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Diet quality and eating patterns in euthymic bipolar patients

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Abstract. – OBJECTIVE: As mood disorders and obesity are interrelated, and both are linked to increased morbidity and mortality, risk factors for obesity should be identified and closely monitored in patients with bipolar disorder (BD). The aim of this study was to determine the diet quality of BD patients and to investigate its putative associations with comorbid obesity and disorders of carbohydrate metabolism, as well as the relationship between diet and clinical features of BD.

PATIENTS AND METHODS: Eating patterns in 113 euthymic BD patients and 160 healthy control subjects were assessed using data obtained from a food frequency questionnaire. Associations of diet quality with subjects' weight, waist circumference (WC), insulin resistance index and clinical features of BD were also analyzed.

RESULTS: BD patients had lower Mediterranean Diet Score than controls. Using principal analysis, four dietary patterns were revealed in the BD group *(western-type, pro-healthy carbohydrates, unhealthy snacks,* and *meats and potatoes)*. Over 70% of patients with BD had Body Mass Index above 25kg/m^2. The values of Fasting Triglycerides Glucose Index and WC were significantly higher in BD patients than in the control group. No significant association between diet quality indices and the clinical course of BD was found.

CONCLUSIONS: In our work, euthymic bipolar patients showed unhealthy dietary patterns and had lower adherence to the Mediterranean diet than the controls. Increased values of insulin resistance indicators in the BD group point to the necessity of monitoring glucose and triglycerides levels and measurement of waist circumference in bipolar patients in the routine clinical practice. The cooperation between psychiatrists, dieticians and other medical professionals are necessary to develop dietary recommendations for patients with bipolar disorder.

Key Words
Diet, Bipolar disorder, Obesity, Insulin resistance, Eating patterns.

Introduction

Mood disorders are a group of recurrent and often chronic diseases, including unipolar disorder (in which the recurrence of depressive episodes is observed) and bipolar disorder (BD), where depressions, as well as manias and/or hypomanias, can be observed. The estimated lifetime prevalence of the unipolar major depressive disorder is about 16%, bipolar disorder -1-1.5%; this figure increases to about 4.5% when the bipolar spectrum is included[1,2]. Mood disorders are associated with a significant burden of disability, not only because of psychiatric symptoms, but also by increasing the risk of developing many somatic disorders and early mortality[3]. Patients with depression, especially those with bipolar disorder (BD), have up to 50% higher risk of developing obesity[4,5].

Obesity itself is a chronic disease with high prevalence[6], serious consequences and increased mortality rates[7]. In the past, it was believed that the risk of obesity in bipolar patients stems from the long-term use of psychotropic drugs[8], but it is stressed that those individuals were obese at a time when drugs were not available (Kretschmer, 1936[9]). The relationship between obesity and affective disorder is also confirmed by studies in newly diagnosed patients. It has been determined that in drug-naïve BD patients, overweight was significantly more prevalent than in other drug-naïve psychiatric patients[9]. When compared to healthy population, those drug naïve newly diagnosed BD patients also had an increased rate of insulin resistance (IR)[10] presumed to be involved obesity and somatic disorders like diabetes mellitus type 2[11,12]. The interaction of different intrinsic neuroendocrine/biological, as well as psychological and behavioral features of BD[13] change the eating patterns of patients, which may contribute

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to the weight gain and obesity development of BD patients (e.g., lifestyle changes associated with affective episodes and mood fluctuations or remission, symptoms of disease phase - hyperphagia[14], limitation of physical activity[15], etc.).

On the other hand, more and more data indicate that a proper diet and nutrition can have a beneficial effect on biological factors that are implicated in affective disorders. Such factors like inflammation, brain plasticity and function, the stress response system, and oxidative processes[16-19] are diet-related and involved in biological pathways of affective illness.

Data increasingly show that some dietary patterns are connected with reduced prevalence and reduced risk of psychiatric illness, namely depression or anxiety. These associations appear to be consistent across countries, cultures and populations[20-25]. Studies[26,27] carried out in recent years indicate that dietary interventions in patients with depression may constitute an effective and accessible treatment strategy in depression. As mood disorders and obesity are interrelated, and both account for a higher risk of morbidity and mortality, it seems clear that in patients with BD, risk factors for obesity and metabolic disorders should be identified and closely monitored, and the occurrence of these disorders should be the target of therapeutic interventions. The National Institute for Health and Clinical Excellence (NICE)[28] recommended advising BD patients on a diet, physical activity and weight loss, monitoring blood pressure and serum glucose level to support patients to control their weight and/or refer patients to a dietician or other specialized services. These recommendations stem from the awareness of the side effects of the administered drugs and do not refer to the intrinsic features of the bipolar disorder itself. Despite those recommendations, a majority of BD patients do not receive the regular physical health monitoring they require in addition to pharmacotherapy[29]. Bipolar patients in many cases depend on psychiatrists' care; compared with other patients, they are less able to explain physical signs or to solve their problems and care for themselves[30]. Psychiatrists tend to focus on mental rather than physical health, their knowledge of somatic diseases is often insufficient. Other doctors have a tendency to regard physical complaints as psychosomatic symptoms and stigmatize people with mental disorders, which results in psychiatric patients receiving inferior medical care[29,30]. There is insufficient awareness among psychiatrists and other physicians that in the treatment of mental disorders, including bipolar disorder, the positive effects of treatment depend not only on the taking of medicines but also on the patient's lifestyle. The doctor should evaluate diagnosis various biopsychosocial factors[31] (such as the patient's diet, physical activity or sleep pattern) and implement appropriate interventions for the patient adapted to the diagnosed specific mental abnormalities. Research which takes into account a variety of biopsychosocial factors relating to the functioning of bipolar patients is therefore needed. Patients' diet seems to be an undisputed modifiable factor which may be the target of a therapeutic or, possibly, prophylactic intervention.

