17).

Our study also showed a decrease in serum vitamin B12 which is significantly and negatively correlated to plasma homocysteine. This may be due to interrelation between metabolisms of the two parameters as discussed earlier (18-20).

CONCLUSION

This study demonstrated a significant association between hyperhomocysteinemia and vitamin B12 deficiency with schizophrenia. But whether these associations are the cause or effect, yet to be proved. Prospective study with a large sample size is needed to further validate this association.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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