ORIGINAL ARTICLE

Impact of micronutrients on anxiety-depressive disorders in type 2 diabetics

Impact des micronutriments sur les troubles anxio-dépressifs chez les diabétiques de type 2

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Abstract

Introduction: Micronutrient deficiencies are common in type 2 diabetics (T2D), promoting the occurrence of anxiety-depressive disorders.
Aim: The objectives of this study were to evaluate the micronutrient status of patients with type 2 diabetes (T2D), screen them for anxiety-depressive disorders, and investigate associations between these disorders and micronutrient intake.
Methods: This was a descriptive cross-sectional study involving 115 type 2 diabetics. They underwent a dietary survey and completed the Hospital Anxiety and Depression Scale (HAD) and Dopamine/Norepinephrine/Serotonin (DNS) questionnaires assessing anxiety-depressive disorders.
Results: Deficiencies in the intake of vitamins (A, E, C, B) and minerals (magnesium, copper, iron, zinc) were noted. Negative and significant associations were found between depression scores and the intake of vitamin B1 ($p=0.01$) and vitamin B6 ($p=0.024$). Similarly, negative and significant associations were found between anxiety scores and the intake of vitamin B6 ($p=0.049$), vitamin B9 ($p=0.019$), and vitamin B12 ($p=0.01$). Referring to the DNS score, we found negative associations between the dopamine score and the intake of vitamin B9 ($p=0.002$), magnesium ($p=0.003$), and copper ($p=0.007$) ; between the norepinephrine score and the intake of vitamin C ($p=0.046$), vitamin B6 ($p<0.001$), magnesium ($p=0.024$), and zinc ($p=0.009$); and between the serotonin score and the intake of vitamin B12 ($p=0.001$), magnesium ($p=0.027$), and zinc ($p=0.047$).
Conclusion: micronutrient deficiencies can exacerbate pre-existing anxiety and depressive disorders in type 2 diabetics. Systematic nutritional education is recommended, emphasizing a balanced and varied diet rich in vitamins and minerals.

Key words: type 2 diabetes, micronutrients, score, anxiety-depressive disorders.

Résumé

Introduction: Les carences en micronutriments sont fréquentes chez les diabétiques de type 2 (T2D) et favorisent l'apparition de troubles anxio-dépressifs.
Objectif: Les objectifs de cette étude étaient d'évaluer le statut en micronutriments chez les diabétiques de type 2 (DT2), de dépister les troubles anxio-dépressifs et d'étudier les associations entre ces troubles et l'apport en micronutriments.
Méthodes: Il s'agit d'une étude descriptive transversale impliquant 115 diabétiques de type 2. Ils ont bénéficié d'une enquête alimentaire et ont répondu aux questionnaires Hospital Anxiety and Depression Scale (HAD) et Dopamine/Norepinephrine/Serotonin (DNS) évaluant les troubles anxio-dépressifs.
Résultats: Des carences en vitamines (A, E, C, B) et en minéraux (magnésium, cuivre, fer, zinc) ont été constatées. Des associations négatives et significatives ont été retrouvées entre les scores de dépression et l'apport en vitamine B1 ($p=0,01$) et en vitamine B6 ($p=0,024$). De même, des associations négatives et significatives ont été retrouvées entre les scores d'anxiété et l'apport en vitamine B6 ($p=0,049$), en vitamine B9 ($p=0,019$) et en vitamine B12 ($p=0,01$). En se référant au score DNS, nous avons identifié des associations négatives entre le score dopamine et les apports en vitamine B9 ($p=0.002$), magnésium ($p=0.003$), et cuivre ($p=0.007$) ; entre le score noradrénaline et les apports en vitamine C ($p=0. 046$), vitamine B6 ($p<0.001$), magnésium ($p=0.024$), et zinc ($p=0.009$) ; et entre le score sérotonine et les apports en vitamine B12 ($p=0.001$), magnésium ($p=0.027$), et zinc ($p=0.047$).
Conclusion: les carences en micronutriments peuvent exacerber les troubles anxieux et dépressifs préexistants chez les diabétiques de type 2. Une éducation nutritionnelle systématique est recommandée, mettant l'accent sur une alimentation équilibrée et variée, riche en vitamines et minéraux.

