PalArch's Journal of Archaeology of Egypt / Egyptology

CORRELATION BETWEEN FOLATE ACID LEVELS AND TOTAL SCORES OF CALGARY DEPRESSION SCALE FOR SCHIZOPHRENIA (CDSS) IN SCHIZOPHRENIA MEN OF BATAK TRANSPORTATION IN PROF PSYCHIATRIC HOSPITAL PROF. DR. M ILDREM MEDAN

Hengky Freddy Sitinjak[1], Bahagia Loebis[2], M. Surya Husada[3]
[1,2,3]Psychiatric Study Program at the Faculty of Medicine, University of North Sumatra, Indonesia. E-mail: hengkysitinjak@yahoo.co.id

Hengky Freddy Sitinjak, Bahagia Loebis, M. Surya Husada: Correlation between Folate Acid Levels and Total Scores of Calgary Depression Scale for Schizophrenia (CDSS) in Schizophrenia Men of Batak Transportation in Prof Psychiatric Hospital Prof. Dr. M Ildrem Medan-- Palarch's Journal Of Archaeology Of Egypt/Egyptology 17(6), 1-14. ISSN 1567-214x
Keywords: males, Batak tribe, depressive symptoms, folic acid.

ABSTRACT
Many different opinions about the timing and progress of depressive symptoms seen in schizophrenia such as positive symptoms that occur due to extrapyramidal side effects caused by antipsychotic drugs and because some characteristics overlap with negative symptoms that can confuse and cause failure to diagnose depressive symptoms. Folic acid is involved in the metabolism of monoamines such as serotonin in the brain, which may be related to mood disorders. To find out the correlation between folic acid levels and total calgary depression scale for schizophrenia (CDSS) scores in men with Batak schizophrenia in the inpatient installation of Prof. Mental Hospital dr. M. Ildrem Medan. This research is a numerical correlative analytic study with a cross-sectional study approach in July to September 2019, where the research subjects are from Batak schizophrenic men in the hospital inpatient installation of Psychiatric Hospital of Prof. dr. M. Ildrem Medan has aged about 21 to 50 years, length of illness ≥ 2 years, a total score of PANSS> 90, and are willing to be respondents and can be interviewed with the nonprobability sampling method for sampling. Correlation between folic acid levels and total CDSS scores was performed using the Pearson test p values obtained <0.001 which indicates that there is a very significant correlation between folic acid levels and CDSS scores. Pearson correlation value of r = -0.64 shows a negative correlation with the strength of a strong correlation. By knowing the correlation between folic acid levels and the total Calgary depression scale for schizophrenia (CDSS) score in men of Batak schizophrenia, it is hoped that the basis for

consideration for examining folic acid levels in men with schizophrenia in depressive symptoms.

I. Introduction

Symptoms of depression in people with schizophrenia have been reported since symptoms have been recognized. The prevalence of depression is found from 7% to 70% which states that depressive symptoms can be observed in all periods of schizophrenia including the initial period. Many differing opinions about the time and progress of depressive symptoms seen in schizophrenia such as positive symptoms that occur due to extrapyramidal side effects caused by antipsychotic drugs and because of some overlapping characteristics with negative symptoms that can be confusing and cause failure to diagnose depression.(1)

Depression is a mood disorder characterized by apathy, bad moods and social withdrawal. Mood instability can act as a mediator between traumatic events such as intimidation and mistreatment and sexual abuse in childhood. Evidence to show that depression is related to schizophrenia ie with problems of violence, arrest, victimization, suicide, problems related to greater substances and have a long-term risk for functional recovery and quality of life.(2)

It is important to note that depressive symptoms can be secondary to comorbid medical disorders, neuroleptic side effects, or psychological reactions to disease. On a clinical perspective, depression may be a prodromal episode of a relapsed psychotic or a post psychotic episode. Several studies have looked at the prevalence of symptoms of depression in long-term treatment of schizophrenia. These sufferings include recurrent hospitalization, deteriorating function deterioration, cognitive decline and poor social abilities.(3)

Kraepelin and Bleuler have provided early clinical characterization of schizophrenia including descriptions of depressive symptoms with more attention to the diagnosis and assessment of this postatopathological form over the past decade. At present, there is a consensus that depressive symptoms commonly occur in schizophrenia representing important differences and symptoms that exist throughout the course of the disease. Depressive symptoms are associated with impaired social and vocational functions, quality of life and increased risk of recurrence. There is an increase in the number of morality in schizophrenia with an increase in suicide rates. The high prevalence of suicidal tendencies in depressed schizophrenia has been repeatedly stated, (4,5)

