Complementary Therapies in Medicine 49 (2020) 102361

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

The effects of probiotic supplementation on mental health, biomarkers of inflammation and oxidative stress in patients with psychiatric disorders: A systematic review and meta-analysis of randomized controlled trials

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ARTICLE INFO

Keywords:
Probiotic supplementation
Inflammation
Oxidative stress
Psychiatric disorders
Meta-analysis

ABSTRACT

Background and objective: In the current meta-analysis of randomized controlled trials (RCTs), the effects of probiotic supplementation on mental health, biomarkers of inflammation and oxidative stress in patients with psychiatric disorders were assessed.

Methods: The following databases were search up to February 2019: PubMed, Scopus, Web of Science, Google scholar and Cochrane Central Register of Controlled Trials.

Results: Twelve studies were included in the current meta-analysis. The findings demonstrated that probiotic supplementation resulted in a significant reduction in Hamilton Depression Rating Scale (HAMD) [Weighted Mean Difference (WMD): -9.60; 95 % CI: -10.08, -9.11]. In addition, a significant reduction in C-reactive protein (CRP) (WMD: -1.59; 95 % CI: -2.22, -0.97), interleukin 10 (IL-10) (WMD: -0.29; 95 % CI: -0.48, -0.11) and malondialdehyde (MDA) levels (WMD: -0.38; 95 % CI: -0.63, -0.13) was found after probiotics supplementation. No significant change was seen in Beck Depression Inventory (BDI) score (WMD: -11.17; 95 % CI: -24.99, 2.65), tumor necrosis factor-α (TNF-α) (WMD: -0.12; 95 % CI: -0.20, -0.05), IL-1B (WMD: -0.34; 95 % CI: -1.43, 0.74), IL-6 (WMD: 0.03; 95 % CI: -0.32, 0.38), nitric oxide (NO) (WMD: -0.54; 95 % CI: -2.16, 1.08), glutathione (GSH) (WMD: 46.79; 95 % CI: -17.25, 110.83) and total antioxidant capacity (TAC) levels (WMD: 15.21; 95 % CI: -59.96, 90.37) after probiotics supplementation.

Conclusion: Overall, the current meta-analysis demonstrated that taking probiotic by patients with psychiatric disorders had beneficial effects on HAMD, CRP, IL-10 and MDA levels, but it did not affect BDI score, other markers of inflammation and oxidative stress.

1. Introduction

Psychiatric disorders are known as major public health problems which cause distress and disability and exits in many forms, including schizophrenia, anxiety and mood disorders.[1,2] These conditions can co-occur with a wide variety of central nervous system (CNS) and metabolic disorders.[3] It is estimated that more than 29.2 % of adults experienced a common mental disturbance within their lifetime.[4] Poor mental health is associated with a considerable lower quality of life, and high economic and social burden.[5] Previous studies have indicated

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https://doi.org/10.1016/j.ctim.2020.102361
Received 11 January 2020; Received in revised form 26 February 2020; Accepted 26 February 2020
Available online 27 February 2020

that the mortality rate among people suffering from mental disorders is two times higher than the general population.[6] The pathological pathways involved in the development of Parkinson's disease (PD) are not completely known, but it is now well-accepted that brain tissue is particularly susceptible to increased inflammation and oxidative stress.[7] Increased peripheral inflammatory markers, elevated production of reactive oxygen species (ROS), reduced activity of antioxidant systems and decreased efficiency in repairing mechanisms are associated with neurological and mental disorders such as major depressive disorders (MDD) and Alzheimer's disease (AD).[8,9] In addition, several psychiatric and neurological diseases may be associated with intestinal dysbiosis which influence the function of CNS via the gut brain axis.[10]

