Int J Nutr Sci 2025;10(1):2-10

International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

Review Article

Association between Dietary Acid Load and Depression, Anxiety, and Stress: A Systematic Review

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ARTICLE INFO

Keywords:
Dietary acid load
Depression
Anxiety
Stress
Mental health

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Received: June 15, 2024
Revised: September 10, 2024
Accepted: September 16, 2024

ABSTRACT

Background: Several studies have suggested a potential association between diet and mental disorders. This systematical review investigated the association between dietary acid load (DAL) and mental health outcomes such as depression, anxiety, and stress.

Methods: Online databases including PubMed, Scopus, and Web of Science searched for published studies using relevant keywords until January 2024.

Results: Seven studies were included in this systematic review, of which 6 were on adults. Five out of six studies on depression evaluated dietary acid load (DAL) with potential renal acid load (PRAL) method of which 3 of them reported a significant association. Three out of five studies that used net endogenous acid production (NEAP) method also presented a significant direct association. Furthermore, five studies examined the relationship between DAL and anxiety and all revealed a significant direct association. Moreover, a direct association between DAL and stress was noticed in two other studies. In terms of children and adolescents, a prospective study found no association between DAL and overall mental health among children and adolescents.

Conclusion: Dietary acid load, especially PRAL, may be associated with psychological disorders like depression, anxiety, and stress among women. However, in the interpretation of these findings, it should be considered that the heterogeneity among studies is high as most of them conducted the study on women and participants had underlying diseases; so the conclusion cannot be extended to the overall population due to the limited number and design of current studies.

Please cite this article as: Zare MJ, Madani S, Ahmadi A. Association between Dietary Acid Load and Depression, Anxiety, and Stress: A Systematic Review. Int J Nutr Sci. 2025;10(1):2-10. doi: 10.30476/ijns.2024.101366.1308.

Introduction

Mental health is one of the significant components of a healthy lifestyle (1). According to the World Health Organization (WHO) report, the worldwide prevalence rate of depression is estimated to be around 4.4%, and for anxiety disorder to be 3.6% (2). Mental disorders such as depression and anxiety are complex conditions that involve biological, social, and environmental factors (3) and can have a profound impact on society, leading to a decrease in quality of life and work performance, as well as an increase in healthcare costs and mortality rates. Therefore, investigations on related factors of mental health can lead to

enhancement in the prevention and treatment of different mental problems (1, 4, 5). Several studies have suggested a potential association between diet and mental disorders (5, 6). For instance, a meta-analysis indicated a significant direct association between the inflammatory potential of diet with depression, anxiety, and distress (7). Also, diet may impact brain function through the impression of the gut-brain barrier axis and gut microbiotome (5, 8, 9). In addition, an inverse association between a high intake of base-inducing foods like vegetables and fruits and a positive association between acid-inducing foods like red or processed meat and depression has been found in some studies (10-13).

Various methods have been developed to assess dietary acid load (DAL), including net endogenous acid production (NEAP) and potential renal acid load (PRAL). NEAP assesses protein to potassium ratio, while PRAL evaluates protein, phosphorus, potassium, magnesium, and calcium intake (14, 15). The relationship between DAL and different aspects of mental health has been investigated in several studies. Milajerdi *et al.* found a significant direct association between DAL and depression and anxiety in adults (16), which was also observed in another cross-sectional study focused on women (17). However, a study in children and adolescents did not find any significant association between DAL and depression or anxiety. Nevertheless, participants with higher DAL exhibited higher levels of emotional problems and hyperactivity (18). As these studies have been conducted on different populations and have used different methods for assessing DAL and mental outcomes; therefore, we conducted a systematic review to summarize all available studies and provide a comprehensive understanding of the association between DAL and depression, anxiety, and stress.

Materials and Methods

Search Strategy

This study was conducted based on the PRISMA guideline for reporting systematic reviews and meta-analyses (19). PubMed, Scopus, and Web of Science online databases were used to search for published studies until January 2024. Keywords used in the search strategy included mental health-related terms and dietary acid load terms. In addition, the reference list of relevant studies was searched for possible eligible studies for review. No restriction was considered for the time of publication or study design.