Mots clés: diabète de type 2, micronutriments, score, troubles anxio-dépressifs.

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Introduction

Diabetes Mellitus affects millions of people all over the world. As of 2015, an estimated 30 million individuals of all ages have diabetes, of which 7.2 million individuals are unaware or did not report having diabetes (1). Type 2 diabetes (T2D) accounts for 90-95% of all diagnosed diabetes cases (1). Moreover, depression and anxiety are highly prevalent among individuals with diabetes (2). Studies indicate that adults diagnosed with T2D have a 1.2 to 1.6 times higher prevalence of depression compared to adults without diabetes (3). The lifetime prevalence of anxiety disorders among individuals with either T1D or T2D is estimated to be 20% higher than individuals without diabetes (4,5).

Individuals Diabetes symptoms such as weakness and fatigue are often seen as ambiguous and therefore reported more often by individuals with depression (6). Studies have examined the biasing impact of negative affect when illness symptoms are vague and difficult to differentiate from the psychophysical responses to emotional distress (7). Moreover, depression and anxiety share several somatic symptoms including, fatigue, changes in appetite, psychomotor slowing and changes in sleep (8). Among individuals with diabetes, the overlapping nature of these somatic symptoms can lead to a misidentification of affective disorders when self-reported screeners for mood symptoms are used (9,10).

The quality of an individual's diet plays an important role in the optimal functioning of their body. A balanced diet must provide the patient with a satisfactory intake of nutrients, particularly micronutrients. A deficiency in one or more of these micronutrients can have effects on the body, especially in type 2 diabetics. These individuals are not spared, according to the literature, where deficiencies in zinc, copper, magnesium, vitamin C and B vitamins have been reported (11). Indeed, the imbalance of the micronutritional status in these vulnerable patients could exacerbate preexisting anxiety-depressive disorders.

Very few studies have examined the impact of micronutrients deficiency on anxiety and depression of T2D. The objectives of our work were to evaluate the micronutrient intake of type 2 diabetics and to study the relationship between these intakes and the anxiety-depressive disorders reported in this population.

Methods

We conducted a cross-sectional descriptive study involving type 2 diabetic patients aged between 18 and 64 years. Patients not included were those with creatinine clearance below 60 ml/min, pregnant and breastfeeding women, patients with digestive malabsorption (celiac disease, crohn's disease, ulcerative colitis), or severe comorbidities (hepatic insufficiency, neoplasia) and patients taking dietary supplements.

All patients were interviewed to determine their age and the duration of their diabetes. A dietary survey was conducted during a dietary interview using the food history method. We referred to the Ciqual table, which specifies the nutritional composition of food products, to convert the food consumed by each patient into nutrients. The "Nutrilog" software, 2022 version available online, was used to analyze the results of this dietary survey and obtain a complete nutritional assessment.

The nutritional assessment provided information on :

- Total energy intake (TEI).
- Macronutrient intake: carbohydrates, fats, proteins, saturated fatty acids (SFA), polyunsaturated fatty acids (PUFA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), monounsaturated fatty acids (MUFA), dietary cholesterol and dietary fiber intake.
- Micronutrient intake :
  - Vitamins : vitamin A (vit A), vitamin D (vit D), vitamin E (vit E), vitamin C (vit C), vitamin B1 (vit B1), vitamin B2 (vit B2), vitamin B3 (vit B3), vitamin B6 (vit B6), vitamin B9 (vit B9), and vitamin B12 (vit B12).
  - Minerals : magnesium (Mg), calcium (Ca), iron (Fe), copper (Cu), zinc (Zn), selenium (Se), and manganese (Mn).

For the nutritional assessment analysis, we referred to the recommendations of the World Health Organization (WHO) (12) concerning the distribution of energy macronutrients: carbohydrates: 5g/kg/day and fats: 1g/kg/day.

