



ALTERATION IN PLASMA HOMOCYSTEINE, VITAMIN D, FOLATE AND VITAMIN C CONCENTRATION IN SCHIZOPHRENIC PATIENTS DUE TO GLUTEN FREE DIET

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ABSTRACT

Schizophrenia is a chronic, psychotic mental disorder. Around 1% of people worldwide are affected by this disease. The function of a healthy brain is dependent on balance nutrition, including Vitamins in the diet. The Homocysteine and Folate levels are negatively interrelated with each other in the schizophrenic patients. Former studies have suggested that the gluten in daily diet is harmful to schizophrenics. So, the present study is designed in an effort to

determine alterations in Plasma Vitamin D, Folate, Vitamin C and Homocysteine in schizophrenics on gluten free diet. Blood samples of 10 males and 10 females schizophrenic patients, placed on a gluten-free diet and 10 males and 10 females placed on normal diet were collected with EDTA and then centrifuged for collection of plasma with age range from 20-30 years. Homocysteine, Vitamin D and Folate were determined by commercially available kit. The vitamin C was determined by stiochiometric oxidation reduction reaction between ascorbic acid (and isoascorbic acid) and oxidizing agent (2, 6-dichlorophenol indophenol). Finally appropriate statistical analysis was applied to analyze the data. In schizophrenics mean plasma Homocysteine concentration was significantly high while Vitamin C, D and Folate were significantly low due to gluten free diet. The patients included in this study showed low vitamins levels and it is possibly due to low vitamins content in gluten-free

products. Therefore, vitamins enriched gluten-free products could be beneficial for schizophrenics.

KEYWORDS: Schizophrenia, Homocysteine, Gluten, Vitamin, Folate.

1. INTRODUCTION

Schizophrenia is a rigorous form of mental illness about 7 per 1000 of the young population is disturbing by this harmful disease generally in the 15-35 years age group. The incidence is low (3 per 10,000), the occurrence is high due to chronicity. In worldwide about 24 million people are affected by this disease. The treatment of this disorder is possible in its early stages. The patients suffering from this disease have an increased threat of early death; they die at least 10 years before than the people of same age group.^[1] It is a multifactor disorder of mind. These factors include biochemical, social, genetic and environmental aspects.^[2] The chances of its development in the population due to genetic factor is around 50% in monozygotic co-twins, approximately 9% when the disease is dominant among first degree families and the opportunity of developing schizophrenia in the off-springs, when the mother is schizophrenic is about 25-50%.^[3] Biological factors include complications which are related to birth such as maternal influenza during winter-spring,^[4] bleeding in pregnancy, obstetric complications during delivery^[5] poor nutrition in early gestation,^[6] maternal illness e.g. thyroid disorder; diabetes mellitus and many other fetal complications like low birth weight babies and babies have small head circumference. Temperature variation at the time of birth, family with lots of clashes and low social class is including in environmental factors. There is reasonably reliable evidence that 5–8% child who born in winter and spring, later develop schizophrenia.^[7] Urban birth is associated with greater risk of schizophrenia instead of later urban living.^[8] The first psychological incident commonly occurs in late adolescence or early adulthood. There are three quarters of persons with schizophrenia who develop the disease between 16 and 25 years of age. Beginning is exceptional after the age of 30 and exceptional after age 40. Men usually develop the illness at age 18–25, however in women; the mean age of beginning is 25–35.^[9] Symptoms of this disorder include hallucinations, delusions, movement disorders, cognitive impairment, and lack of joy in everyday life. They may have opinions of reality that are extremely different from reality seen and shared by others around them. Schizophrenic patients may feel frightened, nervous and chaotic. Hallucinations can occur in schizophrenic patients. The most common type of hallucination in schizophrenia is any sensory form auditory; visual, tactile – hearing voices that other

people do not hear. These patients often have false and illogical beliefs that they are being angry, poisoned or conspired against.^[10] In Young males the onset of schizophrenia is earlier and they suffer worse than females because estrogen probably acts as biological neuroleptic in females avoiding them from schizophrenia. Actually females show affinity to develop schizophrenia after child birth or menopause when serum estrogen level is definitely low.^[3]

Nutrition as a treatment constituent for schizophrenia is a new concept. These patients have a better recovery rate than on a diet lacking some of the nutrients. This is equally true for any serious physical disease. There are many etiologies for the schizophrenia disease. It is recommended that these include mineral deficiency, Vitamin B-3 and B-6 dependency, especially Zinc, and Cerebral reactions.^[11] People with schizophrenia took less exercise. The reasons of their sedentary lifestyle have not been confirmed but reasons that are sedative medication, aspects of the illness and lack of opportunity and awareness may be important^[4,12,13] stated that schizophrenic patients have Celiac and gluten sensitivity. These patients have higher than assumed titers of antibodies link to gluten sensitivity and Celiac Disease. Among these patients, 23.1% had increase levels of IgA-antigliadin antibodies (IgA-AGA) when compared with 3.1% of the normal population. McCreddie et al.^[12] stated that schizophrenic patients made considerably poor option of diet characterized by low fiber and increase fat intake, smoked more profoundly and took less exercise than the normal. Schizophrenics' women were considerably more prone to be over weight than women in the control group. Their fruit and vegetable consumption is less than the suggested intake and only some patients made satisfactory choices of diet. The Folate deficiency was noticed in these patients. The Homocysteine levels of patients with schizophrenia were higher than control group were found.^[14] The Homocysteine and Folate levels were more negatively associated with each other in schizophrenic patient. Negligible importance has been given to the poor dietary status of schizophrenic patients and dietary implementations have inclined to centre on the effect of additional omega-3 fatty acid or vitamins supplementation on mental health with changing consequences.^[15] The physical health and overall lifestyle of these patients are relatively seldom studied. Alteration in plasma Homocysteine, Creatinine, Amino acids, Vitamin B12, Vitamin D and Vitamin C has been reported by many Scientists in schizophrenic patients on gluten free diet.^[13,14,16] However, no work has been reported on these parameters in our socioeconomic status. The present research is designed in an effort to determine alterations in plasma Vitamins and Homocysteine in schizophrenics on gluten free diet.