Inclusion and Exclusion Criteria

Studies with the following criteria were included: (i) Observational studies with prospective, case-control, or cross-sectional designs; (ii) Measurement of the dietary acid load of the diet; and (iii) Assessment of the mental disorders as outcome in all age groups. If a finding from one data set was published in more than one article, a paper with more complete findings was included. Letters, comments, short communications, reviews, meta-analyses, and ecological studies were excluded.

Data Extraction

In this study, two authors separately collected the information in the articles, including the first author's name, date of publication, the characteristics of the participants, age, gender, country, sample size, method of exposure and outcome assessment, length of the follow-up period and the results.

Quality Assessment

The quality of the studies was evaluated by the Newcastle-Ottawa Scale (NOS) indecently by two authors. This checklist consisted of three parts (selection, comparability, exposure/outcome). Finally, based on the scores obtained, the studies were divided into three groups of good, fair, and poor quality. Studies with seven or more points were considered as good; while five to seven were regarded fair and less than five was defined as poor quality (20).

Results

Six-hundred and nine studies were identified in the initial search; while 232 studies were excluded due to duplication. Moreover, after screening by title and abstract, 363 studies were excluded for being unrelated. Fourteen full-text articles of potentially relevant studies remained for full-text review. Of these, 7 studies were excluded because of being irrelevant (n=6) and being review article (n=1) and overall, 7 studies were included. The flow diagram of study selection is displayed in Figure 1.

Characteristics of Studies

Table 1 provides a summary of the characteristics of the studies included in this systematic review. A total of 7 studies were reviewed, consisting of 3 observational cohort studies (18, 21, 22), and 4 cross-sectional studies (16, 17, 23, 24). Of the 6 studies on adults, 4 were conducted on women (17, 21, 23, 25). The studies were conducted in various countries, including Iran (16, 17, 23, 24), USA (21), Germany (18), and Australia (22). Four studies reported data for DAL using both PRAL and NEAP methods (17, 21, 23), while 3 studies reported only PRAL (18, 25), and one presented only NEAP (16). Two studies also demonstrated DAL by following the equation DAL (mEq/day)=[PRAL+(body surface area [m2]×41 [mEq/day])/1.73 m2] (17, 24).

Table 1: Characteristics of included studies.

Study/Year	Type of study/ Country	Participants/ Age	Exposure measure-ment	Outcome measure-ment	Follow-up	Exposure	Outcome	Measures of association OR (95%CI)/ β(95%CI)	Results	Quality of study	Adjustments
Adults											
Bahari	Cross-sectional/ Iran	5631 participants/35-65 years	65-item FFQ	BDI-II BAI	_	PRAL	Depression	1.07 (0.95-1.20)	DAL was not associated with depression in the total population but women with higher DAL or PRAL had higher odds of depression (OR: 1.2; 1.03-1.42, OR: 1.2; 1.03-1.39) respectively; no significant association was observed in men. Higher PRAL was associated with 13% higher odds of anxiety. DAL† was not significantly associated with anxiety.	Good	1, 3, 5, 8, 15, 16, 17, 36, 37, 38
							Anxiety	1.13 (1.01-1.13)			
						DAL†	Depression	1.00 (0.89-1.13)			
							Anxiety	0.97 (0.86-1.09)			
Saul *et al.* (22)	Cohort/ Australia	161 participants with multiple sclerosis/18-59 years	DQES	HADS	10	PRAL	Depression	β=0.09 (0.03-0.15)	Higher DAL may lead to a gradual increase in depression scores over time and a less conceiving association for anxiety in patients with multiple sclerosis	Good	1, 2, 3, 8, 35
							Anxiety	β=0.11 (0.05-0.17)			
						NEAP	Depression	β=0.07 (0.01-0.14)			
							Anxiety	β= 0.10 (0.04-0.16)			
Milajerdi *et al.* (16)	Cross-sectional/ Iran	4378 nonacademic healthy adults (56% women)/36.3±7.8	168-item FFQ	HADS	-	NEAP	Depression	2 (1.52-2.64)	Higher DAL indicates 100% higher odds for depression and 92% for anxiety compared to participants in the lower DAL category	Good	1, 2, 3, 4, 5, 8, 15, 16, 17, 18, 19
							Anxiety	1.92 (1.35-2.74)			
Daneshzad *et al.* (23)	Cross-sectional/ Iran	230 diabetic women/59.9±9.2	168-item FFQ	DASS-21 PSQI	-	NEAP	Depression	1.15 (0.60-2.21)	Although both PRAL and NEAP did not show a significant association with depression, it seems that participants with higher DAL were more likely to have inadequate anxiety, stress, and sleep quality	Good	1, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14
							Anxiety	1.27 (0.67-2.38)			
							Stress	2.13 (1.13-4.01)			
							Sleep quality	2.81 (1.34-5.90)			
						PRAL	Depression	1.88 (0.95-3.73)			
							Anxiety	2.62 (1.35-5.07)			
							Stress	2.59 (1.36-4.94)			
							Sleep quality	3.74 (1.73-8.11)			