Protein intake was evaluated based on the recommendations of the European Food Safety Authority 2017 (EFSA) (13) : proteins : 0.83 g/kg/day

Intake of cholesterol, SFA, MUFA, PUFA, as well as DHA and EPA, was evaluated based on the recommendations of the French National Agency for Food, Environmental and Occupational Health & Safety (ANSES) 2016 and European Food Safety Authority (EFSA) 2017 (14,15).

Fiber intake was considered insufficient if it was below 30g/day [16]. Micronutrient intake was evaluated based on the recommended intake by ANSES 2021 [14]. For micronutrients, we considered individual spontaneous intake satisfactory if it was between 70 and 100% of the recommended dietary allowance (RDA). It was considered insufficient below 70% of the RDA (16).

The total energy expenditure (TEE) over 24 hours is obtained by multiplying the basal metabolic rate (BMR) by a factor depending on the level of physical activity (PAL) (17) :

TEE (kcal/day) = BMR (kcal/day) * PAL

The BMR is estimated using the Black et al. (1996) formula, which is the reference formula (18) :

Men : [1.083*weight (kg)0,48 *Height (m)0,50*Age (years) -0,13] *(1000/4,1855)

women : [0,963* weight (kg)0,48*height (m) 0,50*Age (years) -0,13] *(1000/4,1855)

The result of this formula is in megajoules (MJ). To convert it to kilocalories (kcal), multiply it by 239 (17).

The PAL ranges defined according to the FAO/WHO/UN report (18) are :

- [1.4-1.69] if sedentary or slightly active lifestyle
- [1.70-1.99] if active or moderately active lifestyle
- [2.00-2.40] if vigorous or very active lifestyle

The spontaneous caloric intake (SCI) of each patient determined by the software (NUTRILOG) was evaluated based on their TEE. This intake was considered:

- Hypocaloric if the SCI was lower than the minimum calculated TEE
- Normocaloric if the SCI was between the minimum and maximum calculated TEE
- Hypercaloric if the SCI was higher than the maximum calculated TEE

To calculate energy needs and expenditures, it is sometimes necessary to use a calculated weight different from the patient's actual weight. This reference weight depends on their body mass index (BMI) (19).

Patients completed the HAD (Hospital Anxiety and Depression Scale) questionnaire : anxiety and depression (20). The HAD consists of 14 items rated from 0 to 3, used to screen for anxiety and depression. Even-numbered questions are associated with depression (Score D) and odd-numbered questions with anxiety (Score A). Two scores are obtained, each ranging from 0 to 21 (the maximum total score is 42). These two scores (A and D) are interpreted as follows:

- [0 - 7] : No anxiety and/or depressive disorders
- [8 - 10] : Doubtful symptomatology
- [11 - 21] : Anxiety and/or depressive disorders, possibly severe

Patients also completed the DNS (Dopamine, Norepinephrine, Serotonin) questionnaire validated by the European Institute of Dietetics and Micronutrition (IEDM) and used as a functional mood questionnaire (21). The DNS questionnaire measures the impact of diet on brain function. It highlights the idea that mental resources can be influenced by dietary intake. Furthermore, it allows addressing the patient in their functional symptomatology to achieve a diagnosis consistent with the micronutritional plan.

The DNS score includes three grids, each with an average of 10 questions rated from 0 to 3. Scores are classified as follows ; [0-9]: Low score ; [10-14]: Medium score ; [15-19]: High score ; [20-30]: Very high score.

Statistical Analysis

- Bivariate Analysis :

Simple linear regression analysis was performed to find an association between two quantitative variables (one dependent variable Y and one independent variable X). This association was studied by calculating the regression coefficient b1 indicating the direction of this association and the value of R^2 indicating the strength of the relationship between the two variables.

- Multivariate Analysis :

We performed a multivariate analysis using multiple linear regression to study the link between independents (x0, x1, x2, …) and the dependent variable (y). This relationship is expressed by the equation: $Y = \beta 0 * X0 + \beta 1 * X1 + \beta 2 * X2 + \ldots + \beta n * Xn + \varepsilon$. We included variables with a p-value less than 0.2 in the bivariate study to avoid masking the association by a confounding effect. We checked for the absence of multicollinearity by analyzing the VIF (variance inflation factor) value, which must be less than 10. We verified the normality of the distribution by the residual histogram and the Kolmogorov-Smirnov test.