Symptomatic depression is indeed common in schizophrenia in all phases of the disorder, such as in the first episode, during the initial course of the disorder and after remission, and depression is also present in the residual symptoms of schizophrenia. Recently, there has been an increase in the prevalence of anxiety, depression and substance abuse disorders in people with schizophrenia, which causes distortion of clinical symptoms.Some, maybe most people with schizophrenia experiencing anxiety and depression during the course of his illness, and it has been stated that depression is part of this disorder. In addition, most people with schizophrenia show symptoms of depression during the course of their

illness. Therefore the hypothesis states that the symptoms of depression are an important part of schizophrenia.(3,6,7)

Folic Acid is a natural B vitamin (vitamin B9), the synthetic form is folic acid. When it is low during pregnancy, it can cause congenital neural tube defects in developing fetuses. Folic acid supplementation has been widely studied as a treatment for depression and cardiovascular disease.(8) Folate in food as a complex mixture of conjugated polyglutamate compounds (Folypoly-glutamates) in intestinal wall cells to produce a form of monoglutamate which is more easily absorbed by active membrane transport. (9)

Folate reduces the levels of homocysteine, an amino acid that is thought to worsen some psychiatric symptoms. The folate is also involved in the synthesis of neurotransmitters and in many other metabolic pathways. Homocysteine is one of the nonprotein amino acids produced in the metabolism of one carbon unit. to methione and transsulfuration to cysteine and taurine. The effectiveness of Homocysteine catabolism depends on the availability of folate.(10)

The main mechanism of action of folic acid is through its role as a methyl donor in various biochemical processes of the nervous system and metabolism, and is required for DNA synthesis. Serine reacts with tetrahydrofolate, forming 5, 10- Methylenetetrahydrofolate, folate derivatives involved in DNA synthesis. Methyl groups are donated to cobalamin (B12) with 5-methyltetrahydrofolate, forming methylcobalamin. With the help of the enzyme folate involved in DNA synthesis. amino acids, and convert them to methionine amino acids. Methionine is subsequently converted to S-adenosylmethionine (SAMe), a methyl donor involved in biochemical processes.(11)

*Methylenetetrahydrofolatereductase(MTHFR)*plays an important role in the metabolism of one carbon, which consists of folate, homocysteine, vitamin B12, and DNA methylation, mutations of specific gene loci on Methylenetetrahydrofolate*reductase(MTHFR)*and decreased enzyme activity will affect various physiological events and some psychiatric disorders. Because food is the main source of folate, research reports that low folate levels due to unbalanced food is associated with a higher prevalence of schizophrenia especially in infants with maternal nutritional deficiencies.(12)

Batak tribe is one of the Indonesian ethnic groups located in northern Sumatra. The name of the Batak is a collective theme to identify several ethnic groups who live and come from Tapanuli and East Sumatra.Batak tribes are known for their openness, spontaneity and aggressiveness both physically and verbally. Research conducted by the goddess in 2005 supported this opinion, the results of his study showed that when Batak people were angry they often chose to express their anger when compared to Javanese people who quite often chose to bury their anger. (13)

II. Method

A. Research design

This research is a numerical correlative analytic study with a cross-sectional study approachthe judgeCorrelation between Folic Acid Levels and Total Depression Scale for Schizophrenia (CDSS) in Men with Batak Schizophrenia.

B. Research subject

This research takes place from July to September 2019, where the research subjects are fromBatak schizophrenic men in the hospital inpatient installation. The Soul of Prof. dr. M. Ildrem Medan, aged 21 to 50 years, duration of illness ≥ 2 years, total PANSS Score> 90, and are willing to be respondents and can be interviewed. Taking research subjects with nonprobability sampling method, namely consecutive sampling.

C. Instrument

A problem in assessing depressive symptoms in schizophrenia, mainly due to the lack of development of a specific rating scale for assessing depressive symptoms in schizophrenia. The most commonly used assessment scale is the Hamilton Depression Rating Scale (HDRS) to measure the severity of depressive symptoms in patients with depressive disorders. . However, the use of this scale is also influenced by negative symptoms and extrapyramidal symptoms in schizophrenic patients, so the use of this scale in schizophrenia is doubtful. As a result, to overcome this deficiency, the Calgary Depression Scale For Schizophrenia (CDSS) was developed specifically to assess depressive symptoms in patients with schizophrenia. Some scales, such as the Beck Depression Inventory (BDI), are based on patient reports, but the Beck Depression Inventory (BDI) total score does not fully distinguish depressive symptoms from negative symptoms. Depressive symptoms assessed by the Calgary Depression Scale for Schizophrenia (CDSS) have minimal overlap with other symptoms of schizophrenia.(14,15,16)