Probiotic bacteria provide various health benefits, exert anti-inflammatory effects, ameliorate oxidative stress, modulate host metabolism and brain function.[11] Currently, a meta-analysis demonstrated that probiotic supplementation in healthy subjects led to a significant improvement in preclinical psychological symptoms of anxiety, depression and stress.[12] In addition, a meta-analysis conducted by Mazidi et al.,[13] probiotic administration significantly decreased C-reactive protein (CRP) levels, bud had no significant effect on interleukin 10 (IL-10) and tumor necrosis factor alpha (TNF-α) levels. Another meta-analysis indicated that probiotics could effectively protect the intestinal mucosa, physical and biological barrier by reducing CRP and secretary immunoglobulin A in people with colorectal cancer after the operation, but did not affect IL-6 levels.[14] However, a recent meta-analysis in women with polycystic ovary syndrome did not affect any significant change in CRP concentrations after probiotic supplementation.[15] In addition, several randomized controlled trials (RCTs) have investigated the efficacy of probiotics on biomarkers of inflammation and oxidative stress in patients with psychiatric disorders, but the results are inconsistent. Akkasheh et al. [16] reported that probiotic supplementation for 8 weeks to patients with MDD significantly improved Beck Depression Inventory (BDI), high-sensitivity C-reactive protein (hs-CRP) and glutathione (GSH) levels, but did not influence other biomarkers of inflammation and oxidative stress. Furthermore, a 12-week probiotic and vitamin D co-supplementation in patients with schizophrenia alleviated some indicators of inflammation and oxidative stress.[17] However, the sample size of these trials was small, dosage and formulation of probiotic supplements were different, the quality of studies was variable, and the results were controversial. It is proposed that the reduction in biomarkers of inflammation and oxidative stress following probiotics supplementation might be due to their effects on increasing glutathione (GSH) concentrations and scavenging superoxide and hydroxyl radicals, decreasing gene expression of IL-6 in adipocytes, and decreasing adiposity.[18,19]

Despite numerous RCTs, we are aware of no meta-analysis of RCTs on the effect of probiotic supplementation on parameters of mental health, and biomarkers of inflammation and oxidative stress in patients with psychiatric symptoms. This meta-analysis was conducted to summarize the available evidence of RCTs to determine the effects of probiotic supplementation on parameters of mental health, and biomarkers of inflammation and oxidative stress in patients with psychiatric disorders.

2. Methods

2.1. Search strategy

Eligible RCTs were identified using Cochrane Library, PubMed, Scopus, Web of Science and Google scholar databases for relevant articles published until February 2019, and by manually searching the reference list of the retrieved articles. Databases of International Standard Randomized Controlled Trial Number Register and Meta-register for RCTs were also searched for all ongoing trials. Studies retrieved that evaluated the impact of probiotic and/or synbiotic supplementation on parameters of mental health, and biomarkers of inflammation and oxidative stress by using the following MeSH and text words: patients ["psychotic disorder" OR "depressive disorders" OR "mental disorder" OR "mental health" OR "mood" OR "depression" OR "attention deficit disorder with hyperactivity" OR "attention deficit hyperactivity disorder (ADHD)" OR "autism spectrum disorder" OR "Tourette syndrome" OR "obsessive-compulsive disorder" OR "anxiety disorder" OR "AD" OR "schizophrenia" OR "bipolar disorder"], intervention [("probiotic and/or synbiotic" OR "symbiotic")], and outcomes ["Hamilton Depression Rating Scale (HAMD)" OR "Beck Depression Inventory (BDI)" OR "IL-1B" OR "IL-6" OR "TNF-α" OR "CRP" OR "nitric oxide (NO)" OR "malondialdehyde (MDA)" OR "total antioxidant capacity (TAC)" OR "glutathione (GSH)"]. Additional manual searches including reference lists of related studies; former review studies were reviewed to increase sensitivity in search strategy. Studies included to this meta-analysis had the following criteria: 1) original trials, 2) human trials, 3) intervention and control groups received of probiotic and/or synbiotic supplementation and placebo, respectively and 4) the trials reported mean changes or mean difference of body composition and/or metabolic profiles with standard deviation (SD) for the intervention and control groups.

2.2. Data extraction and quality assessment

Two authors (EA and HM) independently extracted the data and assessed its quality using standard forms and the Cochrane Collaboration risk of bias tool,[20,21] respectively. This tool is based on information on the following domains: randomization generation, allocation concealment, blinding of subjects and outcome assessment, incomplete outcome data, and selective outcome reporting, and other sources of bias. When there was disagreement among them, it resolved by third author (AG). Eligible studies were abstracted: 1) first authors' name 2) publication year 3) age, sex and body composition and/or metabolic profiles of study participants and associated measures of variance 4) study location 5) number of subjects in the intervention and control groups 6) study design 7) duration of the intervention.

3. Data analysis

3.1. Heterogeneity and publication biases

The statistical heterogeneity across the results of the included studies was tested using chi-square test,[22] and quantified by the I^2 statistic.[23] Publication bias was assessed by the funnel plot and tested for statistical significance using the Egger's test.[24]

3.2. Summary measures

We calculated the mean difference for the influence of probiotic supplementation on parameters of mental health, and biomarkers of inflammation and oxidative stress for each included studies. The change score approach was used to obtain the effect sizes, because the correlations between baseline and end measurements were more than 1/2.[25] A meta-analysis was performed to obtain the summary measures for the effect of probiotic supplementation on parameters of mental health, and biomarkers of inflammation and oxidative stress using the inverse variance method. The random effects model was used to report the pooled mean difference with 95 % confidence interval (CI). P-values < 0.05 were considered as statistically significant. Statistical analyses were performed using both Stata version 11.0 (Stata Corp., College Station, TX) and Review Manager 5.3.