2. METHODOLOGY

2.1 Schizophrenic Volunteers Selection Criteria

Following groups were made for this study:

Group I:	Males	(n = 10)	Normal age	(20-30 years)
Group II:	Males	(n = 10)	Schizophrenia age	(20-30 years)
Group III:	Females	(n = 10)	Normal age	(20-30 years)
Group IV:	Females	(n = 10)	Schizophrenia age	(20-30 years)

Schizophrenic patients were also addicted to alcohol, smoking and drugs. Participants were given a Gluten Free Diet for 25 days.

2.2 Intervention Details

Before the initiation, the whole project was submitted to G.C. University, Faisalabad Ethical Review Committee for approval and after approval selected participants were given a Gluten Free Diet for 25 days. A consent form was dully signed by the participant that showed their willingness for the project and confidence on experimental norms. Moreover, all the subjects received similar dietary instruction on a gluten-free diet, and this instruction was provided by the same dietitian. Every effort was made to see that the patients adhered to a strict gluten-free diet. All the patients were seen routinely by the same dietitian for at least one follow-up visit.

2.3 Inclusion Criteria

Subjects were of either gender and of any race, with an age range of 20- 30. A best estimate diagnostic approach was utilized in which information from the Structured Clinical Interview was supplemented by information from family informants, previous psychiatrists, and medical records to generate a diagnosis. All the patients were clinically stable and on the same antipsychotic for at least two months with an unchanged dose for the prior four weeks. Normal subjects were apparently healthy.

2.4 Exclusion Criteria

Pregnant or lactating women were excluded. Pregnancy was determined by pregnancy test. Lactating was determined by participant report.

2.5 Sample Collection

A total of forty (40) blood samples (EDTA added) were collected from normal and schizophrenic individuals and centrifuged immediately. Plasma was separated in small aliquots and stored at -4°C till analysis.

2.6 Physical Parameters

The blood samples of male and female individuals suffering from schizophrenia were collected from District Head Quarter Hospital (DHQ), Faisalabad, Mental Hospital, Lahore, Pakistan Institute of Medical Sciences (PIMS), Islamabad and Benazir General Hospital Rawalpindi. The following physical parameters were studied:-

Age (years): Age of the patients was taken from the record of the hospital.

Height (inches): Height was measured bare footed, using measuring tape.

Weight (kg): Each patients was weighed bare footed and in light clothes using ordinary weighing machine.

Body Mass Index (BMI; kg/m²): BMI was calculated by using following formula:

$$\text{BMI} = \frac{\text{Weight}}{(\text{Height})^2}$$

Body Temperature (°F): Body temperature was recorded by using thermometer.

Blood Pressure (mm/Hg): Systolic and diastolic blood pressure was taken using a sphygmomanometer.

2.7 Plasma Homocysteine

Homocysteine was determined by kit method. Total concentration was estimated by the standard curve made from the standards supplied with the kit. Total Homocysteine (tHcy) was measured by a Homocysteine microtiter plate assay for the determination of tHcy in serum of normal and patients. Serum samples were prepared in polyethylene culture tubes with a reducing agent tris (2-carboxyethyl) phosphine hydrochloride (TCEP) to reduce the protein bound Hcy to free Hcy that was subsequently converted to S-adenosyl-L-homocysteine (SAH) by SAH-hydrolase and quantitated by horseradish peroxidase (HRP-SA) competitive assay (Diazyme, Cat. No. DZ012A, Diazyme Laboratories).

2.8 Plasma Vitamin D

Vitamin D was measured by kit method. The test kit was (OCTEIA 25-(OH)D, Immuno Diagnostic Systems, Boldon, UK) a competitive binding protein assay for the measurement

of 25-OH Vit D. Plasma samples were centrifuged within one hour and then stored samples at -20 °C. Lipemic samples may give erroneous results and must be centrifuged for 10 min. at 13000 rcf (rotational centrifugal force = g) to separate the lipids from the plasma. Samples were mixed well before assaying. A calibration curve was constructed from the standards. Results of the samples were read from that calibration curve.

2.9 Plasma Folic Acid

The kit Chiron Diagnostics was used to assay the Folic acid (FA) in the sample of Human's serum, and other related tissue Liquid. The concentration of Human folic acid in the samples was then determined by comparing the original density of the samples to the standard curve.

2.10 Plasma Vitamin C (mg/dl)

The procedure was based on stiochiometric oxidation reduction reaction between ascorbic acid (and isoascorbic acid) and milk oxidizing agent (2, 6-dichlorophenol indophenol) which was transformed from a strong colored form to its leucoderivate. The titration reagent was gradually added to sample extract. The ending was detected by the color of solution due to slight excess of reagent.

Calculated ascorbic acid or vitamin C using the following equation:

$$\text{Milligrams of ascorbic acid per 100 ml} = \frac{\text{dye conc.} \times \text{milliliters titrated}}{10\text{ml of sample}}$$

2.11 Statistical Analysis

Data thus obtained was analyzed using analysis of variance.^[17] To determine the difference between gender and groups, Duncan Multiple Range (DMR) tests.^[18]

3. RESULTS AND DISCUSSION

3.1 Plasma Homocysteine (μmol/L)

Analysis of variance of Homocysteine of male and female of normal and schizophrenic individuals has been given in Table 1a and 1b. Overall mean Homocysteine of schizophrenic individuals was ($P \leq 0.01$) significantly increased as compared to normal individuals irrespective of their gender (Fig. 1). Overall mean Homocysteine was non-significantly different in males and females irrespective of their groups (Fig. 2). Gender × groups interaction means showed non-significant differences (Fig. 3). In Schizophrenic patients

plasma Homocysteine was increased 98.89% in male and 86.32% in female as compared to normal (Fig. 4).