*Calgary Depression Scale for Schizophrenia (CDSS)*consists of 9 items measured on a Likert type scale. Items on the Calgary Depression Scale for Schizophrenia (CDSS) consist of symptoms of depression 1. Despair, 2. Low self-esteem, 3. Referral ideas, 4. Feelings are blamed, 5. Pathological guilt, 6. Morning depression, 7. Waking up early, 8. Suicide ideas, and 9. Observed depression. Total CDSS score ≥ 6 according to Addington is considered to have a depressive symptom. The cut-off score that is optimized to distinguish the presence or absence of depressive symptoms in schizophrenic patients is 6 or 7, with sensitivity 92.31% and specificity 97.87%. The minimum score is 0 and the maximum score is 27.(16,17)

*Calgary Depression Scale For Schizophrenia (CDSS)*distinguishes well between depressive symptoms, negative, or extrapyramidal symptoms, and is more specific than the Hamilton Depression Rating Scale (HDRS) and Montgomery-Asberg Depression Rating Scale (MADRS) in assessing depressive symptoms in schizophrenic patients. The Calgary Depression Scale for Schizophrenia (CDSS) has good psychometric properties.(18)

D. Procedure

All research subjects were asked to fill in written consent to participate in the study by first being given a detailed and clear explanation. This study is strived to follow the patterns and norms of standard scientific studies. On the

part of the respondent who was interviewed and conducted a blood test, an informed consent was obtained with the delivery of information that the data or confidentiality of the respondent's individual would be guaranteed byauthor. This study was approved by the Research Ethics Committee at the Faculty of Medicine, University of North Sumatra, Medan.

E. Data analysis

After the data is collected, data processing is carried out with the following stages: (1) Editing, a step to examine the completeness of the data obtained through interviews, (2) Coding, is an attempt made to clarify the answers available according to type, (3) Tabulation, is the activity of entering research data into a table based on the studied variables, (4) Data analysis, is the data analyzed using SPSS statistical tests. Normality tests were performed on the data of each group using the Saphiro-Wilk test because the research subjects were ≤ 50. When the data were normally distributed data were analyzed using the Pearson Correlation test. When the data were not normally distributed data were analyzed using the Spearman correlation test.

III. Results

A. Characteristics of Research Subjects

Characteristics of research subjects of 42Research subject in Prof. Mental Hospital Inpatient Installation dr. M. Ildrem Medan, in the following table.

Table 1. Demographic characteristics of study subjects

Demographic Characteristics	n (%)
Age (years)	
21-30	16 (38.1%)
31-40	16 (38.1%)
41-50	10 (23.8%)
Marital status	
Married	29 (69%)
Not Married	13 (31%)
Education	
Elementary school	14 (33.3%)
Middle School	14 (33.3%)
High school	14 (33.3%)
Profession	
Work	9 (21.4%)
Does not work	33 (78.6%)
Length of illness (years)	4 (2-7)

Based on the demographic characteristics of the research subjects, it was found that at the age of 21-30 as many as 16 people (38.1%). aged 31-40 as many as 16 people (38.1%). and aged 41-50 as many as 10 people (23.8%). Marital status in this study subject is married as many as 29

people (69%) and not married as many as 13 people (31%). The educational status was obtained by elementary school as many as 14 people (33.3%). SMP as many as 14 people (33.3%). and SMA as many as 14 people (33.3%). At work, 9 people (21.4%) were employed and 9 people (78.6%) did not work. Median duration of illness is 4 years with a minimum of 2 and a maximum value of 7.

Table 2. Average levels of folic acid

	n	Average ± (sb)	IK95%
Folic Acid Levels	42	19.70 ± 9.40	16.77-22.62

Based on the average levels of folic acid, it was found that the average level of folic acid in the subjects of this study was 19.70 and the standard deviation was 9.40.

Table 3. Average CDSS scores

	n	Median (min-max)
CDSS total score	42	3.50 (1-8)

Based on the average CDSS score, the median total CDSS score obtained in the study subjects was 3.50 with a minimum value of 1 and a maximum value of 8.

Table 4. Correlations between folic acid levels and total CDSS score

	Folic Acid Levels
CDSS Total Score	r = -0.64 p <0.001 n = 42

In table 4 for the correlation test between folic acid levels and the total CDSS score the correlation test was performed using the Pearson test. From the above results obtained p value <0.001 which indicates that there is a very significant correlation between folic acid levels and CDSS scores. Pearson correlation value of r = -0.64 shows a negative correlation with the strength of a strong correlation, this shows that the lower the levels of folic acid, the higher the total CDSS score.