4. Results

4.1. Study characteristics

Seventeen effect sizes from twelve studies were included in the

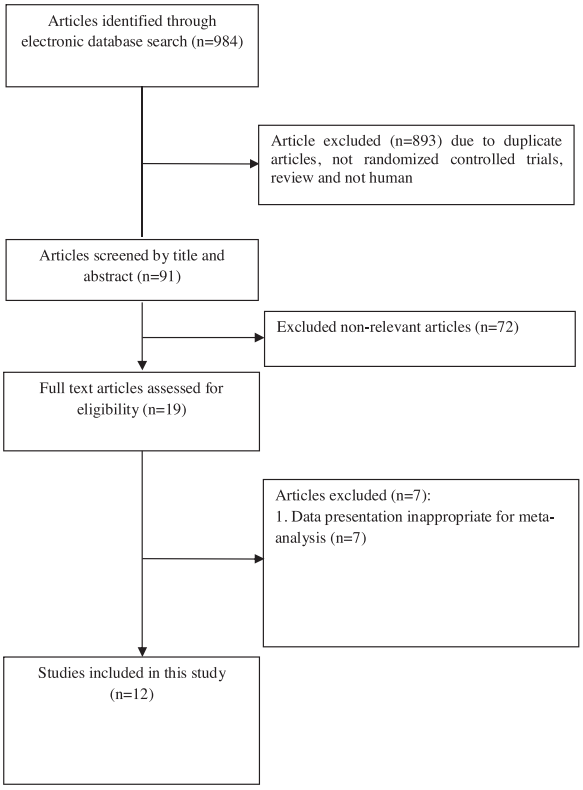

Fig. 1. Literature search and review flowchart for selection of studies.

current systematic review and meta-analysis. Flow-diagram studies are shown in Fig. 1. Studies were published between 2016 and 2019. General characteristics of included studies are presented in Table 1. A total of 656 participants, including 330 individuals in the intervention and 326 individuals in the control groups, were enrolled in these studies. Duration of studies was varied between 6 and 12 weeks. Probiotic supplements were mainly consisted of Lactobacillus or Bifidobacter strains. In some cases, miscellaneous strains of bacteria and in the others a combination of multiple strains were used as the intervention. Use of probiotic capsules, sachets, and probiotic-containing foods were the most predominant forms of supplementation in the included studies.

4.2. Findings for the effects of probiotic supplementation on parameters of mental health

Combining eight effect sizes from 4 studies, we found a significant reduction in HAMD following probiotic supplementation [Weighted Mean Difference (WMD): -9.60; 95 % CI: -10.08, -9.11] (Fig. 2A). Due to the high between-studies heterogeneity (I^2 = 99.7 %), we stratified studies based on participants' age (< 40/≥40 years) (Table 2). This stratification did not change the overall finding. A pooled analysis of 3 studies about the effects of probiotics on BDI failed to find a significant association (WMD: -11.17; 95 % CI: -24.99, 2.65) (Fig. 2B).

4.3. Findings for the effects of probiotic supplementation on inflammatory markers

4.3.1. Effects of probiotic supplementation on CRP levels

A significant reduction in CRP concentrations was found after supplementation with probiotics, as shown when we combined data from 5 available studies (WMD: -1.59; 95 % CI: -2.22, -0.97) (Fig. 2C), which remained significant after subgroup analysis based on study sample size (n < 50/n≥50) (Table 2).

4.3.2. Effects of probiotic supplementation on TNF-α levels

Serum levels of TNF-α was reduced after supplementation with probiotics, as resulted from combination of data from 4 available studies (WMD: -0.12; 95 % CI: -0.20, -0.05) (Fig. 2D). The same findings were reached from subgroup analysis based on study sample size in studies with a sample size of < 50, whereas, no significant effect was seen among those with a sample size of ≥50 (WMD: -0.15; 95 % CI: -0.58, 0.27) (Table 2).