The aim of this work was to determine the diet quality of BD patients and to search for its putative associations with the coexistence of obesity and disorders in carbohydrate metabolism and the relationship between the diet and the clinical features of bipolar disorder.

Patients and Methods

Patients and Controls

One hundred and ninety-nine patients treated for bipolar disorder (BD) for more than 5 years in the outpatient university clinic were screened for the study. Before enrolling in the study, patients were diagnosed by two psychiatrists according to The International Statistical Classification of Diseases and Related Health Problems, 10th Revision - (ICD-10) criteria[32]. At the time of assessment, all patients were euthymic for at least four months, as defined by a score of ≤ 7 on the 17-item Hamilton Depression Rating Scale[33], and a score of ≤ 7 on the Young Mania Rating Scale[34]. The control group constituted a convenience sample of local primary health services' users. Any history of head injury, epilepsy, bariatric treatment, alcohol dependence or diagnosis of dementia, mental retardation or any severe/unstable somatic diseases or taking steroids or immunosuppression resulted in exclusion from the study. Moreover, in the control group, any past or present data on the psychiatric disorder or psychotropic treatment resulted in excluding a person from participation. The study was conducted in accordance with the Helsinki Declaration and the protocol was approved by the Ethics Committee of the Poznan University of Medical Sciences (Resolution no. 121/13). All subjects gave their informed consent after receiving a full explanation of the nature of the procedures of the study.

Measures

Anthropological Measures

Body weight, body height and waist circumferences were measured. Weight was measured in light clothing without shoes to the nearest 0.1 kg, height - in the standing position, without shoes to the nearest 0.01 m (electronic scale WPT 100/200 RadWag Radom Poland). Bodyweight status was described by the body mass index (BMI), expressed as the weight in kilograms divided by the square of the height in meters (kg/m^2). Waist circumference was measured with a retractable measuring tape for precise body measurements over the unclothed abdomen at the narrowest point between the lower rib and iliac crest[35].

Biological Assessment

Blood samples were collected between 8:00 and 9:00 a.m. after an overnight fast of at least 9 hours. Total serum cholesterol, triglycerides, glucose were assayed using colorimetric enzymatic methods in an automated clinical chemistry system. These tests were analyzed in a single laboratory with the same assay to decrease variability. Insulin resistance was assessed using the Fasting Triglycerides and Glucose (TyG) Index computed as the natural logarithm (Ln) of [(fasting triglycerides) (mg/dl) multiplied by fasting glucose (mg/dl)/2][36-40].

Socio-Demographic and Clinical Assessment

A semi-structured socio-demographic questionnaire was used, including information on educational status (number of years of education), living alone or with family, cigarette smoking and alcohol drinking habits. The course of the disease was assessed retrospectively, based on semi-structured interviews, an analysis of medical outpatient charts, and hospitalizations records.

Dietary Assessment

The study used a validated food frequency questionnaire (FFQ) supplied by the Department of Human Nutrition and Hygiene (Poznań University of Life Sciences)[41,42]. Using food frequency questionnaires in the assessment of dietary patterns is a recommended and widely applied method in nutrition research. It is a useful approach for describing the overall diet and examining the interrelations between the diet and its health effects[43-46]. The method of dietary data collection was described in detail elsewhere[41,42,47]. Briefly, individuals participating in the study were given a list of food products and asked to report the frequency of their consumption over the course of the last year (with possible answers: 4-5 times per day, 2-3 times per day, once a day, 4-6 times per week, 2-3 times per week, once a week, 2-3 times per month, once a month, rarely or never) and the frequency of consumption was recalculated and expressed as times/month.

Analysis of Food Data

Using data obtained from FFQ we employed an *a priori* method to measure adherence to the Mediterranean diet (MDiet) and an *a posteriori* method to determine the dietary patterns[43].

The Mediterranean diet (MDiet) adherence was described using the Mediterranean Diet Score (MDS) as proposed by Panagiotakos et al[48] by assessing the frequency of consumption of the main food groups in the Mediterranean diet pyramid. The procedure used for calculating the MDS was described in detail by Bajerska et al[41]. Briefly, food items were grouped according to the Mediterranean diet pyramid, the frequency of consumption of these foods was derived from the FFQ, then it was recalculated and expressed as times/month and assessed (from 0 to 5 or reverse) in respect of each of the 11 food groups that were part of MDiet. Thus, the total dietary score could range from 0 to 55. Higher values of the dietary score indicate greater adherence to the MDiet.

Factor analysis as the *a posteriori* method in both bipolar and control groups was performed. The Kaiser-Meyer-Olkin Measure of Sampling Adequacy was 0.592 for the bipolar group and 0.602 for the control. In both groups, the hypothesis of the identity of the correlation matrix (Bartlett's Test of Sphericity) was rejected. The factor analysis extraction method was the Principal Component Analysis (PCA) and the results were rotated using the Varimax method with Kaiser normalization. To identify the number of PCA-derived patterns to retain, the break-point identified in the scree plot of the eigenvalues and the total variance in the frequency of food consumption were considered. The number of components to be retained were considered at the point at which the scree plot leveled off (eigenvalues > 2.5). The food items were considered a significant component of a dietary pattern if they had a factor loading of $\geq |0.3|$. Higher loading indicated a stronger association between a food item and a dietary pattern, although the value for meaningful factor loading was arbitrary. Dietary patterns were named based on the items of foods exhibiting the strongest correlations and having the highest factor loadings. The summary score for each dietary pattern was derived for each

person and classified into tertiles (bottom, middle, upper); higher tertile represented greater adherence to the dietary pattern. The dietary pattern scores were used to determine the association with clinical, anthropometric and dietary variables.

