Introduction
Conversion is the loss of function of an individual’s motor or sensory organs without any organic pathology. Conversion disorder (CD) is a disease in which symptoms or deficits affect voluntary motor and sensory functions, and it is considered to be related to other medical conditions as well as to psychological factors in the presence of conflict or other stressors before the disease. CD is defined as the physiological outburst of a person’s psychological stress. The arms and the legs may be physically disabled; such a defence may be beneficial both for the subsidence of anxiety, which is the primary gain, and for the individual to get rid of his/her responsibilities, which is the secondary gain. The symptoms of CD are one or more assorted types. Motor symptoms include paralysis or weakness, aberrant movements, such as tremor or dystonia, abnormal gait and limb posturing abnormalities. Episodes of abnormal generalised limb shaking with apparent impaired or loss of consciousness may be similar to epileptic seizures which are also called non-epileptic or psychogenic seizures. Episodes of unresponsiveness resembling syncope or coma may also appear. Other symptoms include diplopia, dysphonia or aphonha, dysarthria or altered articulation and globus which is sensation of a lump in the throat.

Abstract
Objective: To evaluate the association of folic acid and vitamin B12 levels in patients with conversion disorder, and to illuminate the aetiology of conversion disorder by examining depression and somatoform dissociation.
Method: The case-control study was conducted from March 2014 to May 2015 at the Medical Centre of Yuzuncu Yil University, Van, Turkey, and comprised patients diagnosed with conversion disorder and healthy controls. Blood samples were taken from both groups for vitamin B12 and folic acid levels. Data was collected using the Beck Depression Inventory and Somatoform Dissociation Scale. Data was analysed using SPSS 18.
Results: Of the 100 subjects, 55(55%) were cases with a mean age of 27.05±9.04 years and 45(45%) were controls with a mean age of 26.56± 5.96 years. The mean level of B12 was 283.93±122.96 in cases and 324.62±128.82 in controls (p=0.05). The mean level of folic acid was 5.47±1.84 in cases and 6.07±2.26 in controls (p>0.05).
Conclusions: Physicians need to be vigilant about vitamin B12 levels in patients with conversion symptoms.
Keywords: Conversion, Vitamin B12, Folate, Psychopathology. (JPMA 70: 1758; 2020)
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Vitamin B12, folate levels and somatoform dissociation in conversion disorder
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Introduction
Conversion is the loss of function of an individual’s motor or sensory organs without any organic pathology. Conversion disorder (CD) is a disease in which symptoms or deficits affect voluntary motor and sensory functions, and it is considered to be related to other medical conditions as well as to psychological factors in the presence of conflict or other stressors before the disease. CD is defined as the physiological outburst of a person’s psychological stress. The arms and the legs may be physically disabled; such a defence may be beneficial both for the subsidence of anxiety, which is the primary gain, and for the individual to get rid of his/her responsibilities, which is the secondary gain. The symptoms of CD are one or more assorted types. Motor symptoms include paralysis or weakness, aberrant movements, such as tremor or dystonia, abnormal gait and limb posturing abnormalities. Episodes of abnormal generalised limb shaking with apparent impaired or loss of consciousness may be similar to epileptic seizures which are also called non-epileptic or psychogenic seizures. Episodes of unresponsiveness resembling syncope or coma may also appear. Other symptoms include diplopia, dysphonia or aphonha, dysarthria or altered articulation and globus which is sensation of a lump in the throat.

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dissociative disorders in the 10th edition of the International Classification of Diseases (ICD-10).8

Folic acid (vitamin B9) and vitamin B12 deficiency has been known to cause anaemia and neuropsychiatric symptoms, and these vitamin levels have been routinely investigated in psychiatric diseases.9 The clinical features of psychiatric manifestations and other systems may not occur simultaneously. The active forms of vitamin B12 and folic acid act as cofactors in the carbon cycle necessary for the synthesis of deoxyribonucleic acid (DNA), proteins, phospholipids and neurotransmitters. Therefore, they have important roles in neurobiological and haematological functions.10 Vitamin B12 deficiency causes psychiatric symptoms, such as agitation, irritability, negativism, confusion, disorientation, memory loss, impaired concentration, attention deficit, apathy and insomnia. Psychiatric manifestations can occur without the haematological effects sometimes caused by vitamin B12 deficiency.11 Evidence shows that psychiatric disorders develop with the deterioration of the stability of the neuronal cell membrane resulting from the increase or decrease in monoamine levels. Vitamin stores compensate for the deficiency of this vitamin for two years when vitamin B12 is taken inadequately. With the discharge of these deposits, the deficiency of vitamin B12 leads to clinical symptoms. Vitamin B12 levels of 150-300pg/ml generally have clinical manifestations. Clinical signs are strong when the level is <150pg/ml. Neuropsychiatric symptoms can be observed in 35% of patients with B12 vitamin deficiency.12 Currently, there is no definite limit to diagnose vitamin B12 deficiency. One of the limit values widely used by clinicians is 200pg/mL (148pmol/L).13 However, this clinical threshold is not that sensitive and clinical symptoms may be present in many patients with a low normal status.14 Despite the large number of studies investigating B12 and folate levels in various psychiatric disorders, not enough studies have been conducted on CD. The current study was planned to investigate the association of folate and vitamin B12 levels in CD patients, and to illuminate the aetiology of CD by examining somatoform dissociation.