Table 1(a): Analysis of variance of plasma Homocysteine of male and female of normal and schizophrenic individuals.

F-Value	Means Squares	Sum of Squares	Degree of Freedom	Source of Variation
79.082 **	855.625	855.625	1	Group
0.187 NS	2.025	2.025	1	Gender
0.058 NS	0.625	0.625	1	Group x Gender
	10.819	389.500	36	Error
		1247.775	39	Total

** = Significant at $P \leq 0.01$

NS = Non-significant

Table 1(b): Mean Homocysteine ($\mu\text{mol/L} \pm \text{SE}$) of male and female of normal and schizophrenic individuals

Overall Mean	Schizophrenia	Normal	Gender
13.40 \pm 1.27	17.90 \pm 1.03	8.90 \pm 1.13	Male
12.95 \pm 1.29	17.70 \pm 1.04	8.20 \pm 0.95	Female
13.18 \pm 0.89	17.80 \pm 0.71A	8.55 \pm 0.72B	Overall Means

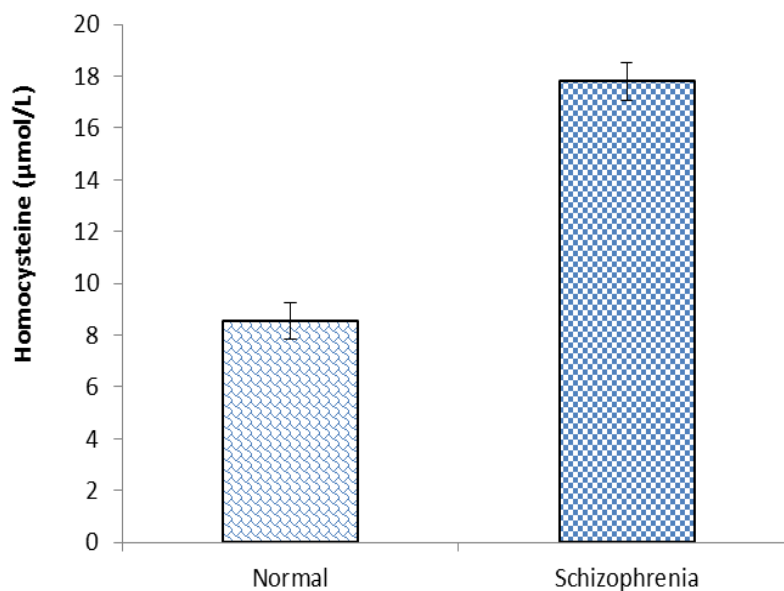


Fig. 1: Overall mean of Homocysteine ($\mu\text{mol/L} \pm \text{SE}$) of normal and schizophrenia individuals irrespective of their gender

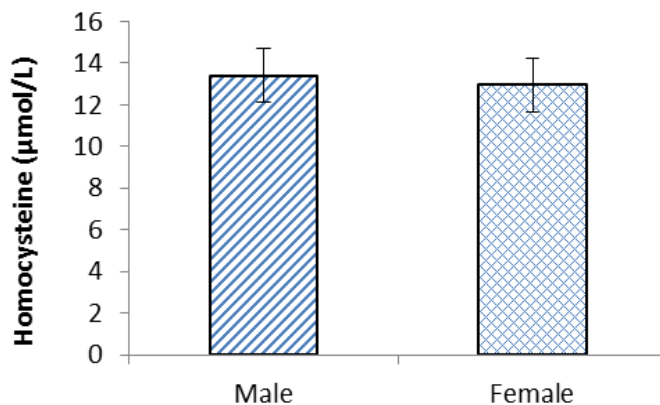


Fig. 2: Overall mean of Homocysteine ($\mu\text{mol/L} \pm \text{SE}$) of male and female irrespective of their group.

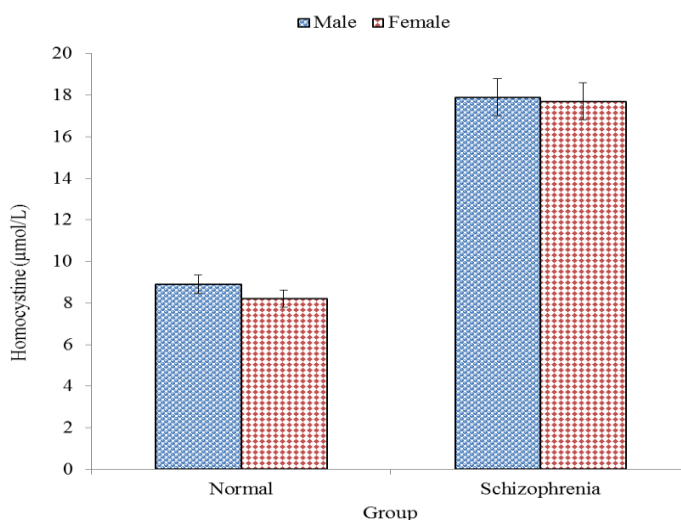


Fig. 3: Mean of Homocysteine ($\mu\text{mol/L} \pm \text{SE}$) of male and female of normal and schizophrenic individuals