Statistical Analysis

To evaluate the normality of the distribution of the variables, the Kolmogorov-Smirnov test was applied. Continuous variables are represented as mean values and standard deviation, while categorical variables are presented as a sample percentage (%). The sociodemographic, lifestyle, and clinical characteristics of the subjects were compared using the Mann-Whitney test for continuous variables and the χ^2 test for categorical variables. Spearman's rank correlation coefficient was used for interdependence analysis for continuous variables. The principal component analysis was performed to identify dietary patterns as described above. To evaluate the differences in the clinical, laboratory and anthropometric variables across tertiles of the dietary patterns scores, the Kruskal-Wallis test was used for continuous variables and the χ^2 test for categorical variables. Dunn's test was used to validate ANOVA for pairwise comparison. The level of statistical significance was set at $p<0.05$. The statistical analysis was conducted with IBM SPSS Statistics for Windows, Version 24.0. (IBM Corp. Armonk, NY, USA).

Results

The group of 199 bipolar patients and 181 controls were screened. Seventy-two BD patients and 15 controls did not meet inclusion criteria, 17 participants (11 BD and 6 controls) were excluded from analysis due to missing data and three bipolar patients withdrew their consent; therefore, 113 bipolar patients and 160 controls were finally included. There were no significant differences in age between BD patients and healthy controls. BD patients were characterized by higher education and, statistically more frequently lived alone. The percentage of smokers was statistically lower than in the control group. Over 2/3 of studied individuals showed BMI > 25 kg/m^2, where a similar percentage of overweight and obese subjects in both groups was indicated. The statistically higher WC was observed in BD group, for both men and women. Bipolar patients had markedly higher serum triglycerides levels. A trend towards higher fasting glucose levels in bipolar patients was also noted. Cholesterol concentrations were not remarkably different between both groups. TyG index as a numerical expression of insulin resistance in BD patients was higher than in the control group and showed a statistically significant difference. Laboratory tests results in bipolar patients and the control group are presented in Table I.

Table I. Demographic, clinical, anthropometric characteristic and laboratory tests results of euthymic bipolar patients and controls. The results are presented as mean (SD) or percentage.

	BD patients (No.=113)	Control group (No.=160)	*p*
Age [years]	57.7 (12.2)	59.7 (15.9)	NS
Education [years]	13.5 (3.1)	10.3 (3.2)	0.0001[1]
Male [%]	21	35	0.008[2]
Current smokers [%]	20.2	28.8	NS
Living alone [%]	21.0	11.6	0.027[2]
BMI [kg/m^2]	28.0 (5.2)	27.9 (5.9)	NS
BMI > 25 [%]	73.9	67.6	NS
BMI > 30 [%]	37.8	30.6	NS
WC in women [cm]	95.1 (12.3)	90.1 (13.4)	0.026[1]
WC in men [cm]	102.6 (13.8)	96.7 (13.1)	0.029[1]
Serum glucose level [mg/dl]	94.8 (24.3)	92.6 (22.9)	0.065
Serum triglycerides level [mg/dl]	173.4	149.8	0.047
Serum cholesterol level [mg/dl]	226.1 (45.8)	217.0 (43.0)	NS
TyG index	4.82 (0.30)	4.58 (0.31)	0.038

SD = standard deviation; WC = waist circumference; TyG index = Fasting Triglycerides and Glucose Index, indicator of insulin resistance. NS non-significant; [1]Mann Whitney test; [2]chi-square test.

Analysis of Dietary Patterns

As *a priori* method to assess adherence to the Mediterranean diet, Mediterranean Diet Score (MDS) was used. Bipolar patients had statistically lower MDS results (mean 28.8 ± 4.9 points) than controls (29.7 ± 3.7 points) with statistical significance p=0.02 (Mann Whitney test). Four components with the PCA (*a posteriori* method) were identified and examined as dietary patterns in each group with 32.67% of the total variance in the frequency of consumption in BD group and 28.87% in control group explained. In both groups similar dietary patterns were observed: *western-type, pro-healthy carbohydrates* and *unhealthy snacks* (Tables II and III). Patients with bipolar disorder showed additionally *meats and potatoes* pattern (Table II), while in controls a pattern named *vegetables and fruits* was identified (Table III). *Western-type* pattern identified in both groups was described by frequent consumption of

Table II. Major dietary patterns in bipolar patients (factor loading matrix). Food items with factor loading less than |0.3| were not included.

Food items	Western-type	Unhealthy snacks	Pro-healthy carbohydrates	Meats and potatoes
Pizza, spaghetti, lasagne		0.54		
Candies, bars, chocolate		0.53		
Hamburgers		0.50		
Ice cream		0.39		
Skimmed milk		-0.38		
Fries	0.73			
Canned fruits	0.66			
Chips, nachos	0.63			
Energizing drinks	0.63			
Cakes, cookies	0.58			
Alcoholic beverages	0.57			
Soda sweetened beverages	0.56			
Pancakes	0.52			
Dumplings	0.48			
Sweetened beverages	0.47			
Hot dogs	0.33			
Potatoes				0.67
Margarine, oil				0.56
Offal meat and offal				0.48
Pork				0.47
Meat, ham, sirloin				0.44
Pastas				0.41
White breads and rolls				0.32
Groats and brown rice			0.53	
Muesli, grains			0.70	
Cornflakes			0.68	
Wholemeal bread, rye bread			0.57	
Eggs			0.67	
Mineral water			0.60	
Yogurt (kefir)			0.41	
Dried fruits			0.35	
Butter			-0.35	
Cabbages				0.56
Cucumbers, onion				0.56
Broad bean, string beans, green peas				0.48
Tomatoes				0.45
Variance explained (%)	10.0	7.14	6.40	8.56

Table III. Major dietary patterns in control group (factor loading matrix). Food items with factor loading less than |0.3| were not included.