Mozaffari *et al.* (17)	Cross-sectional/ Iran	447 healthy women/31.68±7.64	168-item FFQ	DASS-21	-	NEAP	Depression	3.42 (1.87-6.23)	A significant direct association was found between DAL (PRAL, NEAP, DAL†) and depression, anxiety, and stress	Good	1, 3, 4, 5, 6, 7, 8, 10, 15, 19, 27, 29, 34
							Anxiety	3.47 (1.90-6.33)			
							Stress	3.67 (2.04-6.58)			
						PRAL	Depression	3.63(1.97-6.71)			
							Anxiety	3.31 (1.81-6.06)			
							Stress	3.79 (2.09-6.90)			
						DAL†	Depression	3.02 (1.64-5.58)			
							Anxiety	3.25 (1.76-5.98)			
							Stress	3 (1.66-5.43)			
Wu *et al.* (21)	Cohort/ USA	2975 breast cancer survivors (100% women)/50	24-h recalls, 4 times	CES-D	7.3	NEAP	Depression	1.17 (0.98-1.41)	PRAL indicates a significant direct association with depression in breast cancer survivors, especially among younger adults<55 and patients with a sedentary lifestyle	Good	1, 3, 5, 8, 20, 21, 22, 23, 24
						PRAL	Depression	1.34 (1.11-1.62)			
Children											
Bühlmeier *et al.* (18)	Cohort	1685 children and adolescents	80-item FFQ	SDQ	15	PRAL	Mental health	1.04 (0.5-2.15)	No significant prospective association was observed between PRAL and mental health. Association between PRAL and mental health was just significant among 10-year-old cross-sectional analysis	Good	2, 3, 5, 8, 28, 30, 31, 32, 33
								1.25 (1.02-1.53)			
	Cross-sectional 10-years-old	2350 children						1.12 (0.67-1.88)			
	Cross-sectional 15-years-old	2061 adolescents									

BAI: Beck Anxiety Inventory; BDI- II: The Beck Depression Inventory-II; DQES: Dietary Questionnaire for Epidemiological Studies; DSM-5: Diagnostic and Statistical Manual of Mental Disorders-5th Edition; CES-D: Center for Epidemiologic Studies Depression Scale; DASS-21: twenty-one-item Depression, Anxiety and Stress Scale; FFQ: food frequently questionnaire; FSS: Fatigue severity scale; HADS: Hospital Anxiety and Depression Scale; NEAP: net endogenous acid production; PRAL: Potential renal acid load; PSQI: Pittsburgh Sleep Quality Index; SDQ: Strengths and Difficulties Questionnaire; SF-36: Rand 36-Item Short Form Health Survey. †DAL: [PRAL + (body surface area [m2]×41 [mEq/ day]/1.73 m2] ‡Adjustment: age (1), gender (2), body mass index (3), socio-economic status (4), physical activity (5), supplement intake (6), fiber intake (7), energy intake (8), vitamin D (9), medications (10), lipid profile (11), blood pressure (12), sleep duration at night (13), nap time (14), marriage status (15), smoking (16) presence of chronic conditions (17), supplement use and antidepressants use (18), dietary intake of omega-3 fatty acids (19), menopausal status at baseline (20), living alone status (21), number of comorbidities at baseline (22), intakes of vitamin B12 (23), intakes of vegetables (24) metabolic equivalents in minutes per week (25), estrogen and progesterone receptor status (26), hours spent sleeping and outside home (27), study (28), family history of psychological disorders and chronic diseases (29), (30), sedentary behavior (30), pubertal status (31), parental education (32), recruitment region (33), body image (34), dietary reporting (35), education level (36), fiber (37), MUFA (38).