The independence of errors (absence of autocorrelation between residuals) was checked by the Durbin-Watson statistical test. We considered a significant association between the studied variables if the p-value was below the significance threshold of 5%.

Conflicts of interest

All study participants were informed in advance of the type and purpose of the study and gave their consent for the use of their clinical and paraclinical data for the conduct of this study. We declare no conflict of interest in relation to this work. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the National Institute of Nutrition and Food Technology (N 07/2023).

Results

Descriptive Study

Our study involved 115 patients. The average age of the patients was 57.93 ± 7.48 years, with extremes ranging from 26 to 64 years. The majority of the included patients were female (67.8%) with a female-to-male ratio (F/M) of 2.1. The average duration of T2D was 10.94 ± 7.33 years, with extremes ranging from 1 to 30 years.

Table I illustrates the average intake of macronutrients. The average intake of vitamins and minerals is shown in Table II. In our study, deficiencies in the intake of B-group vitamins and vitamins D, A, E, and C were frequent. Similarly, we found deficiencies in mineral intake (magnesium, manganese, copper, iron, and zinc) (Table II).

Table 1. Average macronutrient intake

Parameters	Mean ± Standard Deviation	Min	Max
Carbohydrates (g/kg/day)	4.971 ± 0.919	2.48	7.77
Simple sugars (g/day)	67.6 ± 16.14	31.7	98
Proteins (g/kg/day)	0.948 ± 0.202	0.51	1.65
Lipids (g/kg/day)	1.52 ± 0.297	0.88	2.21
Saturated fatty acids (SFA) (% total energy intake)	12.31 ± 1.33	8.69	14.88
Monounsaturated fatty acids (MUFA) (% total energy intake)	14.98 ± 4.86	6.99	26.23
Polyunsaturated fatty acids (PUFA) (% total energy intake)	6.77 ± 1.61	3.49	10.87
DHA (mg/day)	210 ± 31.61	148	280
EPA (mg/day)	209.16 ± 27.99	120	265
Cholesterol (mg/day)	333.06 ± 45.45	257	425
Fibers (g/day)	31.5 ± 2.88	21.1	39.8

SFA = Saturated Fatty Acids, **MUFA** = Monounsaturated Fatty Acids, **PUFA** = Polyunsaturated Fatty Acids, **DHA** = Docosahexaenoic Acid, **EPA** = Eicosapentaenoic Acid

Using the "Hospital Anxiety and Depression Scale," we noted that 38.3% of patients had definite anxiety and 34.7% had definite depression. According to the DNS scores, these were classified as strong in 19% and very strong in 14.9% of the population, respectively (Figure 1).

Table 2. Vitamin and mineral intake

Parameters	Mean ± Standard Deviation	Min	Max	Micronutrient intake deficiencies (% of patients)
Vitamin A (µg/day)	643.41 ± 191.91	205	1020	47.8
Vitamin D (µg/day)	11.30 ± 3.71	6.05	29.10	52.2
Vitamin E (mg/day)	12.11 ± 4.83	3.15	30.10	22.6
Vitamin C (mg/day)	97.4 ± 46.13	23.40	307	35.7
Vitamin B1 (mg/day)	0.89 ± 0.2	0.49	1.31	32.2
Vitamin B2 (mg/day)	1.16 ± 0.26	0.52	1.85	38.3
Vitamin B3 (mg/day)	12.34 ± 4.22	0.90	31.90	18.3
Vitamin B6 (mg/day)	1.22 ± 0.24	0.77	2.08	40.9
Vitamin B9 (µg/day)	272.81 ± 71.64	103	475	35.7
Vitamin B12 (µg/day)	3.66 ± 1.69	1.12	7.80	42.6
Calcium (mg/day)	757.36 ± 218.36	275	1288	32.2
Magnesium (mg/day)	238.59 ± 51.59	103	411	51.3
Iron (mg/day)	8.17 ± 1.77	4.50	13.70	44.3
Copper (mg/day)	1.28 ± 0.37	0.54	2.9	38.3
Zinc (mg/day)	7.07 ± 2.08	2.32	11.8	37.4
Manganese (mg/day)	2.66 ± 0.79	1.02	4.32	30.4
Selenium (µg/day)	92.09 ± 41.79	42.5	276	19.1