Food items	Western-type	Unhealthy snacks	Pro-healthy carbohydrates	Vegetables and fruits
Candies, bars, chocolate		0.63		
Ice cream		0.47		
Frankfurters, sausages, pies		0.55		
Fries		0.40		
Cakes, cookies		0.57		
Hot dogs	0.82			
Hamburgers	0.79			
Energizing drinks	0.74			
Potatoes	0.67			
Pizza, spaghetti, lasagne	0.55			
Sandwiches	0.54			
Chips, nachos	0.52			
Alcoholic beverages	0.49			
Soda sweetened beverages	0.45			
Canned fruits	0.38			
Groats and brown rice			0.73	
Muesli, grains			0.53	
Cornflakes			0.49	
Skimmed milk			0.44	
Wholemeal bread, rye bread			0.42	
Dried fruits			0.34	
Nuts			0.35	
Peaches, apricots, cherries				0.60
Spinach, lettuce, chicory				0.62
Tomatoes				0.60
Lemons, oranges				0.54
Strawberries, raspberries, blueberries, currants				0.54
Cabbages				0.52
Broad bean, string beans				
Green peas				0.44
Cucumbers, onion				0.49
Lemons, oranges				0.54
Strawberries, raspberries, blueberries, currants				0.54
Apples, pears				0.49
Broad bean, string beans,				
Green peas				0.44
Variance explained (%)	9.23	6.50	6.26	6.75

fries, cookies, pancakes, dumplings, pizza, spaghetti, lasagne, sandwiches, tacos, nachos, fruit drinks, sweetened beverages, canned fruits, soda beverages, energizing drinks (loadings from 0.33 to 0.82). The small differences between the frequency of consumption in analyzed food items between bipolar patients and controls were observed. The pattern named *pro-healthy carbohydrates* was very similar in both groups and was described by frequent consumption of cornflakes, muesli, wholemeal bread, yogurts, dried fruits, eggs, rice, nuts (controls only), skimmed milk (controls only) and mineral water as well as groats and brown rice (loadings from 0.35 to 0.73 and a negative loading with butter -0.38 in BD group). The *unhealthy snacks* pattern noted in both groups was

described by frequent consumption of ice cream, chips, cakes, cookies, hamburgers, frankfurters, candies (loadings from 0.39 to 0.63). Apart from the above-described patterns observed in the entire study group, in the group of euthymic bipolar patients the *meats and potatoes* dietary pattern was noted, characterized by frequent consumption of pork meat, potatoes and heavy carbohydrates like pasta, white bread and rolls (loadings from 0.32 to 0.67) (Table III). As opposed to the patients, persons from the control group showed *vegetables and fruits* pattern described by frequent consumption of salad, green peas, onion, cucumbers, cabbage, tomatoes and various fruits (loadings from 0.44 to 0.62) (Table III).

Table IV presents the comparison of clinical, anthropometric and biochemical characteristics of bipolar patients across tertiles of dietary patterns (for the sake of clarity only the results for first and third tertiles are shown). Higher tertile represented greater adherence to the dietary pattern. Patients with higher adherence to *western-type* dietary pattern and *meats and potatoes* dietary pattern had significantly lower MDS scores. Higher adherence to *meats and potatoes* dietary pattern was connected to the higher serum level of triglycerides, TyG (index of IR) and increased waist circumference. A trend (p=0.06) towards higher cholesterol serum levels in patients with higher adherence to *unhealthy snacks* pattern was also noted.

Analysis of Associations of Clinical, Anthropometric Measures and Diet in the Bipolar Group

Duration of illness was in the range of 6-48 years, mean length of illness was 23.9±11.7 years. The mean number of hospitalization was 1.7±2.6. 79% of patients were treated with lithium for average 16.4 years (±10.4). No association between the course of illness and adherence to Mediterranean diet, insulin resistance expressed with TyG and obesity was found. There were no correlations between these clinical features and MDS and between dietary score and BMI, WC and age in the bipolar group as shown in table V. MDS correlated with pro *healthy carbohydrates* dietary pattern score, and negatively correlated with the *western-type* dietary pattern score. The *unhealthy snacks* and the *meats and potatoes* dietary patterns scores correlate with WC in men, but not in women. The *meats and potatoes* dietary score correlated with TyG index (Table V). Length of past education positively correlated with the *pro-healthy carbohydrates* dietary pattern score, there were no correlations between education length and other dietary patterns. TyG results were associated with BMI and WC in men, but not in women (Table V).

Discussion

Until now, evaluation of the diet and diet-associated factors in patients with bipolar disorder has received very limited attention of researchers. To the best of our knowledge, this is the first study to evaluate diet quality and dietary patterns in a large bipolar patients group. Most studies carried out so far regarding the relationship between nutrition and mental disorders concerned depression. Initially, they have focused on individual nutrients or foods, but subsequently, the dietary patterns which reflected the overall diet have also been analyzed. Analyzing dietary patterns in various populations provides information which may form the basis for evaluating the diet-related morbidity factors and for developing dietary recommendations significant in the therapy, and in the future prevention of specific diseases. Only a small number of papers have so far assessed bipolar patients' diet quality, as summarized in the review by Lopresti et al[18]. Jacka et al[49] suggested that since cross-sectional odds ratio for BD and depression and diet are very similar, the diet may impact mood disorders in a way which is independent of diagnostic category.

In our work, dietary patterns of BD patients and controls were analyzed using data from FFQ with the *a priori* and *a posteriori* approaches. In the *a priori* approach we used the Mediterranean diet score (MDS) assessing the adherence to the Mediterranean style diet. The MDiet is characterized by a high intake of plant foods (vegetables, fruits, legumes, nuts, seeds, olives, whole grains), extra virgin olive oil, moderate intake of fish and low intake of sweets, red meat and processed food[50]. The MDiet has consistently been found to be a healthy dietary pattern in terms of morbidity and mortality (cardiovascular diseases, hypertension, obesity, cancers, type 2 diabetes, Parkinson's disease, Alzheimer's disease)[51-53]. A meta-analysis of prospective and intervention studies has shown that regional versions of the Mediterranean dietary pattern can be proposed for the primary prevention of metabolic syndrome and cardiovascular diseases[54,55].