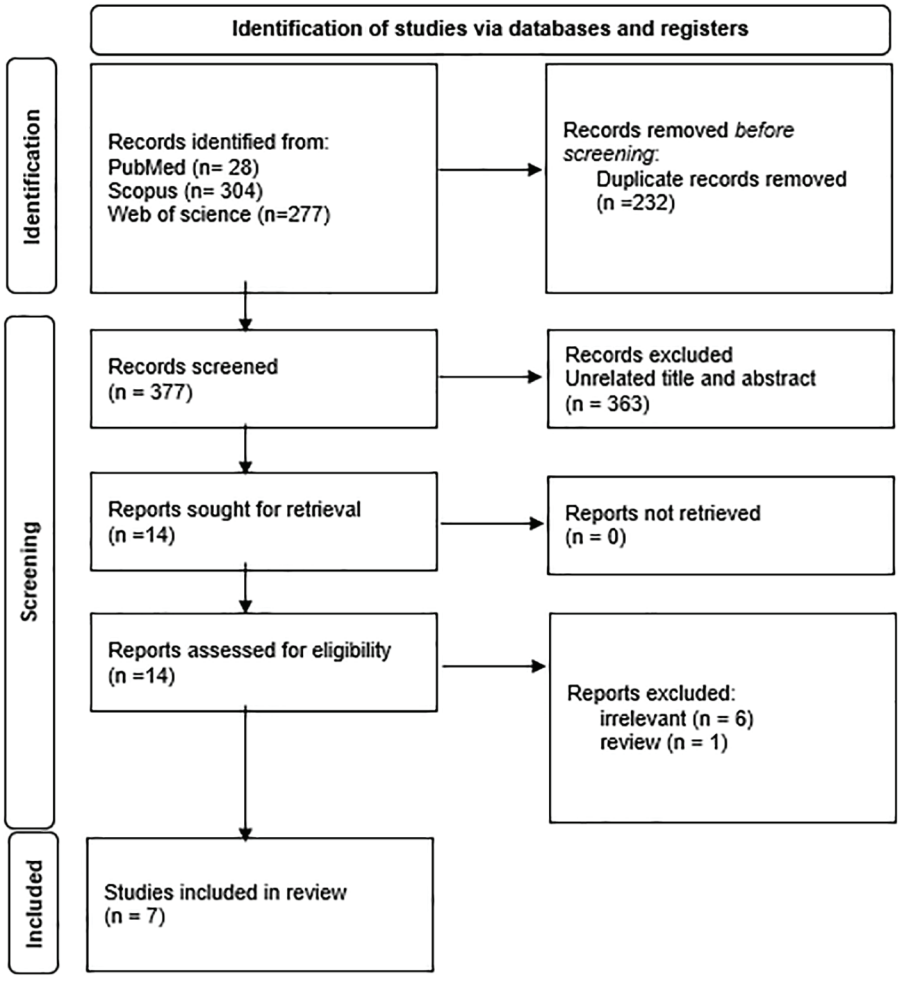

Figure 1: Flowchart of study screening and selection process.

Dietary Acid Load and Depression

Six studies evaluated the association between DAL and depression; while four reporting a significant association. Table 1 summarizes the key results of the included studies. Bahari *et al.* found no significant association between DAL and depression among participants. Meanwhile, in a sex-stratified analysis, the study revealed 20% higher odds for depression in women, while this association was not significant among men (24). A prospective study on patients with multiple sclerosis observed a direct significant association between DAL and depression (22). Milajerdi *et al.* in a cross-sectional study observed a significant direct association between NEAP and depression among healthy adults (16). In another cross-sectional study on healthy women using PRAL, NEAP, and DAL (calculated by PRAL with considering body surface area) method, a significant direct association was visible between DAL and depression (17). Meanwhile, in another cross-sectional study on diabetic women, no significant association was seen between DAL and depression (23). A Longitudinal study by Wu *et al.* (21) on breast cancer survivors noted a significant direct association between PRAL and depression, especially among younger adults (age<55 years) and participants with a sedentary lifestyle had no association by NEAP method.