Patients and Methods

The case-control study was conducted from March 2014 to May 2015 at the Medical Centre of Yuzuncu Yil University, Van, Turkey, and comprised patients diagnosed with conversion disorder and healthy controls. After getting approval from the institutional ethics review committee, the sample size was calculated in the light of literature, keeping the standard deviation (±) for vitamin B12 at 140 effect size (d) 40, and Z value 1.96 for 0.05 type I error rate within the equation n = \( Z^2 / d^2 \) at power 80% and significance level of 5% at 95% confidence interval (CI).13,15

The sample was raised using consecutive sampling from among patients at the Psychiatry Outpatient Department (OPD) who were aged 18-50 years, diagnosed with CD according to the Diagnostic and Statistical Manual of Mental Disorders edition V (DSM-5) criteria while having a normal neurological examination and no other physical or medical complaints, with blood chemicals showing no alcohol or substance abuse. A group of healthy controls was also raised. Informed written consent was obtained from all the participants and those who did not volunteer or were unwilling to give blood samples were excluded.

Blood samples were taken from both the groups for vitamin B12 and folate levels. The samples were centrifuged at 1500g for 10min at 4°C to remove plasma. Folate deficiency was considered to be present at <3ng/mL, and vitamin B12 deficiency was considered present at <200pg/mL.16,17

A socio-demographic data form was filled, which included age, gender, marital status, cultural characteristics. Conversion symptoms were noted using the Beck Depression Inventory (BDI) and the Somatoform Dissociation Scale (SDQ-20) which were filled by the participants.

BDI measures physical, emotional and cognitive indicators seen in depression. It is a self-assessment scale that includes 21 symptom categories. Reliability and validity studies of the scale have been conducted in Turkey.18,19

SDQ-20 is a self-assessment scale which consists of 20 questions for identifying the extent to which each statement is applicable on a five-point likert scale.20,21 It was designed to assess the severity of psychosomatic symptoms that are generally seen in dissociative disorders. The Turkish version of the scale has a one-month test-retest correlation of 0.95, and the cut-off point of 35 yields a sensitivity of 0.84.21

Data was analysed using SPSS 18. Descriptive statistics were initially computed. Chi-square test was performed to examine relationships between the groups and categorical variables. The categorical variables were presented as frequencies and percentages. Mean and standard deviation values for numerical variables were calculated. Mann-Whitney U-test was used where normal distribution of data was not available. Results were considered statistically significant at p<0.05.

Results

Of the 100 subjects, 55(55%) were cases with 45(81.8%)
women and an overall mean age of 27.05±9.04 years, and 45(45%) were controls with 30(66.7%) women and an overall mean age of 26.56±5.96 years (p>0.05) (Table-1). Mean BDI and SDQ-20 scores showed significant differences (p<0.001). There were not significant differences between the groups in terms of mean haemoglobin (Hb), folic acid and vitamin B12 levels (Table-2). However, the mean levels were lower in the cases than the controls. As such, the cases were subsequently divided into low and normal serum B12 groups (Figure). There were 13(23.6%) cases with low vitamin B12 levels compared to 4(8.89%) in the controls (p<0.05).