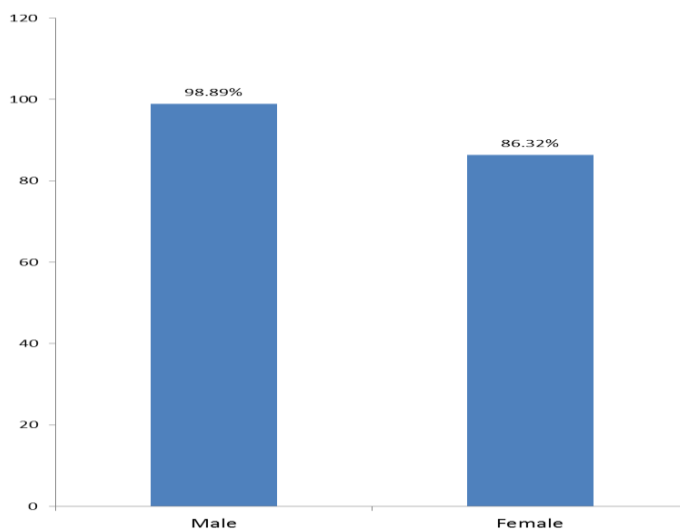


Fig. 4: Percentage of Homocysteine ($\mu\text{mol/L}$) in schizophrenic male and female patients as compared to normal

Plasma Homocysteine level was significantly higher in schizophrenic patients as compared to normal individuals. The high Homocysteine level may be due to a genetic fault associated with methylation inspite of the patient's nutritive conditions, such as the level of Cobalamine or Folate or psychotropic-drug administration.^[19] Another reason of increased Homocysteine level which is postulated ; that the higher serum Homocysteine levels in the patient group may be due to their high stress levels, which permit poisonous materials to easily pass through their serum brain barriers (BBBs).^[20]

The metabolism of Homocysteine is most highly affected by the Folate level and also by numerous environmental factors, such as food, in addition to genetic factors, typically MTHFR.²¹ An increase in plasma Homocysteine is brought about by hypertension, age, vitamin B2, the male gender, vitamin B6, Creatinine, smoking, alcohol consumption, and coffee. Also seeing the option that the patients in our study had a low-Folate diet because they were hospitalized in a mental hospital, where a diet rich of Folate was inaccessible and they are also on gluten free diet which is probably low in Folate so it was assumed that there could be many schizophrenic patients who have a Folate-sensitive Homocysteine metabolism disorder.^[22] The schizophrenic patients who have a Folate-sensitive Homocysteine metabolism disorder, in these patients the plasma Homocysteine level was considerably higher.^[6]

3.2 Plasma Vitamin D (ng/ml)

Table 2a and 2b represent the analysis of variance of plasma Vitamin D concentration of male and female of normal and schizophrenic individuals on gluten free diet. Gender ($P \leq 0.01$) and groups ($P \leq 0.01$) were significantly different. Overall mean plasma vitamin D concentration of schizophrenic individuals was significantly low than normal individuals, irrespective of their gender (Fig. 5). Overall mean plasma vitamin D concentration was significantly low in females as compared to males irrespective of their groups (Fig. 6). However, gender \times groups interaction means were non-significantly different (Fig. 7). In Schizophrenic patients plasma vitamin D was decreased 6.09 % in male and 5.11% decrease in female as compared to normal (Fig. 8).

Table 2(a): Analysis of variance of vitamin D of male and female of normal and schizophrenic individuals.

F-Value	Means Squares	Sum of Squares	Degree of Freedom	Source of Variation
48.803 **	313.488	313.488	1	Group
9.117 **	58.564	58.564	1	Gender
0.374 NS	2.401	2.401	1	Group x Gender
	6.424	231.249	36	Error
		605.702	39	Total

** = Significant at $P \leq 0.01$

NS = Non-significant

Table 2b: Mean vitamin D (ng/ml \pm SE) of male and female of normal and schizophrenic individuals.

Overall Mean	Schizophrenia	Normal	Gender
18.97 \pm 0.87	15.93 \pm 0.41	22.02 \pm 0.97	Male
16.55 \pm 0.83	14.00 \pm 0.31	19.11 \pm 1.17	Female
17.76 \pm 0.62	14.97 \pm 0.33B	20.56 \pm 0.81A	Overall Means

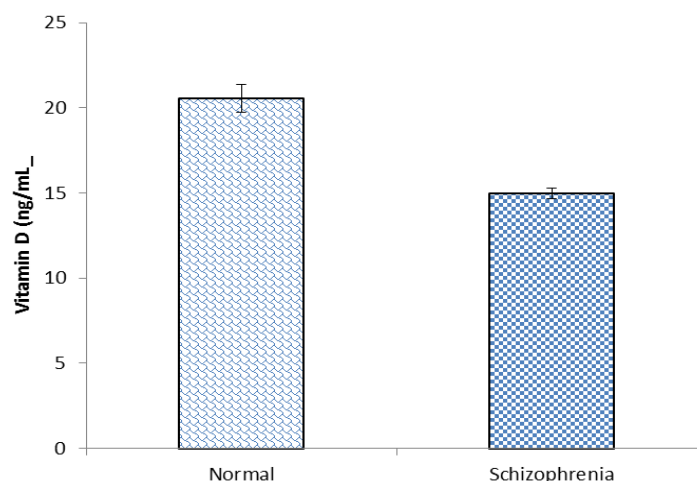


Fig. 5: Overall mean of vitamin D (ng/mL \pm SE) of normal and schizophrenia individuals irrespective of their gender.