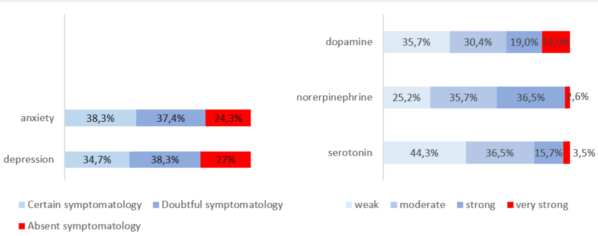

Figure 1. Distribution of Patients According to the HAD/DNA Score

Analytical Study

In the bivariate analysis, significant negative associations were found between the depression score and the intake of vitamin B1 (p=0.01) and vitamin B6 (p=0.024). Additionally, significant negative associations were found between the anxiety score and the intake of vitamin B6 (p=0.049), vitamin B9 (p=0.019) and vitamin B12 (p=0.04) (Table III).

Referring to the DNS score, in the bivariate analysis, we found significant negative associations between the dopamine score and the intake of vitamin B9 (p=0.002), magnesium (p=0.003) and copper (p=0.007). Similarly, significant negative associations were found between the norepinephrine score and the intake of vitamin C (p=0.046), vitamin B6 (p<0.001), magnesium (p=0.024) and zinc (p=0.009). Regarding the serotonin score, significant negative associations were found with the intake of vitamin B12 (p=0.001), magnesium (p=0.027), and zinc (p=0.047) (Table IV).

Table 3. Micronutrient Intake and Anxiety/Depression Score in univariate analysis

	Micronutrient Intake and Anxiety Score		Micronutrient Intake and Depression Score	
Parameters	**Regression Coefficient b ± Standard Deviation**	**p-value**	**Regression Coefficient b ± Standard Deviation**	**p-value**
Vitamin B1	-0.135 ± 1.235	0.150	-0.239 ± 1.118	**0.01**
Vitamin B2	-0.028 ± 0.983	0.765	-0.190 ± 0.891	0.42
Vitamin B3	-0.057 ± 0.061	0.548	-0.175 ± 0.056	0.062
Vitamin B6	-0.184 ± 1.02	**0.049**	-0.210 ± 0.934	**0.024**
Vitamin B9	-0.219 ± 0.004	**0.019**	-0.014 ± 0.003	0.886
Vitamin B12	-0.192 ± 0.149	**0.04**	-0.178 ± 0.138	0.057
Magnesium	-0.143 ± 0.005	0.127	-0.069 ± 0.005	0.461
Iron	-0.05 ± 0.146	0.595	-0.134 ± 0.134	0.154
Copper	-0.045 ± 0.696	0.632	-0.014 ± 0.643	0.885
Zinc	-0.147 ± 0.123	0.118	-0.177 ± 0.113	0.59
Selenium	0.020 ± 0.006	0.831	0.049 ± 0.006	0.606

Table 4. Micronutrient Intake and Dopamine/ Norepinephrine/ Serotonin Score in univariate analysis