**Table-1:** Demographic variables of the CD patients (n = 55) and healthy controls (n = 45).

<table>
<thead>
<tr>
<th></th>
<th>CD patients</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male 10(18.2%)</td>
<td>15 (33.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female 45 (81.8%)</td>
<td>30 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td>Single 21 (38.2%)</td>
<td>32 (71.1%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Married 34 (61.8%)</td>
<td>13 (28.9%)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Illiterate 15 (27.3%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elementary 19 (34.5%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High school 18 (32.7%)</td>
<td>2 (4.4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>College or higher 3 (5.5%)</td>
<td>43 (95.6%)</td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>Attacks or seizures 39 (70.9%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anaesthesia or sensory loss 11 (20%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Weakness or paralysis 3 (5.5%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Speech symptoms 2 (3.6%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Distress factors</td>
<td>Yes 25 (45.5%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 28 (50.9%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Onset of symptoms</td>
<td>0-6 months 29 (52.7%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6-12 months 8 (14.6%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-5 years 18 (32.7%)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

CD: Conversion disorder.
SD: Standard Deviation.

**Table-2:** Comparison of haematological parameters and total scores between groups.

<table>
<thead>
<tr>
<th></th>
<th>CD patients (n = 55)</th>
<th>Controls (n = 45)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean± SD</td>
<td>Mean± SD</td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>23.16±12.8</td>
<td>8.40±7.42</td>
<td>0.001</td>
</tr>
<tr>
<td>SDQ-20 score</td>
<td>43.36±14.67</td>
<td>25.66±5.77</td>
<td>0.001</td>
</tr>
<tr>
<td>SDQ-20&gt;35</td>
<td>35(63.6%)</td>
<td>3(63.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>B12 (pg/ml)</td>
<td>283.92±122.96</td>
<td>324.62±128.81</td>
<td>0.05</td>
</tr>
<tr>
<td>Folic acid (pg/ml)</td>
<td>5.47±1.84</td>
<td>6.07±2.26</td>
<td>0.145</td>
</tr>
<tr>
<td>MCV</td>
<td>88.109±22.909</td>
<td>91.706±38.747</td>
<td>0.565</td>
</tr>
<tr>
<td>Hb</td>
<td>14.16±1.40</td>
<td>14.42±1.58</td>
<td>0.389</td>
</tr>
<tr>
<td>WBC</td>
<td>8.83±7.975</td>
<td>6.99±1.856</td>
<td>0.045</td>
</tr>
</tbody>
</table>

SDQ: Somatoform Dissociation Scale; BDI: Beck Depression Inventory;
MCV: Mean cell volume; Hb: Haemoglobin; WBC: White blood cells
SD: Standard deviation. Significant P values are indicated in bold.

**Discussion**

At the outset, the current study had hypothesised that most patients with CD would exhibit clinically significant low vitamin B12 and folic acid levels compared to the healthy controls. The interest in the relationship between vitamin B12 and folate deficiency and psychiatric disorders has grown recently. Vitamin B12 and folate levels have been investigated in depression, obsessive compulsive disorder (OCD) and schizophrenia. To the best of our knowledge, vitamin B12 and folate levels have never been investigated in CD patients.

Increasing data has implicated biological factors in the development of CD. A structural neuroimaging study suggested macroscopic abnormalities in the brains of patients with CD. Consequently, evidence showed that neural circuits are involved in this pathology. The findings of the current study demonstrated that patients with vitamin B12 deficiency were more likely to have CD. No significant difference was found between the groups in terms of folic acid levels.

Vitamin B12 is essential for the synthesis of S-adenosyl-L-methionine (SAMe) in many important methylation processes of neurotransmitters in the central nervous system.
(CNS). Reduced synthesis of SAMe may decrease monoamine neurotransmitter synthesis. Folic acid and vitamin B12 deficiency diminishes methylation reactions that lead to a decrease in neurotransmitter levels; consequently, intracellular biochemical pathways are adversely affected. Neuropsychiatric symptoms may be caused by these important metabolic pathways. When considered together, all these findings suggest that one carbon metabolism, which involves vitamin B12, may contribute to the aetiology of CD.

The current study found that the CD group had higher points in depression and somatoform dissociation than the control group. Somatoform dissociation was investigated in CD, dissociative disorders and somatisation disorder, and patients with CD and dissociative disorder were found to have high somatoform dissociation scores and differed significantly from somatisation patients in somatoform dissociative symptoms.

In terms of limitations the current study had a cross-sectional design which overlooks the causality factor. Besides, there has been little progress in understanding its pathogenesis and in finding effective treatments as the underlying causes of vitamin B12 deficiency were not examined. Although more detailed studies on this phenomenon are needed, the current findings may provide a point of departure for the future.

**Conclusion**

Vitamin B12 deficiency may be a risk factor for the development of CD.Clinicians should be vigilant about it while dealing with CD patients.

**Disclaimer:** None.

**Conflict of Interest:** None.

**Source of Funding:** None.

**References**