4.3.3. Effects of probiotic supplementation on other inflammatory markers

Findings from the polled analysis of available studies showed no significant effects of probiotic supplementation on levels of IL-1B (WMD: -0.34; 95 % CI: -1.43, 0.74) (Fig. 2E), IL-6 (WMD: 0.03; 95 % CI: -0.32, 0.38) (Fig. 2F) and NO (WMD: -0.54; 95 % CI: -2.16, 1.08) (Fig. 2G); however, it caused a significant reduction in IL-10 levels (WMD: -0.29; 95 % CI: -0.48, -0.11) (Fig. 2H).

4.4. Findings for the effects of probiotic supplementation on biomarkers of oxidative stress

4.4.1. Effects of probiotic supplementation on GSH levels

Probiotic supplementation did not influence GSH levels in a polled analysis of 5 studies (WMD: 46.79; 95 % CI: -17.25, 110.83) (Fig. 2J). Subgroup analysis based on study sample size showed a significant increase in GSH levels following probiotic supplementation among studies with a sample size of ≥50 (WMD: 59.56; 95 % CI: 30.87, 88.26) (Table 2).

4.4.2. Effects of probiotic supplementation on MDA and TAC levels

The current meta-analysis demonstrated that probiotic supplementation led to a significant reduction in MDA levels (WMD: -0.38; 95 % CI: -0.63, -0.13) (Fig. 2K). Combining data from 5 studies, no significant change was found in TAC following consumption of probiotic supplements (WMD: 15.21; 95 % CI: -59.96, 90.37) (Fig. 2L). However, a significant reduction in TAC was seen after probiotic supplementation in studies a sample size of < 50 (WMD: -81.64; 95 % CI: -121.25, -42.02). Otherwise, probiotic supplementation resulted in a significant increase in TAC among studies that recruited ≥50 individuals (WMD: 60.25; 95 % CI: 32.39, 88.10) (Table 2).

5. Discussion

In this meta-analysis, for the first time, we pooled data from available evidence of probiotic supplementation in participants suffered from psychiatric disease. The present study exhibited that taking probiotic supplements by patients with psychiatric disorders improved HAMD, CRP, IL-10 and MDA levels, but did not affect BDI score, and other markers of inflammation and oxidative stress.

6. Effects on parameters of mental health

Psychiatric disease is a complicated condition in which mood and mental disorder lead to impaired individual function.[2] In addition, increased inflammatory markers and disrupted antioxidant defense system could be identified in patients with different types of psychiatric illnesses.[26] Our findings revealed that probiotic supplementation improved HAMD, but did not affect BDI score in patients with psychiatric disorders. In a meta-analysis study by McKean et al.,[12] probiotic supplementation led to a significant reduction in anxiety, depression and stress symptoms in healthy population. In addition, Huang et al. [27] demonstrated that probiotic consumption decreased depression scale score in both healthy and MDD patients. However, in a recent meta-analysis, probiotic supplementation was not effective in decreasing poor mood symptoms in healthy individuals and patients with mental disorder.[28] Depressive symptoms account as one of the strongest predictors of quality of life in mental disorders.[29] It is documented that

Table 1
Characteristics of the studies included in the analysis.