Dietary Acid Load and Anxiety and Stress

A significant direct association was observed between DAL and anxiety in all five studies that evaluated this association. Four studies illustrated a significant direct association between PRAL and anxiety and two between NEAP and anxiety. Two studies assessed the association between DAL and stress and both of them showed a significant direct association. Moreover, one study observed a significant direct association between DAL and sleep among diabetic women.

Dietary Acid Load and Mental Health Among Children and Adolescents

A study conducted by Bühlmeier *et al.* aimed to assess the mental health of children and adolescents using SDQ subscales at the ages of 10 and 15 years, through cross-sectional and prospective associations. The study revealed a significant direct association

between PRAL and emotional problems (Odds Ratio: OR=1.33; 95%Confidence interval: 95%CI=1.15; 1.54) as well as hyperactivity (OR=1.22; 95%CI=1.04; 1.43) in the 10-year-old cross-sectional analysis. However, no significant association was observed in the 15-year-old cross-sectional and prospective analyses (18).

Quality of Studies

Findings on quality assessment of the seven included articles showed the good quality. The results of the quality assessment are available in Appendix 2.

Discussion

This study presents a systematic review of the literature to investigate the association between DAL and mental health outcomes. The review included seven studies, with six conducted on adults. Five out of six studies on depression evaluated DAL with PRAL method of which 3 of them reported a significant association. Three out of five studies that used NEAP method also reported a significant association. Furthermore, five studies examined the relationship between DAL and anxiety, while all showed a significant association. Also, an association between DAL and stress was exhibited in two other studies. In terms of children and adolescents, one study displayed a significant association between PRAL and emotional problems and hyperactivity in a 10-year-old cross-sectional analysis, but no association was indicated in the 15-year cross-sectional and prospective analysis.

Previous researches demonstrated the association between the intake of alkaline food items such as vegetables and a high intake of acidic food items like meat with depression and anxiety (26-29). The overall dietary intake patterns, such as having a Western dietary pattern (mainly acidic), were shown to be associated with the severity of depression (30, 31). In contrast, adherence to a Mediterranean diet (mainly alkaline) revealed an inverse association with psychological disorders (32). There are several hypotheses about the mechanisms by which DAL may affect mental health. One hypothesis is that an acidic diet can induce low-grade metabolic acidosis that can contribute to an elevated glucocorticoid level such as cortisol; and there are increasing evidences for a relationship between high cortisol level and psychological disorders (33-38).

The other possible underlying mechanism is the role of neuroinflammation in mental disorders. It has been shown that inflammation and inflammatory potential of diets can be related to mental disorders (7, 39). A hypothesis suggests a possible relationship between a higher DAL and inflammatory markers such as C-reactive protein (CRP) and the inflammation that leads to mental disorders (17, 40-42). The other is the overstimulation of acid-sensing ion channel 1a (ASIC1a) as a part of degenerin/epithelial Na channels due to a decrease in PH after consuming a diet with higher scores for DAL. ASIC1a, when expressed in the nervous system, especially the amygdala, may be associated with psychological disorders (43-45).

Among the strengths of the current systematic review, the novelty of this issue and the gathering of all available evidences on the association between dietary acid load and mental health outcomes can be described. However, some limitations should be addressed in interpreting the findings as the included studies were only seven studies and three of them have been conducted in Iran. Also, four of the studies conducted on adults were only on women. The high differences between exposure and outcome measurements and the difference between participants' health status resulted in an increase in the rate of heterogeneity in this field. Therefore, the major limitations are the age groups, health status, and gender differences in the study populations. The association between DAL and mental outcomes may be caused by overlaps between vegetable and fruit intake as alkaline and anti-inflammatory food items; on the other hand, protein and especially meat intake is both acidic and pro-inflammatory. It's recommended for future studies to investigate the association between DAL and different aspects of mental health especially in healthy populations of both genders. Moreover, assessing this relationship in patients with chronic kidney diseases (CKD) seems advantageous considering the electrolytes and dietary changes in this condition.