Table IV. Analysis of the relationships of dietary patterns with clinical, anthropometric and biochemical characteristics of bipolar patients (for clarity of the presentation, only the results of the first and third tertile are included).

Dietary pattern	Western-type			Unhealthy snacks			Pro-healthy carbohydrates			Meats and potatoes		
	T1	T3	p^1	T1	T3	p^1	T1	T3	p^1	T1	T3	p^1
Factor scores of dietary pattern	-1.25 to -0.46	0.08 to 5.15		-2.23 to -0.35	0.22 to 5.91		-1.74 to -0.64	0.11 to 3.63		-2.28 to -0.11	0.53 to 3.75	
Females %	81.1	76.6	NS	76.2	79.5	NS	72.7	80.8	NS	78.7	79.4	NS
Age [yrs]	58.84 (12.60)	57.29 (11.16)	NS	57.54 (12.09)	58.41 (10)	NS	60.96 (11.78)	55.98 (11.25)	NS	57.65 (12.66)	57.26 (12.36)	NS
Education [yrs]	13.58 (2.89)	13.17 (3.61)	NS	12.78 (2.85)	13.94 (3.02)	NS	12.36 (3.36)	14.07 (2.74)	NS	13.88 (3.47)	12.79 (2.71)	NS
Living alone	26.4	17	NS	21.4	23.1	NS	12.1	23.1	NS	27.9	11.8	NS
Current smokers	24.5	14.9	NS	14.3	20.5	NS	21.2	19.2	NS	13.1	26.5	NS
BMI [kg/m^2]	28.69 (6.61)	28.17 (5.58)	NS	28.71 (6.33)	27.17 (4.99)	NS	27.87 (5.01)	27.66 (5.94)	NS	27.50 (5.54)	28.63 (6.67)	NS
BMI > 25%	72.7	65.9	NS	71.8	67.6	NS	74.1	64.6	NS	61.5	71.4	NS
BMI > 30%	34.1	31.7	NS	38.5	24.3	NS	25.9	29.2	NS	32.7	32.1	NS
WC [cm] in women	91.8 (18.34)	92.7 (13.05)	NS	88.2 (14.41)	91.7 (15.36)	NS	90.7 (11.73)	88.8 (15.27)	NS	87.6 (13.47)	94.8 (16.49)	0.05
WC [cm] in men	95.0 (5.45)	99.6 (8.98)	NS	93 (7.39)	101.4 (6.10)	NS	96.8 (6.72)	95.7 (9.43)	NS	94.4 (8.97)	101.6 (6.27)	0.001
Serum glucose [mg/dl]	102.48 (31.80)	95.63 (13.66)	NS	99.65 (28.4)	97.27 (19.34)	NS	97.76 (19.01)	100.07 (28.66)	NS	98.06 (27.61)	100.12 (18.48)	NS
TG [mg/dl]	135.09 (81.04)	157.85 (82.74)	NS	157.05 (92.5)	155.21 (93.85)	NS	153.45 (57.11)	160.72 (107.71)	NS	120.98 (57.26)	172.8 (76.87)	0.001
TyG	4.68 (0.29)	4.72 (0.36)	NS	4.75 (0.28)	4.69 (0.41)	NS	4.76 (0.21)	4.72 (0.40)	NS	4.60 (0.31)	4.83 (0.24)	0.002
Serum cholesterol [mg/dl]	214.00 (37.56)	215.93 (6.47)	NS	211.97 (38.4)	228.5 (50.75)	0.06	218.41 (40.67)	215.34 (49.31)	NS	217.70 (46.35)	209.93 (42.40)	NS
MDS	30.50 (4.09)	26.20 (3.36)	0.001	28.72 (3.56)	28.31 (4.75)	NS	28.09 (3.26)	28.46 (4.64)	NS	30.09 (3.92)	27.48 (3.72)	0.001

T1- bottom tertile, T3- upper tertile; BMI- body mass index; WC- waist circumference, TG -serum triglycerides level; TyG- Fasting Triglycerides and Glucose Index; MDS- Mediterranean Diet Score; data are presented as the mean (SD) for continuous variables and as % for categorical variables; *p*-values were derived from chi-square for categorical variables test and Kruskall Wallis test for continuous variables; NS not significant.

Table V. Associations of clinical, anthropometric measures, Mediterranean diet adherence score (MDS) and PCA derived dietary pattern scores (Spearman's rank correlation coefficient) in the group of euthymic bipolar patients.

	MDS	Dietary pattern				BMI [kg/m^2]	WC - females [cm]	WC - males [cm]	TyG
		western-type	unhealthy snacks	pro-healthy carbo-hydrates	meats and patatoes				
Age [years]	0.031	-0.022	-0.028	-0.154	-0.033	0.01	0.13	0.31	-0.04
Education [years]	0.153	-0.006	0.168	0.197[1]	0.185	-0.22[1]	-0.28[1]	-0.16	-0.17
BD duration [years]	-0.222	0.053	-0.037	0.018	0.065	0.11	0.15	-0.13	0.09
Lithium therapy [years]	-0.006	0.066	-0.011	0.001	-0.081	0.07	0.12	-0.04	-0.19
Number of hospitalizations	0.069	-0.057	0.157	-0.032	0.070	0.06	0.01	0.06	0.13
MDS	–	-0.453[1]	-0.098	0.031[2]	0.368	0.08	0.05	-0.26	-0.02
BMI [kg/m^2]	0.03	-0.114	-0.093	-0.072	0.061	–	0.08	0.54[2]	0.59[2]
WC – females [cm]	0.15	0.030	0.077	-0.199	0.159	–	–	–	0.32
WC – males [cm]	-0.13	0.252	0.550[2]	0.014	0.211[2]	–	–	–	0.56[2]
TyG	0.153	0.029	-0.031	-0.113	0.324[2]	0.59[2]	–	–	–

MDS- Mediterranean Diet Score; TyG- Fasting Triglycerides and Glucose Index; BMI- body mass index; WC- waist circumference; [1]$p<0.01$; [2]$p<0.001$.