Authors (Ref)	Publication year	Sample size (control/ intervention)	Duration (wk)	Gender	Assessment method	Age (years)	Intervention (type and dosage)	Type of bacteria	Disease	Outcomes
Akkasheh et al.[16]	2016	20/20	8	F/M	DSM-IV and a score of ≥15 on the 17-item HAMD	36.2 ± 8.2, 38.3 ± 12.1	6×10^9 CFU/g probiotic	*L.acidophilu, L.casei, B.bifidum*	MDD	BDI TAC, GSH CRP
Akbari et al.[41]	2016	30/30	12	F/M	NINDS-ADRDA criteria and revised criteria from the National Institute on Aging-Alzheimer's Association	82.00 ± 9.25 77.67 ± 14.35	200 ml probiotic milk containing *L.acidophilus, L.casei, B.bifidum, L.fermentum* 2×10^9 CFU/g	*L.acidophilus, L.casei, B.bifidum, L.fermentum*	AD	TAC, GSH, MDA, NO CRP
Pinto-Sanchez et al.[47]	2017	20/18	6	F/M	Mild to moderate depression based on HADS	41 ± 22.9, 44.8 ± 20.7	$1.0E+3 \times 10^9$ CFU/g probiotic	*B.longum* NCC3001	IBS with mild to moderate anxiety and/or depression	CRP, TNF-a, IL-1B, IL-6, IL-10
Kazemi et al.[48]	2019	36/38	8	F/M	NR	36 ± 8.47, 36.15 ± 7.85	$\geq 10 \times 10^9$ CFU/5 g sachet probiotic	*L.helveticus* R0052, *B.longum* R0175 (CNCM strain I-3470)	MDD	BDI
Miyaoka et al.[49]	2018	20/20	8	F/M	DSM-IV and a score of ≥16 on the 17-item HAMD.	41.9 ± 4.2, 44.2 ± 15.6	60 mg probiotic	*C.butyricum* MIYAIRI 588	TRD	BDI, HAMD-17
Agahi et al.[50]	2018	23/25	12	F/M	Diagnosed by NINDS-ADRDA criteria and revised criteria from the National Institute on Aging-Alzheimer's Association	80.57 ± 8.5, 79.70 ± 7.6	3×10^9 CFU probiotic	*L.fermentum, L.plantarum, B.lactis, L.acidophilus, B.bifidum, B.longum*	AD	TAC, GSH, MDA, NO TNF-a, IL-6, IL-10
Ghaderi et al.[17]	2019	30/30	12	F/M	DSM-IV and PANSS ≥55	43.2 ± 6.0, 44.8 ± 8.3	8×10^9 CFU probiotic + 50000IU vitamin D every 2 weeks	*L.acidophilus, B.bifidum, L.reuteri, L.fermentum*	Schizophrenia	TAC, GSH, MDA, NO CRP
Ghorbani et al.[51]	2018	20/20	6	F/M	DSM-V and HAMD score of 17 to 23	35.50 ± 5.27, 34.45 ± 3.95	1000 mg probiotic + 100 mg fructooligosaccharide	*L.casae, L.acidofilus, L.bulgarigus, L.rhamnosus, B.breve, B.longum, S.thermophilus*	Moderate depression	HAMD-17
Lew et al.[52]	2018	51/52	12	F/M	Moderate stress based on PSS-10	32.1 ± 11.4, 31.3 ± 10.8	2×10^{10} CFU/g probiotic	*L.plantarum* P8	Stressed adults	TNF-a, IL-1B, IL-10
Rudzki et al.[53]	2019	30/30	8	F/M	DSM-IV	38.90 ± 12, 39.13 ± 9.96	2×10^{10} CFU probiotic	*L.plantarum* 299v	MDD	HAMD-17 TNF-a, IL-1B, IL-6
Majeed et al.[54]	2018	20/20	12	F/M	DSM-IV	43.88 ± 9.8, 40.36 ± 10.28	2×10^{10} CFU probiotic	*B. coagulans* MTCC 5856	MDD in IBS	HAMD-17
Tamtaji OR et al.[55]	2018	26/27	12	F/M	NINDS-ADRDA criteria and revised criteria from the National Institute on Aging-Alzheimer's Association	78.5 ± 8.0, 76.2 ± 8.1	2×10^9 CFU probiotic + 200 μg selenium	*L.acidophilus, B.bifidum, B.longum*	AD	TAC, GSH, MDA, NO CRP

NR: not reported.
AD, Alzheimer's disease; HAMD, Hamilton Depression Rating Scale; QIDS-SR16, Quick Inventory of Depressive Symptomatology; DASS, Depression, Anxiety and Stress Scale; HADS, Hospital Anxiety and Depression scale; PANSS, Positive and Negative Syndrome Scale; PSS-10, Cohen's Perceived Stress Scale; IBS, Irritable bowel syndrome; TRD, treatment-resistant major depressive disorder; MDD, Major depressive disorder.