	Micronutrient and Dopamine Score		Micronutrient and Norepinephrine Score		Micronutrient and Serotonin Score	
Parameters	**Regression Coefficient b ± Standard Deviation**	**p-value**	**Regression Coefficient b ± Standard Deviation**	**p-value**	**Regression Coefficient b ± Standard Deviation**	**p-value**
Vitamin C	-0,285 ± 0,21	0.410	-0,187 ± 0,011	**0,046**	-0.131±1.32	0.356
Vitamin B2	-0.118 ± 2.09	0.210	-0.015 ± 1.88	0.869	-0.043 ± 1.8	0.646
Vitamin B3	-0.063 ± 0.131	0.502	-0.161 ± 0.116	0.087	-0.125 ± 0.112	0.182
Vitamin B6	-0.020 ± 2.22	0.836	-0.416 ± 1.8	**<0.001**	0.155 ± 1.89	0.935
Vitamin B9	-0.286 ± 0.007	**0.002**	-0.171 ± 0.007	0.068	-0.192±0.002	0.328
Vitamin B12	-0.135 ± 0.323	0.149	-0.081 ± 0.29	0.390	-0.301 ± 0.267	**0.001**
Magnesium	-0.278 ± 0.01	**0.003**	-0.211 ± 0.009	**0.024**	-0.206 ± 0.009	**0.027**
Zinc	-0.139 ± 0.263	0.14	-0.243 ± 0.231	**0.009**	-0.186 ± 0.225	**0.047**
Copper	-0.252 ± 1.45	**0.007**	-0.080 ± 1.33	0.395	-0.131±1.22	0.156
Iron	-0.103 ± 0.311	0.272	-0.030 ± 0.28	0.754	-0.131 ± 0.267	0.164
Selenium	-0.116 ± 0.013	0.218	-0.105 ± 0.012	0.262	-0.122±0.221	0.203

In the multivariate analysis, a significant association was noted between the dopamine score and the intake of vitamin B9 (p=0.029) and magnesium (p=0.021). A significant negative association was found between the norepinephrine score and the intake of vitamin B6 (p<0.001). Serotonin score was associated with vitamin B12 (p=0.002) and magnesium (p=0.02) intake (Table V).

Table 5. Micronutrient Intake and Dopamine/ Norepinephrine/ Serotonin Score in multivariate analysis

Micronutrient Intake and Dopamine Score		
Parameters	**Regression Coefficient b ± Standard Deviation**	**p-value**
Vitamin B12	-0.025 ± 0.32	0.791
Vitamin B9	-0.212 ± 0.008	0.029
Magnesium	-0.21 ± 0.01	0.021
Zinc	0.16 ± 0.287	0.879
Copper	-0.168 ± 1.54	0.087
R^2 = 0.163		
Micronutrient Intake and Norepinephrine Score		
Parameters	**Regression Coefficient b ±Standard Deviation**	**p-value**
Vitamin C	-0.099 ± 0.01	0.267
Vitamin B3	-0.101 ± 0.123	0.308
Vitamin B6	-0.407 ± 2.01	<0.001
Vitamin B9	0.130 ± 0.007	0.170
Magnesium	-0.101 ± 0.009	-0.252
Zinc	0.117 ± 0.247	0.231
R^2 = 0.244		
Micronutrient Intake and Serotonin Score		
Parameters	**Regression Coefficient b ± Standard Deviation**	**p-value**
Vitamin B3	-0.073 ± 0.112	0.516
Vitamin B12	-0.845 ± 0.270	0.002
Magnesium	-0.02 ± 0.008	0.02
Iron	-0.394 ± 0.251	0.12
Zinc	-0.117 ± 0.247	0.237
R^2 = 0.253		

Discussion

Negative and significant associations were found between depression scores and the intake of vitamin B1 and vitamin B6. Similarly, negative and significant associations were found between anxiety scores and the intake of vitamin B6, vitamin B9 and vitamin B12.

Modern diets, often characterized by unbalanced nutritional intake, lead to micronutrient deficiencies. Type 2 diabetics, in particular, are not spared from these deficiencies. The deterioration of micronutrient status in this vulnerable population has been well established through several studies (22,23). These micronutrient deficiencies can impact brain function, causing fatigue, concentration disorders, anxiety and depression. In this context, we conducted a cross-sectional descriptive study on 115 type 2 diabetic (T2D) patients. The objectives of this work were to assess the micronutritional status of patients with T2D, to screen them for anxiety and depressive disorders using HAD and DNS questionnaires, and to investigate associations between these disorders and micronutrient intake.