IV. Discussion

This study is a numerical correlative analytic study with a cross-sectional approach that is describing and analyzing a situation in a given moment. In the study analyzed is the correlation between levels of folic acid

and the total Calgary Depression Scale for Schizophrenia (CDSS) scores in men with schizophrenia of the Batak tribe who are undergoing treatment in the hospital. The Soul of Prof. M. Ildrem Medan, involving 42 subjects who met the inclusion and exclusion criteria. This research was carried out after obtaining approval from the research ethics committee of the Faculty of Medicine, University of North Sumatra, Director of the Hospital. The Soul of Prof. M. Ildrem Medan and from research subjects by filling out informed consent.

For statistical analysis IBM SPSS Statistics version 22 is used with Pearson correlation test data analysis if the data is normally distributed. For normality test data, Sapphiro-Wilk normality test is used because the number of subjects from this study is ≤ 50 subjects.

In the table. 1 on the sociodemographic characteristics for age in this study obtained the most age is age 31-40 as many as 16 people (38.1%) and ages 21-30 as many as 16 people (38.1%), ages 41-50 as many as 10 people (23 , 8%). This study is the same as that conducted by Arthy and colleagues in Indonesia in 2015 explained that the most age is age 31-45 years by 8 people (57%), aged 18-30 years by 3 people (21.4%) and aged 44-55 years as many as 3 people (21.4%).(19)

Based on the table. 1 in this study researchers only took male subjects. This study is the same as conducted by Orum and friends in Turkey in 2018 explained that the levels of folic acid in men are higher than women, this is due to differences in hormones, characteristics of diet, menstrual periods and so on.(20)

In table.1 In the marital status, subjects with married status were 29 people (69%) and not married 13 people (31%). Based on the level of elementary school education is 14 people (33.3%), junior high school is 14 people (33.3%) and high school is 14 people (33.3%). Likewise with the employment status found subjects who worked as many as 9 people (21.4%) and subjects who did not work 33 people (78.6%) .The medium value for the duration of illness in this study was 4 years with a minimum value of 2 and a maximum value 7

In the table. 2 the mean value of folic acid levels in this subject was 19.70 nmol / L and the standard deviation was 9.40 nmol / L. The subjects in this study were in the acute phase of treatment. This study is the same as that conducted by Arthy and colleagues in Indonesia in 2015 obtained the average folic acid level of 15.92 nmol / L and the standard deviation of 5.28 nmol / L.(19)

In the table. 3 obtained a median total CDSS score in the study subjects obtained a median of 3.50 with a minimum value of 1 and a maximum value of 8. In some subjects this study obtained a decrease in levels of folic acid.

In the table. 4 obtained p value <0.001 which indicates that there is a very significant correlation between CDSS score and folic acid levels. Pearson correlation value of r = -0.64 shows a negative correlation with the strength of a strong correlation, this shows that the lower the levels of folic acid, the higher the total CDSS score. This study is different from the study conducted by Roffman and colleagues in 2017 conducted in hospitalized schizophrenia patients by comparing 2 groups, namely the intervention group with the addition of supermene L-methylfolate 15 mg and the placebo group for 12 weeks. the effectiveness of folic acid supplementation

is influenced by genotype variants in relation to folic acid metabolism in plasma. In the study the results obtained are changes in plasma metlyfolate levels at 12 weeks. However there was no significant difference in the depressive symptom assessment of the intervention group by measuring the CDSS score (p = 0.44).(21)

The strength of this study is that it is the first study conducted in Indonesia to find out the correlation between folic acid and the total score of the Calgary depression scale for schizophrenia (CDSS) in batak tribal schizophrenic men. The limitations of this study do not compare with healthy control groups.

V. Reference

Balci G, Oter G, Akdag H, Bekki A, et al. Factors Associated with depression in patients with schizophrenia. Journal of Mood Disorders. 2016, 6 (2): p. 54-62.

Upthegrove R, Marwaha S, and Max Birchwood. Depression and Schizophrenia: Cause, Consequence, or Trans-diagnostic Issue? Schizophrenia bulletin. 2016, 43 (2), p. 240-244.

El-Bahy M, Mohamed W. Prevalence of depression in schizophrenia patients evaluated by the Calgary Depression Scale in Shebin El-Kom, Menoufiya. Middle East Current Psychiatry. 2013, 20: p. 191-196.