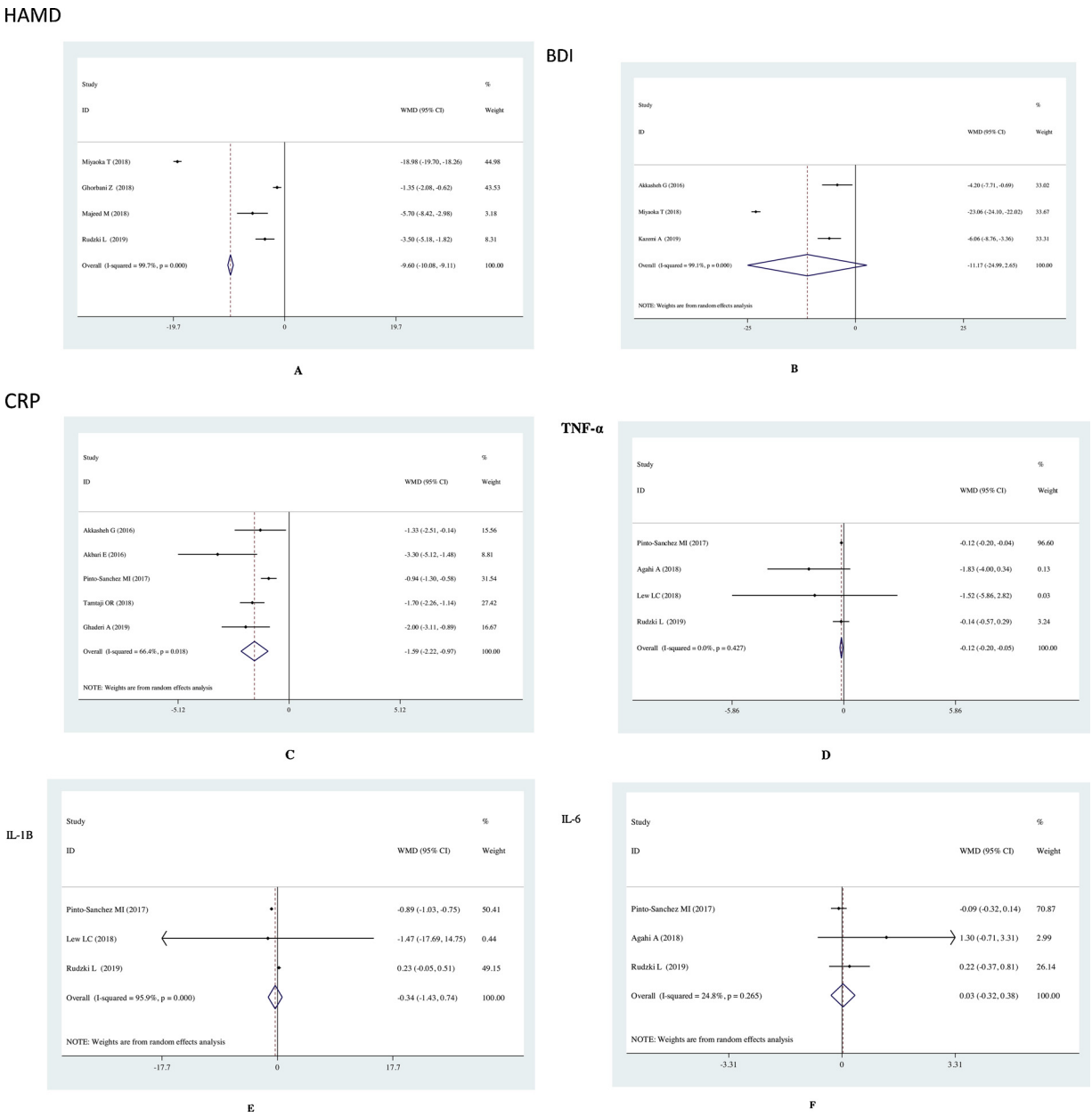

Fig. 2. Meta-analysis mental health and biomarkers of inflammation and oxidative stress weighted mean difference estimates for A) HAMD, B) BDI, C) CRP, D) TNF-α, E) IL-1B, F) IL-6, G) NO, H) IL-10, J) GSH, K) MDA and L) TAC in the probiotics supplements and placebo groups (CI = 95 %).

there is a significant association between BDI score and health-related quality of life.[30] In addition, a variety of unfavorable health behaviors are related to depressive disorders.[31] The exact mechanism by which probiotics exert beneficial psychological effects are not elucidated, it is postulated that probiotic bacteria promote biosynthesis of neurotransmitters, including gamma-aminobutyric acid, norepinephrine, serotonin, dopamine, and acetylcholine which influence brain activity and improve mood symptoms.[32] In addition, probiotic consumption increases the expression of brain-derived neurotrophic factor which plays an important role in neural plasticity, memory, neural health and has antidepressant effects.[33] Moreover, probiotics modify intestinal microbiota composition and inflammatory immune system reactions which has a great impact on the gut-brain axis and possibly modulates emotional state.[34]

7. Effects on inflammatory markers

In the present study, we demonstrated that the use of probiotic supplements in patients with psychiatric disorders reduced CRP and IL-10 levels, but did not influence other inflammatory markers. A meta-analysis conducted by Aqaeinezhad et al.,[35] ptobiotic supplementation in patients with rheumatoid arthritis decreased CRP concentrations. Mazidi et al. [13] reported that probiotic administration significantly improved CRP, while did not change IL-10 and TNF-α concentrations. In addition, a meta-analysis indicated that probiotic consumption in patients with colorectal cancer reduced CRP values; while IL-6 levels remained unchanged.[14] However, results of the present study differ from findings of a previous meta-analysis study by Samah et al. [36] that found no significant effect of probiotics on CRP concentrations. The peripheral inflammatory signals can reach the brain and amplify inflammation in CNS which results in altered brain performance in areas mediating mood and cognition.[9] In addition, inflammatory state