In our study, deficiencies in the intake of B-group vitamins and vitamins D, A, E, and C were found. Similarly, we identified deficiencies in mineral intake (magnesium, manganese, copper, iron, and zinc). We found significant negative associations between depression and anxiety scores and deficiencies in B-group vitamins (B1, B6, B9, and B12). Additionally, significant negative associations were found between DNS scores and deficiencies in minerals (magnesium, copper, zinc) and vitamins (vitamin C, vitamin B6, vitamin B12).

Our study had some limitations, indeed, we assesd micronutrient intake only through dietary surveys because measuring micronutrient levels is not a common practice and requires a budget. Moreover, micronutritional status is influenced by many factors difficult to evaluate, such as gut microbiota and genetics.

Micronutrient Intake

Vitamins and minerals are necessary in small amounts, but their presence is crucial for cellular metabolism. Our study demonstrated that micronutrient deficiencies are very common among type 2 diabetics. Vitamin D deficiency was the most frequent, found in 52.2% of diabetic patients. For B-group vitamins, deficiencies in B1, B2, B3, B6, B9 and B12 were common, observed in 32.2%, 38.3%, 18.3%, 40.9%, 35.7% and 42.6% of patients, respectively.

For other vitamins, deficiencies in vitamins A, E, and C were found in 47.8%, 22.6%, and 35.7% of patients, respectively. Regarding minerals, deficiencies in magnesium, manganese, copper, iron, and zinc were noted in 51.3%, 30.4%, 38.3%, 44.3%, and 37.3% of patients, respectively. According to the S.U.V.I.M.A.X study, 77% of women and 72% of men have magnesium intakes below two-thirds of the recommended daily allowance (RDA) (24). A Tunisian study conducted in 2021 on diabetic patients also found deficiencies in vitamins D, C, B12, and B9 in 95%, 60%, 58%, and 50% of diabetics, respectively. In the same study, deficiencies in copper, magnesium, and calcium intake were found in 60%, 65%, and 80% of diabetics, respectively (25). Similarly, a study conducted in Iran showed deficiencies in vitamin D (75.3%), vitamin C (58.5%), vitamin B6 (54.4%) and vitamin B9 (61.2%) (26). According to the Val de Marne study, 80% of individuals did not meet the RDA for zinc and vitamin B6 and 40% had a deficiency in vitamin B9 and 100% in magnesium (27).

Prevalence of Anxiety and Depressive Disorders in Type 2 Diabetics

The results of our study highlight a high prevalence of anxiety and depressive disorders in type 2 diabetics. Using the "Hospital Anxiety and Depression Scale," we noted that 38.3% of patients had definite anxiety and 34.7% had definite depression, thus highlighting the extent of these disorders in this population. Our results are similar to the studies by Jagielski and Hudson (28,29), where depression and anxiety were present in 40% of people with diabetes. In the study by Collins et al., conducted on 1456 type 2 diabetic patients, the prevalence of anxiety and depression was 32% and 22.4%, respectively. In other studies, the prevalence of anxiety and depressive disorders was higher, around 60% (30-32). However, in other works, depressive disorders were estimated at around 17%, while the prevalence of anxiety disorders was around 29% (33,34).

Micronutrient Intake and Anxiety-Depressive Disorders

In our study, we found significant negative associations between the HAD anxiety score and the intake of vitamins B6 (p=0.049), B9 (p=0.019) and B12 (p=0.04). Similarly, significant negative associations were also found between the HAD depression score and the intake of vitamin B1 (p=0.01) and vitamin B6 (p=0.024).

A study conducted in Japan (35) showed that people with panic attacks and thus highly prone to anxiety had low blood levels of vitamin B6. Due to its importance as a cofactor in many metabolic reactions in the body, a deficiency in vitamin B6 can have repercussions on many bodily functions and can be associated with various symptoms: skin, hematological, and neurological. Among the neurological signs are mood disorders, depressive tendencies, and anxiety. Cobalamins are currently being evaluated to determine if they could help in the management of mood disorders (36,37).