Woff RS, Obermeier M, Seemuller F, Jager M, Messer T, et.al.Evaluating Depressive Symptoms and Their Impact Calgary Depression Scale. Acta Psychiatrica Scandinavica: 2010.

Schennach R, Obermeier M, Seemuller F, Jager M, Schmauss M, et.al. Evaluating Depressive Symptoms in Schizophrenia: A Psychometric Comparison of the Calgary Depression Scale for Schizophrenia and the Hamilton Depression Rating Scale. Psychopathology. 2012; 45: 276-85

Hasan A, Faikal P, Wobrock T, Lieberman J, Glenthoj B, et.al. World Federation of societies of Biological Psychiatry (WFSBP) Guidelines for Bilogical Treatment of Schizophrenia. Part 3: 2015 Update Management of special circumstances: Depression, Sufficiency, Substance Use Disorders and Pregnancy and Lactation. The World Journal of Biological Psychiatry: 2015; 16: 142-70

Lewis S, Escalano PR, Keith SJ. Phenomenology of Schizophrenia. In: Saddock BJ, Saddock VA, Kaplan & Saddock's Comprehensive Textbook of Psychiatry, 9ed. Philadelphia: Lippincott Williams & Walkins; 2009: p. 1433-51

Torrey EF, Davis JM. Adjunct Treatment for Schizophrenia and Bipolar Disorder: What to try When You Are Out of Ideas. Clinical Schizophrenia & Related Psychoses. 2012 January: p. 208-16.

Borba CP, Fekadu A, Teferra S, Bekele D, Shibre T, et.al. A Placebo-Controlled Trial of Folate with B12 in patients with Schizophrenia with Residual Symptoms in Ethiopia Using Sequential Parallel Comparison Design. British Journal of Medicine & Medical Research. May; 4 (23): p. 4090-104

Moustafa AA, Hewedi DH, Eissa AM, Frydecka D, Misiak B. Homocysteine Levels in Schizophrenia and Affective Disorders Focus on Cognition. Behavioral Neuroscience. 2014 October; 8: p.1-10.

Thorne Research, Inc. Folic Acid Monograph. Alternative Medicine Review. 2009; 10 (3).

Wan L, Li Y, Zhang Z, Sun Z, He Y, et. al. Methylenetetrahydrofolate reductase and psychiatric diseases. (2018) 8: 242: p.1-12

Suciati R, Agung IM. Differences in Emotional Expressions in Batak, Javanese, Malay and Minangkabau people. Journal of Psychology. December 2016; 12 (2): p. 99-108.

Hasan A, Faikal P, Wobrock T, Lieberman J, Glenthoj B, et.al. World Federation of societies of Biological Psychiatry (WFSBP) Guidelines for Bilogical Treatment of Schizophrenia. Part 3: 2015 Update Management of special circumstances: Depression, Sufficiency, Substance Use Disorders and Pregnancy and Lactation. The World Journal of Biological Psychiatry: 2015; 16: 142-70

Lako IM, Bruggeman R, Knegtering H, Wiersma D, Schoevers RA, et.al. A Systematic review of instruments to measure depressive symptoms in patients with schizophrenia. Journal of Affective Disorders. 2012; 140; 38-47.

Reyes MM, Mendoza R, Dominguez M, Caballero A, Tania MB, Diaz T, et.al. Depressive Symptoms are evaluated by the Calgary Depression Scale for Schizophrenia (CDSS): Genetic Vulnerability and sex effects. Psychiatry Research. 2011; 189; 55-61.

Suttajit S, Srisurapanont M, Pilakanta S, Charnsil C, Suttajit S. Reliability and validity of the Thai version of the Calgary Depression Scale for Schizopherenia. Neuropsychiatric Disease and treatment. 2013; 9; 113-118.

Addington J, Shah H, Liu L, Addington D. Reliability and Validity of the Calgary Depression Scale for Schizophrenia (CDSS) in Youth at Clincal High Risk for Psychosis. Schizophrenia Research. 2014; 153 (0); 64-67.

Arthy C, Amin M, Effendy E. Comparison of folic acid levels in schizophrenia patients and control groups. Earth and environmental science 125 (2018) .p 1-3.

Orum MH, Kara MZ, Egilmez OB. Determination of vitamin B12, folate and ferritin levels of patients in a psychiatric clinic: A one-year retrospective study. 2018; 4 (2) .p 71-78.

Roffman JL, Petruzzi LJ, Tanner AS, Brown HE, Eryilmaz H, et. al. Biochemical, physiological and clinical effects of L-methyfolate in schizophrenia: a randomized controlled trial. Molecular psychiatry (2017) 00. p 1-7.