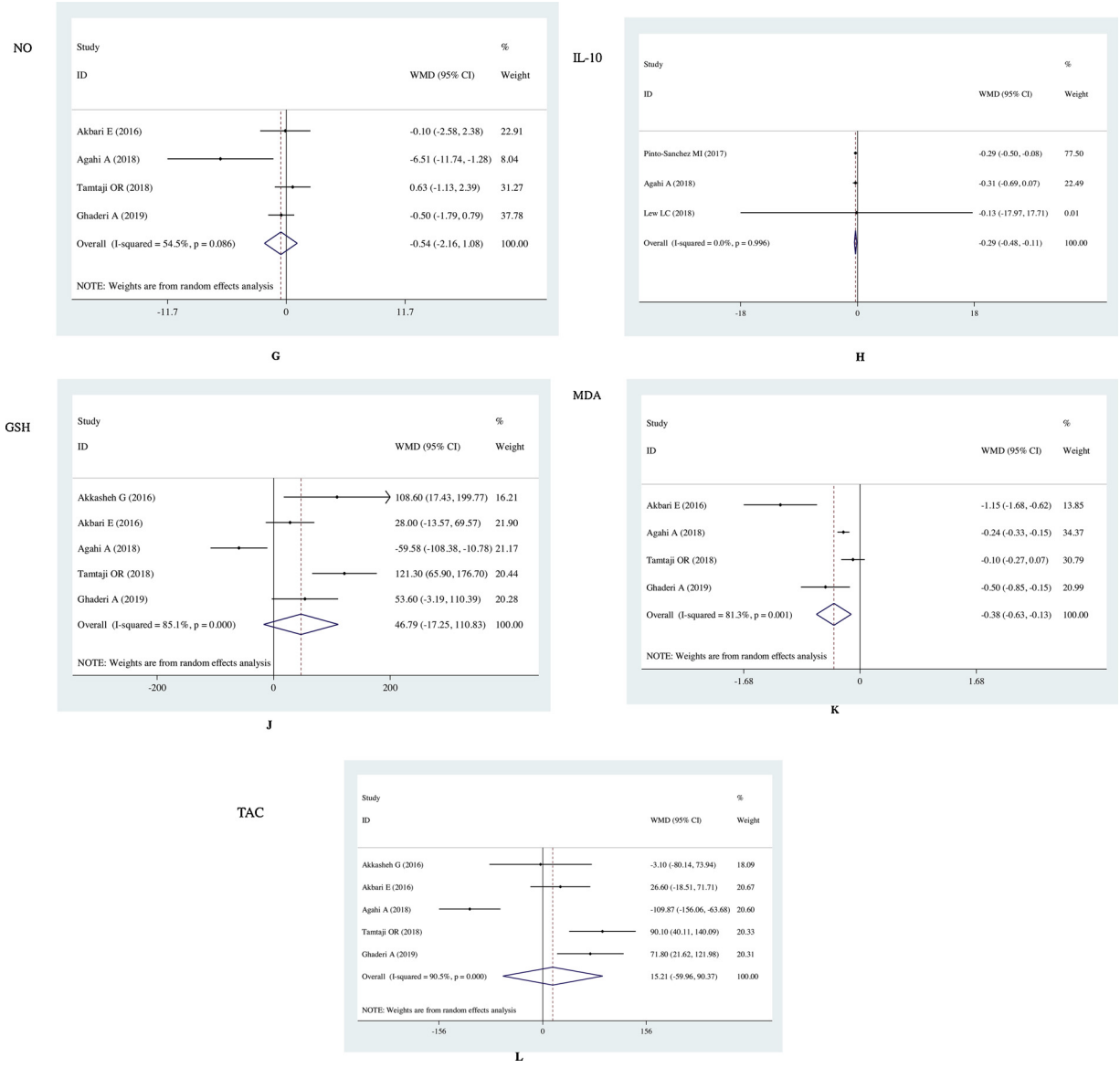

Fig. 2. (*continued*)

influence the synthesis of adverse tryptophan cathabolites which promote apoptosis, hippocampal damage and disrupt neural plasticity.[37] It is indicated that increased levels of inflammatory markers such as TNF-α in depression contributes to treatment resistance.[38] Moreover, some evidence suggested that anti-inflammatory treatments may have antidepressant properties.[39] The role of probiotics in alleviating inflammatory response can be explained by production of short chain fatty acids which decrease enzymatic synthesis of CRP in the liver,[19] and modulation the activity of Toll-like receptor, nuclear factor kappa-B, and mitogen-activated protein kinase pathways which reduce the

Table 2
Subgroup analyses for the effects of probiotic supplementation on parameters of mental health and biomarkers of inflammation and oxidative stress among patients with psychiatric disorders.