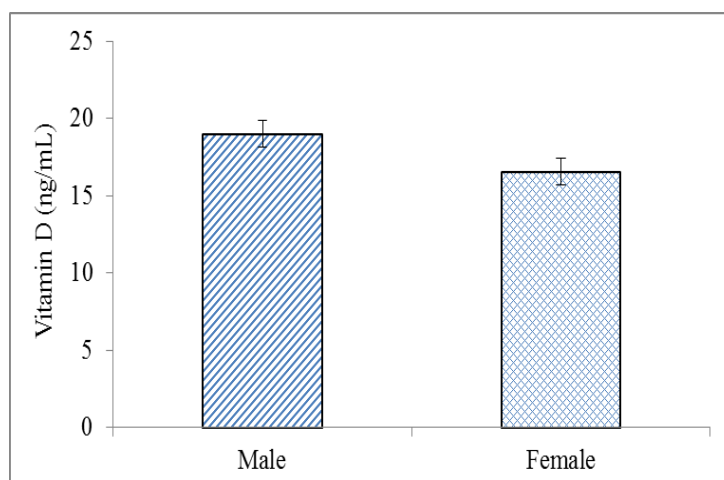


Fig. 6: Overall mean of vitamin D (ng/mL \pm SE) of male and female irrespective of their group.

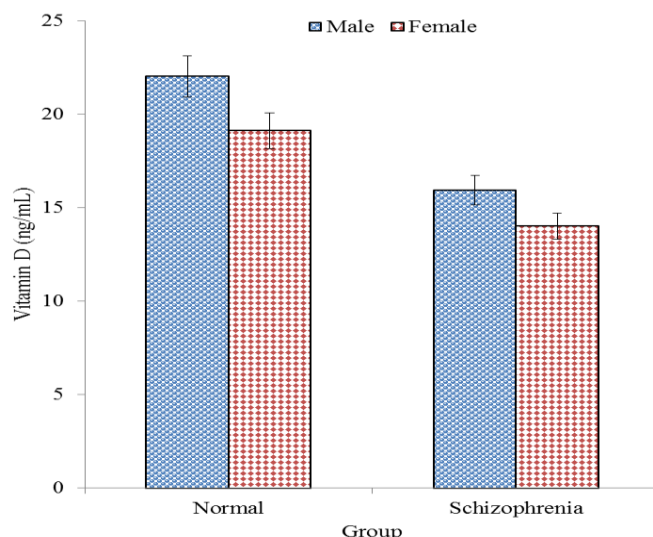


Fig. 7: Mean of vitamin D (ng/mL \pm SE) of male and female of normal and schizophrenic individual

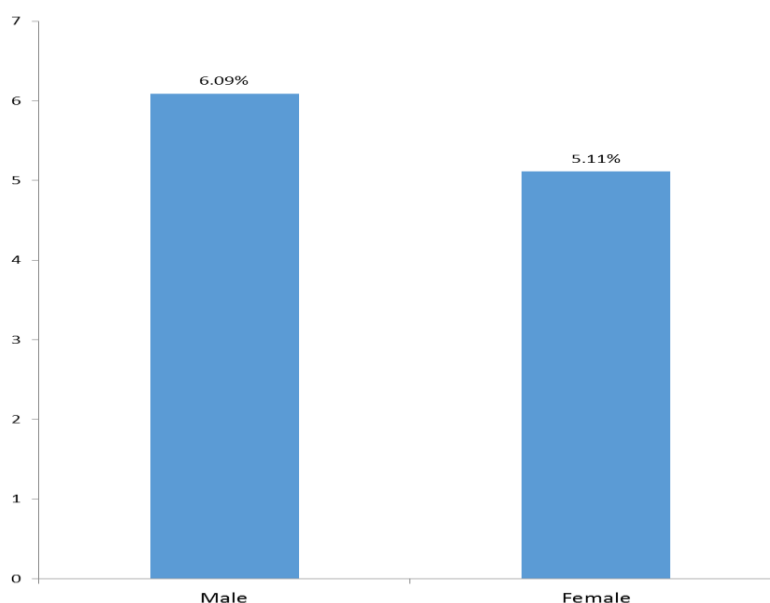


Fig. 8: Percentage of vitamin D (ng/mL) in schizophrenic male and female patients as compared to normal.

In present study the level of plasma Vitamin D was significantly decreased in patients with schizophrenia as compared to normal. The reason of low vitamin D may be that these patients are often suffering from celiac disease. The villi which help to blend and absorb fat are often worn with celiac disease and due to which the absorption of fat absorption is compromised. The failure to sufficiently absorb fat will not only disturb absorption of vitamins E, D and A, but it will extremely affect hormone, creating hormonal imbalance as well because Hormones are made from cholesterol – fat.^[23]

Gluten-free products are often low in Vitamin B, Calcium, Vitamin D, Iron, Zinc, Magnesium and Fiber.^[24] Also the gluten-free diet can be a low nutrient diet; so it may be the reason of decreased vitamin D concentration in schizophrenic patients on gluten free diet.^[25] Another factor that may contribute to decreased vitamin D concentration in the plasma of schizophrenic patients is the low sun exposure of large areas of the body because these patients are hospitalized so the exposure to the sun is limited or a low intake of calcium and vitamin D.^[26] One other factor that may contribute to low vitamin D concentration in schizophrenic patients the Level of vitamin D may be low because most commercial gluten-free products are not enriched with extra vitamins.^[27] Cigarette smoking is frequently observed in patients with schizophrenia^[28] and Smokers have a tendency to take a diet that is deficient in vitamin D. Present study showed that plasma Vitamin D concentration was significantly low in females as compared to males. Decreased in Vitamin D in females may be due to the reason that males generally had a higher intake than did females.^[29]

3.3 Plasma Vitamin C (mg/dl)

Table 3a and 3b represent the analysis of variance of plasma vitamin C concentration of male and female of normal and schizophrenic individuals on gluten free diet. Gender ($P \leq 0.01$) and groups ($P \leq 0.01$) were significantly different. However gender \times groups interaction means were non-significantly different. Overall mean plasma vitamin C concentration of schizophrenic individuals was significantly low than normal individuals, irrespective of their gender (Fig. 9 and Fig. 10). On the other hand overall mean plasma vitamin C concentration was non-significantly low in females as compared to males irrespective of their groups (Fig. 11). In Schizophrenic patients plasma vitamin C was decreased 27.65 % in male and 26.7% in female as compared to normal (Fig. 12).