In this study, euthymic bipolar patients had worse adherence to MDiet as assessed with the MDS compared to controls. We are not aware of the results of other studies concerning bipolar patients and MDiet adherence. However, it should be highlighted that in population studies in Poland and other Eastern European countries high adherence to the Mediterranean diet has only rarely been observed[56], but the Mediterranean style diet has continually been associated with a reduced risk of total and cardiovascular diseases related deaths[56], as well as a reduced risk of breast and lung cancer[44].

In our group of euthymic bipolar patients, no correlations of the Mediterranean diet adherence score with clinical features of mood disorder (duration of the disease, number of hospitalizations, duration of lithium therapy) was found. To our best knowledge, there was no report of the association of adherence to the MDiet and BD risk, the onset of illness or its clinical features. To search for this association, a prospective longitudinal study should be carried out. Given the hypothesis that the impact of diet on mood disorders may be independent of diagnostic category[49] the results of studies on depression should be taken into consideration. In systematic reviews and meta-analyses high adherence to the Mediterranean diet was consistently associated with reduced risk of depressive symptoms[57-59] and a protective role of the Mediterranean diet pattern with regard to the prevention of depressive disorders was suggested[57,60]. Even short-term adherence to the Mediterranean-style diet had the potential to improve mood[61].

The *a posteriori* approach derives dietary patterns independently of the existing knowledge of food and nutrition and their health/diseases relations. In our work, using PCA (in the *a posteriori* approach), four dietary patterns in both bipolar and control groups were identified. The *western-type* and *unhealthy snacks* patterns identified in both groups were characterized by high consumption of not recommended food items (such as fries, pizza, hamburgers, chips, cookies, sweetened beverages and soda sweetened beverages). In BD patients only the *meats and potatoes* dietary pattern rich in various refined carbohydrates, with a marked frequency of fat and meats consumption, was noted. Such dietary patterns are related to increased rates of obesity, non-communicable diseases such as cancer, stroke, cardiovascular diseases, type-2 diabetes mellitus, and neurodegenerative diseases[62-66]. In our work, the dietary pattern with high vegetables and fruits intake was found exclusively in the control group. Epidemiologic studies[67,68] consistently show that dietary patterns with high fruit and vegetables as well as nuts and legumes intake are associated with lower rates of mortality and cardiovascular diseases and type 2 diabetes. Both in the group of patients with bipolar disorder and in the control group, a common dietary pattern (labeled *pro-healthy carbohydrates*) was also observed. This pattern included almost the same food items in both groups (namely groats and brown rice, muesli, grains, cornflakes, wholemeal bread, rye bread, nuts). Consequently, out of the four patterns identified in the BD patients group, three may be regarded as unhealthy, while in the control group two patterns out of four were considered healthy: *pro-healthy carbohydrates* and *vegetables and fruit* pattern. Therefore, it can be stated that the overall diet quality of bipolar patients was worse than that in the control group. The diet pattern called *pro-healthy carbohydrates* seen in the BD group could constitute - according to Jacka et al[24] – an attempt to reduce weight or prevent weight gain; it is also possible that, as food frequency was self-assessed, patients might report 'healthy' eating because such diet patterns are socially desirable.

As mentioned above, there are a few studies on the diet of patients with BD. It is difficult to compare their results due to differences in dietary assessment methods, different groups of patients, different ways of diagnosing BD or assessing the severity of mood disorders. In an Australian study[49] BD patients have had higher scores of the unhealthy western-style diet (processed meats, pizza, chips, white bread, etc.) than healthy controls. Our patients showed a similar pattern named *meats and potatoes* – with meats, offal, potatoes, white bread prevailing in their diet. However, any further comparison between both groups would be difficult since the Australian BD group was selected from an epidemiological survey and consisted of 23 persons, exclusively women. A study[69] conducted in the USA has been based on answers to dietary-related questions in the Veterans Affairs Large Health Survey of Veteran Enrollees. No differences in the reported fruit and vegetable intake between BD patients and subjects without serious mental illness have been observed. In our work, the dietary pattern with high intake of vegetables and fruit was identified only in the control group, not in the BD group. However, it must be noted that in the American study no information was given regarding the basis for diagnosing BD. On the

other hand, the analysis of the results of large epidemiological studies carried out in several European countries, the United States, Canada, Puerto Rico, Taiwan, Korea, and New Zealand has indicated a robust correlational relationship between greater seafood consumption and lower prevalence rates of bipolar disorders[70]. Polish BD patients, as well as the controls, did not report the noticeable frequency of consumption of fish or any seafood and such food items were not included in any dietary pattern. In our study, bipolar patients presented a dietary pattern defined by us as *meats and potatoes*, with a high frequency of consumption of unhealthy carbohydrates (like potatoes, white bread, rolls, pasta). Similar characteristics of consumption in BD patients have been reported by Elsmlie et al[8]. They used the 24-hour diet recall method mainly to assess the percentage of energy derived from various food sources in 89 euthymic bipolar patients. Higher energy intake from carbohydrates in BD patients, higher total energy intake in female patients, and no excessive intake of fat among the bipolar patients were observed. In this work, the dietary pattern of bipolar euthymic patients showed a higher frequency of consumption of fatty meats like pork, offal, oil and margarine. Only one Japanese study has compared food frequency intake in unipolar and bipolar patients (although diagnosis and assessment of symptoms severity have depended on self-rating scales)[71]. At the time of assessment, all patients were depressed and treated with antidepressants in an outpatient clinic. Japanese authors identified three dietary patterns called *plant foods and fish products*, *fish*, and *western/meat*. In male patients with bipolar depression, the *plant foods and fish products* pattern showed an inverse relationship with depressive symptoms[71]. In our study, the v*egetables and fruits* pattern was identified in the control group, and was not observed in bipolar patients. The results of the first dietary intervention as adjunctive treatment of BD are interesting, as they indicate that a high-quality diet is associated with better outcomes in BD[72]. A high-quality diet was defined as a diet rich in fruits and vegetables, whereas poorer-quality diets included more saturated fats, refined carbohydrates, and alcohol.