Although mood swings are largely due to life events, psychological, relational, or social circumstances, adaptation to these events ultimately depends on the neurotransmitters present in the central and peripheral nervous system. The balance of their biosynthesis can vary due to genetic, environmental, and nutritional factors. These factors intervene at different levels in the synthesis, release, mobilization, and action of neurotransmitters. Many studies have since confirmed the importance of dietary precursors and mineral and vitamin cofactors (iron, magnesium, zinc, vitamin C, B-group vitamins - B1, B3, B6, B9 and B12) in the synthesis of brain neurotransmitters (38,39).

In our study, we found significant negative associations between the dopamine score and the intake of vitamin B9 (p=0.002), magnesium (p=0.003), and copper (p=0.007). In multivariate analysis, a significant association was noted between the dopamine score and the intake of vitamin B9 (p=0.029) and magnesium (p=0.021). Similarly, we identified significant negative associations between the norepinephrine score and the intake of vitamin C (p=0.046), vitamin B6 (p<0.001), magnesium (p=0.024), and zinc (p=0.009). In multivariate analysis, a significant negative association was found between the norepinephrine score and the intake of vitamin B6 (p<0.001). Furthermore, we observed significant negative associations between the serotonin score and the intake of vitamin B12 (p=0.001), magnesium (p=0.027), and zinc (p=0.047). In multivariate analysis, significant negative associations were found between this score and the intake of vitamin B12 (p=0.002) and magnesium (p=0.02).

To function properly, the brain uses enzyme precursors, vitamins, and minerals provided by our diet and necessary for the synthesis of neurotransmitters that manage our behavior, actions, moods and sleep. If these raw materials are insufficient, the synthesis of these neurotransmitters would be reduced, potentially leading to behavioral changes due to decreased activity. Among the neurotransmitters present in the brain, three have major importance : dopamine, norepinephrine and serotonin (40).

Dopamine: Acts as a "starter." It plays an important role in initiating action and is involved in several cognitive functions such as learning, attention, and thought structuring. It is also involved in mood and emotion regulation. Its synthesis occurs in several steps and requires the presence of phenylalanine and tyrosine, with the main source being dietary proteins. Tyrosine is then converted to L-Dopa by tyrosine hydroxylase. This process requires B-group vitamins (B2, B3, B6, B9, and B12) and iron as cofactors. Then, L-Dopa is converted to dopamine by DOPA decarboxylase in the presence of certain cofactors, which are vitamin B6, magnesium and zinc (40).

Norepinephrine: Is involved in action amplification, pleasure seeking, reward, and learning and memory processes. A norepinephrine deficiency could result in memory disorders, reduced pleasure, anhedonia, and moral suffering. For the synthesis of this neurotransmitter, an enzyme, dopamine beta-hydroxylase, transforms dopamine into noradrenaline, involving previously cited cofactors plus copper and especially vitamin C, which is necessary for the hydroxylation of dopamine to give norepinephrine. Magnesium is involved in its storage (39).

Serotonin: Serotonin is an indoleamine acting as a "brake," involved in impulse control and action inhibition. Hypoactivity of the serotonergic system can lead to aggression, disinhibition, irritability and anxiety. Serotonin is synthesized in neurons and enterochromaffin cells of the gastrointestinal plexus from tryptophan. Its synthesis involves multiple decarboxylation steps and requires certain cofactors (B vitamins, iron, zinc and magnesium) (41).

Magnesium can also act as a neuroprotector, capable of regulating the permeability of the blood-brain barrier. A relationship between stress reactions, such as anxiety and magnesium deficiency has been reported by Tarasov et al. These results highlight the importance of dietary precursors ; mineral and vitamin cofactors (magnesium, zinc, vitamin C, and B vitamins) in the synthesis of brain neurotransmitters (42).

Colin S., in his study conducted in 2018, demonstrated the importance of various micronutrients in the treatment of anxiety and depression (43).

Conclusion

Modern diets are characterized by the emergence of ultra-processed foods with a high caloric content and low micronutrient intake. This diet consists of empty or hollow calories, leading to micronutrient deficiencies that can exacerbate pre-existing anxiety and depressive disorders in type 2 diabetics. Systematic nutritional education is recommended, emphasizing a balanced and varied diet rich in vitamins and minerals.

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