Table 3(a): Analysis of variance of vitamin C of male and female of normal and schizophrenic individuals.

F-Value	Means Squares	Sum of Squares	Degree of Freedom	Source of Variation
13.894**	2.172	2.172	1	Group
0.484NS	0.076	0.076	1	Gender
0.018NS	0.003	0.003	1	Group x Gender
	0.156	5.626	36	Error
		7.877	39	Total

NS = Non-significant

** = Significant at $P \leq 0.01$

Table 3(b): Mean of vitamin C (mg/dl±SE) of male and female of normal and schizophrenic individuals.

Overall Mean	Schizophrenia	Normal	Gender
1.356±0.092	1.321±0.122	1.391±0.144	Male
0.890±0.081	0.838±0.097	0.942±0.132	Female
1.123±0.071	1.080±0.094B	1.167±0.108A	Overall Means

Mean sharing similar letter in a row or in a column are statistically non-significant ($P>0.05$).

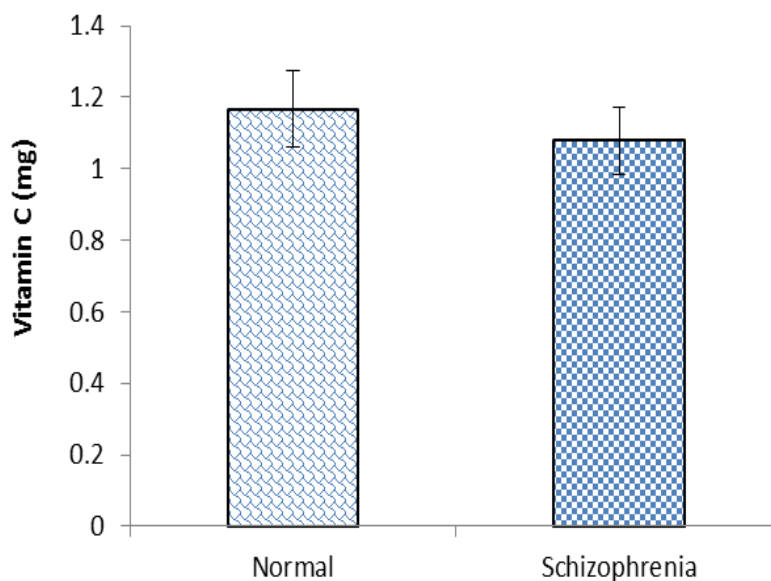


Fig. 9: Overall mean of vitamin C (mg/dl±SE) of normal and schizophrenia individuals irrespective of their gender.

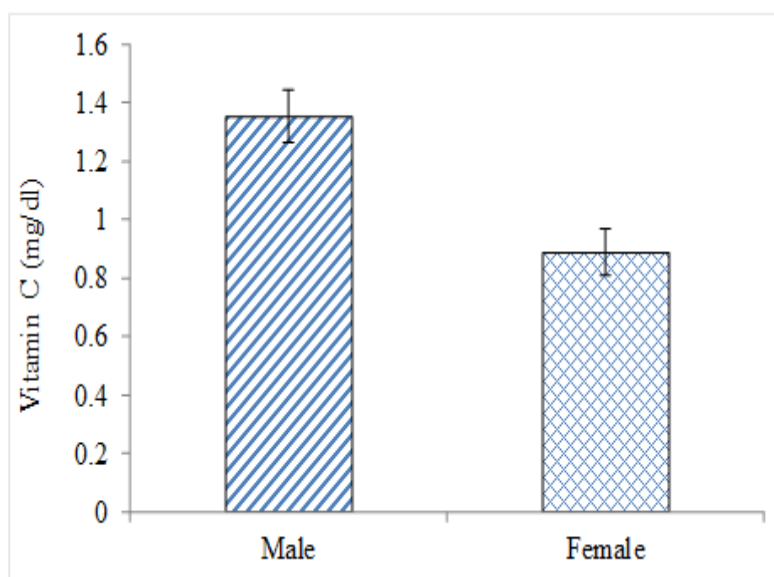


Fig. 10: Overall mean of vitamin C (mg/dl±SE) of male and female irrespective of their group

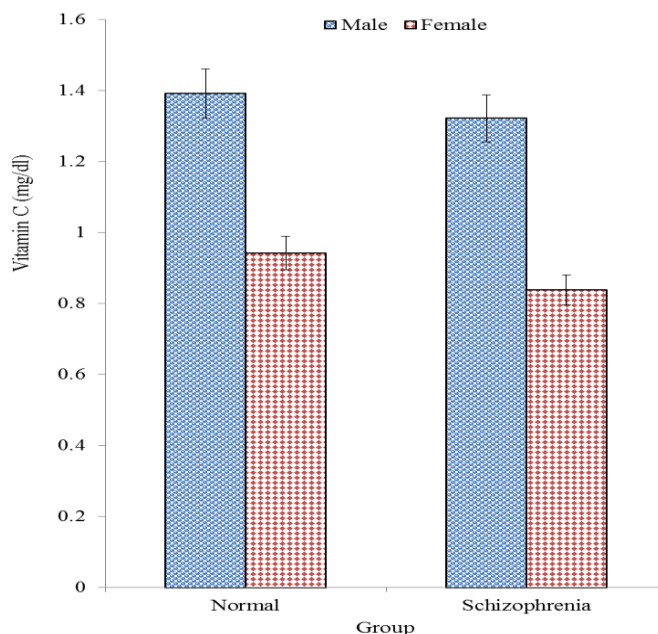


Fig. 11: Mean of Vitamin C (mg/dl±SE) of male and female of normal and schizophrenic individuals.