Conclusion

It seems that dietary acid load, especially PRAL, could be associated with anxiety and depression, especially in women. However, these conclusions are not robust due to the limited number and design of current studies. Future prospective studies in both gender and different age groups should be conducted to conclude the association between dietary acid-base intake and mental health.

Acknowledgment

No fund or collaboration was provided for this study to be appreciated.

Funding

No fund was received for this study.

Authors' Contribution

A.A determined the subject of systematic review, MJ.Z and S.M did the initial screening, data extraction, quality assessment and wrote the main text of the manuscript, A.A rechecked the data extraction, quality assessment and written text.

Conflict of Interest

All of authors declare not to have any of conflict of interest.

References

1 Bideshki MV, Jowshan MR, Sherafati N, et al. Association between Dietary Inflammatory Index, Mean Adequacy Ratio, Dietary Energy Density and Mental Health among Iranian Women. *Int J Nutr Sci*. 2024;9:109-117. doi: 10.30476/IJNS.2024.101191.1296.

2 Organization WH. Depression and other common mental disorders: global health estimates. World Health Organization; 2017.

3 Sa MN, Suman G, Rajan B. Assessment of Nutritional Status and Influencing Factors among Elderly in Mathikere, Urban Bengaluru, Karnataka of India. *Int J Nutr Sci*. 2024;9:56-61. DOI: 10.30476/IJNS.2024.99721.1258.

4 Renowening Y, Suradi S, Probandari A. Correlation of Smoking Habits, Physical Activities and Fat Intake with Cognitive Ability in Indonesian Elderly. *Int J Nutr Sci.* 2019;4:186-191. DOI: 10.30476/IJNS.2019.83497.1037.

5 Sarris J, Logan AC, Akbaraly TN, et al. International Society for Nutritional Psychiatry Research consensus position statement: nutritional medicine in modern psychiatry. *World Psychiatry.* 2015;14:370-1. DOI: 10.1002/wps.20223. PMID: 26407799.

6 Bremner JD, Moazzami K, Wittbrodt MT, et al. Diet, stress and mental health. *Nutrients*. 2020;12:2428. DOI: 10.3390/nu12082428. PMID: 32823562.

7 Chen GQ, Peng CL, Lian Y, et al. Association Between Dietary Inflammatory Index and Mental Health: A Systematic Review and Dose-Response Meta-Analysis. *Front Nutr.* 2021;8:662357. DOI: 10.3389/fnut.2021.662357. PMID: 34026809.

8 Sandhu KV, Sherwin E, Schellekens H, et al. Feeding the microbiota-gut-brain axis: diet, microbiome, and neuropsychiatry. *Transl Res.* 2017;179:223-44. DOI: 10.1016/j.trsl.2016.10.002. PMID: 27832936.

9 Hosseini-Asl SMK, Mehrabani G, Masoumi SJ. Key Focus Areas in Pouchitis Therapeutic Status: A Narrative Review. *Iran J Med Sci*. 2024;49:472-486. DOI: 10.30476/ijms.2024.100782.3326. PMID: 39205822.

10 Quirk SE, Williams LJ, O'Neil A, et al. The association between diet quality, dietary patterns and depression in adults: a systematic review. *BMC Psychiatry*. 2013;13:175. DOI: 10.1186/1471-244X-13-175. PMID: 23802679.

11 Saghafian F, Malmir H, Saneei P, et al. Fruit and vegetable consumption and risk of depression: accumulative evidence from an updated systematic review and meta-analysis of epidemiological studies. *Br J Nutr*. 2018;119:1087-101. DOI: 10.1017/S0007114518000697. PMID: 29759102.

12 Godos J, Currenti W, Angelino D, et al. Diet and mental health: Review of the recent updates on molecular mechanisms. *Antioxidants*. 2020;9:346. DOI: 10.3390/antiox9040346. PMID: 32340112.

13 Bahrami H. Reducing Dietary Acid Load to Lower Cancer Risk: An Overview of Nutritional Strategies. *Int J Nutr Sci*. 2024;9:94-100. DOI: 10.30476/IJNS.2024.99025.1238.