As it could have been predicted, our analysis indicated a correlation between the Mediterranean Diet Score and the dietary patterns in patients with BD. A positive correlation between the MDS and the *pro-healthy carbohydrates* dietary pattern scores and a negative correlation with the *western-type* pattern scores were found. Significantly lower MDS scores were observed in patients with higher adherence to the *western-type* and *meats and potatoes* dietary patterns. The Mediterranean-style diet includes healthy grains and nuts defined according to the PCA as *pro-healthy carbohydrates*. On the other hand, the *western-type* dietary pattern was related to higher consumption of food items not belonging to the Mediterranean diet, such as refined carbohydrates, processed meat, white bread, etc.

While there are few studies on the relationship between diet and BD, much more attention has so far been paid to the links between different aspects of diet and depression. For example, research has shown that unhealthy western-style diets are linked to the risk of depression. In the systematic review of observational studies Rahe et al[20] indicated that dietary patterns may exert influence on the onset of depression. Depression risk was inversely associated with a diet rich in fruits, vegetables, nuts and legumes according to a systematic review of prospective cohort studies[72] as well as a diet with a high intake of fruit, vegetables, fish, and whole grains[21]. In the British population, a higher risk of depression linked to a higher score on the western-style diet pattern was observed[74]. In a study of nearly 9,000 adults, participants whose diets involved a consistent intake of fast foods were as much as 40% more likely to develop depression than those who did not consume fast foods, with the risk for depression increasing along with the amount of fast foods consumed[75]. A recently published meta-analysis[76] showed that the western-style/unhealthy dietary pattern was associated with an increased risk of depression. Research on diet and depression has revealed an inverse association between diet quality and depression in various populations, such as Norwegian[24], Australian[17], and American[77,78] in both cross-sectional[17,77,79] and in longitudinal studies[60,74].

Considering Jacka et al's statement quoted above[49] on the relationship between diet and mood disorders in general and not broken down into unipolar depression and BD, this information may indicate the possible impact of the diet on the course of both types of mood disorders in terms of depressive recurrences. Our study did not reveal the relationship between diet and the course of BD; however, this result should be treated with great caution, due to its cross-sectional character and the retrospective way of collecting data on mood fluctuations.

As research results indicate that some food patterns, namely those with a higher intake of seafood, vegetables, fruits and nuts, can be associated with a reduced risk of depression, it appears that this should be taken into account in medical recommendations in the treatment of BD. The existing evidence suggests that healthy, recommended dietary practices may reduce the risk of development of depression and help to treat this disorder. It is to be hoped that the results of further controlled intervention studies will allow the introduction of dietary recommendations specific to BD in the future.

In our work, we also searched for links between diet and obesity/overweight in BD patients. Our findings showed that mean BMI in both groups was within the range of overweight (BMI more than 25 and less than 30), and more than one third of the participants in both groups were obese (BMI>30); the values did not differ between BD patients and the controls. The percentage of persons with obesity in the group of patients was 37.8%, which is consistent with data provided by other authors[80] and it was slightly higher than that in the control group (similarly to the percentage of persons with obesity). However, the differences were not statistically significant. Consequently, we did not confirm observations made by other authors regarding higher percentage of overweight and obesity (defined with BMI) in bipolar patients[8,81,82]. As obesity and overweight were associated with a worse course of BD[83], a greater intensity of depressive symptoms, poorer treatment results and the risk of early mortality[84], an accurate and as early as possible diagnosis of obesity is indispensable.

As waist circumference (an indicator of central adiposity) better explains obesity-related health risk[85] and is a stronger marker of a health risk than BMI[86] it is emphasized that a BMI measure does not reliably reflect the quantity of visceral adipose tissue. Waist circumference measurement is particularly useful in patients who are classified as normal or overweight on the BMI scale (a range to 29.9 kg/m^2). An increased waist circumference (an indicator of central adiposity) can be considered as a symptom of future obesity, and the driving force of metabolic syndrome and cardiovascular disease and type 2 diabetes[87,88]. The proposed Europid sex-specific cut-off points are 94 cm (men) and 80 cm (women) for an increased risk, and 102 cm (men) and 88 cm (women) for a substantially increased risk of diabetes and other metabolic disturbances[89]. In our patients and controls, the WC measurement was above recommended ranges and markedly higher in BD than in controls for both sexes. It is recommended to monitor changes in waist circumference over time, in addition to measuring BMI, to estimate the increased abdominal fat even in the absence of changes in BMI[90]. Obesity in BD patients may be primary (associated with symptoms of depression, particularly atypical depression[14], or personality traits[91]) or secondary to treatment[80], caused by consumption of sweet carbohydrate/fat rich foods for mood enhancement[92]. Other possible mechanisms are also postulated, including among others hypercortisolemia or changes in the perception of hunger[93], probably related to adipose-derived hormones like adiponectin and leptin[94] or gustatory system dysfunctions[95]. Development of obesity in BD is probably contingent upon a number of factors. Its negative effects (increased morbidity and mortality) indicate the need for obesity monitoring, prophylaxis and treatment.