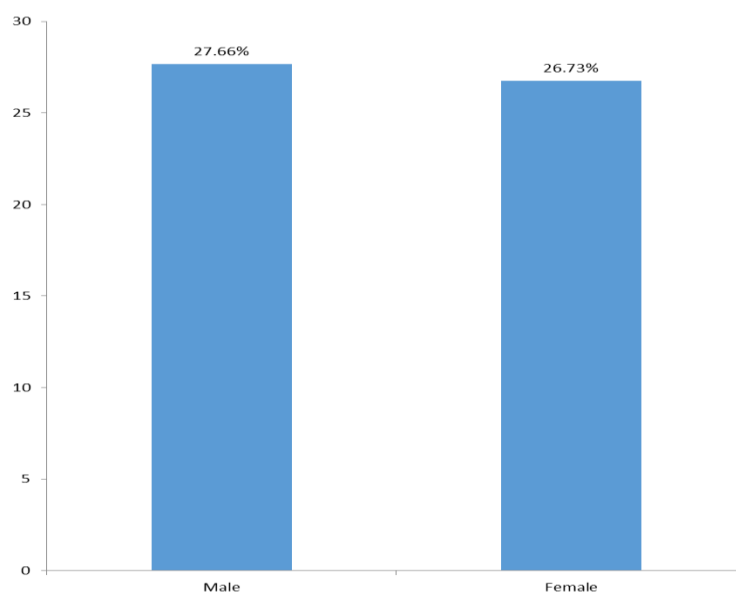


Fig. 12: Percentage of vitamin C (mg/mL) in schizophrenic male and female patients as compared to normal.

The study showed that plasma concentration of Vitamin C was significantly decreased in schizophrenic patients. In gluten free diet the concentration of vitamin C is low that may be the reason of decreased plasma concentration of vitamin C in patients group.^[30] Also the stress, smoking and infections may contribute to decreases vitamin C concentration in schizophrenic patients.^[31] Another reason of decreased plasma vitamin C level in our study may be the cigarette smoking. Cigarette smoking is frequently observed in patients

with schizophrenia^[28] and cigarette smoking is related with decreased serum vitamin C levels because smoking may impair the absorption of vitamin C and increased the urinary excretion.^[32] The Patients with schizophrenia are more vulnerable than normal subjects to oxidative damage as observable from increased malondialdehyde (MDA) levels in plasma due to which antioxidant levels are low in Schizophrenic patients when compared to control as clear from reduced levels of vitamins C and E in the plasma.^[33] That's why in schizophrenic patients antioxidant defense is Impaired and lipid peroxidation is increased. One other factor of decreased plasma vitamin C concentration is responsible for schizophrenia could increase ascorbic acid consumption.^[34] The critical-phase metabolic response to an inflammatory disease reduces plasma vitamin C concentration, sometimes to unnoticeable levels and increases metabolic clearance of ascorbic acid.

3.4 Plasma Folate (nmol/L)

Analysis of variance of Folate of male and female of control and schizophrenic individuals has been given in Table 4a and 4b. Overall mean Folate of schizophrenic individuals was ($P \leq 0.01$) significantly decreased as compared to normal individuals irrespective of their gender (Fig. 13). Overall mean Folate was non-significantly different in males and females irrespective of their groups (Fig. 14). Gender \times groups interaction means showed non-significant differences (Fig. 15). In Schizophrenic patients plasma Folate was decreased 5.03 % in male and 11.04 % in female as compared to normal (Fig. 16).

Table 4(a): Analysis of variance of Folate of male and female of normal and schizophrenic individuals.

F-Value	Means Squares	Sum of Squares	Degree of Freedom	Source of Variation
95.683**	785.794	785.794	1	Group
0.014NS	0.113	0.113	1	Gender
0.011NS	0.087	0.087	1	Group x Gender
	8.213	295.650	36	Error
		1081.645	39	Total

** = Significant at $P \leq 0.01$

NS = Non-significant

Table 4(b): Mean Folate (nmol/L \pm SE) of male and female of normal and schizophrenic individuals

Overall Mean	Schizophrenia	Normal	Gender
6.32 \pm 1.21	1.84 \pm 0.72	10.80 \pm 1.08	Male
6.21 \pm 1.18	1.83 \pm 0.71	10.60 \pm 1.05	Female
6.27 \pm 0.83	1.84 \pm 0.49A	10.70 \pm 0.73B	Overall Means

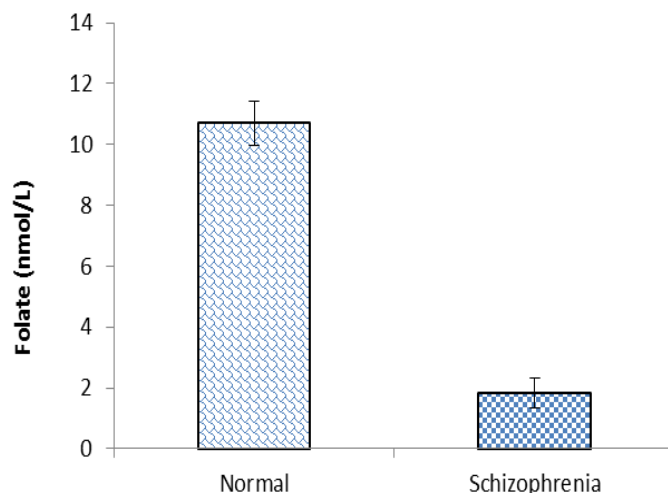


Fig. 13: Overall mean of Folate (nmol/L±SE) of normal and schizophrenia individuals irrespective of their gender.