14 Remer T, Manz F. Estimation of the renal net acid excretion by adults consuming diets containing variable amounts of protein. *Am J Clin Nutr.* 1994;59:1356-61. DOI: 10.1093/ajcn/59.6.1356. PMID: 8198060.

15 Frassetto LA, Todd KM, Morris Jr RC, et al. Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. The *Am J Clin Nutr.* 1998;68:576-83. DOI: 10.1093/ajcn/68.3.576. PMID: 9734733.

16 Milajerdi A, Hassanzadeh Keshteli A, Haghighatdoost F, et al. Dietary acid load in relation to depression and anxiety in adults. *J Hum Nutr Diet.* 2020;33:48-55. DOI: 10.1111/jhn.12658. PMID: 31173421.

17 Mozaffari H, Siassi F, Guilani B, et al. Association of dietary acid-base load and psychological disorders among Iranian women: A cross-sectional study. *Complement Ther Med.* 2020;53:102503. DOI: 10.1016/j.ctim.2020.102503. PMID: 33066849.

18 Bühlmeier J, Harris C, Koletzko S, et al. Dietary acid load and mental health outcomes in children and adolescents: results from the GINIplus and LISA birth cohort studies. *Nutrients*. 2018;10:582. DOI: 10.3390/nu10050582. PMID: 29738509.

19 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71. DOI: 10.1136/bmj.n71. PMID: 33782057.

20 Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of

nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603-5. DOI: 10.1007/s10654-010-9491-z. PMID: 20652370.

21 Wu T, Hsu FC, Pierce JP. Acid-Producing Diet and Depressive Symptoms among Breast Cancer Survivors: A Longitudinal Study. *Cancers (Basel)*. 2020;12:3183. DOI: 10.3390/cancers12113183. PMID: 33138152.

22 Saul A, Taylor BV, Blizzard L, et al. Long-term dietary acid load is associated with depression in multiple sclerosis, but less evidence was found with fatigue and anxiety. *Mult Scler Relat Disord*. 2023;69:104415. DOI: 10.1016/j.msard.2022.104415. PMID: 36434910.

23 Daneshzad E, Keshavarz SA, Qorbani M, et al. Association of dietary acid load and plant-based diet index with sleep, stress, anxiety and depression in diabetic women. *Br J Nutr*. 2020;123:901-12. DOI: 10.1017/S0007114519003179. PMID: 31806069.

24 Bahari H, Seifi N, Foroumandi E, et al. Dietary acid load, depression, and anxiety: results of a population-based study. *BMC Psychiatry*. 2023;23:679. DOI: 10.1186/s12888-023-05163-3. PMID: 37723484.

25 Tessou KD, Lemus H, Hsu FC, et al. Independent and Joint Impacts of Acid-Producing Diets and Depression on Physical Health among Breast Cancer Survivors. *Nutrients*. 2021;13:2422. DOI: 10.3390/nu13072422. PMID: 34371931.

26 Liu MW, Chen QT, Towne SD, et al. Fruit and vegetable intake in relation to depressive and anxiety symptoms among adolescents in 25 low- and middle-income countries. *J Affect Disord*. 2020;261:172-80. DOI: 10.1016/j.jad.2019.10.007. PMID: 31634676.

27 Matison AP, Mather KA, Flood VM, et al. Associations between nutrition and the incidence of depression in middle-aged and older adults: A systematic review and meta-analysis of prospective observational population-based studies. *Ageing Res Rev*. 2021;70:101403. DOI: 10.1016/j.arr.2021.101403. PMID: 34246793.

28 Nucci D, Fatigoni C, Amerio A, et al. Red and Processed Meat Consumption and Risk of Depression: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2020;17:6686. DOI: 10.3390/ijerph17186686. PMID: 32937855.

29 Lassale C, Batty GD, Baghdadli A, et al. Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies. *Mol Psychiatry*. 2019;24:965-86. DOI: 10.1038/s41380-018-0237-8. PMID: 30254236.