Fat accumulation and abdominal obesity are strongly associated with insulin resistance and diabetes as their consequences (as well as many other somatic comorbidities). Detection and monitoring of IR by calculation of the HOMA (Homeostatic Model Assessment for Insulin Resistance)[96] is expensive and not easily available as glucose and insulin blood levels assessment is necessary. Another method, namely calculation of the TyG index as a marker of insulin resistance derived from serum triglycerides and glucose levels[37] has been postulated to be useful. In our work, bipolar patients tended to have higher serum glucose levels (p=0.065) and had significantly higher triglycerides levels (p=0.047) and TyG index (p=0.038) than the controls. In the BD group, the TyG scores were associated with BMI and waist circumference in male patients. An analysis of the relationships between biochemical parameters and the diet has shown, not surprisingly, that a high TyG score is remarkably associated with the *meats and potatoes* dietary pattern, which is loaded with refined carbohydrates (associated with hyperglycemia and IR). Insulin resistance and, consequently, diabetes are associated with depression[97-99], with some authors postulating an important role of glycemic pathology in affective disorders[100,101], and the progress of the illness[102], therefore IR monitoring is necessary.

Our research results, combined with the results obtained by other authors, unequivocally indicate the necessity for monitoring of the diet of patients with bipolar disorder. It is of multi-fold importance: first of all, it may help reduce the risk

of obesity and insulin resistance, which increase the risk of patient's early death, further somatic comorbidities and, probably, have a negative impact on the course of BD[103]. Dietary interventions, changes in the diet, and nutrition improvement may provide an efficacious and accessible treatment strategy for both the management of affective disorders and management/prevention of common somatic comorbidities. Dietary interventions are well accepted, relatively inexpensive and easy to implement as the patterns of dietary intake may be easily understood and interpreted by patients with mood disorders and translated into dietary recommendations. Making changes in the diet can also improve patients' functioning by increasing their sense of control and coping with the illness.

In the routine psychiatric practice, BMI assessment is often neglected or based on a patient's interview only (thus frequently being unreliable). Body weight and waist circumference should be measured as a simple and objective method of monitoring weight gain, abdominal obesity, and the obesity-related morbidity risk. Also in patients with BD, biochemical factors associated with the diet and obesity should be monitored. It seems that in the conditions of outpatient psychiatric care, determination of fasting glucose and triglycerides as well as of the TyG index in order to monitor co-occurrence of insulin resistance and screening towards diabetes type 2 should prove effective. These methods, which are inexpensive and generally available, provide important information of double importance in BD patients: first, associated with obesity and its comorbidities and secondly, with BD and the course of the disease. However, despite a growing body of evidence confirming the relationship of impairment of glucose metabolism (i.e., IR) and obesity in BD, they both remain under-detected and undertreated. There are no recommendations to screen affective patients for insulin resistance as well as for central obesity. It seems advisable that the new guidelines of procedure in BD should include a recommendation to measure WC, screen patients for glucose and TG levels and calculate the TyG index. In the authors' opinion, in the course of management of BD as a highly prevalent, lifelong, and recurrent disease, interdisciplinary co-operation is required. At the research level, psychiatrists may collect nutrition-related data about patients, however they do not have the knowledge of how to interpret them, while dieticians do not have the ability to examine mentally ill patients. During routine clinical practice, a dietician would be informed by the psychiatrist on how to account for the disease during their work, about the medications taken by the patient and about the impact of his/her mental condition, which would help them develop a diet adapted to the patient's needs. In turn, the psychiatrist would monitor the condition of the patient during the check-up visits and provide support in implementing dietary recommendations.

We are aware of the limitations of this study. The first of them is the fact that it is cross-sectional, and therefore it does not show the direction and nature of the interdependencies between studied parameters (for example, whether insulin resistance is a consequence of BD, associated with a poor lifestyle of patients, or whether insulin resistance is a predisposing factor for BD, having a negative impact on the course of the disease). Another limitation of our work was including only euthymic BD patients, as our intention was to assess the dietary pattern independently of mood symptoms. In the future, a prospective longitudinal study should be carried out in order to evaluate the complex interrelations of mood fluctuations and changes in the diet, nutrition and weight of bipolar patients. Our bipolar sample may not be representative of the entire bipolar population as they were tertiary care clinic patients, with long duration of illness and closed psychiatric care, involving a fixed visit plan and regular psychiatric assessment. We did not evaluate data on bipolar participants' medications which may have impacted their eating behavior. Approximately 45% of patients with bipolar disorder take medications associated with weight gain[104], which was also the case in the group studied, however an object of our study was the patients' diet and not the medications taken by them. Another limitation of the work was caused by the fact that the methods selected, and in particular the PCA, require subjective and arbitrary decisions in determining the number of factors to retain, in choosing the method of rotation of the initial factors, and in naming the dietary patterns. We should also take into account the social desirability bias as data derived from food frequency questionnaires are self-reported which could impact reliability. Nevertheless, previous validation studies have shown an adequate quality of such research method.

Despite the limitations, our results may supplement still insufficient data on diet quality of individuals with bipolar disorder, thus enhancing the possibility to provide a comprehensive ap-

proach to BD prevention and treatment targeting lifestyle factors, such as the eating patterns of bipolar patients. In view of the growing evidence for the significance of nutrition and obesity in affective patients (relevant to psychiatric and somatic state), it seems necessary to monitor and improve the diet of these patients, to influence both their mental and somatic health[30].

Conclusions

Bipolar euthymic patients eat less healthy; there are differences in dietary patterns in euthymic BD patients compared with healthy controls. BD patients show an increased waist circumference and an increased fasting triglycerides and glucose index (TyG) and disturbances in both these parameters are closely associated with insulin resistance. The results of our study point to the expediency of measuring waist circumference in order to monitor the possible central obesity in patients with BD. They also indicate that further research (particularly prospective studies) into the relationships between diet, nutrition, and BD should be conducted and that further close co-operation of psychiatrists, dieticians and other medical experts is necessary to develop dietary recommendations for patients with bipolar disorder.

Conflict of Interests

The authors declare that they have no conflict of interest.

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