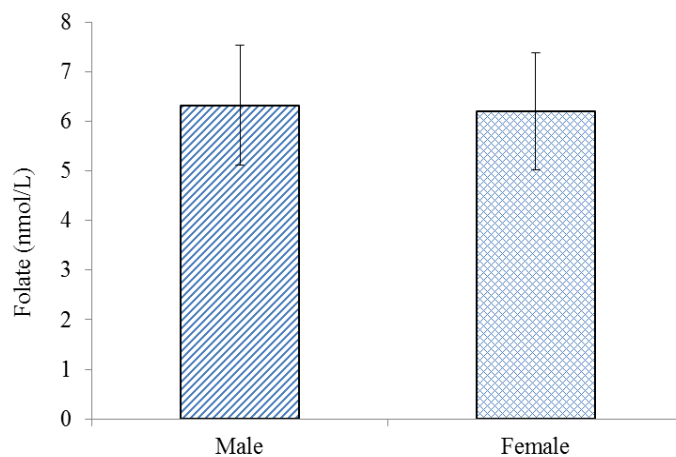


Fig. 14: Overall mean of Folate (nmol/L±SE) of male and female irrespective of their group

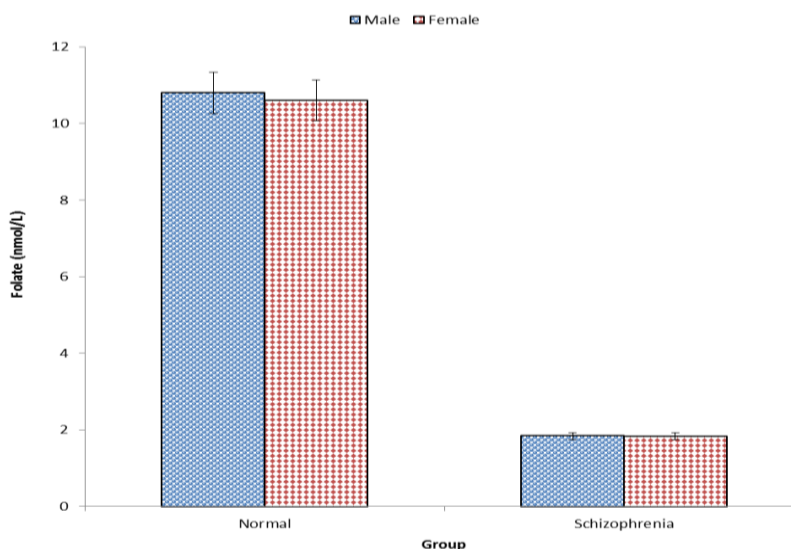


Fig. 15: Mean of Folate (nmol/L±SE) of male and female of normal and schizophrenic individuals.

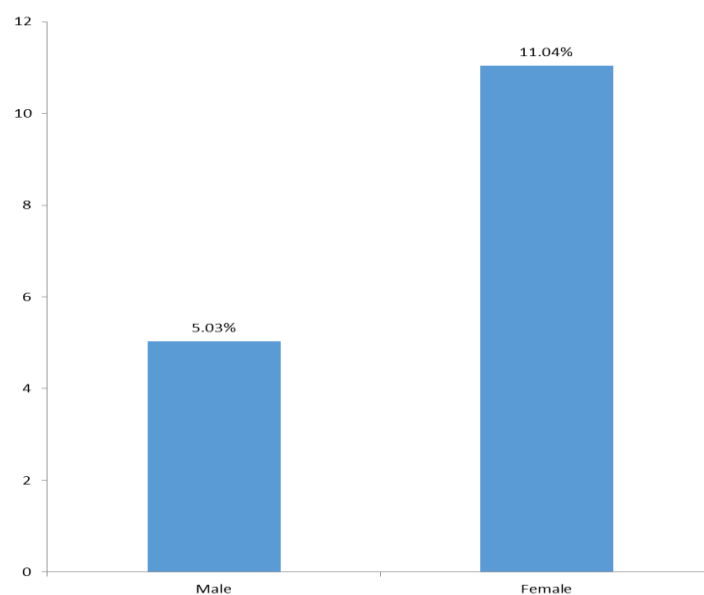


Fig. 16: Percentage of Folate (nmol/L) in schizophrenic male and female patients as compared to normal

Plasma Folate level was significantly lower in schizophrenic patients as compared to normal individuals. The lower Folate index values in schizophrenic patients may be associated with poor dietary intake. Containing two genes: GCPII (glutamate carboxy peptidase II), which controls the absorption of Folate and may be lacking in people with schizophrenia, and MTHFR (methylene tetrahydro folate reductase), which stimulates Folate for use in the brain.^[35]

Another reason of low Folate levels in our subjects may reflect decreased dietary intake, as was described among schizophrenic patients.^[36] These patients often ingest less Folate because of idiosyncratic dietary patterns, due to which a low Folate level could be a result. Gluten-free diet is often low in B vitamins. So, it may be the reason of low Folate concentration in schizophrenic patients. The higher smoking rates among schizophrenic patients than among the general population, cigarette smoking may lower the Folate concentrations.^[28] Also Schizophrenic patients stick to diet free of gluten for several days can also develop Folate deficiency, probably due to low Folate content in gluten-free foodstuffs.

4. CONCLUSION

It is concluded that in patients with schizophrenia on gluten free diet there was an increase in plasma Homocysteine level and Creatinine while decrease in body weight, BMI, vitamin D, Folate, Vitamin C, triiodothyronine (T3) and Thyroxine (T4). Limited

data and little information on the present study needs more work, further studies are necessary to correlate the changes in Homocysteine, Creatinine, Vitamins and Thyroid Hormones profile in schizophrenic patients being treated with gluten free diet.

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