Variables		Subgroups	Number of effect sizes	Pooled WMD	95 % CI	I^2 (%)	Between-study I^2 (%)
HAMD	Participants' age	< 40 year	2	−1.69	−2.37, −1.02	81.0	< 0.001
		≥40 year	2	−18.10	−18.80, −17.41	98.8	
CRP	Study sample size	n < 50	2	−0.97	−1.32, −0.63	00.0	< 0.01
		n≥ 50	3	−1.87	−2.35, −1.39	27.8	
GSH	Study sample size	n < 50	2	−22.13	−65.15, 20.90	90.2	< 0.01
		n≥ 50	3	59.56	30.87, 88.26	71.5	
TAC	Study sample size	n < 50	2	−81.64	−121.25, −42.02	81.6	< 0.001
		n≥ 50	3	60.25	32.39, 88.10	46.1	
TNF-α	Study sample size	n < 50	2	−0.12	−0.20, −0.04	57.9	0.88
		n≥ 50	2	−0.15	−0.58, 0.27	0.0	

HAMD: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory; CRP: C-reactive protein; GSH: Glutathione; IL-1B: Interleukin-1Beta; IL-6: Interleukin-6; IL-10: Interleukin-10; TNF-α: Tumor necrosis factor-alpha; NO: Nitric oxide; TAC: Total antioxidant capacity; MDA: Malondialdehyde.

expression of pro-inflammatory cytokines.[40]

8. Effects on biomarkers of oxidative stress

Results of our study indicated that probiotic supplementation significantly reduced MDA levels, bud did not affect other biomarkers of oxidative stress. However, when we stratified studies by the participants' age, a significant increase in GSH levels was seen after probiotic supplementation in adults. In addition, intake of probiotics resulted in a significant increase in TAC in studies with adults as well as those with a sample size of ≥50. Several clinical studies have investigated the effects of probiotics on oxidative stress in patients with mental illness. Two studies showed that probiotic supplementation reduced MDA concentrations in subjects with AD [41] and schizophrenia.[17] In addition, Akkasheh et al. [16] reported that probiotic supplementation led to a significant increase in TAC levels. However, in a meta-analysis conducted by Aqaeinezhad et al.,[35] it was reported that probiotic supplementation did not affect TAC and MDA levels in RA patients. Dysregulation in oxidative balance leads to tissue damage and has been implicated in the pathogenesis of neuropsychiatric disorders.[42] Decreased antioxidant capacity and increased ROS cause damage to protein, DNA, and membrane fatty acids and thereby results in cell apoptosis, neurodegeneration and brain volumetric changes. Enhanced oxidative status also contributes to triggering autoimmune responses in mental disorders,[26] and provokes lipid peroxidation which increases the risk of atherosclerosis in depressed individuals.[43] Furthermore, elevated MDA levels can influence the metabolism of serotonin by inhibiting the ligand binding site of serotonin.[44] Moreover, a significant inverse correlation has been reported between antioxidants and the severity of clinical symptoms of psychiatric disorders and some studies reported that antioxidant therapy improved mental outcomes in these conditions.[45] Probiotic supplementation may lead to the modulation of oxidative stress by several mechanisms, including metal ion chelating ability, regulating ROS levels by application of their antioxidant enzyme system, generation antioxidant metabolits such as GSH, regulating the antioxdant system of host, preventing the genration of hydroxy radicals and mediation signaling of Nrf2, protein kinase C and other antioxidant signaling pathways.[46]

9. Conclusions

Overall, the current meta-analysis demonstrated that taking probiotic by patients with psychiatric disorders had beneficial effects on HAMD, CRP, IL-10 and MDA levels, but did not affect other markers of inflammation and oxidative stress.

Availability of data and material

The primary data for this study is available from the authors on direct request.

Author contributions

EA, AM, HM, and AG contributed in conception, design, data collection, statistical analysis and drafting of the manuscript. HJ, MAM and JH contributed in conception and manuscript drafting. The final version was confirmed by all authors for submission.

Funding

The research grant provided by Research Deputy of Arak University of Medical Sciences (AUMS).

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

The present study was supported by a grant from the Vice-chancellor for Research, AUMS, Arak, and Iran.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2020.102361.

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