30 Li Y, Lv MR, Wei YJ, et al. Dietary patterns and depression risk: A meta-analysis. *Psychiatry Res*. 2017;253:373-82. DOI: 10.1016/j.psychres.2017.04.020. PMID: 28431261.

31 Jacka FN, Pasco JA, Mykletun A, et al. Association of Western and traditional diets with depression and anxiety in women. *Am J Psychiatry*. 2010;167:305-11. DOI: 10.1176/appi.ajp.2009.09060881. PMID: 20048020.

32 Shafiei F, Salari-Moghaddam A, Larijani B, et al. Adherence to the Mediterranean diet and risk of depression: a systematic review and updated meta-analysis of observational studies. *Nutr Rev*. 2019;77:230-9. DOI: 10.1093/nutrit/nuy070. PMID: 30726966.

33 Carnauba RA, Baptistella AB, Paschoal V, et al. Diet-Induced Low-Grade Metabolic Acidosis and Clinical Outcomes: A Review. *Nutrients*. 2017;9:538. DOI: 10.3390/nu9060538. PMID: 28587067.

34 Zajkowska Z, Gullett N, Walsh A, et al. Cortisol and development of depression in adolescence and young adulthood - a systematic review and meta-analysis. *Psychoneuroendocrinology*. 2022;136:105625. DOI: 10.1016/j.psyneuen.2021.105625. PMID: 34920399.

35 Herane Vives A, De Angel V, Papadopoulos A, et al. The relationship between cortisol, stress and psychiatric illness: New insights using hair analysis. *J Psychiatr Res*. 2015;70:38-49. DOI: 10.1016/j.jpsychires.2015.08.007. PMID: 26424422.

36 Zorn JV, Schür RR, Boks MP, et al. Cortisol stress reactivity across psychiatric disorders: A systematic review and meta-analysis. *Psychoneuroendocrinology*. 2017;77:25-36. DOI: 10.1016/j.psyneuen.2016.11.036. PMID: 28012291.

37 Maurer M, Riesen W, Muser J, et al. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. *Am J Physiol Renal Physiol*. 2003;284:F32-40. DOI: 10.1152/ajprenal.00212.2002. PMID: 12388390.

38 Weiner ID. Untangling the complex relationship between dietary acid load and glucocorticoid metabolism. *Kidney Int*. 2016;90:247-9. DOI: 10.1016/j.kint.2016.04.011. PMID: 27418088.

39 Osimo EF, Baxter LJ, Lewis G, et al. Prevalence of low-grade inflammation in depression: a systematic review and meta-analysis of CRP levels. *Psychol Med*. 2019;49:1958-70. DOI: 10.1017/S0033291719001454. PMID: 31258105.

40 de Nadai TR, de Nadai MN, Albuquerque AA, et al. Metabolic acidosis treatment as part of

a strategy to curb inflammation. *Int J Inflam*. 2013;2013:601424. DOI: 10.1155/2013/601424. PMID: 23841017.

41 Najjar S, Pearlman DM, Alper K, et al. Neuroinflammation and psychiatric illness. *J Neuroinflammation*. 2013;10:43. DOI: 10.1186/1742-2094-10-43. PMID: 23547920.

42 Wu T, Seaver P, Lemus H, et al. Associations between Dietary Acid Load and Biomarkers of Inflammation and Hyperglycemia in Breast Cancer Survivors. *Nutrients*. 2019;11:1913. DOI: 10.3390/nu11081913. PMID: 31443226.

43 Wemmie JA, Zha X-m, Welsh MJ. Acid-sensing ion channels (ASICs) and pH in synapse physiology. Structural and functional organization of the synapse: Springer; 2008. p. 661-81.

44 Coryell MW, Ziemann AE, Westmoreland PJ, et al. Targeting ASIC1a reduces innate fear and alters neuronal activity in the fear circuit. *Biol Psychiatry*. 2007;62:1140-8. DOI: 10.1016/j.biopsych.2007.05.008. PMID: 17662962.

45 Rauch SL, Shin LM, Wright CI. Neuroimaging studies of amygdala function in anxiety disorders. *Ann N Y Acad Sci*. 2003;985:389-410. DOI: 10.1111/j.1749-6632.2003.tb07096.x. PMID: 12724173.